

Acute Care Surgery and Trauma

Evidence Based Practice

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Edited by
Stephen M Cohn

Acute Care Surgery and Trauma: Evidence Based Practice

Edited by

Stephen M. Cohn MD FACS

Witten B. Russ Professor of Surgery

University of Texas Health Science Center

San Antonio, Texas, USA

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Contributors

Greg A. Abrahamian MD

Assistant Professor of Surgery, Department of Surgery
Transplant Center, University of Texas Health Science
Center at San Antonio, Texas, USA

Omid Noormohammadi, Alicia Logue MD

University of Texas Health Science Center
San Antonio, Texas, USA

Joshua B. Alley MD

Major USAF MC, Staff General Surgeon
Wilford Hall Medical Center, Lackland AFB
Texas. Clinical Assistant Professor, Department of
Surgery, University of Texas Health Science Center
San Antonio, Texas, USA

Jayson D. Aydelotte MD

Director of Trauma, Department of Surgery
Walter Reed Army Medical Center
Washington, DC, USA

Michael M. Badellino MD

Associate Professor of Surgery
Penn State College of Medicine
Program Director, General Surgery Residency
Lehigh Valley Health Network
Allentown, Pennsylvania, USA

Hany Bahouth MD BSc

General and Trauma Surgeon, Director
Acute Care Surgery, Rambam Health Campus
Haifa, Israel

Heidi I. Becker MD

Assistant Professor
Department of Ophthalmology, University of Texas
Health Science Center at San Antonio
San Antonio, Texas, USA

Stephen W. Behrman MD FACS

Associate Professor of Surgery, Department of Surgery
The University of Tennessee Health Science-Center
Memphis, Tennessee, USA

Greg J. Beilman MD FACS

Professor of Surgery, Department of Surgery
University of Minnesota
Minneapolis, Minnesota, USA

Robert Benjamin MD FACS

Chief of Trauma Services
William Beaumont Army Medical Center
Department of Surgery
El Paso, Texas, USA

Bethesda MD

Department of Surgery
Madigan Army Medical Center, Tacoma
Fort Lewis, Washington, USA

Juliane Bingener MD

Department of Surgery, Mayo Clinic
Rochester, Minnesota, USA

COL Lorne H. Blackburne MD FACS

U.S. Army Institute of Surgical Research
Fort Sam Houston
San Antonio, Texas, USA

Juan J. Blondet MD

Postdoctoral Fellow, Department of Surgery
University of Minnesota
Minneapolis, Minnesota, USA

Col. W. Brian Perry MD USAF MC

Wilford Hall Medical Center, Lackland AFB
San Antonio, Texas, USA

Susan E. Brien MD MEd CSPQ FRCSC CPE

Associate Director, Professional Affairs, Royal College
of Physicians and Surgeons of Canada
Ottawa, Ontario, Canada

Steven Brower MD

Division of General Surgery
Memorial Health Medical Center
Savannah, Georgia, USA

Gabriel E. Burkhardt MD Capt USAF MC

Vascular Surgery Resident, Wilford Hall United States
Air Force Medical Center, Lackland Air Force Base
The University of Texas Health Science Center
at San Antonio, San Antonio, Texas, USA

Christopher Busken MD

Division of General Surgery
Memorial Health Medical Center
Savannah, Georgia, USA

Leopoldo C. Cancio MD FACS

Colonel, Medical Corps, U.S. Army, U.S., Army Institute
of Surgical Research, Fort Sam Houston
San Antonio, Texas, USA

Robert Chen MD FRCPC

Attending Anaesthetist and Intensivist
Assistant Professor
St. Michael's Hospital, Department of Anaesthesia
University of Toronto,
Toronto, Canada, USA

Clarence E. Clark III MD

Chief Resident, General Surgery
Department of Surgery
University of Texas Health Science Center San Antonio
and Wilford Hall Medical Center
San Antonio, Texas, USA

Charles F. Cobb MD

Associate Professor of Surgery, Drexel University
College of Medicine, Allegheny General Hospital
Department of Surgery
Pittsburgh, Pennsylvania, USA

Mark Cockburn MD

New Rochelle, New York, USA

Rebecca Coefield MD

Division of General Surgery
Memorial Health Medical Center
Savannah, Georgia, USA

Raymond P. Compton MD FACS

Paris Surgical Specialists,
Chief of Surgery, Henry County Medical Center
Paris, Tennessee, USA

Marshall A. Corson MD

Associate Professor of Medicine
Head, Section of Cardiology Medical Center
Division of Cardiology
University of Washington Medical Center
Seattle, Washington, USA

Bruce A. Crookes MD FACS

Assistant Professor of Surgery, Division of Trauma
Burns and Critical Care, Department of Surgery
University of Vermont College of Medicine
Burlington, Vermont, USA

Marc A. de Moya MD FACS

Assistant Professor of Surgery
Harvard Medical School
Division of Trauma, Emergency Surgery
and Surgical Critical Care, Massachusetts General Hospital
Boston, Massachusetts, USA

Amy P. De Rosa DO

Resident Surgeon
MCRMC: Department of General Surgery
Michigan State University
East Lansing, Michigan, USA

Daniel L. Dent MD

Associate Professor, Division of Trauma and Emergency
Surgery, University of Texas Health Science Center
San Antonio, Texas, USA

James C. Doherty MD MPH

Director of Trauma Surgery and Critical Care
Advocate Christ Medical Center
Oak Lawn, Illinois
Clinical Assistant Professor of Surgery, University of
Illinois College of Medicine, Chicago, Illinois, USA

Matthew O. Dolich MD FACS

Associate Clinical Professor, Department of Surgery
University of California, Irvine
Orange, California, USA

Joseph J. DuBose MD

Division of Acute Care Surgery, Trauma and Surgical
Critical Care, Wilford Hall Medical Center
Lackland AFB, Texas
Clinical Instructor, Trauma and Surgical Critical Care
Division of Trauma and Surgical Critical Care
Los Angeles County, University of Southern
California Hospital
Los Angeles, California, USA

COL Brian J. Eastridge MD FACS

Director, Joint Trauma System
U.S. Army Institute of Surgical Research
Fort Sam Houston, San Antonio, Texas, USA

Matthew J. Eckert MD

Department of Surgery, Madigan Army Medical Center
Fort Lewis, Washington, USA

Akpofure Peter Ekeh MD

Associate Professor
Wright State University
Department of Surgery, Boonshoft School of Medicine
Dayton, Ohio, USA

Robert M. Esterl Jr. MD

Professor of Surgery, Department of Surgery
Transplant Center, University of Texas Health Science
Center at San Antonio, Texas, USA

Ara J. Feinstein MD MPH

Ryder Trauma Center, Jackson Memorial Hospital
Division of Trauma and Surgical Critical Care
DeWitt Daughtry Family Department of Surgery
Miami, Florida, USA

Aaron M. Fields MD

Assistant Program Director
Critical Care Fellowship, Staff Intensivist
Staff Anesthesiologist, United States Air Force
Wilford Hall Medical Center
Lackland AFB, Texas, USA

Antonio Jorge V. Forte MD Resident

Plastic Surgery, Section of Plastic Surgery
Department of Surgery
Yale University School of Medicine
New Haven, Connecticut, USA

Renato Freitas MD PhD

Adjunct Professor of Plastic Surgery
Federal University of Parana
Curitiba, Brazil

Eugene Y. Fukudome MD

Resident, Department of Surgery
Massachusetts General Hospital
Boston, Massachusetts, USA

Alberto Garcia MD

Assistant Professor of Surgery, Universidad del Valle
Chief Emergency Department, Fundacion Valle de Lili
Cali, Colombia

Joseph E. Glaser MD

Resident, Department of General Surgery
New York Hospital of Queens, Flushing
New York, USA

Joel E. Goldberg MD FACS

Assistant Professor of Surgery, Brigham
and Women's Hospital
Boston, Massachusetts, USA

Gerald Gollin MD

Associate Professor of Surgery and Pediatrics
Loma Linda University School of Medicine
Division of Pediatric Surgery
Loma Linda, California, USA

Steven Granger MD

Department of Surgery
Intermountain Medical Center
Salt Lake City, Utah, USA

M. Kelly Green MD

Resident, Department of Ophthalmology
University of Texas Health Science Center at San Antonio
San Antonio, Texas, USA

Mark Gunst MD MPH

Division of Acute Care Surgery
Trauma and Surgical Critical Care
Wilford Hall Medical Center
Lackland AFB, Texas, USA

Fahim Habib MD

Assistant Professor of Surgery
University of Miami, Miller School of Medicine
Miami, Florida, USA

Ryan T. Hagino MD FACS

Associate Professor, Division of Vascular Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

S. Morad Hameed MD MPH FRCS

Assistant Professor of Surgery and Critical
Care Medicine, University of British Columbia
Vancouver, Canada

Stephen O. Heard MD

Professor, Departments of Anesthesiology and Surgery
University of Massachusetts Medical School
Worcester, Massachusetts, USA

Antonio Hernandez MD

Assistant Professor
Director of Cardiothoracic & Transplant Anesthesiology
Department of Anesthesiology
University of Texas Health Science Center
San Antonio, Texas, USA

John J. Hong MD

Chief, Section of Trauma Research
Division of Trauma/Surgical Critical Care
Lehigh Valley Health Network
Allentown, Pennsylvania, USA

Jerry Lee Howard MD

Department of Surgery, Lehigh Valley Health Network
Allentown, Pennsylvania, USA

Kenji Inaba MD MSc FRCS FACS

Assistant Professor of Surgery
University of Southern California
Division of Trauma Surgery
and Surgical Critical Care
Los Angeles, California, USA

Brent Izu MD

Resident in Surgery
Wright State University Department of Surgery
Boonshoft School of Medicine
Dayton, Ohio, USA

Elan Jeremitsky MD

Division of Trauma Surgery
Department of Surgery
Allegheny General Hospital
Pittsburgh, Pennsylvania, USA

Igor Jeroukhimov MD

Head of Trauma Unit Attending in General Surgery
Division of Surgery, Hasaf Harofei Medical Center
Affiliated with Tel Aviv University
Zerelin, Israel

Maria Fernanda Jimenez MD

Assistant Professor of Surgery, Javeriana University,
Bogota, Colombia

Robert Kelly MD

Division of General Surgery,
Memorial Health Medical Center
Savannah, Georgia, USA

David R. King MD Major USAF MC

Instructor of Surgery, Division of Trauma
Emergency Surgery, Surgical Critical Care
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts, USA

Yoram Klein MD

Assistant Professor of Surgery Chief, Division of Trauma and Emergency Surgery, The Hebrew University School of Medicine - Kaplan Medical Center
Rehovot, Israel

Lydia Lam MD

Critical Care Fellow, Division of Trauma and Surgical Critical Care, Los Angeles County University of Southern California Hospital
Los Angeles, California, USA

Teofilo Lama MD

Trauma and Critical Care Services
Saint Mary's Medical Center
West Palm Beach, Florida, USA

Peter A. Learn MD

Clinical Assistant Professor of Surgery
University of Texas Health Science Center
San Antonio, Texas
Wilford Hall, USAF Medical Center
Lackland AFB, Texas, USA

Alan Lisbon MD

Associate Professor of Anaesthesia
Harvard Medical School, Acting Chair, Anesthesia Critical Care and Pain Medicine
Beth Israel Deaconess Medical Center
Boston, Massachusetts, USA

Peter P. Lopez MD

Assistant of Professor of Surgery
Division of General and Laparoscopic Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Alexandra A. MacLean MD

Assistant Professor of Surgery, Weill Medical College
Cornell University, Attending Surgeon
New York Hospital of Queens
Flushing, New York, USA

Sapoori Manshahi MD

Assistant Professor of Surgery
Department of Surgery
University of Minnesota
Minneapolis, Minnesota, USA

Deborah L. Mueller MD FACS

Associate Professor of Surgery
Division of Trauma and Emergency Surgery
Department of Surgery, University of Texas Health Science Center
San Antonio, Texas, USA

Paras Nikolaos MD PhD

Transplant Institute, Miller School of Medicine
University of Miami
Miami, Florida, USA

Doron Norman MD

Orthopedic Surgeon, Director, orthopedic surgery B
Rambam Health Campus
Haifa, Israel

Terence O'Keeffe MB ChB BSc FRCS(Ed) MSPH

Division of Trauma, Critical Care and Emergency Surgery, Department of Surgery, University of Arizona
Tucson, Arizona, USA

Adrian W. Ong MD

Assistant Professor of Surgery
Drexel University College of Medicine
Allegheny General Hospital
Department of Surgery
Pittsburgh, Pennsylvania, USA

Michael D. Pasquale MD

Associate Professor of Surgery
Penn State College of Medicine
Chief, Division of Trauma/Surgical Critical Care
Lehigh Valley Health Network
Allentown, Pennsylvania, USA

Edgar J. Pierre MD

Assistant Professor of Anesthesiology
Surgery and Care Critical
Department of Anesthesiology, University of Miami
Miami, Florida, USA

Brad H. Pollock MPH PhD

Professor and Chairman
Department of Epidemiology and Biostatistics
School of Medicine, University of Texas Health Science Center at San Antonio
San Antonio, Texas, USA

Michelle A. Price MEd PhD

Assistant Professor of Surgery, University of Texas Health Science Center at San Antonio
San Antonio, Texas, USA

Basil A. Pruitt, Jr., MD

Clinical Professor
Department of Surgery
The University of Texas Health Science Center at San Antonio
San Antonio, Texas, USA

Juan Carlos Puyana MD

Associate Professor
Surgery and Critical Care Medicine
University of Pittsburgh - Chief Medical Officer
IMITS Center, UPMC
Pittsburgh, Pennsylvania, USA

Todd E. Rasmussen MD Lt Col USAF MC

Chief Division of Surgery
Wilford Hall USAF Medical Center
Lackland Air Force
Texas
Associate Professor of Surgery, The Uniformed Services University of the Health Sciences
Bethesda, Maryland, USA

Bipin K. Ravindran MD MPH

Fellow, Cardiology and Cardiac Electrophysiology
Department of Medicine, Division of Cardiology
University of Washington
School of Medicine
Seattle, Washington, USA

V. Seenu Reddy, MD MBA FACS

Assistant Professor
Division of Thoracic Surgery
Director Thoracic Aortic Surgery
Department of Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Peter M. Rhee MD MPH

Professor of Surgery, Chief, Section of Trauma
Critical Care and Emergency Surgery
Arizona Health Sciences Center
Department of Surgery
Tucson, Arizona, USA

Raul J. Rosenthal MD FACS

The Bariatric Institute
Cleveland Clinic Florida
Weston, Florida, USA

Amanda Saab MD

Resident in Anesthesiology
Department of Anesthesiology, University of Miami
Miami, Florida, USA

Shaul Sagiv MD

Assistant Professor of Orthopedic Surgery, Chief
Division of Spine and Orthopedic Trauma
The Hebrew University School of
Medicine – Kaplan Medical Center
Rehovot, Israel

David Sahar MD

Division of Plastic and Reconstructive Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Anne Saladyga MD

William Beaumont Army Medical Center
El Paso, Texas, USA

Edan Sarid MD

Research Assistant,
The Yitzhak Robin Trauma Division
Tel Aviv Sourasky Medical Center
Department of Surgery B
Tel Aviv, Israel

Stephanie A. Savage MD Major USAF MC

Surgical Critical Care/Chief of Trauma
Wilford Hall Medical Center
Lackland AFB, Texas, USA

Mark D. Sawyer MD

Consultant in Surgery
Division of Trauma, Critical Care, and
General Surgery, The Mayo Clinic
Rochester, Minnesota, USA

Patrick Schaner MD

Division of Plastic and Reconstructive Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

John G. Schneider MD

Resident, Department of Surgery
University of Vermont College of Medicine
Burlington, Vermont, USA

Carl I. Schulman MD MSPH FACS

DeWitt Daughtry Family Department of Surgery
Division of Trauma and Critical Care
University of Miami Miller School of Medicine
Miami, Florida, USA

Steven D. Schwartzberg MD

Chief of Surgery, Cambridge Health Alliance
Visiting Associate Professor Surgery
Harvard Medical School
Cambridge, Massachusetts, USA

Wayne H. Schwesinger MD FACS

Professor of Surgery
Division of General and Laparoendoscopic Surgery
Department of Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Maureen K. Sheehan MD FACS

Assistant Professor
Division of Vascular Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Joseph H. Shin MD FACS

Chief of Plastic Surgery
Department of Surgery, Baystate Medical Center
Tufts Medical School
Springfield, Massachusetts, USA

Joseph H. Shin MD FACS

Chief of Plastic Surgery
Department of Surgery, Baystate Medical Center
Tufts Medical School
Springfield, Massachusetts, USA

Paula K. Shireman MD FACS

Departments of Surgery and Medicine and
The Sam and Ann Barshop Institute for Longevity and
Aging Studies at the University of Texas
Health Science Center
South Texas Veterans Health Care System
San Antonio, Texas, USA

Kent R. Van Sickle MD

Division of General and Laparoendoscopic Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Renato da Silva Freitas MD PhD

Adjunct Professor of Plastic Surgery
Federal University of Parana
Curitiba, Brazil

Richard K. Simons MChB FRCS

Associate Professor of Surgery
University of British Columbia
Vancouver, Canada

Dror Soffer MD

Director, The Yitzhak Rabin Trauma, Division
Assistant Professor of Surgery, Tel Aviv Sourasky
Medical Center, Department of Surgery B
Tel Aviv, Israel

K. Vincent Speeg MD PhD

Professor of Medicine/Gastroenterology
Transplant Center, University of Texas Health
Science Center at San Antonio, Texas, USA

Kenneth D. Stahl MD FACS

Assistant Professor of Surgery and
Director of Patient Safety, DeWitt Daughtry Family
Department of Surgery, Division of Trauma and
Surgical Critical Care, Director of Patient Safety Research
William Lehman Injury Research Center
The University of Miami Leonard M. Miller
School of Medicine
Miami, Florida, USA

Scott R. Steele MD FACS

Colon and Rectal Surgery, Madigan Army Medical Center
Department of Surgery
Assistant Professor of Surgery
Uniformed Services University
Fort Lewis, Washington, USA

Ronald Stewart MD

University of Texas Health Science Center
San Antonio, Texas
Clinical Instructor, Trauma Surgery
San Antonio, Texas
Institute of Surgical Research
San Antonio, Texas, USA

Balachundhar Subramaniam MBBS MD

Assistant Professor of Anaesthesia, Harvard Medical
School, Director of Cardiac Anesthesia Research
Beth Israel Deaconess Medical Center
Boston, Massachusetts, USA

Erik J. Teicher MD

Division of Trauma/Surgical Critical Care
Lehigh Valley Health Network
Allentown, Pennsylvania, USA

Pedro G.R. Teixeira MD

Research Fellow
University of Southern California
Division of Trauma Surgery and
Surgical Critical Care
Los Angeles, California, USA

Burke Thompson MD MPH

Associate Director of Trauma
Moses Cone Health System, Trauma Program
Moses Cone Memorial Hospital
Greensboro, North Carolina, USA

Boulos Toursarkissian MD

Associate Professor and Chief
Division of Vascular Surgery
University of Texas Health Science Center
San Antonio, Texas, USA

Olga N. Tucker MD FRCSI

The Academic Department of Surgery
The Queen Elizabeth Hospital
Birmingham, United Kingdom

Andreas G. Tzakis MD PhD FACS

Professor of Surgery
Transplant Institute, Miller School of Medicine
University of Miami
Miami, Florida, USA

George C. Velmahos MD PhD MEd

John F. Burke
Professor of Surgery
Harvard Medical School, Chief, Division of Trauma
Emergency Surgery, and Surgical Critical Care
Massachusetts General Hospital
Boston, Massachusetts, USA

Cynthia L. Villarreal MA

Faculty Associate
Department of Surgery
University of Texas Health Science
Center at San Antonio
San Antonio, Texas, USA

Mohan N. Viswanathan MD

Assistant Professor of Medicine
Division of Cardiology Section of Cardiac
Electrophysiology
Department of Medicine
University of Washington School of Medicine
Seattle, Washington, USA

J. Matthias Walz MD

Assistant Professor
Departments of Anesthesiology and Surgery
University of Massachusetts Medical School
Worcester, Massachusetts, USA

Howard Wang MD

University of Texas Health Science Center
San Antonio, Texas
Division of Plastic and Reconstructive Surgery
San Antonio, Texas, USA

Steven E. Wolf MD

Betty and Bob Kelso Distinguished Professor in
Burns and Trauma, Vice-Chairman for Research
Department of Surgery, University of Texas
Health Science Center
Chief and Task Area Manager, Clinical Trials
United States Army
San Antonio, Texas, USA

"The questions never change . . . just the answers!"

—Owen Wangenstein

Preface

JOHN HUNTER, FATHER OF EVIDENCE-BASED SURGERY



The first surgeon to apply evidence to the field of surgery was probably John Hunter (1728–1793, Fig. P.1). His approach to medicine is exemplified by his management of gunshot wounds.

Conventional practice dictated that army surgeons open up a gunshot wound—a technique known as “dilatation”—prize out the musket ball or shot with their fingers or forceps prior to cleaning away any debris and dressing the wound. The principle of dilatation stemmed from the belief that gunpowder was poisonous, dating back to its first use in European warfare in the thirteenth century. This doctrine almost certainly increased death and suffering. The acts of incising flesh within a wound were exceedingly painful before the advent of anaesthetic agents and often lead to tremendous loss of blood. In addition, dilatation frequently introduced fatal infection as military surgeons often treated their casualties on muddy, manure-ridden battlefields.

During the conquest of Belle-Ile in 1761, during Britain’s Seven Year War with France, Hunter observed the outcomes of five French soldiers but had been shot in the exchange of gunfire who had managed to hide out in an empty farmhouse. “The first four men had nothing done to their

wounds; indeed very little was done to the men themselves; for they lay in an uninhabited house for more than four days with hardly any subsistence,” Hunter noted. “The wounds were never dilated, nor were they dressed all this time. . . . All of them healed as well, and as soon as the like accidents do in others who have all the care that possibly can be given of them.” Therefore, neglected through accident rather than design, their injuries had healed better than those of their British counterparts who had been subjected to the surgeon’s knife. Hunter believed that wounded soldiers had a better chance of survival by letting nature take its course. While his colleagues dismissed his examples as mere curiosities, Hunter adapted his methods to suit his observations in the first systematic application of scientific evidence to practice.

Hunter’s aim was that young surgeons attending his lectures would always “ask the reasons of things”. He wanted them to take nothing for granted, to subject every common superstition and unproven therapy to scrutiny. Essentially, he aimed to equip them to elevate surgery to the rank of a science. (Adapted from *Knife Man*, by W. Moore, 2005)

EVIDENCE-BASED SURGERY

Using evidence-based studies, this textbook focuses on the critical management questions of the day. The book uses publications from the past decade and predominantly cites those published manuscripts that provide Level I and II evidence using the Oxford scale (with permission from the Centre for Evidence-Based Medicine) (see Table P.1).

Each chapter is organized around the several key questions on the particular topic. These questions have been judged by the authors as essential in delineating the current status of evidence-based material related to the specific subject. A summary of these questions and answers along with the strength of the recommendations appear in each chapter. (*Disclaimer:* The authors used the Oxford table, shown in Table P.1, to judge the quality and integrity of the evidence reviewed, but these decisions were at times subjective.) In many instances, there are little high-quality data found on these various topics. The evidence-based surgery reviews are submitted to stimulate the development of future clinical trials and provide credible answers to age-old surgical management questions.

Table P.1 Oxford Centre for Evidence-Based Medicine Levels of Evidence (May 2001)

Level	Therapy/Prevention, Etiology/Harm	Prognosis	Diagnosis	Differential Diagnosis/Symptom Prevalence study	Economic and Decision Analyses
Ia	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR [†] validated in different populations	SR (with homogeneity*) of Level I diagnostic studies; CDR [†] with Ib studies from different clinical centers	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level I economic studies
Ib	Individual RCT (with narrow confidence interval [‡])	Individual inception cohort study with ≥80% follow-up; CDR [†] validated in a single population	Validating** cohort study with good ^{†††} reference standards; or CDR [†] tested within one clinical center	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multiway sensitivity analyses
Ic	All or none [§]	All or none case series	Absolute SpPins and SnNouts ^{††}	All or none case-series	Absolute better-value or worse-value analyses ^{††††}
IIa	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >II diagnostic studies	SR (with homogeneity*) of IIb and better studies	SR (with homogeneity*) of Level >II economic studies
IIb	Individual cohort study (including low-quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; derivation of CDR [†] or validated on split-sample ^{§§§} only	Exploratory** cohort study with good ^{†††} reference standards; CDR [†] after derivation, or validated only on split-sample ^{§§§} or databases	Retrospective cohort study or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multiway sensitivity analyses
IIc	“Outcomes” research; ecological studies	“Outcomes” research		Ecological studies	Audit or outcomes research
IIIa	SR (with homogeneity*) of case control studies		SR (with homogeneity*) of IIIb and better studies	SR (with homogeneity*) of IIIb and better studies	SR (with homogeneity*) of IIIb and better studies
IIIb	Individual case-control study		Nonconsecutive study; or without consistently applied reference standards	Nonconsecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor-quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations.
IV	Case-series (and poor-quality cohort and case-control studies ^{§§})	Case-series (and poor-quality prognostic cohort studies***)	Case-control study, poor or nonindependent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
V	Expert opinion without explicit critical appraisal, or based on physiology, bench research or “first principles”	Expert opinion without explicit critical appraisal or based on physiology, bench research, or “first principles”	Expert opinion without explicit critical appraisal or based on physiology, bench research, or “first principles”	Expert opinion without explicit critical appraisal or based on physiology, bench research, or “first principles”	Expert opinion without explicit critical appraisal or based on economic theory or “first principles”

Users can add a minus sign, −, to denote the level that fails to provide a conclusive answer because of either a single result with a wide confidence interval (such that, e.g., an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm); or a systematic review with troublesome (and statistically significant) heterogeneity. Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

Abbreviations: CDR, clinical decision rule; RCT, randomized controlled trial; SR, systematic review.

*By *homogeneity* we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted, studies displaying worrisome heterogeneity should be tagged with a − at the end of their designated level.

[†]CDRs are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category.

[‡]See foregoing note for advice on how to understand, rate, and use trials or other studies with wide confidence intervals.

[§]Met when *all* patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but *none* now die on it.

(Continued)

Table P.1 (Continued)

^{§§}By poor-quality *cohort study* we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and nonexposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor-quality *case-control study* we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

^{§§§}Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into “derivation” and “validation” samples.

^{††}An absolute SpPin is a diagnostic finding whose specificity is so high that a positive result rules *in* the diagnosis. An absolute SnNout is a diagnostic finding whose sensitivity is so high that a negative result rules *out* the diagnosis.

^{†††}Good, better, bad, and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.

^{††††}Good reference standards are independent of the test and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a nonindependent reference standard (where the test is included in the reference, or where the testing affects the reference) implies a Level IV study.

^{†††††}Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.

^{**}Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g., using a regression analysis) to find which factors are significant.

^{***}By poor-quality prognostic cohort study, we mean one in which sampling was biased in favor of patients who already had the target outcome, the measurement of outcomes was accomplished in < 80% of study patients, outcomes were determined in an unblinded, nonobjective way, or there was no correction for confounding factors.

^{****}Good follow-up in a differential diagnosis study is > 80%, with adequate time for alternative diagnoses to emerge (e.g., 1–6 months acute, 1–5 years chronic).

Source: Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes, since November 1998.

Table P.2 Grades of recommendation

A	Consistent Level I studies
B	Consistent Level II or II studies <i>or</i> extrapolations from Level I studies
C	Level IV studies <i>or</i> extrapolations from Level II or III studies
D	Level V evidence <i>or</i> troublingly inconsistent or inconclusive studies of any level

Extrapolations are where data are used in a situation that has potentially clinically important differences than the original study situation.

Stephen M. Cohn

Foreword

This textbook focuses on important surgical management issues where one or more problems are addressed using scientific evidence from the published literature. This foreword describes the criteria used for weighing the evidence provided by published research studies. Why evidence-based medicine? The primary use of evidence-based medicine (EBM) is to help make informed decisions by combining individual clinical expertise with the best available external clinical evidence. This approach optimizes decision making for the care of individual patients (1).

Surgical management issues presented herein are oriented toward interventions. Although gathering evidence from intervention studies is the most common use of EBM, the objectives of patient-oriented research studies can alternatively include determining the etiology of a health problem, determining the accuracy and utility of new tests, and identifying prognostic markers. In this book, EBM is used to assess the safety and efficacy of new treatments and rehabilitative or preventive interventions. The evidence from multiple studies is often combined to make clinical inferences and select the most appropriate treatment plan for individual patients. The goal of this chapter is to describe the ways evidence is evaluated and integrated.

ASSESSING THE VALIDITY OF INTERVENTION STUDIES

Four attributes define the strength of evidence provided by a published intervention study. The first is the level of the evidence—dictated by the type of study design that was used. The second is the quality of evidence—directly related to lack of bias. The third is statistical precision—the degree to which true effects can be distinguished from spurious effects due to random chance. The fourth is the choice of a study endpoint to measure an effect—an endpoint's appropriateness to truly represent a clinically meaningful effect—and the magnitude of the observed effect. For practical reasons, the selection of study subjects is almost always a compromise. The degree to which a chosen study population represents an intended target population must also be considered; selection bias can compromise a study's weight of evidence.

Study Design

Several different types of studies are used in clinical research. Case reports and case series can document the effects of an intervention or clinical course. However, these are subject to selection bias, often use subjective outcome assessment,

and are imprecise due to the small samples. Case reports and case series have no control groups for comparisons. Case-control studies include subjects who have developed the outcome of interest (cases) and a group of unaffected subjects (controls). Case-control studies can be performed in a more timely manner and are often much less expensive than other study designs. However, a temporal relationship between cause and effect can only be inferred, and not directly measured, because of the retrospective in nature of case-control studies. Also, case-control studies are subject to biased recall of antecedent exposures. Selection bias is an important concern, especially the selection of controls. Case-control studies are most often used for very rare outcomes or when there is a long induction period between an exposure and the outcome.

Prospective cohort studies recruit subjects who are free of the outcome of interest. Subjects are then dynamically followed over time for the occurrence of the outcome. Recruitment may be selective and based on accruing an equal number of subjects into preselected exposures categories; matching on other factors is possible to reduce confounding and improve the precision of comparisons across exposure groups. Alternatively, recruitment to cohort studies need not be based on predetermined categories of exposure; these are typically studies with several exposures of interest. An alternative design is the historical cohort study. These studies use preexisting information, often in a comprehensive database, to historically classify exposure status. The database is then gleaned for information about subsequent outcome events. Except for randomized controlled trials, prospective cohort studies are more expensive than other designs. An exposure of interest, such as a new surgical procedure versus a conventional procedure, may be linked to unknown or unmeasurable potential confounders. Because cohort studies are not randomized, the distribution of these unknown or unmeasurable confounders may not be balanced between the treatment groups, thus leading to confounding. Prospective studies are more time consuming than case-control studies. A major advantage of cohort designs are that they provide a clear picture of the temporal relationship between a cause and an effect. Matching can efficiently reduce confounding. A cohort study is generally simpler and less expensive to conduct than a randomized controlled trial.

Randomized controlled trials (RCTs) provide the greatest weight of evidence compared to other designs. In these studies, the allocation of subjects to an exposure of interest is done solely for the purpose of obtaining an unbiased estimate of the treatment effect. The key advantage

of RCTs is their lower likelihood of confounding bias. Whereas controlling for known confounders can be performed using techniques such as restriction, stratified block design, or statistical adjustment, randomization tends to balance the distribution of unknown or unmeasurable confounders between treatment groups. RCTs can also be more easily blinded. The disadvantages of RCTs are recruitment barriers (particularly for subjects who prefer not to be experimented on) and, because of their prospective nature, higher costs than nonprospective designs such as case-control studies. Even with those limitations, RCTs represent the gold standard; they provide the strongest weight of evidence.

Other study designs are used less frequently in medical research. Cross-sectional studies collect both exposure and outcome information simultaneously and may be more applicable for prevalent rather than acute conditions. Cross-sectional studies do not address cause and effect temporal relationships. Cross-over designs are studies in which all subjects serve as their own controls. Half the study population receives the primary treatment first and then crosses over to receive the second treatment. The other half receives the treatments in reverse order. An assumption of cross-over studies is that the residual effects of a treatment disappear by the time the groups are crossed over. This is clearly not applicable for many surgical interventions where a subject's condition is permanently altered by the therapy (e.g., limb amputation). Pharmaceutical trials where the washout period for the new drug is too long or of unknown duration cannot be evaluated with cross-over designs.

Bias

The strength of scientific evidence provided by an individual study is dependent on a number of key factors. All of these factors must be properly considered before attempting to make clinical inferences from a published study. Ideally, results are published for studies that are both internally and externally valid. Compromised validity lowers a study's weight of evidence.

The design of all patient-oriented research studies is strongly associated with the degree to which bias can potentially impact the study results and conclusions. The internal validity for a particular study is affected by observer bias, measurement bias, confounding, and statistical precision. These potential problems manifest themselves in different ways for different study designs.

Internal validity refers to a study's lack of bias; bias is a systematic error that affects inferences derived from the results of a study. Internally valid studies are free of bias. *External validity* refers to the generalizability of a study and addresses the issue of whether results derived from the assessment of a study-specific population can be extrapolated to another population of interest. Internal validity should be the primary consideration when reviewing a publication. If a study is not internally valid, one need not consider whether it is externally valid, that is, biased study results should never be extrapolated to another population. For intervention studies, internal validity addresses whether observed changes (study results) can be attributed to the treatment effect or whether they are attributed to other, alternate explanations, such as bias or lack of statistical precision.

There are a number of internal validity considerations. Measurement bias is inaccuracy related to the method of measuring values for a study. Examples include miscalibrated blood pressure readings, inaccurate height measurements, flawed laboratory methods that give erroneous values, or less than optimal coding that fails to accurately reflect clinically meaningful categories. Observer bias is inaccuracy related to measuring a study outcome where the observer knows the intervention group assignment. Observer bias is more likely to occur when the chosen outcome measure is subjective. Examples of softer, more subjective measures include the occurrence of symptoms or toxicities, patient self-report measures, and interpretations of physical examination findings. If observers know which treatment a patient is receiving, their outcome assessments may be biased. Blinded designs are sometimes used to reduce observer bias. Double blinding is a technique in which neither the observer nor the patient knows the treatment assignment. However, blinding may be impractical for many surgical interventions (such as total limb versus partial limb amputation) or for regimens with very idiosyncratic symptom or toxicity profiles. Confounding bias is the mixing up of effects so that the primary effect under study cannot be separated from the influence of extraneous factors. For example, failing to account for preoperative disease severity in a randomized trial evaluating two surgical approaches might lead to confounding if the severity distribution differed between groups.

Statistical Precision

Statistical precision for a study results in the ability to distinguish real effects from those due to random chance, that is, chance associations. For example, with just 10 subjects (5 in each group) in an RCT comparing a new postsurgical antibiotic regimen to a conventional regimen for sepsis prophylaxis is likely to result in an extreme finding that can be attributed to random chance, not the true biological drug effect. Chance errors are less likely to occur with larger sample sizes. Trials are always planned to limit the likelihood of chance errors; acceptable levels of error (for Type I and Type II statistical errors) are selected, and the target minimum detectable effect size is chosen. Formal sample size/power calculations are performed during the study's design to ensure adequate statistical precision.

External Validity

External validity is a function of whether a study's results can be generalized. The question is, "Does the study population possess unique characteristics that might modify the effect of an intervention in a way that would render it ineffective in some other group?" Subjects accrued to a trial may not be representative of the population to which the intervention is intended to be applied. There is a tendency for published surgical and nonsurgical intervention studies to enroll subjects at larger academic institutions. The characteristics for these referred patients may not be representative of patients seen at smaller nonacademic centers. Even within a center, subjects that volunteer to participate in a study may not be representative of the institution's entire clinical population.

Selection bias can occur with the self-selection of individuals who volunteer to participate in a research study.

Both researchers and participants may bring a multitude of characteristics to a clinical study, some inherent and some acquired. These can include factors such as gender, race/ethnicity, hair, eye and skin color, personality, mental capability, physical status, and psychological attitudes such as motivation or willingness to participate. Differences in the distribution of these factors between a source population and a protocol-enrolled study population may introduce selection bias. For example, some investigators may preferentially select more athletic-looking subjects for an elective orthopedic surgery clinical trial. Multicenter trials may improve the generalizability of a study, but such studies may still suffer from selection bias.

WEIGHT OF EVIDENCE

Study design, lack of bias, statistical precision, and external validity are elements that affect a study's weight of evidence. Each of these factors must be considered when evaluating a published study. For practical reasons, the investigator who is designing a new study is always confronted with trade-offs between these factors and cost. For example, having highly restrictive eligibility criteria reduces confounding but lowers the generalizability of a study. The choice of a more objective endpoint for an antibiotic trial (e.g., death versus confirmed sepsis) decreases observer bias at the cost of decreased statistical precision—fewer deaths compared to the number of incident sepsis cases. Investigators are faced with many challenges when designing intervention studies. Because resources are almost always limited, design compromises are made that ultimately impact the overall weight of evidence provided by a study.

LITERATURE REVIEWS

Reviews of published studies can take multiple forms. Reviews can be done of single studies. Single studies may be used as the basis for making treatment decisions. There may be a very large RCT that appropriately evaluated a single clinical endpoint with high validity. This may be sufficient for medical decision making. Alternatively, narrative reviews or systematic reviews evaluate multiple publications.

NARRATIVE REVIEWS

Narrative reviews often address a broad set of clinical questions and are thus less focused on a specific question. They appear more often in the literature and are more qualitative and less quantitative. In contrast, systematic reviews are usually focused on a specific clinical issue, incorporate objective criteria for selection of published studies, include an evaluation of quality and worthiness, and often use a quantitative summary to synthesize combined results.

Narrative reviews are often one of the first academic endeavors that young physicians complete during their training. Their subjective nature increases the likelihood that inferences are affected by imprecision and bias. Often, a count of included studies supporting or refuting a particular issue is determined and a winner is declared. For narrative reviews, little consideration may be given to issues of study design, sample size/statistical power, or study validity.

SYSTEMATIC REVIEWS

Systematic reviews are a staple of EBM (2). They provide the best means for combining evidence from multiple studies. They follow a defined protocol to identify, summarize, and combine information. Systematic reviews may restrict the inclusion of studies to specific study designs, such as RCTs, or they may include a broader set of designs. Systematic reviews can be very labor intensive and costly. They may attempt to use information from unpublished studies. There are significant challenges in combining evidence from studies that use different designs, or different endpoints, or that vary by other methodological characteristics.

A protocol for a systematic review uses a strict set of guidelines for selecting and amalgamating information from the literature. The Cochrane Collaboration (see www.cochrane.org) guidelines for developing a systematic review protocol requires a background section explaining the context and rationale for the review; a statement of the objectives; a clear definition of the inclusion and exclusion criteria for studies (including study designs, study populations, types of interventions, and outcome measures); the search strategy for identification of studies; and the methodological approach to the review process, including the selection of trials, assignment of methodological quality, data handling procedures; and data synthesis. Data synthesis includes statistical considerations such as choice of summary effect measures, assessment of heterogeneity of effect across studies, subgroup analyses, use of random or fixed effects statistical models, and assessment of publication bias.

Meta-Analysis

Systematic reviews often (but not always) include a meta-analysis. The goals of meta-analysis are to provide a precise estimate of the effect and determine if the effect is robust across a range of populations (3). Often a component of systematic reviews, meta-analyses tally the results of each study identified by the reviewer and then calculate the average of those results, if appropriate. Data are first extracted from each individual study and then used to calculate a point estimate of effect along with a measure of uncertainty, for example, the 95 percent confidence interval. This is repeated for each of the studies included in the meta-analysis. Then a decision is made about whether the results can be pooled to calculate an average result across all the studies. The decision to combine or not combine studies is made by an assessment of the heterogeneity of effect across studies. Observed statistical heterogeneity suggests that the true underlying treatment effects in the trials are not identical; that is, the observed treatment effects have a greater difference than one should expect due to random error alone. Importantly, uncovering heterogeneity may be the primary goal of a meta-analysis. Analysis of heterogeneity may elucidate previously unrecognized differences between studies. Only in the absence of significant heterogeneity can study results be combined and a summary measure of effect calculated. Calculation of summary measures relies on a mathematical process that gives more weight to the results from studies that provide more information (usually those with larger study populations) or with higher quality. Often, data for all included studies are

plotted on a graph known as a forest plot, which includes a graphical representation of the magnitude of effect for each study and its degree of uncertainty (plotted as confidence intervals). Meta-analysis can evaluate the impact of potential confounders on the treatment effect.

Publication Bias

All studies are subject to Type I errors where evidence is found to reject a null hypothesis when there is no true effect, or Type II errors where evidence is found to not reject the null hypothesis when a true effect exists. Studies with statistically significant results ("positive" studies) are more likely to be accepted for publication than those without statistically significant results ("negative" studies). Even adequately powered studies with very low Type II error rates are less likely to be accepted for publication than are smaller positive studies.

LEVELS OF EVIDENCE AND GRADES OF RECOMMENDATIONS

All reviews evaluate historical information and are therefore subject to systematic bias and random error. For different study objectives (e.g., determining the impact of a therapeutic or preventive intervention), the Oxford Centre for Evidence-Based Medicine Levels of Evidence displays the level of evidence based on a review of the literature, study design, and quality. The highest level of evidence for a therapeutic intervention is provided by systematic reviews of large RCTs that show homogeneity of effect across trials (Level 1a); the next highest is for an individual RCT with a narrow confidence interval (Level 1b); this is followed by an all-or-none effect related to the introduction of a treatment (Level 1c). The level of evidence decreases

with weaker study designs, such as cohort studies (Level 2), followed by case-control studies (Level 3), case series (Level 4), and at the lowest level, expert opinion (Level 5). Grades of recommendations are based on consistency of higher level studies: An A grade shows consistency across Level 1 studies; a B grade shows consistency across Level 2 or 3 studies or extrapolations from Level 1 studies; a C grade shows consistency across Level 4 studies or extrapolations from Level 2 or 3 studies; a D grade shows Level 5 evidence or inconsistency across studies of any level.

SUMMARY

EBM is not limited to the evaluation of RCTs and meta-analysis. A broader range of external evidence can be brought to bear on addressing clinical questions (1). Practice guidelines developed using EBM can have a positive impact on patient outcomes. EBM guidelines have reduced mortality from myocardial infarctions and also improved care for persons with diabetes and other common medical problems. EBM supplements physicians' judgments that might otherwise be based solely on anecdotal clinical experience. Surgical practice can benefit from EBM and should be incorporated into the standard of care.

REFERENCES

1. Sackett DL, Rosenberg WMC, Gray JAM, et al. Evidence based medicine: What it is and what it isn't. *Br Med J* 1996; 312: 71-2.
2. Egger M, Smith GD, Altman DG, eds. *Systematic Reviews in Health Care. Meta-Analysis in Context*, 2nd edition. London: BMJ Publishing Group, 2001.
3. Borenstein M, Hedges LV, Higgins JPT, et al. *Introduction to Meta-Analysis*. New York: Wiley, 2009.

Brad H. Pollock MPH PhD

*Professor and Chairman, Department of Epidemiology
and Biostatistics, School of Medicine, University of Texas
Health Science, Center at San Antonio, San Antonio, Texas, USA*

Introduction

Sir William Osler said, “To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all” (1). Today we can expand on that aphorism by saying, “to practice surgery without scientific understanding is like sailing without a rudder.” Surgeons must use their understanding of disease pathogenesis and knowledge of treatment effectiveness to define the science of surgery, which enables them to achieve early diagnosis and apply appropriate treatment with resultant maximum salvage and optimum outcomes.

Surgical practice has always been based on the scientific understanding of the day. That understanding has slowly evolved to a knowledge base that is continually expanding and being refined by sophisticated high-technology laboratory studies and the randomized controlled clinical trials of today. Until the 19th century, scientific understanding was commonly based on personal observation and opinion or, at best, anatomic dissections and comparisons. The impact of recommendations based on scientific thought generated in that fashion and the credence accorded such were related directly to the prominence and reputation of the individual making the recommendation. Historically, surgical authority, as the determinant of surgical treatment, has migrated from individual to individual and from country to country, for example, from Hippocratic Greece to Galenic Rome.

The retardation of surgical progress and impairment of patient care due to ascientific surgical dogma are well illustrated by the tortured history of wound care. Hippocrates (460–377 B.C.) recommended making pus form in the wound as soon as possible for the counterintuitive purpose of reducing inflammation (2). When Rome gained medical ascendancy, Galen (130–200 A.D.), by being a proponent of suppuration as a beneficial, even essential component of wound healing, furthered the concept of “laudable” pus (2,3). In the 13th century, Theodoric published *Chirurgia*, in which he advanced the then-heretical opinion that the formation of pus was not necessary for wound healing. That opinion was largely ignored, even though the concept of pus-free healing was supported by Henri de Mondeville of France in his 14th-century textbook *Chirurgie* (2). Guy de Chauliac further extended the authority of French surgeons by publication of his seven-part work, *La Grande Chirurgie*, in 1363. Unfortunately, de Chauliac fully supported the importance of laudable pus and has thus been credited by some with having arrested progress in wound care for more than five centuries (4).

The limitations of authoritarian opinion and dogma in the absence of scientific understanding are further illustrated by the “gunpowder as poison” controversy. In 1460, Heinrich von Pfolspeundt prepared his *Buch Der Bündth-Ertznei*, in which he mentioned “powder-burns” caused by gunshots (5). The concept of poisoned gunshot wounds was extended by Brunschwig, who in his 1497 book *Dis Ist Das Buch Der Chirurgia Hantwirckung Der Wundartzny* recommended using boiling oil or cautery to make wounds suppurate. In the next century, during the siege of Turin, Ambroise Paré noted the absence of severe inflammation in casualties treated without the customary boiling oil. Despite that observation, Paré persisted in a search for a “perfect” salve to stimulate suppuration in the belief that suppuration was required for optimum healing (6). In 16th-century England, Clowes advocated avoiding cautery, but in the next century, Richard Wiseman, whom some consider to have been the father of English surgery, reintroduced cautery and recommended incorporating raw onions in the dressings to counteract the effects of the gunpowder (2,7). In the last decade of the 18th century (1794), John Hunter, on the basis of his experience in the treatment of war wounds, proposed in his posthumously published book *A Treatise on the Blood, Inflammation, and Gun-shot Wounds* that a gunshot wound should be treated like other wounds. Hunter’s stature at the time was so great that early American surgeons such as Jones, Morgan, and Shippen commonly traveled to England to work with him and complete their training. Consequently, his opinion was considered to have resolved the controversy. Unfortunately, Hunter also recommended that gunshot wounds should not be opened or made larger (6). That recommendation, which made the subsequent appearance of laudable pus virtually certain, did little to improve the control of infection in war wounds. Infections in patients with war wounds remained common and were associated with prohibitively high mortality rates, for example, 97% in patients with pyemia in the U.S. Civil War (8).

The modifications in surgical care that reduced the incidence of infection in war wounds occurred only after Middleton Goldsmith, a Union Army surgeon in the U.S. Civil War, reported that topical antiseptics with bromine could reduce the mortality rate of hospital gangrene from 38% and higher to 2.6% (8). Pasteur identified bacteria as the cause of putrefaction in 1861, and Lister documented that intraoperative antiseptics could effect a threefold reduction of postamputation mortality (6). As has often been the case, those scientific advances supporting changes in

surgical care were slowly accepted and the resultant therapeutic innovations were incorporated into clinical practice with reluctance. Lister's reports on the effectiveness of his antiseptic methods, which appeared beginning in 1869, were initially received with considerable skepticism and even outright rejection by leaders of American surgery. At the 1882 and 1883 meetings of the American Surgical Association, more speakers decried the Lister system than supported it, and one surgeon even considered it doubtful that "microscopic germs cause suppuration" (9).

Authoritarianism and tenacious adherence to dogma in the absence of scientific evidence is not peculiar to surgery, as documented by the professional career of Benjamin Rush and his unrelenting advocacy of exhaustive therapy by which patients were purged, blistered, sweated, and bled, often to the point of exhaustion, as indicated by the name of the therapeutic regimen. Rush, who became the national authority of this kind of therapy, was frequently consulted when it was unsuccessful, and his typical recommendation for more of the same resulted in exhaustive therapy being renamed "heroic" therapy (8). Even with the new name it did little to help the wounded Stonewall Jackson, who did not survive his injury and the heroic therapy he received (10). During the Civil War, reports of deaths due to the toxicity of calomel and tartar emetic, which were components of Rush's therapy, led Surgeon General Hammond to bar those drugs from the formulary of the Union Army. Loud objections to that action by the proponents of heroic therapy gave Secretary of War Stanton an excuse to court-martial Hammond (8). Physician reports of survival of many patients who would ordinarily have received heroic therapy but did not and the deaths attributed to its toxic components ultimately led to its abandonment.

Scientific understanding occurs as an end-product of laboratory and/or clinical research, which were both virtually nonexistent in the United States until the mid-19th century. At that time, entrance to medical school in the United States did not require any basic science knowledge, and there were no laboratories for either undergraduates or medical students at universities and medical schools. Yale University, which founded the Sheffield Scientific School in 1869, was the first to offer a course to prepare students for studies in medical science. In 1871, the first university laboratory for experimental physiology was established by Henry Bowditch at Harvard Medical School, and the second laboratory of physiology was established at Johns Hopkins University School of Medicine five years later (11). Even though those laboratories were productive and produced graduates that established other laboratories and conducted scientific research, physicians were considered to be—and actually were—largely clinicians and only rarely scientists.

In the early part of the 20th century, the Flexner Report severely criticized medical schools and identified measures to improve their quality (12). Thereafter, the establishment of more full-time professorships in surgery and academic emphasis on research as an obligation of each faculty member increased both laboratory and clinical research activity (13). Since 1930, when Congress established the National Institutes of Health (NIH), those institutes have been the principal source of funding for biomedical research (14). That funding support has recently doubled,

and in a recent fiscal year the NIH budget is \$29.5 billion (15). The research sponsored by the NIH, other federal agencies, charitable organizations, professional societies, and commercial entities has rapidly expanded the knowledge base of surgical science extending from the level of the whole organism to organ, tissue, cellular, subcellular, and nanotech levels. Scientific surgery, as presented in this volume, can be defined by its concordance with scientific principles, standards of care, and practice guidelines based on valid research results and the outcomes of rigorous clinical trials.

For the past 50 years, the ever-expanding understanding of disease pathophysiology, as revealed by research findings and rapidly disseminated by modern informatics capabilities, has made it possible to identify scientific surgery with greater ease and assurance than in the past. Concurrently, authoritarian personal opinion has receded as the primary guide to medical practice. Development of evidence-based practice (EBP) has been facilitated by construction of extensive computerized databases and organized programs of information analysis such as the Cochrane Collaboration, which orchestrates reviews of specific topics by selected experts. EBP is promulgated in the form of practice recommendations, such as the practice management guidelines developed by the Eastern Association for the Surgery of Trauma and annotated surgical practice algorithms such as those constructed for Critical Decisions in Trauma by the Western Trauma Association (16,17,18). Other professional societies focused on other aspects of surgical disease have formulated similar practice guidelines, standards of care, and practice algorithms (19).

Evidence-based medicine or practice, which developed in the last decade of the 20th century, consists of a five-step process (20). A question of clinical relevance is developed on which a systematic review of pertinent literature typically is conducted using electronic databases to identify publications to be reviewed. The selected studies are evaluated for both design and scientific quality. The data from those studies deemed to be eligible on the basis of sufficient scientific quality are extracted, amalgamated, and analyzed. Data extraction for EBP can be done by performance of a quantitative meta-analysis or simply by making a qualitative comparison of study outcomes ranked according to a predetermined scale of evidence strength (20). The fifth and final step is to use the results of the meta-analysis or qualitative comparison to formulate standards, guidelines, or options of practice. None of these practice recommendations are absolute because scientific surgical practice is also affected by patient choice and surgical innovation. Consequently, practice standards, guidelines, or options should be viewed as continually evolving recommendations that the scientific surgeon can use to design treatment adaptations to meet the unique needs of individual patients.

There is a hierarchy of evidence used to classify clinical studies, develop practice guidelines, and define scientific surgery as a component of EBP. As the authors in this volume demonstrate, scientific surgery is based on the non-biased review and analysis of the publications constituting the current knowledge base related to the diagnosis, treatment, and outcomes of a specific surgical disease or problem. The evidence of therapeutic studies to be analyzed in the development of EBP can be classified according to the

scientific rigor with which the evidence has been generated. Class or Level I evidence consists of that derived from prospective randomized controlled trials (RCTs) of sufficient size using appropriate design and methodology or the systematic review of Level I RCTs. Class or Level II evidence consists of prospective cohort studies, RCTs with less than 80% follow-up, and systematic reviews of Level II studies or nonhomogeneous Level I studies. Class or Level III evidence consists of case-control studies, retrospective cohort studies, and systematic reviews of Level III studies. Class or Level IV evidence consists of case series, case reviews, and case reports. Class or Level V evidence consists of expert opinion. Yet another class of evidence called "technology assessment" is used for the evaluation of devices, for example, skin substitutes can be evaluated in terms of reliability, therapeutic potential, and cost-effectiveness. In similar fashion, the evidence generated by prognostic studies investigating outcomes, diagnostic studies investigating diagnostic tests, and economic and decision analyses to develop an economic or decision model is assigned to one of four or five levels of scientific quality, with subdivisions in a variable number of those levels depending on the type of study being analyzed (21,22).

Although RCTs are considered to generate gold standard scientific evidence, their validity and strength are often compromised. Common limitations include inadequate blinding, failure to report a sample size calculation, lack of defined primary endpoint, incomplete or inaccurate reporting, and unexplained exclusion of patients from analysis. The consort statement has been developed to improve the reporting of RCTs and assist the reviewer in assessing adequacy of enrollment, allocation to treatment, follow-up, and number of patients analyzed. For each RCT, a consort statement should be prepared by the authors or, if absent, by the reviewers. The checklist, which is used to prepare the consort statement, consists of 22 separate items beginning with the title and abstract and ending with consideration of generalizability and overall interpretation of the results as related to current evidence. Specific items comprising the checklist include a description of methods and participants, interventions, objectives, and outcomes. Particular attention is given to sample size, randomization in terms of sequence generation, allocation concealment, and implementation, blinding and statistical methods, study duration, number of participants analyzed in each group, and a specific statement about analysis by "intention to treat" (23). A consort flow diagram should be provided or prepared to describe the procession of patients through the enrollment, intervention allocation, follow-up, and analysis phases of the trial, as was done by the authors reporting the results of the ProTECT trial (24). Consort Statement 2001 is available online at several Web sites, including *Journal of the American Medical Association*, *The Lancet*, and BioMed Central.

The emphasis of scientific surgery is the identification of safe and effective treatment with optimum outcomes and, some would add, greatest cost-effectiveness. Efficacious treatment, however, must never be compromised in the name of cost-effectiveness if real or projected cost savings will reduce diagnostic accuracy or impair long-range outcomes.

The evaluation and analysis of available evidence is then used to develop the recommendations that guide

surgical practice. Practice recommendations are similarly classified according to the scientific rigor and clinical certainty of the evidence analyzed (See Figure). To be considered a standard of care, the recommendation should be supported by Class I evidence. However, if prospective randomized controlled trials are neither practical nor ethical, Class II evidence of strong clinical certainty can be used to support a standard of care recommendation. More often, the recommendations resulting from evidence analysis result in practice management guidelines. Guidelines are typically based on a combination of Class II and Class III evidence. The weakest level of practice recommendations has been called "options." Options typically are based on Class III evidence and lack rigorous scientific support, but reflect current recommendations of recognized authorities. Authoritarian edicts have not disappeared; they have simply been reclassified to the lowest level of "evidence" (21,22,25).

The Cochrane Library, which represents the evidence database of the Cochrane Collaboration, includes the Cochrane Database of Systematic Reviews, which can be used to support "scientific surgery" decision making and practice recommendations. A Cochrane review evaluates, in structured format, the effects of various aspects of medical care on prevention, treatment, and rehabilitation of health care problems. The reviews are constructed to assist those involved in all levels of medical care in making informed decisions about the utilization and expenditure of health care resources. Typically, a review group and its related editorial team discuss possible review titles, following which the prospective review authors attend a protocol workshop and prepare a plan by which the review will be conducted. The review is then carried out with the editorial team providing the necessary statistical, methodological, and trial searching activities (26).

The methodology used in each review is clearly displayed to enable the reader to assess the validity of the review's conclusions. The search strategy, which may include searches of non-English articles and unpublished records, is fully described. The clinical studies included in the review are then evaluated according to preestablished criteria. If the database is large enough and sufficiently homogeneous, a meta-analysis may be used for statistical summary to improve the estimate of a clinical effect, as compared to the results of individual studies. Additionally, a meta-analysis permits evaluation of individual studies within the meta-analysis and assessment of the effects of intervention on specific subsets of patients. Generalizability of the review is enhanced by the involvement of multinational editorial teams, and the reviews are commonly updated on nearly an annual basis. New evidence is incorporated in those updates and criticisms, deficiencies, and errors are addressed and eliminated.

The format of a Cochrane review begins with a brief summary of the review in language for lay readers. Subsequent sections include a structured abstract that is typically posted on the MEDLINE medical database, background information, and a short statement of the objectives. Considerable attention is given to selection criteria in which the types of studies, participants, interventions, and outcome measures for endpoints are described. The search strategy utilized to identify relevant studies is detailed and may range from searches of electronic databases to hand searching of journals or conference proceedings. Review methodology

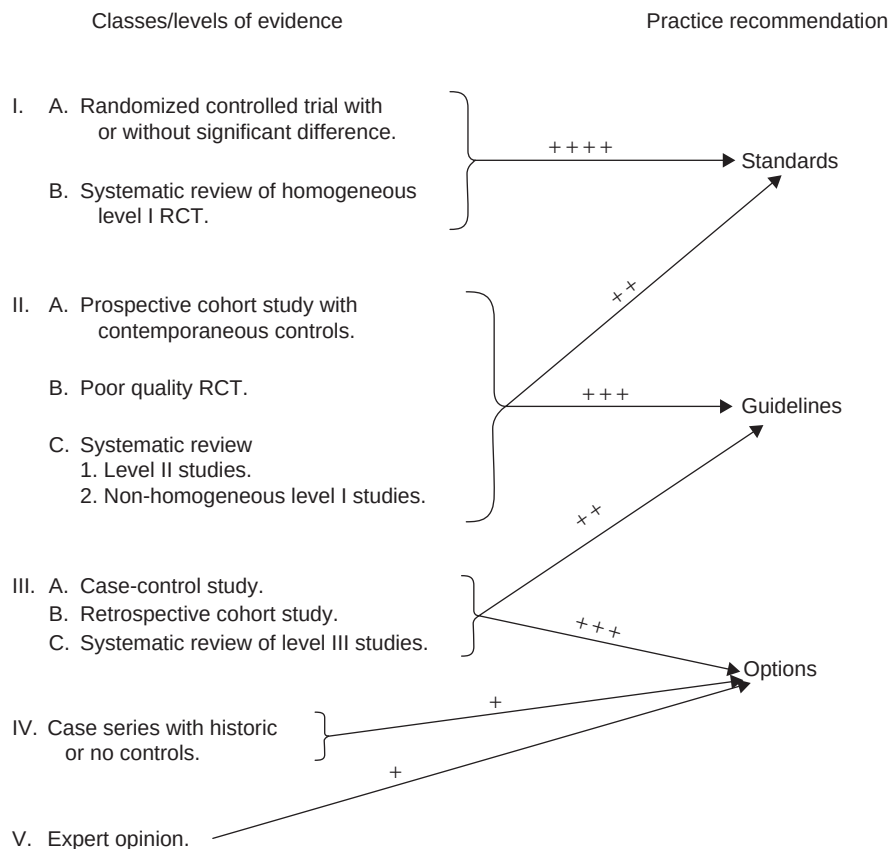


Figure Development of evidence-based scientific surgery recommendations. +–++++: relative strength of evidence. Source: Adapted from Refs. 20 and 21.

is described in terms of selection criteria, quality assessment, data extraction, data analysis, and inclusion of subgroups. This is followed by a section describing the number and size of the studies and an assessment of their methodological quality. The results are then presented in text and, if a meta-analysis was performed, in graphic form. Last, an interpretation and assessment of results is followed by the authors' conclusions in terms of practice application and research potential (27).

The quality of the Cochrane reviews is ensured by members of the editorial team and by selected external referees. Although the authoritarianism of individuals has been reduced by this approach to EBP, it has been replaced by authoritarianism of the members of review groups and editorial teams, members of which may be volunteers with self-assigned experts or superannuated authorities with dated expertise. Additionally, the clinical relevance of reviews is often limited. In the case of burn care, less than 1% of the Cochrane Database of Systematic Reviews, issue 3, 2005, had relevance to burn patient care and management (28). Greater involvement of clinical surgeons in the Cochrane Library has been recommended as a means of enhancing it as an evidence-based medical and surgical resource.

There are several intrinsic weaknesses in the sources of data that are typically analyzed to develop evidence-based medicine. First and foremost is the fact that even high-quality studies with negative outcomes are not likely to be published, whereas commercially funded studies,

particularly those originating in the United States, are more likely to be published (29). Concern has also been raised about the difficulty in assessing the quality of the trials selected for review in terms of inadequate study power to answer the question posed; inadequate concealment of patient selection, resulting in nonapparent patient selection bias; and missing data requiring exclusion of patients or imputation of data, which may compromise the strength of the study. The use of standardized mean differences for data extraction in meta-analyses has also been seriously questioned. Gøtzsche and colleagues found that a high proportion of such meta-analyses, 63%, had errors that could negate or even reverse the findings of the study (30). Those authors recommend caution in the evaluation of meta-analyses using the standardized mean difference for data transformation. Other limitations of meta-analyses consist of bias and confounding, which are often unrecognized and may be more prominent in larger studies in which sufficient details may be absent. The noted limitations speak for establishing uniformity of design, data collection, and analysis for all clinical trials entered into meta-analyses.

As a possible adjunct to evidence-based scientific surgery, Clarke and others have proposed the application of artificial intelligence to assist surgeons in developing an initial treatment plan for patients with major injury. A computerized decision tree based on expert trauma surgeons' extensive experience has been evaluated as a mechanism

to influence decisions of a surgeon at points where treatment decisions have to be made. Use of the decision tree increased the accuracy of surgeons dealing with simulated clinical problems and, as such, supports the usefulness of the annotated Critical Decisions in Trauma algorithms developed by the Western Trauma Association (17,18,31).

The goal and ultimate end result of scientific surgery is improved patient care and optimum patient outcomes achieved by informed surgeons practicing evidence-based scientific surgery. Historically, it has often been difficult to overcome dogmatic dictates and reach those goals with other than painfully slow velocity. Resistance to scientific surgery persists, perhaps not as overtly as manifested by the American Surgical Association members who refused to accept the germ theory of disease. Tatsioni and colleagues have recently emphasized the persistence of medical practice based on authoritarian claims from frequently cited observational studies in spite of well-published highly regarded evidence to the contrary produced by randomized trials (32). To counterbalance that resistance to change, the recent revision and updating of the Advanced Trauma Life Support Course by the American College of Surgeons' Committee on Trauma on the basis of evidence analysis exemplifies the power of EBP to maintain the currency and relevance of scientific surgery (33). The importance of constant evolution and rapid updating of practice guidelines when new data become available has recently been highlighted by the results of the Perioperative Ischemic Evaluation trial, which confirmed the ineffectiveness of the perioperative β -blocker therapy recommended by the American College of Cardiology and the American Heart Association (34).

The answer to the question posed in the title of this chapter, "why scientific surgery?" is twofold: Scientific surgery is cost-effective and optimizes outcomes as manifested by rapidity and certainty of diagnosis and by promoting efficient application of the existing knowledge base and technology to decrease hospital stay and reduce mortality. Evidence-based scientific surgical care using computerized clinical decision support has been reported to markedly decrease the cost per case for trauma patients and the average length of hospital stay at a Level I major urban trauma center (35). The fewer complications and lower mortality in patients undergoing colorectal surgery performed by diplomates of the American Board of Surgery further document the advantages of scientific surgery as practiced by board-certified surgeons (36).

The application of the information presented in this volume will guide the scientific surgeon in providing state-of-the-art care ranging from standards of care to practice guidelines to options, depending on the level of supporting evidence. More important, scientific surgery will optimize the application of medical resources and, most important, allow the surgeon to apply principles of scientific surgery to address the unique needs of individual patients.

REFERENCES

- Osler W. Books and Men in Aequanimitas: With Other Addresses to Medical Students Nurses and Practitioners of Medicine. New York: McGraw Hill, 1932.
- Haeger K. The Illustrated History of Surgery. London: Harold Starke, 1989.
- Graham H. Surgeons All. New York: Philosophical Library, 1957.
- Johnson PC. Guy de Chauliac and the *Grand Surgery*. SG & O 1989; 169: 172–6.
- Rutkow IM. Surgery: An Illustrative History. St. Louis, MO: Mosby, 1993.
- Pruitt BA Jr. Combat casualty care and surgical progress. Ann Surg 2006; 243: 715–29.
- Watt J. Some forgotten contributions of naval surgeons. JR Soc Med 1983; 78: 753–61.
- Rutkow IM. Bleeding in Blue and Gray: Civil War Surgery and the Evolution of American Medicine. New York: Random House, 2005.
- Ravitch MM. A Century of Surgery, vol. I. Philadelphia: Lippincott, 1981, pp. 22–33.
- Albin MS. The wounding, amputation and death of Thomas Jonathan "Stonewall" Jackson: some medical and historical insights. Bull Anesth History 2001; 19: 4–7.
- Pruitt BA Jr. The integration of clinical care and laboratory research. A model for medical progress. Arch Surg 1995; 130: 461–71.
- Flexner A. Medical Education in the United States and Canada, Bulletin 4. New York: New York Carnegie Foundation for the Advancement of Teaching, 1910.
- Lee FS, Cannon WB, Pearce RM. Medical research in its relations to medical schools. Proc Assoc Am Med Coll 1917; 27: 19–31.
- Pruitt BA Jr. Centennial changes in surgical care and research. Ann Surg 2000; 232: 287–301.
- Biophysical Society Legislative Update. eweiss@biophysics.org (accessed December 21, 2007).
- Diaz JJ Jr, Bokhari F, Mowery NT, et al. Guidelines for management of small bowel obstruction. J Trauma 2008; 64: 1651–64.
- Moore FA, Davis JW, Moore EE, et al. WTA critical decisions in trauma: management of adult blunt splenic trauma. J Trauma 2008; 65: 1007–11.
- Dais JW, Moore FA, McIntyre RC Jr, et al. WTA critical decisions in trauma: Management of pelvic fracture with hemodynamic instability. J Trauma 2008; 65: 1012–15.
- Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary. Circulation 2007; 116: 1971–96.
- Gray M. Evidence-based decision making for the wound care clinician: what is the process, where are the resources? Ostomy Wound Manage 2008(Suppl): 3–6.
- Fisher CG, Wood KB. Introduction to and techniques of evidence-based medicine. Spine 2007; 32: S66–72.
- Gibran NS. Practice guidelines for burn care, 2006. J Burn Care Res 2006; 27: 437–8.
- Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001; 134: 663–94.
- Wright DW, Kellermann AL, Hertzberg VS, et al. ProTECT: a randomized clinical trial of progesterone for acute traumatic brain injury. Ann Emerg Med 2007; 49: 391–402.
- Wright JG. Practical guide to assigning levels of evidence. J Bone Joint Surg Am 2007; 89: 1128–30.
- An introduction to Cochrane reviews and the Cochrane Library, in the Cochrane Collaboration. www.cochrane.org.
- What is a Cochrane review, in the Cochrane Collaboration. www.cochrane.org.
- Wasiak J, Cleland H. How relevant and useful is the Cochrane Library as a resource for evidence in burn care, practice, and management. J Burn Care Res 2006; 27: 386–93.
- Lynch JR, Cunningham MRA, Warme WJ, et al. Commercially funded and United States-based research is more likely

- to be published; good-quality studies with negative outcomes are not. *J Bone Joint Surg Am* 2007; 89: 1010–18.
30. Gøtzsche PC, Hróbjartsson A, Marić K, et al. Data extraction errors in meta-analyses that use standardized mean differences. *JAMA* 2007; 298: 430–7.
 31. Clarke JR. Decision making in surgical practice. *World J Surg* 1989; 13: 245–51.
 32. Tatsioni A, Bonitsis NG, Ioannidis JPA. Persistence of contradicted claims in the Literature. *JAMA* 2007; 298: 2517–26.
 33. Kortbeek JB, Al Turki SA, Ali J, et al. Advanced Trauma Life Support, 8th edition, the evidence for change. *J Trauma* 2008; 64: 1638–50.
 34. Messerli FH, Bangalore S. When guidelines need guidance. *Am J Med* 2008; 121: 742–3.
 35. Moore FA. Evidence-based medical information technology: the next generation. *J Trauma* 2007; 63: 1195–205.
 36. Holmboe ES, Lipner R, Greiner A. Assessing quality of care: Knowledge matters. *JAMA* 2008; 299: 338–40.

Basil A. Pruitt, Jr., MD

*Clinical Professor, Department of Surgery,
The University of Texas Health Science,
Center at San Antonio, San Antonio, Texas, USA*

Evidence for Injury Prevention Strategies: From Private Practice to Public Policy

Michelle A. Price and Cynthia L. Villarreal

Evidence-Based Injury Prevention Summary		
Question	Answer	Grade
What is the estimated number of lives saved by the implementation of primary safety belt laws in the United States?	Evidence supports the benefit of primary belt laws in reducing injuries and fatalities.	A
What evidence exists on the effectiveness of SBI for alcohol problems for reducing subsequent injury among emergency room patients?	Evidence supports SBI to reduce short-term recidivism, but additional research on long-term effects is needed.	A
What are the applications of preventive medicine to the control of domestic violence?	Screening programs increase victim identification; however, evidence on intervention effectiveness is limited.	B
What is the evidence for the effectiveness of clinician counseling regarding firearm safety?	Evaluation of gun safety programs in primary care settings have resulted in inconsistent outcomes.	B
What is the effectiveness of injury prevention counseling delivered by a health care provider in improving safety practices among pediatric patients?	There is sufficient evidence to suggest that injury prevention counseling improves safety practices among the pediatric population.	A

INTRODUCTION

Traumatic injury is a preventable disease. In the United States, unintentional and intentional injuries are the leading cause of death among persons under age 35 and the fourth leading cause of death among persons of all ages (1). The three leading mechanisms of major trauma are motor vehicle collisions, firearms, and falls. In 2000, the estimated annual injury-attributable medical expenditures cost totaled \$117 billion, representing approximately 10% of the total U.S. medical expenditures (2). These expenditures are similar to other leading public health concerns, such as obesity (9.1%) and smoking (6.5% to 14.4%). These estimates, however, do not represent the true economic burden on society because they do not include the lost life value due to premature mortality, loss of patient and caregiver time, insurance costs, property damage, litigation, and diminished quality of life.

The development of trauma systems from the prehospital arena to rehabilitation services has been effective in reducing morbidity and mortality from injury. Nevertheless, 50% of deaths still occur at the scene or within minutes of the event. Thus, the mission of trauma care must include injury prevention in addition to advances in resuscitation, definitive care, and rehabilitation. The American College of Surgeons has recognized the importance of injury prevention initiatives in reducing the injury death and disability rate (3). For this reason, an organized injury prevention

program is required for trauma center verification. Similarly, the American College of Surgeons Committee on Trauma has recently added a requirement for trauma centers to provide alcohol screening followed by a brief intervention for those testing positive for alcohol or those identified as having an alcohol problem. Injury prevention strategies in the health care system are provided on a continuum ranging from hospital-funded, community-based educational programs to anticipatory guidance in a primary care setting (prior to injury) and targeted interventions with injured patients with the goal of reducing the likelihood of future reinjury. Community education programs are usually conducted by trauma center outreach staff and include unintentional injury prevention (e.g., infant car seat installation training and home safety) and violence prevention programs (e.g., domestic violence and suicide prevention). The most effective programs are empirically based, conducted for a sufficient duration, and delivered in a culturally appropriate format to a cohesive target community (4).

In this chapter, we review the available literature concerning the prevention of unintentional and violent injury via public policy, emergency center and clinic base intervention. We focus on the most prevalent mechanism of unintentional injury (motor vehicle collisions and alcohol related injury) as well as violent injuries (e.g., domestic violence and handguns). Finally, we review the effectiveness of physician or health care provider injury prevention counseling in primary care settings.

WHAT IS THE ESTIMATED NUMBER OF LIVES SAVED BY THE IMPLEMENTATION OF PRIMARY SAFETY BELT LAWS IN THE UNITED STATES?

Motor vehicle traffic collisions are the leading cause of death among people ages 1–44 years in the United States (5). Studies indicate that motor vehicle collisions are the leading cause of traumatic brain injuries where in the brain is injured in 70% of all collisions and the spinal cord in 5% of all collisions (6,7). Unrestrained motor vehicle occupants account for 60% of the vehicle occupant deaths (8). Research has shown that safety belts are the single most effective means of reducing collision-related injury and mortality (9). The National Highway Traffic Safety Administration (12), suggests that lap/shoulder belts, when used properly, reduce the risk of fatal injury to front-seat passenger car occupants by 45% and the risk of moderate to critical injury by 50%. Furthermore, for light truck occupants, safety belts reduce the risk of total injury by 60% and moderate to critical injury by 65%.* Due to the fact that safety belts are very effective, laws have been established to encourage their use. Safety belt laws are divided into two categories: primary and secondary. A primary safety belt law allows a law enforcement officer to stop a vehicle and issue a citation when the officer observes an unbelted driver or passenger, whereas secondary laws allow officers to issue a ticket for not wearing a seat belt only when there is another citable traffic violation (10). Primary laws are more effective than secondary laws for increasing safety belt use and reducing traffic fatalities (11). In the United States, only 25 states have primary safety belt use laws (12). Over time, with the expansion of safety belt use laws to additional states, seat belt use rates have steadily increased, especially in the past decade in response to a national agenda to increase safety belt use.

Studies suggest that passing a primary law can increase safety belt use rates among nonusers by 40% (12). In 1994 the overall observed shoulder belt use rate was 58%, a decade later that number had risen to 80%, and in 2005 the national average was 82% (12). Among states with primary versus secondary safety belt use laws, the average safety belt use rate was about eight percentage points higher in those states who had primary enforcement laws: 83% versus 75% (10). In a study done by the Insurance Institute for Highway Safety (13), states that strengthened their laws from secondary enforcement to primary saw an estimated 7% decline in driver death rates. If the 28 states that still have secondary safety belt laws would have changed their safety belt law, more than 5,000 lives could have been saved since 1996 (13).

Recommendations: Educating patients and supporting community-based initiatives to increase safety belt use has great potential in the continuation of saving lives, preventing injuries, and reducing the economic costs associated with motor vehicle collisions. Passage and enforcement of primary safety belt use laws are the most effective strategy to increase use, which will decrease serious injuries and fatalities associated with motor vehicle collisions. Physicians and other health care providers should encourage patients to use safety belts as well as participate in the policy-making process in those states without primary safety belt laws. Trauma surgeons can play a particularly poignant role in advocating for the passage of these laws because they

can speak to state legislators and the media regarding their experiences with motor vehicle collision patients who were unrestrained. Recommendation grade: A.

WHAT EVIDENCE EXISTS ON THE EFFECTIVENESS OF SCREENING AND BRIEF INTERVENTION FOR ALCOHOL PROBLEMS FOR REDUCING SUBSEQUENT INJURY AMONG EMERGENCY ROOM PATIENTS?

In trauma systems today, nearly 50% of patients have positive blood alcohol concentrations (14). According to the Centers for Disease Control and Prevention, alcohol is the leading contributor to both intentional and unintentional injuries in the United States (5). Research has also shown that alcohol use contributes to patients having multiple traumatic injuries over time supporting the need to provide screening and brief intervention (SBI) to reduce the likelihood of subsequent trauma among patients (15). Yet until recently, relatively few trauma patients who were under the influence of alcohol were screened for alcohol abuse, referred for treatment, or even acknowledged as having alcohol in their system.

One of the greatest challenges to addressing alcohol problems is identifying patients who are in need of treatment. A promising technique for doing this is SBI. Hospital emergency rooms in many states use this technique to identify patients with problem drinking and addiction. In 2007, the American College of Surgeons (ACS) instituted the requirement that ACS-verified Level I trauma centers screen all trauma patients for high-risk alcohol use and provide intervention to patients with elevated blood alcohol levels (15). Research done by Babor and Kadden (16) suggests that trauma centers present a unique opportunity to implement screening and brief interventions. Gentilello and colleagues demonstrated that many patients with alcohol problems are more likely to receive health care from a trauma surgeon than from a primary care practitioner (18). Furthermore, a study conducted by Schermer and colleagues (17) reveals that 83% of trauma surgeons believe that a trauma center is an appropriate place to provide alcohol interventions.

The purpose of SBI in trauma settings is to prevent substance abuse–related disabilities in persons at risk or prevent further harm among those in the early stage of substance abuse (16). SBI can be accomplished using a variety of tools that assist clinicians in asking about alcohol use, assessing the problem severity, advising the patient to decrease alcohol use, and monitoring progress. Two widely used brief instruments are the AUDIT and the CAGE. The AUDIT helps identify excessive drinking as the cause of the presenting illness and provides a framework for intervention to help risky drinkers reduce alcohol use (therefore avoiding dangerous consequences) (19). The AUDIT is also used to identify alcohol dependence and some specific consequences of harmful drinking. The CAGE instrument has been shown to be both sensitive and specific for identifying persons who meet criteria for alcohol abuse and dependence (20). The CAGE is a very short and simple screening instrument that asks about attempting to cut down on alcohol, being annoyed by others criticizing you about your drinking, feeling guilty about drinking, and having an eye-opener (an alcoholic beverage) in the morning.

Brief interventions for risky drinking and alcohol abuse are strongly supported by evidence in terms of their feasibility and effectiveness in medical settings, including primary health care (21). SBI is not only effective in reducing subsequent injuries but reduces alcohol-related costs to health care facilities. Brief alcohol counseling sessions have reduced recidivism by 50% and have significantly reduced both binge drinking episodes and drinks consumed per week (22,23). Four studies have shown that SBI among trauma patients significantly reduces self-reported drinking, injuries, and other alcohol dependence symptoms (24–27). Monti et al. found that a single intervention session in the emergency department (versus standard treatment) reduced alcohol-related injuries 50% (versus 21%) (25). Studies done by Longabaugh et al. and Hungerford et al. concluded that SBI done in the emergency department significantly reduced alcohol-related negative consequences for up to one year (26,27). Gentilello found that a single 40-minute session reduced weekly drinking by 22 drinks compared to 7 drinks among the control group, with a 47% reduction in hospital readmission among study participants (24).

Furthermore, cost benefit analysis research conducted by Gentilello and colleagues showed that SBI conducted in trauma centers could save hospitals \$1.82 billion a year and that for every dollar spent on screening and intervention, \$3.81 in health care costs were saved (23). The Substance Abuse and Mental Health Services Administration indicates that trauma centers are in an ideal position to take advantage of the teachable moment generated from an injury by implementing SBI for at-risk and dependent drinkers (14). Although data show that screening injured patients for the presence of an alcohol problem reduces subsequent alcohol use, hospital readmissions, and related consequences, many trauma centers do not provide the service (23). With successful implementation of injury prevention strategies such as SBI, the overall public health approach available in trauma hospital settings will make great strides in improving prevention services among this vulnerable population.

Recommendations: Trauma surgeons, emergency department physicians, and other health care providers are key personnel who can detect alcohol problems using existing screening tools that are easy to administer, reliable, and effective in reducing repeat trauma. Screening tools and physician guides are available on the American College of Surgeons Web site (28) and the National Institute of Alcohol Abuse and Alcoholism (29). Recommendation grade: A.

WHAT ARE THE APPLICATIONS OF PREVENTIVE MEDICINE TO THE CONTROL OF DOMESTIC VIOLENCE?

Violence prevention encompasses a wide spectrum of interpersonal violence (i.e., child maltreatment, intimate partner violence, sexual violence, and elder abuse) and self-directed violence (i.e., self-harm and suicide). Much of the research on evidenced-based prevention practices in health care settings has focused on domestic or intimate partner violence (IPV). Annually in the United States, women experience approximately 4.8 million IPV assaults or rapes and men experience about 2.9 million IPV assaults (30). In a study of the prevalence of domestic violence victimization among women attending general practice, Richardson and

colleagues found that 41% had experienced IPV and 17% had experienced it within the last year (31).

Health care services play a central role in the care of IPV victims, however, the effectiveness of health care professionals' responses has been a focus of concern since the 1970s (32). Nelson et al. systematically reviewed the evidence for screening women and the elderly for IPV and found that despite the extensive literature, few studies provide data on detection and management to guide clinicians (33). Ramsey et al. conducted a systematic review of the effectiveness of health professional screening and intervention for IPV among women presenting in emergency departments, primary care facilities, or antenatal clinics (34). Eight of the nine screening studies meeting inclusion criteria found higher rates of IPV identification at the sites using screening tools (35–42). In those studies reporting relative risk, the likelihood of positive identification after the introduction of a screening protocol ranged from 1.49 (1.08–1.97) (35) to 6.78 (2.35–19.56) (42). This concurs with an earlier systematic review conducted by Waalen et al. (43). However, the one randomized controlled trial did not find evidence of increased identification rates related to the introduction of screening procedures (44). The authors also reviewed six studies (nine papers) (35,38,39,42,45–49) meeting inclusion criteria for evaluating the effectiveness of IPV interventions in health care settings and found no relation between type of intervention or setting and the effect of the intervention (34). Only two of the studies reviewed measured rates of domestic violence as an outcome measure (46,49) with the more robust study detecting a reduction in physical and nonphysical abuse following counseling and advocacy support intervention (49).

Recommendation: IPV screening programs moderately increase rates of victim identification in health care settings; however, there is limited evidence of effectiveness of associated interventions. Therefore, it would be premature to recommend implementation of a universal screening program. Further research using randomized clinical trials is required to better quantify the effectiveness of IPV prevention strategies in health care settings. Health care professionals should, however, receive training on selectively screening for IPV for patients who meet specific criteria with well-validated, brief screening tools such as the Hurt, Insulted, Threatened, or Screamed at instrument (50) or the Partner Violence Screen (51). Recommendation grade: B.

WHAT IS THE EVIDENCE FOR THE EFFECTIVENESS OF CLINICIAN COUNSELING REGARDING FIREARM SAFETY?

In the United States during 1979–2004, firearm injury was the second leading cause of injury death (behind motor vehicle traffic deaths) (52). During that period, the firearm death rate declined 3%. In 2004, there were 29,569 firearm deaths in the United States (or 10.0 deaths per 100,000 population). Since the mid-1980s, organized medicine has crafted policies and programs to reduce firearm morbidity and mortality (53). Longjohn and Christoffel found five policy consensus areas among 14 national medical societies: access prevention, gun commerce, research, public education, and clinical counseling (54).

The American Academy of Pediatrics recommends violence prevention anticipatory guidance at every health maintenance visit, including urging gun removal from homes (55). The evidence on the effectiveness of patient counseling regarding gun removal or safer storage behaviors has been equivocal (56). In a investigation of gun safety counseling coupled with a gun lock giveaway in a pediatric outpatient setting, Carbone et al., (57) found significant improvements in safe gun storage behaviors among families in the intervention group (62%) versus the control group (27%). In a similar study conducted in a family practice clinic, Albright and Burge (58) found improved storage behaviors among gun-owning patients who received either verbal counseling alone (64%) or verbal counseling plus a gun safety brochure (58%) compared to controls (33%). Conversely, two earlier studies that used the Steps to Prevent Firearm Injury (STOP) did not find significant effects. Oatis et al. (59) did not find statistically significant declines in gun ownership or improvement in storage practices among participants who received safety counseling and written materials during a well-child visit at a pediatric practice. Similarly, Grossman and colleagues (60) found that the gun safety counseling intervention did not lead to changes in gun ownership or significant changes in storage practices.

Recommendation: Research on the effectiveness of physician counseling regarding gun removal and safe storage has been limited with mixed results. Further study is warranted (61). Recommendation Grade: B.

WHAT IS THE EFFECTIVENESS OF INJURY PREVENTION COUNSELING DELIVERED BY A HEALTH CARE PROVIDER IN IMPROVING SAFETY PRACTICES AMONG PEDIATRIC PATIENTS?

Injury is the leading cause of death and a substantial cause of disability for children and adolescents (62). Given the pervasive and preventable nature of these injuries, prevention counseling or anticipatory guidance should be integrated into physician visits and other health care settings to educate parents, caretakers, and children about age-appropriate behavioral risks and safety strategies. Over the last decade, however, the proportion of children receiving injury prevention counseling was relatively unchanged from 40% in 1994 to 42.4% in 2003 (63).

There is sufficient evidence that clinical counseling can influence child safety seat use and use of a functioning smoke alarm in the home (64–66). A review of the literature on childhood injury prevention counseling in primary care settings illustrated that the majority of studies (18 out of 20) demonstrated positive outcomes in increasing overall knowledge and safety practices along with decreasing childhood

injury rates (66). Furthermore, a systematic review of more than 20 randomized controlled trials of a variety of injury prevention interventions in clinical settings suggested a strong improvement in safety practices, which included child safety seat and safety belt restraint use (64).

Injury prevention counseling has been successfully implemented in the pediatric population (64,67,68). Research shows that parents and children are often receptive to injury-prevention counseling during a sick visit, especially if it is related to an injury, a recent emergency department visit, or injury to a sibling (69). Due to the fact that pediatricians come into contact with parents a great deal in the first five years of a child's life for routine care, the American Academy of Pediatrics and Bright Futures recommend that clinicians use this opportunity to provide injury prevention counseling (70,71). The Injury Prevention Program, developed in 1983 by the American Academy of Pediatrics, includes a safety counseling schedule, age-appropriate safety sheets for families, and interventions that have been proven to effectively improve safety practices among parents and caregivers (66,67,72).

Recommendations: Physicians and health care providers should use routine doctor visits, emergency department visits, and other health care visits as teachable moments to educate the patient and parents on age-appropriate injury prevention. Recommendation grade: A.

CONCLUSIONS

Physicians in office-based practices, hospital outpatient/follow-up clinics, and emergency departments all have a unique opportunity to educate patients on injury prevention. Major influences in physicians' decisions to incorporate injury prevention counseling into routine care include confidence in the ability to counsel, perceptions regarding counseling effectiveness, training, practice setting, and office time constraints (63,73–77). Injury prevention counseling does not have to be time consuming and extensive, but substantive enough to increase knowledge. Effective prevention programs can include physician or nurse counseling, the use of computerized educational materials, public service announcements, and educational videos in waiting areas (78,79). Due to the fact that physicians and health care providers have time constraints, the most efficient strategy is to educate patients or caregivers on specific topics that are appropriate for the patient's age, time of year, and other common injuries seen in that population (67,80,81). Physicians can also play an active role in advocating for prevention programs and policies and working with community stakeholders and policy makers with a vested interest in reducing injuries and saving lives.

Summary of Evidence-Based Injury Prevention Studies

Author	Ref.	Year	Evidence level	Groups	Design	Follow-up	Endpoint
Dunn et al.	22	2003	II	Trauma patients (no control group)	CS	6 and 12 months	Hazardous drinking patterns
Whitlock et al.	21	2004	II	Varied	SR	Varied	Varied
Gentilello et al.	23	2005	II	Injured patients, 18 years or older, positive blood alcohol content	PCS	None	None
Monti et al.	25	1999	I	Motivation interview versus standard care	RCT	3 and 6 months	Alcohol interventions, harm reduction
Longabaugh et al.	26	2001	I	Brief intervention versus brief intervention with booster session versus standard care	RCT	12 months	Ongoing intervention, decrease alcohol recidivism
Hungerford et al.	27	2003	II	Convenience sample of alcohol positive patients	PCS	4 months	Increased feasibility of alcohol screening and counseling
Nelson et al.	33	2004	II	Varied	SR	Varied	Varied
Ramsey et al.	34	2002	II	Varied	SR	Varied	Varied
Carbone et al.	57	2005	II	Gun safety counseling session, STOP 2 brochure plus a gun lock versus anticipatory guidance	PCS	1 month	Gun ownership, gun storage practices
Albright & Burge	58	2003	I	Verbal counseling alone versus counseling plus a gun safety brochure versus no counseling	RCT	60–90 days	Gun ownership, gun storage practices
Otis et al.	59	1999	IV	STOP gun safety counseling plus brochure (no control group)	CS	≥1 year	Gun ownership, gun storage practices
Grossman et al.	60	2000	I	Gun safety counseling with STOP brochure plus gun lock coupon versus standard care	RCT	3 months	Gun ownership, gun storage practices
DiGuseppi et al.	64	2000	I	Varied	SR	Varied	Varied
DiGuseppi et al.	65	2001	I	Varied	SR	Varied	Varied
Bass et al.	66	1993	II	Varied	SR	Varied	Varied

Abbreviations: CS, case study; RCT, randomized controlled trial; PCS, prospective cohort study; RCS, retrospective cohort study; SR, systematic review; NR, not reported.

REFERENCES

- Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). U.S. Department of Health and Human Services, National Center for Injury Prevention and Control, 2002.
- Department of Health and Human Services. Medical expenditures attributable to injuries—United States, 2000. *Morbidity and Mortality Weekly Report* 2004.
- American College of Surgeons Committee on Trauma. Resources for Optimal Care of the Injured Patient. 2006.
- Nilsen P. What makes community based injury prevention work? In search of evidence of effectiveness. *Injury Prev* 2004; 10: 268–74.
- Centers for Disease Control and Prevention, Web-based Injury Statistics Query and Reporting System (WISQARS). U.S. Department of Health and Human Services, National Center for Injury Prevention and Control, 2007.
- Ruff RM, Marshall LF, Klauber MR, et al. Alcohol abuse and neurological outcome of the severely head injured. *J Head Trauma Rehab* 1990; 5: 21–31.
- Kreutzer JS, Doherty R, Harris JA, et al. Alcohol abuse among persons with traumatic brain injury. *J Head Trauma Rehab* 1990; 5: 9–20.
- National Transportation Safety Board. Safety Report: Actions to Reduce Fatalities, Injuries, and Crashes. Washington, DC: 2007.
- Centers for Disease Control and Prevention. Impact of primary laws on adult use of safety belts—United States 2002. *Morbidity and Mortality Weekly Report* 2004; 257–60.
- National Highway Traffic Safety Administration. Traffic Safety Facts: Strengthening Safety Belt Use Laws—Increase Belt Use, Decrease Crash Fatalities and Injuries. Washington, DC: U.S. Department of Transportation, 2004.
- Schultz RA, Elder RW, Sleet DA, Thompson RS. Primary enforcement seat belt laws are effective even in the face of rising belt use rates. *Accid Anal Prev* 2004; 36: 491–3.
- National Highway Traffic Safety Administration. Traffic Safety Facts: Estimated Minimum Savings to a State's Medicaid Budget by Implementing a Primary Seat Belt Law. Washington, DC: U.S. Department of Transportation, 2007.
- Insurance Institute for Highway Safety. Effectiveness of Primary Belt Laws. Arlington, VA: 2005.
- Substance Abuse and Mental Health Services Administration. Results from the 2005 National Survey on Drug Use and Health: National Findings, in Series H-30. 2006.
- American College of Surgeons Committee on Trauma. Alcohol screening and brief intervention for trauma patients. 2007.
- Babor TF, Kadden RM. Screening and interventions for alcohol and drug problems in medical settings: What works? *J Trauma Inj Inf Crit Care* 2005; 59: S80–S87.
- Schermer CR, Gentilello LM, Hoyt DB. National survey of trauma surgeons' use of alcohol screening and brief intervention. *J Trauma Inj Inf Crit Care* 2003; 55: 849–56.
- Gentilello LM, Rivara FP, Donovan DM. Alcohol problems in women admitted to a Level I trauma center. *J Trauma Inj Inf Crit Care* 2000; 48: 108–14.
- Saunders JB, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification test (AUDIT): WHO collaborative project on early detection of persons

- with harmful alcohol consumption—II. *Addiction* 1993; 88: 791–804.
20. Ewing JA. Detecting alcohol: The CAGE questionnaire. *JAMA* 1984; 252: 1905–07.
21. Whitlock EP, Polen MR, Green CA. Behavioral counseling interventions in primary care to reduce risky/harmful alcohol use by adults: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 2004; 140: 557–68.
22. Dunn CW, Zatzick DF, Russo J. Hazardous drinking by trauma patients during the year after injury. *J Trauma Inj Inf Crit Care* 2003; 54: 707–12.
23. Gentilello LM, Ebel BE, Wickizer TM, et al. Alcohol interventions for trauma patients treated in emergency departments and hospitals: A cost benefit analysis. *Ann Surg* 2005; 241: 541–50.
24. Gentilello LM, Rivara FP, Donovan DM. Alcohol interventions in a trauma center as means of reducing the risk of injury recurrence. *Ann Surg* 1999; 230: 473–83.
25. Monti PM, Colby SM, Barnett NP. Brief intervention for harm reduction with alcohol positive older adolescents in a hospital emergency department. *J Consult Clin Psychol* 1999; 67: 989–94.
26. Longabaugh R, Woolard RF, Nirenbert TD. Evaluating the effects of a brief motivational intervention for injured drinkers in the emergency department. *J Stud Alcohol* 2001; 62: 806–16.
27. Hungerford DW, Williams JM, Furbee PM. Feasibility of screening and intervention for alcohol problems among young adults. *Am J Emerg Med* 2003; 21: 14–22.
28. American College of Surgeons Web site. www.facs.org/trauma/publications/sbirtguide.pdf
29. National Institute of Alcohol Abuse and Alcoholism Web site. pubs.niaaa.nih.gov/publications/aa65/AA65.htm
30. Tjaden P, Thoennes N. Extent, Nature, and Consequences of Intimate Partner Violence: Findings from the National Violence Against Women Survey. Washington, DC: Department of Justice, 2000.
31. Richardson J, Coid J, Petruckevitch A, et al. Identifying domestic violence: cross sectional study in primary care. *Brit Med J* 2002; 324: 274.
32. Stark E, Flitcraft A. *Women at Risk: Domestic Violence and Women's Health*. London: Sage, 1996.
33. Nelson HD, Nygren P, McInerney Y, et al. Screening women and elderly adults for family and intimate partner violence: a review of the evidence for the U.S. preventive services task force. *Ann Intern Med* 2004; 140: 387–404.
34. Ramsay J, Richardson J, Carter YH, et al. Should health professionals screen women for domestic violence? Systematic review. *Brit Med J* 2002; 325: 314.
35. Harwell TS, Casten RJ, Armstrong KA, et al. Results of a domestic violence training program offered to the staff of urban community health centers. *Am J Prevent Med* 1998; 15: 235–42.
36. Olson L, Anctil C, Fullerton L, et al. Increasing emergency physician recognition of domestic violence. *Ann Emerg Med* 1996; 27: 741–6.
37. Roberts GL, Lawrence JM, O'Toole BI, et al. Domestic violence in the emergency department. *Gen Hosp Psych* 1997; 19: 12–15.
38. Fanslow JL, Norton RN, Robinson EM, et al. Outcome evaluation of an emergency department protocol of care on partner abuse. *Aust N Z J Pub Health* 1998; 22: 598–603.
39. Fanslow JL, Norton RN, Robinson EM. One year follow-up of an emergency department protocol for abused women. *Aust N Z J Pub Health* 1999; 23: 418–20.
40. Morrison LJ, Allan R, Grunfeld A. Improving the emergency department detection rate of domestic violence using direct questioning. *J Emerg Med* 2000; 19: 117–24.
41. Covington DL, Diehl SJ, Wright BD, et al. Assessing for violence during pregnancy using a systematic approach. *Mat Child Health J* 1997; 1: 129–33.
42. Wiist WH, McFarlane J. The effectiveness of an abuse assessment protocol in public health prenatal clinics. *Am J Pub Health* 1999; 89: 1217–21.
43. Waalen J, Goodwin MM, Spitz AM, et al. Screening for intimate partner violence by health care providers: barriers and interventions. *Am J Prevent Med* 2000; 19: 230–7.
44. Thompson RS, Rivaro FP, Thompson DC, et al. Identification and management of domestic violence: a randomized clinical trial. *Am J Prevent Med* 2000; 19: 253–63.
45. Shepard MF, Elliott BA, Falk DR, et al. Public health nurses' responses to domestic violence: a report from the Enhanced Domestic Abuse Intervention Project. *Pub Health Nurs* 1999; 16: 359–66.
46. Muellerman RL, Feighny KM. Effects of an emergency department-based advocacy program for battered women on community resource utilization. *Ann Emerg Med* 1999; 33: 62–6.
47. McFarlane J, Soeken K, Reel S, et al. Resource use by abused women following an intervention program: associated severity of abuse and reports of abuse ending. *Pub Health Nurs* 1997; 14: 244–50.
48. McFarlane J, Parker B, Soeken K, et al. Safety behaviors of abused women after an intervention during pregnancy. *J Obstet Gyn Neonat Nurs* 1998; 27: 64–9.
49. Parker B, McFarlane J, Soeken K, et al. Testing an intervention to prevent further abuse to pregnant women. *Res Nurs Health* 1999; 22: 59–66.
50. Sherin KM, Sinacore JM, Li XQ, et al. HITS: a short domestic violence screening tool for use in a family practice setting. *Fam Med* 1998; 30: 508–12.
51. Feldhaus KM, Kosiol-McLain J, Amsbury HL, et al. Accuracy of 3 brief screening questions for detecting partner violence in the emergency department. *JAMA* 1997; 277: 1357–61.
52. Centers for Disease Control and Prevention. QuickStats: Age-adjusted death rates for leading causes of injury deaths, by year—United States, 1979–2004. *Morbidity Mortal Weekly Rep* 2006.
53. U.S. Department of Health and Human Services, Bureau of Maternal and Child Health and Resources Development, and Office of Maternal and Child Health. Surgeon General's Workshop on Violence and Public Health. Rockville, MD: U.S. Department of Health and Human Services, 1986.
54. Longjohn MM, Christoffel KK. Are medical societies developing a standard for gun injury prevention? *Inj Prev* 2004; 10: 169–73.
55. American Academy of Pediatrics, Committee of Practice and Ambulatory Medicine. Recommendations for preventive pediatric health care. *Pediatrics* 2000; 105: 645–6.
56. Dowd MD. Firearm injury prevention: Reasons for optimism. *Arch Pediatr Adolesc Med* 2005; 159: 1081–2.
57. Carbone PS, Clemens CJ, Ball TM. Effectiveness of gun-safety counseling and a gun lock giveaway in a Hispanic community. *Arch Pediatr Adolesc Med* 2005; 159: 1049–54.
58. Albert WG, Simpson RI. Evaluating an educational program for the prevention of impaired driving among grade 11 students. *J Drug Ed* 1985; 15: 57–71.
59. Oatis PJ, Buderer NMF, Cummings P, et al. Pediatric practice based evaluation of the Steps to Prevent Firearm Injury program. *Inj Prev* 1999; 5: 48–52.
60. Grossman DC, Cummings P, Koepsell TD, et al. Firearm safety counseling in primary care pediatrics: a randomized, controlled trial. *Pediatrics* 2000; 106: 22–6.
61. Albright T, Burge SK. Improving firearm storage habits: impact of brief office counseling by family physicians. *J Am Board Fam Pract* 2003; 16: 40–6.
62. Pressley JC, Barlow BA. Preventing injury and injury-related disability in children and adolescents. *Semin Pediatr Surg*, 2004; 13: 133–40.
63. Chen J, Kresnow M, Simon TR, et al. Injury-prevention counseling and behavior among US children: results from the

- second injury control and risk survey. *Pediatrics* 2007; 119: 958–65.
64. DiGiuseppi C, Roberts IG. Individual-level injury prevention strategies in the clinical setting. *Future Child* 2000; 10: 53–82.
 65. DiGiuseppi C, Higgins JP. Intervention for promoting smoke alarm ownership and function. *Cochrane Database Systematic Review* 2001(2).
 66. Bass JL, Christoffel KK, Widome M, et al. Childhood injury prevention counseling in primary care settings: a critical review of the literature. *Pediatrics* 1993; 92: 544–50.
 67. Gardner HG. Office-based counseling for unintentional injury prevention. *Pediatrics* 2007; 119: 202–6.
 68. Miller TR, Galbraith M. Injury prevention counseling by pediatricians. *Pediatrics* 1995; 96: 1–4.
 69. Gielen AC, Wilson MEH, McDonald EM, et al. Randomized trial of enhanced anticipatory guidance for injury prevention. *Arch Pediatr Adolesc Med* 2001; 155: 42–9.
 70. Green M, ed. *Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents*. Arlington, VA: National Center for Education in Maternal and Child Health, 1994.
 71. Committee on Practice and Ambulatory Management. Recommendation for preventive health care. *Pediatrics* 1995; 96: 373.
 72. Barkin S, Fink A, Gelber L. Predicting clinician injury prevention counseling for young children. *Arch Pediatr Adolesc Med* 1999; 153: 1226–31.
 73. Cheng TL, DeWitt TG, Savageau JA, et al. Determinants of counseling in primary care pediatric practice. *Arch Pediatr Adolesc Med*, 1999; 153: 629–35.
 74. Cohen LR, Runyan CW. Barriers to pediatric injury prevention counseling. *Inj Prev* 1999; 5: 36–40.
 75. Ewing GB, Selassie AW, Lopez CH, et al. Self-report of delivery of clinical preventive services by U.S. physicians, comparing specialty, gender, age, setting of practice, and area of practice. *Am J Prev Med* 1999; 17: 62–72.
 76. Becher EC, Cassel CK, Nelson EA. Physician firearm ownership as a predictor of firearm injury prevention practice. *Am J Public Health*, 2000; 90: 1626–8.
 77. Wright MS. Pediatric injury prevention. *Arch Pediatr Adolesc Med*, 1997; 151: 1039–43.
 78. Lin SX, Hyman D, Larson E. Provision of health counseling in office-based practices and hospital outpatient clinics. *Prev Med* 2005; 40: 542–6.
 79. Kottke TE, Edwards BS, Hagen PT. Counseling: implementing our knowledge in a hurried and complex world. *Am J Prev Med* 1999; 17: 295–8.
 80. Berman BA, Yancey AR, Bastani R. African-American physicians and smoking cessation counseling. *J Natl Med Assoc* 1997; 89: 534–42.
 81. Webster DW, Wilson ME, Duggan AK, et al. Firearm injury prevention counseling: a study of pediatricians' beliefs and practices. *Pediatrics* 1992; 89: 902–7.

Trauma Systems

S. Morad Hameed and Richard K. Simons

Summary of Evidence on Aspects of Trauma Systems and Corresponding Recommendations			
Question	Statement	Evidence	Recommendation
Can surgeons play an important role in public health?	Surgeons have a important role in public health	IIa	B
Can trauma systems prevent injury?	Trauma systems prevent injury recidivism associated with alcohol abuse	Ib	A
	Trauma system implementation has been associated with reductions in mortality from motor vehicle crashes	IIc	B
	Trauma systems should play a more active role in injury prevention	IIc	B
Once a severe injury occurs, how long do we have?	Prompt intervention after major trauma is a first principle of trauma systems	V	D
Prehospital care: Scoop and run or stay and play?	Prehospital intubation in traumatic brain injury should be selective and attempted with care when necessary	IIb	B
	Prehospital fluid resuscitation should be limited in patients with penetrating mechanisms in urban environments	1b	B
	Scene time and interventions in trauma should be minimized if possible until more is known about the effects of specific interventions	IIa	B
	Local analyses should be done to determine trauma center catchments that may be more rapidly served by air medical transport	IIb	B
	Trauma systems must be made more accessible in rural environments, where injury severity adjusted mortality is high	IIc	B
Are trauma centers accessible?	Trauma systems increase survival	IIc	B
Do trauma systems save lives?	Specific structural and process factors influence trauma system performance	IIb	—
What features of trauma systems make a difference?	Trauma center volume influences outcome	IIc	B
	Trauma center designation influences outcome	IIc	B
	Further optimization or trauma system performance will depend on the collection and analysis of data on injury-related disability	V	D
What are the long-term outcomes of trauma systems?	A systematic approach to trauma care improves survival	IIa	B
Can trauma systems help build safer societies, and at what cost?	Inclusive trauma systems improve survival	IIc	B
	Inclusive trauma systems may improve survival in mass casualty and multicaseualty situations	Needed	
	Trauma systems are cost-effective	IIb	B
	Trauma systems have the potential to reduce morbidity and mortality in low-income settings	Needed	

There are few problems in surgery, or in health care in general, that are more pressing than trauma. Each year, more than 100 million people are injured worldwide, and more than 5 million people die as a result of injury. The epidemic is global, with low- and middle-income countries shouldering 90% of the burden of injury (1). In the United States, trauma is the fourth leading cause of death; because of its heavy impact among the young, it results in the loss of more years of life than the three other leading causes of death (heart disease, stroke, cancer) combined. When non-fatal injuries are accounted for, injury results in the loss of 5.1 million years of productive life annually. Americans spend over \$150 billion in direct costs each year on the

consequences of trauma (1). The emotional and social costs to patients and families, though difficult to quantify, are also staggering.

In 1966, while considering the impact of injury on society, the U.S. National Academy of Sciences and the National Research council observed that “public apathy to the mounting toll from accidents must be transformed into an action program under strong leadership” (2). Its recommendations for a national strategy for injury control, which included mobilization of public awareness and wide and formal collaboration on injury prevention, emergency medical care, and trauma research, transformed fatalistic attitudes about trauma into the perception of trauma as

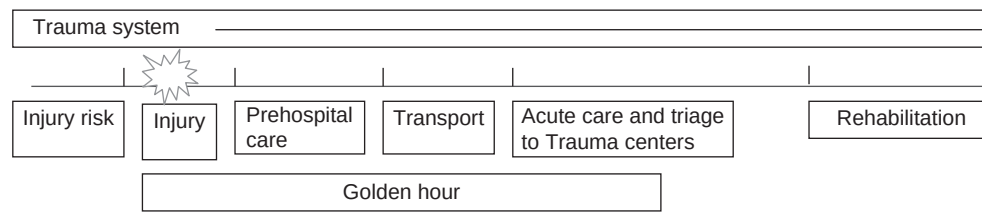


Figure 2.1 Structure of trauma systems.

Trauma systems represent society's most complete and multimodal response to injury, from prevention to prompt and effective acute care to rehabilitation and reintegration into society.

a public health problem with achievable solutions and ushered trauma care into the modern era. But trauma is a complex epidemic to confront. Risk is highly influenced by the interplay of social, economic, environmental, and even geographic factors, and outcome is highly influenced by our ability to rapidly interrupt shock and its downstream consequences and restore cognitive and musculoskeletal integrity and function. To be effective, injury control must begin even before the moment of impact, be prepared to efficiently integrate and apply multidisciplinary knowledge to acute care, and end only when risk is eliminated and patients return to their places in society.

In the decades since 1966, surgeons have taken the lead in the development of trauma systems (Fig. 2.1), which can be thought of as a comprehensive public health response to injury and that have been described as “an astounding achievement of modern health care” (3). During this time, mortality from unintentional injury in the United States has fallen from 55 per 100,000 population in 1965, to 37.7 per 100,000 in 2004 (4) as innovative injury prevention strategies have been broadly implemented and access to sophisticated trauma care within an hour of injury has been provided to 84.1% of all Americans (5). Trauma systems have been built out of necessity, often without the luxury of high-level evidence, but their rapid evolution has been guided by the careful analysis of available data. This chapter summarizes some of the best recent evidence on the impact of trauma systems on prevention and trauma care, outlines areas where more data are required, and briefly describes the exciting threshold to which trauma system development has brought us.

A PUBLIC HEALTH APPROACH

Can Surgeons Play an Important Role in Public Health?

It can be argued that the American College of Surgeons (ACS) was decades ahead of the National Academy of Science/National Research Council in recognizing injury as a priority for advocacy and action. In 1922, it established the Committee on Trauma (ACS-COT) to provide surgical leadership in trauma care. Later, as ACS members returned home from wars in Korea and Vietnam “with their organizational and technical skills honed in combat and the College advocating reform and improvements of standards

at home (surgeons), gained a pre-eminent role in the care of injured patients” (6). Since its publication in 1976, the ACS-COT *Resources for Optimal Care of the Injured Patient* (7) has set the standards for trauma care, and each new edition has been broader in scope and more influential than the last. Increasingly, governments are using the criteria described in this document to guide designation of trauma centers and regionalization of injury control efforts.

The ACS-COT considers injury control to be most effectively accomplished in a public health framework that includes approaches to prevention, optimization of access to acute care, acute care itself, rehabilitation, and research. In each of these areas, the ACS-COT promotes pursuit of the three core functions of public health: ongoing *assessment* of injury data and the epidemiology of injury, evidence-based *policy development*, and ongoing *assurance* of efficacy of processes. From this perspective, a trauma system can be defined an integrated set of health care resources devoted to taking a comprehensive approach to injury control.

Even a brief perusal of the ACS-COT *Resources* manual or the current trauma literature makes it clear that surgeons have played a major role in the development of every aspect of the public health model of trauma systems. Advances in the assessment, policy development, and assurance aspects of injury prevention, prehospital care, acute care, and rehabilitation have been driven by the systematic collection and analysis of injury data in ACS-COT-mandated trauma registries. As frontline providers of clinical care, surgeons have ready access to and a profound understanding of injury data, and will therefore always have a substantial role in the interpretation of these data to policy makers, the design and advocacy of injury control strategies, and the ultimate development of injury control policy. Surgeons have an important role in public health.

Recommendation grade: B.

INJURY PREVENTION

Can Trauma Systems Prevent Injury?

In a classic study of injury mortality, traumatic deaths were found to occur in a trimodal distribution, with 45% of deaths occurring within one hour of injury, 34% of deaths occurring within one to four hours, and 20% of deaths after a week (8). Although a more recent study, also nicely done, showed a less prominent late mortality peak (with

only 7.6% of deaths occurring beyond one week), a phenomenon attributed to the increasing maturity of trauma systems (9), these mortality studies are both remarkably illustrative of the importance of a systems approach to injury control. Deaths occurring within one hour of trauma often occur at the scene and are mostly attributable to catastrophic, nonsurvivable head or cardiovascular injuries. This first mortality peak is thought to be more amenable to injury prevention strategies than to advances in acute or rehabilitative care. The magnitude of this peak is so great that some investigators believe that the most significant advances in injury control in the future will come mainly from prevention initiatives (10). (The second and third peaks in mortality are more accessible to acute trauma care measures and are discussed in the next section.)

Trauma surgeons are in a unique position to identify the determinants of injury and to inform the development of effective injury prevention strategies. Perhaps the best example of trauma center–led injury prevention is provided by a prospective randomized controlled trial of a brief intervention for alcohol abuse that demonstrated substantial reductions in alcohol consumption (22 versus 7 drinks per week) and reinjury risk (47%) in the intervention group (11). On a larger scale, trauma systems, through research, cooperation with industry, public awareness efforts, and legislation, have contributed to and documented a substantially reduced risk of injury from motor vehicle crashes through the use of seat belts (relative risk of injury 0.42) (12). Progress such as this has prompted the ACS-COT to recognize injury prevention as a priority for all trauma centers, and require Level I and II trauma centers to recruit prevention coordinators. However, a comprehensive survey of U.S. trauma centers revealed that despite a strong interest in injury prevention, less than 20% of them have dedicated coordinators, and more than two-thirds have no specific funding for injury prevention programs (13). Even where evidence exists for the cost-effectiveness of hospital-based injury prevention strategies, as is the case with the alcohol screening and brief intervention initiative (14), resource limitations and competing priorities resulted in its adoption by only half of surveyed trauma centers.

Despite these challenges, public health measures directed at injury control have already achieved some great successes and should be pursued further in mature trauma systems. In the United States, as a result of consistent efforts to change legislation, engineering, and behavior, the annual mortality rate from motor vehicle crashes has fallen from 18 to 1.7 deaths per million miles traveled since 1925 (15). Similarly, deaths from occupational injuries fell from 37 to 4 per 100,000 workers between 1933 and 1997 (16). But more work is needed. Injuries from all causes are still extremely common, and some segments of the population remain particularly vulnerable (17–21).

Recommendations: Trauma systems prevent injury recidivism associated with alcohol abuse. Recommendation grade: A. Trauma system implementation has been associated with reductions in mortality from motor vehicle crashes. Recommendation grade: A. Trauma systems should play a more active role in injury prevention. Recommendation grade: B.

CLINICAL TRAUMA CARE

Over the years, the perspective of trauma systems has widened from regionalized expert trauma centers to multidimensional approaches to injury control that include public policy, prevention, prehospital care, acute medical care, and rehabilitation. All of these areas have grown up together, and it is difficult to examine their progress and effects in isolation. Still, some insights into their value and potential can result from this approach.

The Golden Hour: Once a Severe Injury Occurs, How Long Do We Have?

As we have seen, observational studies (11,12) have documented an important second peak in mortality between one and six hours after injury. Many of these injuries may be responsive to timely control of hemorrhage and restoration of oxygen delivery (22). French surgeons in World War I observed a steady rise in mortality among wounded soldiers as delays to definitive care increased. Only 10% of soldiers who received care within an hour of being injured died, whereas 70% of soldiers waiting 10 or more hours died (23). This mortality pattern, which was cited by R. Adams Cowley in his Golden Hour concept when he started using military helicopters to transport wounded patients in Maryland in 1969 (24), was likely the result of progressive, unchecked shock. In World War II and conflicts in Korea, Vietnam, and the Middle East, combat mortality rates have fallen as delays to definitive care and duration of unchecked shock have been minimized through innovations such as helicopter transport and forward surgical hospitals (7).

Modern studies have consistently shown that shock or compromised delivery of life-sustaining oxygen (as evidenced by regional or systemic markers of anaerobic metabolism) are associated with surgical complications, organ failure, and death (25). Entire military and civilian trauma systems, have been built to deliver systematic and aggressive care within this Golden Hour after injury (25). Observed decreases in trauma-associated multiorgan failure and mortality are likely attributable to early resuscitation (26). The principle of prompt intervention where oxygen delivery is impaired has sound physiologic basis and support from decades of observations that reductions of delays improve survival.

Recommendation: Prompt intervention after major trauma is a first principle of trauma systems. Recommendation grade: D.

Prehospital Care: Scoop and Run or Stay and Play?

It seems clear that once an injury has occurred, early and aggressive care can reduce morbidity and save lives. But what constitutes “early” and what is meant by “aggressive” have been the matter of some debate. Surprisingly, early advanced life support of trauma patients by well-trained paramedics in the field (including thorough assessment, invasive airway control, and prompt resuscitation with intravenous fluids), although intuitively appealing as a means to correct hypoxia and hypotension, has not consistently been shown to improve outcomes. In fact, several observational studies have suggested that increasing availability of prehospital intubation for airway protection

and ventilatory support is associated with similar or worse outcomes in trauma patients with head injuries (27–29) and hypovolemia (30). A prospective, alternate day trial (31) of prehospital bag valve mask ventilation versus intubation in children requiring ventilatory support also revealed no benefit from the more invasive approach. There is also some evidence that a less invasive approach to initial fluid resuscitation may be beneficial: Another prospective, alternate day trial of penetrating trauma in an urban environment suggested that survival increases if paramedics defer intravenous fluid resuscitation in patients sustaining penetrating torso trauma until a time when surgical hemostasis has been achieved (32). The conclusions from these early studies have favored the notion that a “scoop and run” prehospital strategy, minimizing potentially harmful on site interventions and prolonged scene times, may improve outcomes after severe injury.

Prehospital care issues were recently reexamined in one of the largest and most comprehensive studies of prehospital care to date. Stiell and colleagues investigated the effect of system-wide introduction of advanced life support skills for paramedics on survival after severe injury in 2,867 patients. This before–after, controlled clinical trial suggested that augmentation of paramedic skills was not associated with improved survival (81.8% basic, 81.1% advanced) and was associated with *worse* survival in the subset of patients ($n = 598$) with Glasgow Coma Scale score lower than 9 (60.0% basic, 50.9% advanced). Intubation in the field was associated with increased mortality [odds ratio (OR) 2.8]. Interestingly, administration of prehospital intravenous fluids did not appear to be associated with improved outcome (33).

The reasons for failure of advanced paramedic training to make a significant impact on trauma outcomes are not well understood. Recent studies of jurisdictions that place a strong emphasis on aggressive prehospital care (e.g., Montreal) were not able to show a difference between aggressive field resuscitation and rapid transport approaches (7,34). It is possible that a combination of technical factors leading to inadvertent hypoxia or hyperoxia, aspiration, hypocapnea, hypotension, or intracranial hypertension during intubation can compound or exacerbate the primary injury and compromise recovery (35). Until these factors are better characterized individually, it is reasonable to apply advanced life support measures in the prehospital setting selectively and with care to avoid hypoxia and hypotension and to continue to expedite patients' transfer to definitive care.

This brings us to the issue of mode of transport. At our center, trauma patients frequently arrive by helicopter still in the early stages of shock, leading to the frequent impression that air transport routinely saves lives by lowering the duration of hypoperfusion. Does helicopter transport reduce prehospital time, and if so, does it save lives and provide good value for money? Despite the ubiquity of air transport, its use is not supported by high-level evidence. In general, ground ambulance transport (GAT) is widely available and can be readily dispatched. Air medical transport by helicopter (AMT) may take longer to dispatch in some jurisdictions, but often has more sophisticated medical capability (advanced paramedics or physicians) and is faster once launched. Geographic analyses have suggested that distance thresholds from trauma centers to injury locations

exist: beyond certain distances AMT is consistently faster than GAT (36,37). However, the consistency of this association appears highly dependent on trauma system–specific factors, such as numbers of helicopters, locations of landing pads, weather conditions, and so on (38). Some investigators have estimated reductions in mortality of 20–50% with AMT, whereas other studies have not documented a survival benefit (42). More studies are needed to characterize the value of, and optimum algorithms for helicopter transport in trauma.

Recommendations: Prehospital intubation in traumatic brain injury should be selective and attempted with care when necessary. Recommendation grade: B. Prehospital fluid resuscitation should be judicious in patients with penetrating mechanisms in urban environments. Recommendation grade: B. Scene time and interventions in trauma should be minimized until more is known about the effects of specific interventions. Recommendation grade: B. Local analyses should be done to determine trauma center catchments that may be more rapidly served by air medical transport. Recommendation grade: B.

Trauma Centers: Are They Accessible?

Assuming patients in the early Golden Hour receive prompt and judicious prehospital care, where do they go next?

At the heart of trauma systems, trauma centers focus expertise and resources to bring high-quality care to patients with severe and complex injuries and take the lead in their communities on prevention and quality improvement initiatives and scientific research. Between 1991 and 2002, the number of trauma centers in the United States more than doubled from 471 to 1,154 (190 Level I, 263 Level II, and 701 Level III–V hospitals) (39). Access to Level I and Level II centers has grown to provide coverage to 69.2% of Americans within 45 minutes and 84.1% within 60 minutes of injury (5). This level of access is a phenomenal achievement, but more work is still needed for access to become universal. Approximately 46.7 million Americans, mostly in rural areas, still cannot get to Level I or II care within one hour of injury. The observation that injuries sustained in rural environments have higher injury severity adjusted mortality than those in urban environments, (40) may in part be attributable to the poor reach of trauma systems into these areas. Promotion of policies, such as the Emergency Medical Treatment and Active Labor Act, which requires trauma centers to receive severely injured patients if capacity exists, may help establish access as an entrenched and fundamental property of trauma systems (41).

Recommendation: Trauma systems must be made more accessible in rural environments, where injury severity adjusted mortality is high. Recommendation grade: B.

Do Trauma Systems Save Lives?

Access to trauma centers is important because these centers are widely considered to improve outcomes. But do we know this for sure? Numerous investigators have explored this question from three different angles: structure, process and outcome. The *structure* of trauma centers include the presence of in-house trauma attendings and multidisciplinary

trauma teams, well-equipped trauma bays, ready access to operating theaters, the presence of clinical protocols and educational curricula, research capacity and injury prevention activity, and participation in external review and designation. A few studies have suggested that the presence of trauma attendings in house and other structural interventions reduce time to definitive treatment, cost, and even mortality (42–44), prompting organizations such as the ACS-COT and the Trauma Association of Canada to provide trauma surgeon response time guidelines. *Process* in trauma systems is assessed using measures of function: How fast does the trauma team respond, how long does it take to get to the operating room? Implementation of trauma systems has also been shown to improve processes of care (45). Finally, and most important, *outcome* of trauma patients, including mortality, length of stay, and functional measures, may all provide insights into how well a trauma center is fulfilling its mandate.

The trauma systems literature is dominated by this outcome bottom line, particularly by mortality, because it has been most consistently measured. Because randomized trials of trauma center versus non-trauma center performance are not feasible (and probably no longer ethical), assessments of trauma centers have mostly used three types of observational designs: analyses of preventable deaths, comparisons to national norms, and population based studies. *Analyses of preventable deaths* by expert panels provided the earliest justification for the regionalization of trauma care in dedicated centers. In a striking example, West and colleagues compared the proportion of preventable in hospital trauma deaths in San Francisco County, where trauma care was regionalized to a single trauma center, to that in Orange County, where more than 40 centers participated in trauma care. They found only 1% of deaths in San Francisco to be preventable, while a staggering 73% of deaths were considered preventable in Orange County (46). Four years later, after the implementation of regionalized trauma care in Orange County, the proportion of preventable deaths fell to an eighth of its previous level (47). Other analyses of preventable death such as the one by Gruen and colleagues (48) are also interesting because they demonstrate the scope and intensity of the clinical work carried out by trauma centers every day and the impact of process on outcome. These investigators noted that some preventable deaths might have been partly due to problems with airway control, delayed control of acute thoracic/abdominal/pelvic hemorrhage, inadequate venous thromboembolism or gastrointestinal prophylaxis, lengthy initial operative procedures rather than damage control surgery in unstable patients, overresuscitation with fluids, and complications of feeding tubes. Other early trauma center studies have involved *comparisons of trauma center patient outcomes to national norms* (using Trauma and Injury Severity Score methodology and comparisons to reference data from the Major Trauma Outcomes Study), and use of *population-based methods* to examine populations with and without access to trauma systems. Each of these strategies provided early evidence in favor of trauma centers and systems (49).

In one of the most widely cited population-based studies of trauma system effectiveness, investigators from the University of Washington led by Nathens examined the effect of trauma systems on motor vehicle crash mortality in 22 states using the national Fatality Analysis Reporting

System database. After adjusting for differences in injury prevention legislation and general injury mortality trends, the study found that an 8% mortality reduction attributable to trauma systems was evident by 15 years following trauma system implementation (50). Celso and colleagues published another landmark study (51) of the effectiveness of trauma systems. Their review of the literature and meta-analysis examined 14 population-based studies, published between 1992 and 2004, comparing mortality rates before and after implementation of trauma systems or comparing mortality in jurisdictions with and without trauma systems. Like the Nathens study, these were all *ecological studies*—retrospective observational studies examining the health of populations or communities using time trends (mortality before and after trauma system implementation) and geographical comparisons (mortality in jurisdictions with without trauma systems) (52). Improved odds of survival were noted in 8 of the 14 studies, and a meta-analysis including 6 of the studies demonstrated a 15% reduction in mortality where trauma systems were present. Since the publication of this meta-analysis, more rigorous evidence for trauma system effectiveness has accumulated. In another landmark trial, Mackenzie and colleagues used data from the National Study on the Costs and Outcomes of Trauma (NSCOT) to compare mortality between Level I trauma centers and large nontrauma centers in metropolitan areas of 14 states. After carefully adjusting for differences between the patient populations, the authors found that in hospital and one-year mortality were significantly lower for trauma centers (RR 0.80 and 0.75, respectively), and that this effect was more pronounced in younger patients with more severe injuries (53).

Trauma centers have also shown promise in the management of pediatric injuries. Based on observed improved traumatic brain injury outcomes in high-level pediatric trauma centers, the ACS has recommended that children with such injuries be managed at these facilities. However, a recent study of six U.S. states suggests that almost a third of children do not get to high-level care. Access for children is an important research priority.

Recommendation: Trauma systems increase survival.
Recommendation grade: B.

What Features of Trauma Systems Make a Difference?

The mounting evidence for trauma system effectiveness has led some authors to conclude that “the positive impact of trauma systems has been definitely established” and that new research efforts in this area should focus on the further refinement of the structure and processes of trauma care (54). In the absence of high-quality evidence, early trauma systems were built on a foundation of expert opinion. But their rapid evolution has depended on and will continue to depend on close and ongoing evaluation of their structure and processes. In Quebec, such evaluation and evidence-based and context-specific evolution has resulted in a decline in mortality from severe injury from 51.8% in 1992 to 8.6% in 2002 (55). In a study of over 72,000 patients, investigators in Quebec probed the specific strengths of trauma systems and demonstrated that mortality following severe injury is strongly affected by structural and process issues, such as advance notification of trauma centers by prehospital crews (OR 6.1), the presence of hospital-based

performance improvement programs (OR 0.44), and by trauma center experience (OR 0.98) and tertiary designation (OR 0.68) (56).

The effect of experience and trauma center designation has also received attention from other research groups. To define the experience effect, Nathens and colleagues compared outcomes in trauma patients treated at 31 university-affiliated Level I and Level II trauma centers. They observed that as trauma center volumes increase, hospital lengths of stay decrease, perhaps reflecting more rapid recovery in more experienced centers. This relationship descends to a plateau once injury admissions exceeded 600 (Injury Severity Score > 15) per year. Also, odds of death from severe injuries relative to the smallest centers were shown to start decreasing above the 600 admissions threshold, again suggesting that about 600–650 major trauma admissions per year might be the boundary between low- and high-volume trauma centers. After adjustment for confounders, Nathens's group found significantly lower mortality among patients presenting to high-volume trauma centers with penetrating abdominal trauma and hypotension (OR 0.02) and with multisystem injuries with low Glasgow Coma Scale (OR 0.49) (57). However, an analysis of 12,254 patients from the National Trauma Data Bank, focusing on a slightly different population of severely injured patients and using different volume thresholds, found ACS-COT trauma center *designation* (i.e., degree of preparedness and resources for trauma care) to be more predictive of outcome than patient volume (58). Disability at discharge (20.3% versus 33.8%) and mortality (25.3 versus 29.3) were significantly lower in Level I than in Level II centers, but trauma volumes were not associated with outcome differences. These studies are not directly comparable, but both suggest that care provided in dedicated trauma centers, either because of experience or preparedness, has the potential to reduce morbidity and save lives.

Recommendation: Trauma center volume and designation influences outcomes. Recommendation grade: B.

Beyond Saving Lives: What Are the Long-term Outcomes of Trauma Systems?

Virtually all of the studies cited use in-hospital survival as the metric for trauma system success. However, as mortality from multisystem trauma has fallen, both in military and civilian settings, many survivors are returning home to their communities and productive life. Unfortunately, data on the long-term functional outcomes after traumatic conditions such as shock, multiorgan failure, traumatic brain injury, and pelvic and long bone fractures are expensive and not routinely collected. When these data are collected, the results are often surprising: Gabbe and colleagues found that six months after major trauma, only 42% of patients had returned to work, and only 32% characterized their recovery as good (59). Outcome measures at the time of hospital discharge, such as the modified Functional Independence Measure and the Glasgow Outcome Score, which are often used as indicators of functional recovery, were not found to be reliably predictive of long-term outcomes, emphasizing how little insight we get from hospital data on ultimate outcomes. Holbrook and colleagues at the University of California, San Diego, found

that adolescents sustaining major trauma have significant and sustained deficits in quality of life compared to national norms (60). These findings, and others by this group, highlight the urgency of data collection, continued research, and action in this area.

Recommendations: Long-term outcomes in severe trauma are poor. Further optimization of trauma system performance will depend on the collection and analysis of data on injury-related disability V.

FUTURE DIRECTIONS

Can Trauma Systems Help Build Safer Societies, and at What Cost?

In recent years, the concept of trauma systems has transitioned from regionalization of trauma care to (often single) specialized high-volume trauma centers to a more holistic and multidisciplinary or *systems* approach to injury control that starts with injury prevention and emphasizes a wider response to trauma including pre- and posthospital care. Nathens's study of the effect of trauma systems on motor vehicle crash survival found that seat belt legislation, helmet use, and established speed limits, in addition to presence of trauma centers, were independently associated with better survival. A more recent study of motor vehicle occupant survival also demonstrated the beneficial effects of preventive strategies but failed to show an association between trauma center presence and outcome (61). It is becoming increasingly evident that the observed successes of trauma systems cannot be attributed to any one component or measure, but rather to a systematic approach to injury control.

More effective and universal acute care of injury continues to be an area of intense interest for trauma systems. Trauma investigators have speculated that a more participatory or *inclusive* approach to trauma care, which involves all of a region's acute hospitals (to the extent that their resources permit), could streamline the triage and early care of injured patients and extend the reach of trauma systems beyond the catchments of large, urban trauma centers to more rural and remote regions. A recent comparison of American states with the traditional, single trauma center-based exclusive trauma systems with states with inclusive trauma systems, used administrative discharge data from 24 states to demonstrate that states with the highest levels of inclusiveness (38–100% of hospitals designated as Level I–V trauma centers) had the lowest odds of mortality (OR 0.77) after adjustment for factors such as injury mechanism and trauma system maturity. The authors of this study speculated that early care of patients in inclusive systems at local trauma centers and more efficient transfers to higher levels of trauma care when needed may have been responsible for the observed advantage of inclusive systems (62). These conclusions about sharing the work in inclusive trauma systems may seem to be at odds with other studies documenting the importance of the volume–outcome relationship in severe trauma, but it is likely that the benefits of inclusive systems will be maximized if triage is accurate, with all severe injuries rapidly referred and transported to high-volume or designated high-level centers (63). Currently, high-volume trauma centers in the United States, which account

for 7% of all hospitals, care for 60% of severely injured patients (64). The need for rapid and accurate assessment of patient needs and accurate triage to appropriate facilities is underscored by a report from Sampalis and colleagues (65) in Montreal, who found that severely injured patients initially taken to less specialized hospitals, then transferred to trauma centers, had almost twice the mortality of those transferred directly to trauma centers. The interesting challenge of modern trauma systems will be to reconcile these sorts of observations about prehospital care, triage, trauma center performance, and inclusiveness and adapt them to their own specific regional needs.

The role of trauma systems in building safer societies will also be shaped by the increasing threats of multiple and mass casualty situations. Natural disasters and acts of war and terrorism have already tested both military and civilian trauma systems in North America and around the world. It is believed that more inclusiveness in the delivery of trauma care, with a high proportion of hospitals able to respond promptly and according to their established capabilities, will increase the capacity of our response to these situations. Disaster preparedness has become an essential mandate of trauma systems, and research in this area using simulation or extrapolation from previous experiences is a priority if trauma systems are to remain effective and relevant (66–68).

Such considerations would seem to justify the high cost of maintaining trauma system preparedness. A survey of the additional capabilities and costs associated with 24-hour trauma system preparedness in 10 trauma centers in Florida suggested that the annual costs of such preparedness is \$2.7 million per center. Most of these costs were attributed to physician on-call coverage. The authors note that these costs of preparedness may not translate to billable patient care and are therefore not recouped (69). The financial benefits of preparedness in terms of reductions in morbidity and mortality, however, are difficult to quantify accurately and are probably undervalued. A more global economic evaluation of trauma care examined the cost per quality adjusted life year (cost/QALY) gained by treatment at a tertiary trauma center in Ottawa, Canada. The investigators found that the increase in cost/QALY for treatment at a tertiary trauma center compared to a nontrauma center (\$4,303) compared favorably with other established health care interventions (70). Another analysis of the Florida trauma system confirmed that although care at trauma centers was more expensive, it was associated with a reduction in mortality of 18%, resulting in a cost of \$35,000 per life saved at trauma centers. Again, when restored productivity was considered, the authors concluded that trauma center care compared very favorably with other established medical interventions (71). However, Fishman and colleagues raised an important issue regarding the unintended consequences of trauma systems: Does trauma care adversely affect outcomes of nontrauma patients? They found that patients presenting to the emergency department with acute coronary syndromes during a concurrent trauma activation had nearly twice the number of adverse cardiac events at 30 days. Although this was a small study, it suggests that future evaluations of trauma system costs should take into account possible collateral consequences (72).

Recommendations: A systematic approach to trauma care improves survival. Recommendation grade: B. Inclusive trauma systems improve survival. Recommendation

grade: B. Inclusive trauma systems may improve survival in mass casualty and multicase situations. Evidence needed. Trauma systems are cost-effective. Recommendation grade: B.

Global Health: Can Trauma Systems Save Lives in Low-resource Settings?

Perhaps the ultimate challenge and responsibility of established trauma systems is to find ways in which their successes can be applied to advance global safety and health. As we have seen, trauma systems, despite providing good value for money, are expensive to establish and run. We have also seen that low-income countries, without prevention or health care budgets of this scale, shoulder a disproportionate amount of the burden of injury because of unsafe roads (73) and working conditions, violence (74), and poor access to organized and comprehensive trauma care. A lack of resources should not be a deterrent to the pursuit of advances in trauma care; hundreds of thousands of lives stand to be improved or saved if trauma systems can find more universal applications. Study after study has shown that trauma systems prevent injury and improve outcomes in part because they are successful in reorganizing available resources and focusing them on achieving high standards of injury control.

Recognizing the promise of a public health/trauma systems approach to injury control in low-resource settings, the International Association for Trauma and Surgical Intensive Care and the World Health Organization, along with a number of prominent trauma organizations from around the world, set out to identify fundamental priorities for trauma care that must be achieved regardless of the level of individual or societal wealth. The results of their deliberations were published in 2004 in *Guidelines for Essential Trauma Care* (75). These guidelines are the low-resource counterpart to the ACS-COT *Resources for Optimal Care of the Injured Patients*. They are geared to economies that spend as little as US\$3–4 per capita per year on health, are rallying points for advocacy, create tangible goals, and can be modified to fit local circumstances (76). They represent the starting point for action on injury control at the global level. Data collection to guide implementation of initiatives such as the Essential Trauma Care project and other injury control policies has often been absent in low-income settings. However, early initiatives in this area have suggested that trauma registries may be feasible and would play an important role (77).

The magnitude of surgical illness, the surgical workforce crisis, and the absence of systems of care, including trauma systems in many low-income countries, have created a critical opportunity for research, policy development, and investment. Ozgediz and colleagues have noted that the creation of new partnerships between U.S. surgical training institutions and surgical associations with their counterparts in the developing world could serve as a means of sharing knowledge, skills, and resources to make a meaningful impact on global health (78). With unprecedented enthusiasm for global health promotion among North American surgical trainees, with established strategies for the implementation and improvement of trauma systems, and with solid evidence to support their benefit, the next

decades of trauma system development promise to be even more exciting than the last.

Recommendation: Trauma systems have the potential to reduce morbidity and mortality in low-income settings. Evidence needed.

SUMMARY

A goal, which we did not achieve, was to use an evidence based scientific method to support recommendations completely. Although our intention was sincere, we learned that, often, current data are lacking to definitively establish one recommendation over another

—ACS-COT Resources for the Optimal Care of the Injured Patient

In recent years, the value of trauma systems has been supported by a wealth of Level II data (population-based cohort and ecological studies), and trauma systems have become an important feature of the public health landscape. They provide data for injury prevention and stand ready for injury and mass casualty. They also illustrate that comprehensive public health approaches can make a difference in diseases with complex determinants and rapid and severe consequences. Perhaps because of these factors, the principles of trauma systems have been applied widely. But as the ACS-COT points out, gaps in the trauma systems literature and the persistence of injury as a major public health issue around the world mean that the work is still far from accomplished. New insights into the specific factors that make trauma systems effective are beginning to emerge and will continue to guide trauma system development. More studies are needed, including economic evaluations so that long-term benefits can be accounted for and trauma systems remain efficient. More analyses involving outcomes other than hospital death are also needed (79) so that the heavy impact of prehospital deaths including suicide (80) and nonfatal mortality on society can be measured, and so that trauma systems may adjust accordingly. Innovative analyses of access to trauma systems are needed so that their reach might be extended further into rural and remote communities (81,82). Trauma systems, which provide the framework for emergency response, must also clarify their roles in mass casualty and disaster situations. Ongoing insights from military experiences may be essential to this effort (83). From the start, trauma systems have emphasized accountability and improvement and have worked to ensure that evidence is collected and acted on. Initiatives such as the NSCOT, collecting high-quality data, will provide important insights for the future development of trauma systems on many fronts. Finally, local successes have global implications. Surgeons working in trauma systems have an exciting opportunity to share knowledge and insights and tackle problems together with their colleagues in low-income countries.

REFERENCES

1. Rug E. Injury: A leading cause of the global burden of disease WHO/HSC/PVI/99.11. Geneva: WHO, 1999.
2. Committee on Trauma and Committee on Shock, National Research Council. *Accidental death and disability: The neglected disease of modern society*. Washington, DC: National Academy of Sciences/National Research Council, 1996.
3. Ciesla DJ. Trauma systems and access to emergency medical care. *J Trauma* 2007; 62: S51.
4. Morbidity and Mortality Weekly Report November 2, 2007; 56; 1137–40.
5. Branas CC, MacKenzie EJ, Williams JC, et al. Access to trauma centers in the United States. *JAMA* 2005; 293: 2626–33.
6. Nathens AB, Brunet FP, Maier RV. Development of trauma systems and effect on outcomes after injury. *Lancet* 2004; 363: 1794–801.
7. *Resources for Optimal Care of the Injured Patient* 2006. Committee on Trauma, American College of Surgeons.
8. Trunkey DD. Trauma. *Sci Am* 1983; 249: 25–35.
9. Demetriades D, Kimbrell B, Salim A. Trauma deaths in a mature urban trauma system: is “trimodal” distribution a valid concept? *J Am Coll Surg* 2005; 201: 343–8.
10. Stewart RM, Myers JG, Dent DL, et al. Seven hundred fifty-three consecutive deaths in a Level I trauma center: The argument for injury prevention. *J Trauma* 2003; 54: 68–70.
11. Gentilello LM, Rivara FP, Donovan DM, et al. Alcohol interventions in a trauma center as a means of reducing the risk of injury recurrence. *Ann Surg* 1999; 230: 473–83.
12. McGwin G, Metzger J, Alonso JE, et al. Restraint systems in vehicles—seat belts and airbags. *J Trauma* 2005; 23: 7–9.
13. McDonald EM, MacKenzie EJ, Teitelbaum SD, et al. Injury prevention activities in U.S. trauma centres: are we doing enough? *Injury* 2007; 38: 538–47.
14. Gentilello LM, Ebel BE, Wickizer TM, et al. Alcohol interventions for trauma patients treated in emergency departments and hospitals: A cost benefit analysis. *Ann Surg* 2005; 241: 541–50.
15. Morbidity and Mortality Weekly Report 1999; 48: 369–74.
16. Centers for Disease Control and Prevention. Achievements in public health, 1900–1999. Improvements in workplace safety—United States. *Mortal Morbid Weekly Rep* 1999; 48: 461–9.
17. Karmali S, Laupland K, Harrop AR, et al. Epidemiology of severe trauma among status aboriginal Canadians: a population-based study. *Can Med Assoc J* 2005; 172: 1007–11.
18. Cubbin C, LeClere FB, Smith GS. Socioeconomic status and the occurrence of fatal and nonfatal injury in the United States. *Am J Public Health* 2000; 90: 70–7.
19. Centerwall BS. Race, socioeconomic status, and domestic homicide. *JAMA* 1995; 273: 1755–8.
20. Birken CS, Parkin PC, To T, et al. Trends in rates of death from unintentional injury among Canadian children in urban areas: Influence of socioeconomic status. *Can Med Assoc J* 2006(Oct 10); 175: 867.
21. Bell N, Schuurman N, Hameed SM. A multilevel analysis of the socio-spatial pattern of assault injuries in Greater Vancouver, British Columbia. *Can J Public Health* 2009; 100: 73–7.
22. MacLeod JB, Cohn SM, Johnson EW, et al. Trauma deaths in the first hour: Are they all unsalvageable injuries? *Am J Surg* 2007; 193: 195–9.
23. Santy P, Marquis Moulinier. De shock traumatique dans les blessures de guerre, analysis d’observations. *Bull Med Soc Chir* 1918; 44: 205.
24. Cowley RA, Hudson F, Scanlan E, et al. An economical and proved helicopter program for transporting the emergency critically ill and injured patient in Maryland. *J Trauma* 1973; 13: 1029–38.
25. Hameed SM, Aird WC, Cohn AM. Oxygen delivery. *Crit Care Med* 2003; 31: S658–S667.
26. Durham RM, Moran JJ, Mazuski JE, et al. Multiple organ failure in trauma patients. *J Trauma* 2003; 55: 608–16.
27. Eckstein M, Chan L, Schneir A. Effect of prehospital advanced life support on outcomes of major trauma patients. *J Trauma* 2000; 48: 643–8.
28. Murray JA, Demetriades D, Berne TV, et al. Prehospital intubation in patients with severe head injury. *J Trauma* 2000; 49: 1065–70.

29. Davis DP, Peay J, Sise MJ, et al. The impact of prehospital endotracheal intubation on outcome in moderate to severe traumatic brain injury. *J Trauma* 2005; 59: 933–9.
30. Shafi S, Gentilello L. Pre-hospital endotracheal intubation and positive pressure ventilation is associated with hypotension and decreased survival in hypovolemic trauma patients: an analysis of the national trauma data bank. *J Trauma* 2005; 59: 1140–7.
31. Gausche M, Lewis RJ, Stratton SJ, et al. Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome: a controlled clinical trial. *JAMA* 2000; 283: 783–90.
32. Bickell WH, Wall MJ Jr, Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med* 1994; 331: 1105–9.
33. Stiell IG, Nesbitt LP, Pickett W, et al. The OPALS major trauma study; impact of advanced life-support on survival and morbidity. *Can Med Assoc J* 2008; 178: 1141–52.
34. Liberman M, Mulder D, Lavoie A, et al. Multicenter Canadian study of prehospital trauma care. *Ann Surg* 2003; 237: 153–60.
35. Davis DP. Should invasive airway management be done in the field? *Can Med Assoc J* 2008; 178: 171–3.
36. Lerner EB, Billittier AJ, Sikora J, et al. Use of a geographic information system to determine appropriate means of trauma patient transport. *Acad Emerg Med* 1999; 6: 1127–33.
37. Mitchell AD, Tallon JM, Sealy B. Air versus ground transport of major trauma patients to a tertiary trauma centre: a province-wide comparison using TRISS analysis. *Can J Surg* 2007; 50: 129–33.
38. Karanicolas PJ, Bhatia P, Williamson J, et al. The fastest route between two points is not always a straight line: an analysis of air and land transfer of nonpenetrating trauma patients. *J Trauma* 2006; 61: 396–403.
39. MacKenzie EJ, Hoyt DB, Sacra JC, et al. National inventory of hospital trauma centers. *JAMA* 2003; 289: 1515–22.
40. Muellemann RL, Wadman MC, Tran TP, et al. Rural motor vehicle crash risk of death is higher after controlling for injury severity. *J Trauma* 2007; 62: 221–6.
41. Spain DA, Bellino M, Kopelman A, et al. Requests for 692 transfers to an academic Level I trauma center: implications of the emergency medical treatment and active labor act. *J Trauma* 2007; 62: 63–7.
42. Luchette F, Kelly B, Davis K, et al. Impact of the in-house trauma surgeon on initial patient care, outcome, and cost. *J Trauma* 1997; 42: 490–5.
43. Rogers FB, Simons R, Hoyt DB, et al. In-house board-certified surgeons improve outcome for severely injured patients: a comparison of two university centers. *J Trauma* 1993; 34: 871–5.
44. Cornwell EE, Chang DC, Phillips J, et al. Enhanced trauma program commitment at a Level 1 trauma center. *Arch Surg* 2003; 138: 838–43.
45. Olson CJ, Arthur M, Mullins RJ, et al. Influence of trauma system implementation on process of care delivered to seriously injured patients in rural trauma centers. *Surgery* 2001; 130: 273–9.
46. West JG, Trunkey DD, Lim RC. Systems of trauma care. A study of two counties. *Arch Surg* 1979; 114: 455–60.
47. West JG, Cales RH, Gazzaniga AB. Impact of regionalization. The Orange County experience. *Arch Surg* 1983; 118: 740–4.
48. Gruen RL, Jurkovich GJ, McIntyre LK, et al. Patterns of errors contributing to trauma mortality: lessons learned from 2,594 deaths. *Ann Surg* 2006; 244: 371–80.
49. Mullins RJ, Mann NC. Population-based research assessing the effectiveness of trauma systems. *J Trauma* 1999; 47: S59–S66.
50. Nathens AB, Jurkovich GJ, Cummings P, et al. The effect of organized systems of trauma care on motor vehicle crash mortality. *JAMA* 2000; 283: 1990–4.
51. Celso B, Tepas J, Langland-Orban B, et al. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. *J Trauma* 2006; 60: 371–78.
52. Coggon D, et al. Ecological studies in epidemiology for the uninitiated 1997. www.bmj.com/epidem/epid.6.html; accessed August 30, 2008.
53. MacKenzie EJ, Rivara FP, Jurkovich GJ, et al. A national evaluation of the effect of trauma-center care on mortality. *New Eng J Med* 2006; 354: 366–78.
54. Mulder DS, Liberman M, Sampalis J. Editorial comment. *J Trauma* 2006; 60: 371–8.
55. Liberman M, Mulder DS, Lavoie A, et al. Implementation of a trauma care system: evolution through evaluation. *J Trauma* 2004; 56: 1330–5.
56. Liberman M, Mulder DS, Jurkovich GJ, et al. The association between trauma system and trauma center components and outcome in a mature regionalized trauma system. *Surgery* 2005; 137: 647–58.
57. Nathens AB, Jurkovich GJ, Maierreggio RV, et al. Relationship between trauma center volume and outcomes. *JAMA* 2001; 285: 1164–71.
58. Demetriades D, Martin M, Salim A, et al. The effect of trauma center designation and trauma volume on outcome in specific severe injuries. *Ann Surg* 2005; 242: 512–7.
59. Gabbe BJ, Simpson PM, Sutherland AM, et al. Functional measures at discharge: are they useful predictors of longer term outcomes for trauma registries? *Ann Surg* 2008; 247: 854–9.
60. Holbrook TL, Hoyt DB, Coimbra R, et al. Trauma in adolescents causes long-term marked deficits in quality of life: adolescent children do not recover preinjury quality of life or function up to two years postinjury compared to national norms. *J Trauma* 2007; 62: 577–83.
61. Shafi S, Nathens AB, Elliott AC, et al. Effect of trauma systems on motor vehicle occupant mortality: a comparison between states with and without a formal system. *J Trauma* 2006; 61: 1374–9.
62. Utter GH, Maier RV, Rivara FP, et al. Inclusive trauma systems: do they improve triage or outcomes of the severely injured? *J Trauma* 2006; 60: 529–37.
63. Position paper on trauma care systems. Third National Injury Control Conference, April 22–25, 1991, Denver, CO. *J Trauma* 1992; 32: 127–9.
64. Diggs BS, Mullins RJ, Hedges JR, et al. Proportion of seriously injured patients admitted to hospitals in the US with a high annual injured patient volume: a metric of regionalized trauma care. *J Am Coll Surg* 2008; 206: 212–9.
65. Sampalis JS, Denis R, Frechette P, et al. Direct transport to tertiary trauma centers versus transfer from lower level facilities: Impact on mortality and morbidity among patients with major trauma. *J Trauma* 1997; 43: 288–96.
66. Hoyt DB, Coimbra R. Trauma systems. *Surg Clin North Am* 2007; 87: 21–35.
67. Champion HR, Mabee MS, Meredith JW. The state of US trauma systems: public perceptions versus reality—implications for US response to terrorism and mass casualty events. *J Am Coll Surg* 2006; 203: 951–61.
68. Currier M, King DS, Wofford MR, et al. Katrina experience: lessons learned. *Am J Med* 2006; 119: 986–92.
69. Taheri PA, Butz DA, Lottenberg L, et al. The cost of trauma center readiness. *Am J Surg* 2004; 187: 7–13.
70. Seguin J, Garber BG, Coyle D, et al. An economic evaluation of trauma care in a Canadian level trauma hospital. *J Trauma* 1999; 47: S99–S103.
71. Durham R, Pracht E, Orban B, et al. Evaluation of a mature trauma system. *Ann Surg* 2006; 243: 775–85.

72. Fishman PE. The impact of trauma activations on the care of emergency department patients with potential acute coronary syndromes. *Ann Emerg Med* 2006; 48: 347–53.
73. Ameratunga S, Hajar M, Norton R. Road-traffic injuries: confronting disparities to address a global-health problem. *Lancet* 2006; 367: 1533–40.
74. World Health Organization. World Report on Violence and Health. 2002; www.who.int/violence_injury_prevention/violence/world_report/en/index.html
75. World Health Organization. Guidelines for Essential Trauma Care. 2004; www.who.int/violence_injury_prevention/publications/services/guidelines_traumacare/en/index.html.
76. Mock C, Joshipura M, Gossen J, et al. Strengthening trauma systems globally: the essential trauma care project. *J Trauma* 2005; 59: 1243–6.
77. Schultz CR, Ford HR, Cassidy LD, et al. Development of a hospital-based trauma registry in Haiti: an approach for improving injury surveillance in developing and resource-poor settings. *J Trauma* 2007; 63: 1143–54.
78. Ozgediz D, Riviello R, Rogers SO. The surgical workforce crisis in Africa: a call to action. *Bull Am Coll Surg* 2008; 93: 10–6.
79. Mann NC, Mullins RJ, MacKenzie EJ, et al. Systematic review of published evidence regarding trauma system effectiveness. *J Trauma* 1999; 47(3 Suppl): S25–S33.
80. Schecter WP, Klassen C, O'Connor P, et al. Suicide: the unmet challenge of the trauma system. *Arch Surg* 2005; 140: 902–4.
81. Schuurman N, Bell N, Hameed M, et al. A model for identifying and ranking need for trauma service in non-metropolitan regions based on injury risk and access to services. *J Trauma* 2008; 65: 54–62.
82. Osterwalder JJ. Could a regional trauma system in eastern Switzerland decrease the mortality of blunt polytrauma patients? A prospective cohort study. *J Trauma* 2002; 52: 1030–6.
83. Eastridge BJ, Jenkins D, Flaherty S, et al. Trauma system development in a theater of war: experiences from operation Iraqi freedom and operation enduring freedom. *J Trauma* 2006; 61: 1366–72.

Evidence-Based Review of Trauma Outcomes

Michael M. Badellino, John J. Hong, and Michael D. Pasquale

Clinical Questions			
Question	Answer	Level	Grade of recommendation
Can the principles of EBM be used to assess trauma outcomes?	Yes	I II III	B
Can application of the concepts of EBM actually improve outcome?	Yes	I II III	B
Can application of the concepts of EBM be applied to specifically improve trauma outcome?	Yes	I II III	B

The proper practice of scientific surgery has always required that the individual surgeon base patient management decisions on clinical evidence of effectiveness. The progress of surgery through the 20th century has been fostered by vibrant support from clinical and bench research initiatives. The application of this general process by individual surgeons has not been universal, however. Clinical practice has often been guided by anecdote, cultural practices, or reliance on evidence of questionable value.

WHAT ARE EVIDENCE-BASED OUTCOME EVALUATIONS?

Since the 1980s, the principles of evidence-based medicine (EBM) have provided a framework and process that allows the conscientious, explicit, and judicious use of current best evidence from clinical care research in the management of individual patients (1). EBM is therefore a method of patient care, decision making, and teaching that integrates high-quality research evidence with pathophysiologic reasoning and clinician experience (2,3). In short, EBM systematically searches for the best evidence rather than relying on expert opinion or anecdote (4). The core process in EBM is to base clinical decisions on the best available evidence while at the same time understanding and being able to rate the quality or power of that evidence. The inherent difficulties of any individual having the time or expertise to accomplish the latter are reflected in the establishment of multidisciplinary working groups to evaluate quality of evidence, such as the Canadian and U.S. Preventive Services Task Forces. Another group, the Grading of Recommendations Assessment, Development and Evaluation working

group, has a mission to create highly structured, transparent, and informative system for rating quality of evidenced (5,6). An important point to keep in mind when evaluating data, is that best evidence in any particular outcome study may *not* come from multicenter, randomized, controlled clinical trials, generally recognized as the gold standard for evidence, but rather less powerful studies (4).

Several landmark studies by the Institute of Medicine (IOM) published in the early part of this decade have firmly established safety efforts, quality improvement processes, and outcome measures as critical and essential elements of health care policy (7,8,9). Outcome measures can no longer be limited to time-honored standards of clinical endpoints, such as morbidity and mortality, but must include patient-centered outcomes such as quality of life and patient satisfaction and as well as measures of compliance with practice guidelines. The tools and data sources required to assess these parameters must include audits, clinical registries, scoring systems, and administrative databanks.

In many respects, trauma surgeons, centers, and researchers have been at the forefront of outcome evaluation for several decades. Almost since their inception, trauma centers and systems have had to answer to regulatory bodies, governmental and private, and have had to prove a standard of care based primarily on outcome measures. Indeed, accreditation of trauma centers is nothing less than a critical assessment of surgical outcomes in a particular center using evidence-based, validated methodology. A review of several recent presidential addresses at the Eastern Association for the Surgery of Trauma highlights the great concern and interest among trauma surgeons for the methods and application of EBM (10–13).

CAN THE PRINCIPLES OF EBM BE USED TO ASSESS TRAUMA OUTCOMES?

The development of the processes of EBM has also led to a refinement of the definition of generally recognized outcome parameters. In a broad sense, outcomes have historically been grouped as either clinical endpoints (live, die, etc.) or some intermediate outcome (blood pressure, blood glucose level, etc.). In trauma, clinical endpoints have traditionally included survival, morbidity, length of stay, and cost. Although the definition of each of these outcomes seems intuitive, the endpoints for each variable may differ considerably. Survival may be 30 days or 1 year, morbidity rates may be confounded by preexisting disease, and cost estimates are notoriously difficult to quantify. Thus, great caution must be exercised in interpreting data using these endpoints. Recently, so-called quality-of-life endpoints are being recognized as important measures to be included in surgical outcome studies and processes.

Although it has been observed that historically trauma practice has often not been based on rigorous data, nonetheless penetration of EBM principles into clinical trauma care is ever increasing. This is illustrated by a large number of trauma-related outcome studies that have emerged in the past 10 years (11,14–33).

The great limitation to the more widespread application of evidence-based outcome evaluations (EBOEs) to trauma care in general is the fact that the initial care on the injured patient, both pre- and initial-hospital, does not lend itself easily to the design of gold standard of randomized controlled trials (RCTs). Thus, Level I recommendations are difficult to draw. Nonetheless, as mentioned previously, reasonable best evidence in these cases may be generated from well-designed, Class II and III studies that are multi-institutional with large sample sizes.

Perhaps the most influential and illustrative outcome evaluation project in trauma is the recently completed National Study on Costs and Outcomes in Trauma. As reported by MacKenzie and colleagues, in a study of over 5,000 trauma patients treated at trauma and nontrauma centers, in-hospital mortality rates were significantly lower at trauma centers (34). Using propensity score weighting to adjust for differences in severity of injury, preinjury illness, and age, the authors reported a 25% risk reduction for death among patients treated at a trauma center as compared to a nontrauma center. This difference in mortality rate was maintained up to 1 year following injury. Previous studies of trauma center effectiveness had been poorly designed due to reliance on in-hospital mortality data and difficulties in adjusting for referral bias. By using proper stratification techniques, collecting data on covariates influencing survival and propensity score weighting, the authors have produced evidence of high quality. The public health implications of this study are still being debated.

Answer: Yes, the principles of EBM may be used to assess trauma outcomes. Recommendation grade: B.

CAN APPLICATION OF THE CONCEPTS OF EBM ACTUALLY IMPROVE OUTCOME?

Perhaps the quintessential example of how the principles of EBM can improve patient outcome is found in a review

of the over 15-year experience with the National Surgical Quality Improvement Program (NSQIP). Initially begun in the Veterans Health Administration in 1991, NSQIP has established new methods for the assessment and improvement of quality in surgery. In 2004, the American College of Surgeons (ACS) made the program available to the private sector. In its essence, NSQIP provides a national, validated, peer-controlled program that aims to improve the quality of surgical care by applying risk-adjusted outcomes for comparative assessment. According to Khuri et al., the program has demonstrated its efficacy in reducing postoperative complications in the Veterans Health Administration, and has demonstrated that safety is indistinguishable from overall quality of surgical care, adverse outcomes are primarily determined by the quality of the system, and reliable comparative data are imperative to ensure safety from adverse outcomes (35).

In response to a pivotal IOM study in 1999, several related EBOE initiatives were designed and implemented. The Agency for Healthcare Research and Quality (AHRQ) established the Center for Quality Improvement and Safety. This center, in turn, has become a leader in education and training in patient safety practices and has developed evidence-based best practices for the National Quality Forum (NQF). The NQF in turn, has developed evidence-based safe practices that the Joint Commission requires hospitals to practice. These are only a few of the many EBM initiatives that can trace their genesis to the IOM study. In 2005, the IOM revisited the issue of safety, in light of the many EBM initiatives developed, and reported modest but real decreases in medication error rates, complications of anticoagulation, and numbers of serious infections (36–38).

Although compliance with management guidelines per se does not directly address outcomes, such a relationship is clearly implied (39). Perhaps a signature achievement of the Eastern Association for the Surgery of Trauma has been the Management Guideline Project. For approximately 15 years, since prompted by a seminal presidential address by Dr. Michael Rhoades, the Committee on Management Guidelines has led the way not only in trauma clinical guideline development, beginning with the topics of blunt cardiac injury, cervical spine evaluations, penetrating colon injury, and deep venous thrombosis prophylaxis, but also in the very process of guideline development (10,11). Studies of compliance with guidelines for head injury and advanced trauma life support guidelines have suggested a direct and positive effect on outcome (40,41).

Answer: Yes, application of the concepts of EBM actually improve outcome. Recommendation grade: B.

CAN APPLICATION OF THE CONCEPTS OF EBM BE APPLIED TO SPECIFICALLY IMPROVE TRAUMA OUTCOME?

EBM can be used to improve trauma outcome by utilizing a process that applies problem identification and critical evidence review to produce changes in clinical practice which results in outcome improvement. This process most often results in the creation of newer, evidence-based standards of care, often applied clinically by development and attention to clinical guidelines or protocols (40).

Clinical protocols are institutional manifestations of evidence-based best practices. They often take the form of algorithm-based pathways that suggest specific patient care interventions, in specific disease states, usually arranged around critical decision-making points or “nodes.” The flow of care from these nodes is based not on anecdote or institutional culture but on evidence-based national guidelines or best evidence available as determined by specific institutions. Probably the most effective protocols are focused, simple, dichotomous (if *a* then *b*) and annotated and referenced at key nodes to the best evidence that was used in the protocol development. Well-designed clinical protocols will also have a positive effect on practice-based learning by physicians and nurses and allow audits to assess institutional adherence to standards of care. The use of clinical management protocols to direct intensive care unit ventilator management has been demonstrated to improve outcomes (41).

Evidence-based guidelines have been defined as systematically developed statements of generally accepted management strategies based on best available evidence” (40). Particular valuable guidelines are often developed by national organizations (e.g., EAST) or multidisciplinary consensus conferences. Guidelines are not standards of care, but recommendations based on best evidence. Adherence to well-designed, evidence-based management guidelines should be expected to produce outcome improvement. Indeed, studies of compliance with guidelines for head injury and advanced trauma life support have suggested a direct and positive effect on outcome (42,43). Despite these findings, there remains some debate regarding this relationship (39,44).

Answer: Yes, application of the concepts of EBM can be applied to specifically improve trauma outcome. Recommendation grade: B.

WHAT GROUPS OR INITIATIVES ARE CURRENTLY USING EBOES?

IOM

Perhaps no organization using outcome research has caught the public eye as profoundly as the IOM. Beginning with a 1999 report, “To Err Is Human: Building a Safer Health System,” the IOM, an independent think tank commissioned by Congress, has been at the forefront of outcomes research. This study estimated that as many as 98,000 Americans die annually as a result of medical error and called for a national effort to remediate this unacceptable situation (8). The widespread coverage this report received in the media and the response by Congress has had profound effects on medicine in the United States. In turn, this has ushered in a growth era of EBM. The specific impact this and other studies by the IOM has had on trauma care is evidenced in the real attention given to the issue of patient safety by such groups as the ACS Committee on Trauma. The IOM report has prompted initiatives by several other governmental and nongovernmental agencies as detailed shortly.

AHRQ

The AHRQ is a government agency tasked with studying evidence-based guidelines throughout the United States. The AHRQ has established several areas where the principles of EBM can be applied to improve safety and quality

and include antibiotic and deep vein thrombosis prophylaxis, central venous catheter management, and enteral nutrition (45,46). In cooperation with the American Medical Association and American Health Insurance, the AHRQ has created a electronic database of evidence-based clinical practice guidelines to assist health care providers in obtaining reliable, relevant data on which to base best practices (47).

Leapfrog

The Leapfrog group is a cooperative initiative between public and private health care payers as well as several leading U.S. companies who are large purchasers of health care. This group has been active in identifying evidence-based characteristics that are believed to impact the quality of health. These include computer physician order entry, electronic medical records, high-volume institutions, and staffing of intensive care units.

ACS

The ACS has been a leader in advancing outcome studies and evidence-based trauma guidelines. Perhaps the most recent initiatives, the NSQIP and the Surgical Care Improvement Project are the most noteworthy. Under the auspices of the Committee on Trauma, the National Trauma Data Bank and National Trauma Registry of the American College of Surgeons are repositories of invaluable Class III EBM Studies (48).

VA

The development in 1974 of the Veterans Administration (VA) Decentralized Hospital Computer Program, later the Veterans Health Administration (VHA)’s computerized patient record system, ushered in a modern era of intense concern for surgical quality within the VHA, as measured by outcomes evaluations. Indeed, this database serves as a paradigm of the type required to perform critical data analysis as part of an EBOE. The VHA has developed several noteworthy surgical quality programs, including the Neurosurgery Consultants Board and the Continuous Improvement of Cardiac Surgery Program, and is a major participant in NSQIP.

CAN ONE DEVELOP A PROCESS THAT UTILIZES THE CONCEPTS OF EBM TO ASSESS OUTCOME?

A process for EBOE has resulted from work by the AHRQ (45). The model consists of a 10-step process that is rigorous and practical. Central to the process are the concepts of development, implementation, and revision.

The core basic concepts of EBM can be used to fashion a process to assess outcome. In general, the process will begin with the definition of a specific problem or outcome to be studied. In complex systems, this is best accomplished by a multidisciplinary team. This is followed by critical appraisal of existing, pertinent literature, with particular attention to appropriateness of study design (avoidance of Type I error) power, sample size, and level and class of recommendation. Outcome studies are particularly susceptible to selection bias, loss of power due to risk adjustment, and small sample size (Type II error). The product of this effort is the development of a clinical trial, quality

database, practice guideline, clinical pathway, or protocol. RCTs remain the gold standard for clinical research but may not be practical, especially in the trauma population. The use of Class II studies, such as retrospective analyses,

cohort, or case-controlled studies, as well as Class III studies, such as clinical series, databases, and case reports, can also provide valuable evidence that is simply unavailable at the Class I level.

Evidentiary Table

Ref.	#	YR	Level	Randomization/Group/ Intervention	Design	Follow-up	Major endpoint	Minor endpoint
Intensive Care								
Gattinoni et al.	14	01	Ib	Prone positioning in ARDS	MC/RCT	10 days	Survival	P/F ration
ARDS Network	15	00	Ib	Low tidal volume ventilation in ARDS	MC/RCT	28 days	Survival	Vt
Herbert et al.	16	99	Ib	Restrictive transfusion strategy	MC/RCT	30 days	Survival	Hg
Organ/System								
Maenza et al.	19	96	IIb	Blunt cardiac trauma/myocardial contusion	Meta-analysis		Complications	
Harbreth et al.	20	04	III	Adult splenic injury/trauma center level	Retrospective		Treatment	LOS
Chan et al.	30	05	III	Spinal cord injury/ASIA subgroups	Retrospective	3 mos.	Functional status	
Davis et al.	31	03	III	Intubation in traumatic brain injury	Prospective		Survival	Neurologic outcome
Demetriades et al.	21	05	IIb	Colon injuries/treatment	MC/prospective	72 hrs	Survival	Complications
Wang et al.	28	04	III	Intubation in traumatic brain injury	Registry		Survival	Neurologic outcome
System/Outcome								
Holbrook et al.	17	01	IIb	Gender effect	MC/prospective	18 mos.	Functional outcome	
Gausche et al.	18	00	IIb	Out-of-hospital intubation	Controlled		Survival	Neurologic outcome
Simons et al.	22	02	III	Designation of trauma centers	Comparative		Survival	
Nathens et al.	23	01	III	Trauma center volume	MC/retrospective		Survival	LOS
Larson et al.	24	04	III	Air ambulance use	Retrospective		Survival	LOS
Napolitano et al.	25	01	III	Gender differences following blunt trauma	Retrospective/cohort		Survival	Complications
Osler et al.	26	01	III	Pediatric trauma center designation	Retrospective		Survival	Injury severity
Ferrera et al.	27	00	III	Geriatric trauma	Prospective		Outcome	
Jacobs et al.	29	99	III	Air medical transport	Retrospective		Outcome	

Abbreviations: MC, multicenter; LOS, length of stay; RCT, randomized controlled trial.

REFERENCES

- Davidoff F, Haynes B, Sackett D, et al. Evidence based medicine. *Br Med J* 1995; 310: 1085–6.
- Cook D. Evidence based critical care medicine: a potential tool for change. *New Horiz* 1998; 6: 20.
- Guyatt GH, Sackett D, Sinclair J. Users guide to the medical literature IX. A method for grading health care recommendations. Evidence Based Medicine Working Group. *JAMA* 1995; 274: 1800.
- McCleod R. Evidenced based surgery: what it is and what it is not. *ACS Clinical Congress* 2003; 1.
- Schunemann H, Oxman A, Brozak J, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *Br Med J* 2008; 336: 1106.
- Guyatt G, Oxman A, Kunz R, et al. What is “quality of evidence” and why is it important to clinicians? *Br Med J* 2008; 336: 995.
- Committee on Enhancing Federal Healthcare Quality Programs, Institute of Medicine, Corrigan J, Eden J, Smith B, eds. *Leadership by Example: Coordinating Government Roles in Improving Health Care Quality*. Washington, DC: National Academy Press, 2002.
- Kohn L, Corrigan J, Donaldson M, eds. Institute of Medicine (US) Committee on Quality of Healthcare in America. *To Err Is Human: Building a Safer Health System*. Washington, DC: National Academy Press, 2000.
- Institute of Medicine (US) Committee on Quality of Health Care in America. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academy Press, 2001.
- Rhodes M. Practice management guidelines for trauma care: Presidential address, seventh scientific assembly of the Eastern Association for the Surgery of Trauma. *J Trauma* 1994; 37: 635.
- Fabian T. Evidence-based medicine in trauma care: whither goest thou? *J Trauma* 1995; 47: 225.

12. Moore F. Evidence-based medical information technology: the next generation. *J Trauma* 2007; 63: 1195.
13. Pasquale M. Outcomes for trauma: Is there an end (result) in site. *J Trauma* 2008; 64: 60.
14. Gattinoni L, Tognoni G, Presenti A, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 2001; 345: 568.
15. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342: 1301.
16. Herbert P, Wells G, Blajchman M, et al. A Multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999; 340: 409.
17. Holbrook T, Hoydt D, Anderson J. The importance of gender on outcome after major trauma: functional and physiologic outcomes in women versus men. *J Trauma* 2001; 50: 270.
18. Gausche M, Lewis R, Stratton S, et al. Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome. *JAMA* 2000; 283: 783.
19. Maenza R, Seaberg D, D'Amico F. A meta-analysis of blunt cardiac trauma: ending myocardial confusion. *Am J Emerg Med* 1996; 14: 237.
20. Harbrecht B, Zenati M, Ochoa J, et al. Management of adult blunt splenic injuries: comparison between Level I and Level II trauma centers. *J Am Coll Surg* 2004; 198: 232.
21. Demetriades D, Murray J, Chan L. Penetrating colon injuries requiring resection: diversion or primary anastomosis? An AAST multicenter study. *J Trauma* 2001; 50: 765.
22. Simons R, Kasic S, Kirkpatrick A, et al. Relative importance of designation and accreditation of trauma centers during evolution of a regional trauma system. *J Trauma* 2002; 52: 827.
23. Nathans A, Jurikovich G, Maier R. Relationship between trauma center volume and outcomes. *JAMA* 2001; 285: 1164.
24. Larson J, Dietrich A, Abdessalam S, et al. Effective use of the air ambulance for pediatric trauma. *J Trauma* 2004; 56: 89.
25. Napolitano L, Greco M, Rodriguez A, et al. Gender difference in adverse outcomes after blunt trauma. *J Trauma* 2001; 50: 274.
26. Osler T, Vane D, Tepas J, et al. Do pediatric trauma centers have better survival rates than adult trauma centers? An examination of the National Pediatric Trauma Registry. *J Trauma* 2001; 50: 96.
27. Ferrara P, Bartfield J, D'Andrea C. Outcomes of admitted geriatric trauma victims. *Am J Emerg Med* 2000; 18: 575.
28. Wang H, Peitzman A, Cassidy L, et al. Out-of-hospital endotracheal intubation and outcome after traumatic brain injury. *Ann Emerg Med* 2000; 44: 439.
29. Jacobs L, Gabram S, Stajnkrycer M, et al. Helicopter air medical transport: Ten year outcomes for trauma patients in a New England program. *Conn Med* 1999; 63: 677.
30. Chan S, Chan A. Rehabilitation following traumatic spinal cord injury in a tertiary spinal cord injury center: a comparison with an international standard. *Spinal Cord* 2005; 43: 489.
31. Davis D, Hoydt D, Ochs M, et al. The effect of paramedic rapid sequence intubation on outcome in patients with severe traumatic brain injury. *J Trauma* 2003; 54: 444.
32. Harrison T, Laskosky J, Jazaeri O, et al. "Low dose" recombinant activated factor VII results in less blood loss and blood product use in traumatic hemorrhage. *J Trauma* 2005; 59: 150.
33. Shafi S, Nathans A, Parks J, et al. Trauma quality improvement using risk adjusted outcomes. *J Trauma* 2008; 64: 599.
34. MacKenzie E, Rivara F, Jurokovich G, et al. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med* 2006; 354: 366.
35. Khuri S. Safety, quality and the National Surgical Quality Improvement Program. *Gen Surg News* 2006; 11(S).
36. Leape L, Berwick D. Five years after to err is human: what have we learned? *JAMA* 2005; 293: 2384.
37. Joint Commission on Accreditation of Healthcare Organization. Sentinel event trends: Potassium chloride events by year. 2006; 3 www.jointcommission.org/sentinelevents/statistics.
38. Whittington J, Cohen H. OSF's journey in patient safety. *Qual Manag Health Care* 2004; 13: 53.
39. Rhodes M, Fallow W. How guidelines can serve as outcome tools. *J Surg Outcomes* 1999; 2: 9.
40. Institute of Medicine (US) Committee on Clinical Practice Guidelines, Field MJ, Lohr KN, eds. Guidelines for Clinical Practice: From Development to Use. Washington, DC: National Academy Press, 1992.
41. Collin G, Atkinson N, Furrow K, et al. Decreasing the duration of mechanical ventilation through the use of a ventilator management protocol. *Crit Care Med* 1999; 27: 110.
42. Lewell M, McCauley W, Anderson S. Review of the compliance with advanced trauma life support protocol among patients referred to a Level I trauma center. *Ann Emerg Med* 1999; 34: 531.
43. Palmer S, Bader M, Qureshi A. The impact on outcomes in a community hospital setting of using the AANS traumatic brain injury guidelines. *J Trauma* 2001; 50: 657.
44. Pasquale M, Fabian T. Practice management guidelines for trauma from the Eastern Association for the Surgery of Trauma. *J Trauma* 1998; 44: 941.
45. Agency for Healthcare Policy and Research. Interim Manual for Clinical Practice Guideline Development. Rockville, MD: Agency for Healthcare Policy and Research, 1991.
46. Shojania K, Duncan B, McDonald K, et al., eds. Making Health Care Safer. A Critical Analysis of Patient Safety Practice. AHRQ Publication No. 01-E058, Rockville, MD: Agency for Healthcare Policy and Research July 20, 2001.
47. National Guideline Clearinghouse www.guideline.gov.
48. Kincaid E, Chang M, Letton R, et al. Admission base deficit in pediatric trauma: a study using the National Trauma Data Bank. *J Trauma* 2001; 51: 332.

Evidence-Based Surgery: Military Injury Outcomes

Brian J. Eastridge

Clinical Questions		
Issue	Recommendation	Strength of recommendation
What is the role of a trauma system in combat injury outcomes?	Trauma systems are responsible for improvements in outcome after combat injury and should be a key element of the battlefield medical system.	C
What are the impact damage control measures on the morbidity and mortality of combat injury?	1. Damage control resuscitation should be considered for combat injury requiring massive transfusion.	B
	2. Damage control surgery techniques, including extraabdominal procedures, should be entertained for severe battlefield injury with unstable physiology.	C
	3. The indication for resuscitative thoracotomy should be considered in all patients in extremis, excluding isolated brain injury.	B
What are the contemporary techniques and outcomes of colon surgery performed on the battlefield?	Colon diversion should be performed in patients with high-energy colon injury patients that would not tolerate complications.	C
What are the contemporary techniques and outcomes of vascular surgery performed on the battlefield?	1. Damage control techniques, including shunting, should be utilized to optimize revascularization outcomes.	B
	2. In the combat environment, arterial reconstruction should be performed with autogenous material.	B
	3. In the context of battlefield venous injury, venous ligation is safe and effective option for the management of venous vascular injury.	B
	4. Proximity extremity injury should be evaluated by angiography to mitigate the risk of occult vascular injury.	B
What are the contemporary techniques and outcomes of burn surgery performed on the battlefield?	Burn casualties should be resuscitated based on urine output.	B

INTRODUCTION

The development of trauma care has been a synergistic relationship between the military and civilian medical environments for the past two centuries (1,2). During the Civil War, military physicians realized the utility of prompt attention to the wounded, early debridement, and amputation to mitigate the effects of tissue injury and infection and evacuation of the patient from the battlefield. World War I saw further advances in the concept of evacuation and the development of echelons of medical care. With World War II, blood transfusion and resuscitative fluids, including plasma, were widely introduced into the combat environment, and surgical practice was improved to care for wounded soldiers. From his World War II experiences, Dr. Michael DeBakey, the surgical consultant to the Army Surgeon General, noted that wars have always promoted advances in trauma care due to the concentrated exposure of military hospitals to large numbers. Wartime medical

experience fostered a fundamental drive to improve outcomes by improving practice (3). In Vietnam, more highly trained medics at the point of wounding and prompt aeromedical evacuation decreased battlefield mortality rate even further (4). In addition, concerted efforts to gather combat injury data led to increased insight into the management of injury and improvements in trauma care in the United States (5–7). This chapter reviews the current evidence, including recent practice guidelines, for the prevention and management of upper gastrointestinal bleeding.

WHAT IS THE ROLE OF A TRAUMA SYSTEM IN COMBAT INJURY OUTCOMES?

Trauma centers and trauma systems in the United States have had a remarkable impact on improving outcomes of injured patients (1,4,8–20), reducing mortality by up to 15% in mature systems. With the onset of the conflicts in Iraq

and Afghanistan, a military trauma system was developed and modeled after the successes of civilian systems, and modified to account for the realities of combat. The stated vision of the Joint Theater Trauma System was to ensure that every soldier, marine, sailor, or airperson injured on the battlefield has the optimal chance for survival and maximal potential for functional recovery. The system implementation mandated placement of infrastructure elements, including a trauma registry, performance improvement capability, and research. Data derived from the trauma registry were responsible for several hundred scientific manuscripts and the production of over 30 evidence-based clinical practice guidelines used to optimize combat casualty care. The Joint Theater Trauma System improved information dissemination and performance along the continuum of care, from battlefield wounding through the entire evacuation process, the result being the lowest case fatality rate (10.4%) in the history of warfare (21).

Recommendation

Trauma systems are responsible for improvements in outcome after combat injury and should be a key element of the battlefield medical system. Strength of recommendation: C.

WHAT ARE THE IMPACT DAMAGE CONTROL MEASURES ON THE MORBIDITY AND MORTALITY OF COMBAT INJURY?

In conjunction with damage control resuscitation concepts, which have decreased mortality from 60% to <20% after combat injury requiring massive transfusion (22–26) damage control surgery techniques have dramatically altered the outcomes of soldiers, sailors, airpersons, and marines injured on the battlefield. In the Vietnam War, it was recognized in several case series that temporizing surgical procedures demonstrated a survival advantage when compared to definitive surgical therapy (5). Though apparently temporarily misplaced in antiquity after the Vietnam War, the technique regained notoriety in the treatment of civilian trauma after a hallmark publication by Stone and colleagues that advocated abbreviated celiotomy in patients with abdominal injury with associated coagulopathy and hypothermia (27). Within the past decade, a number of authors have also described the expansion of this life-saving surgical practice to include thoracic, vascular, orthopedic, and neurosurgical procedures (28–32). Eastridge demonstrated the utility of damage control surgical concepts in the current conflict. Of the 1,118 patients in the study, 771 patients required operative intervention. Fifty (6.5%) of the operative patients required damage control procedures. The mechanism of injury precipitating damage control therapy was 90% penetrating (52% gunshot wound, 32% improvised explosive device, 6% indirect fire) and 10% blunt (motor vehicle crash). In this series, damage control procedures were 76% abdominal, 16% vascular, and 8% thoracic. Patients requiring damage control procedures had worse measures of physiology on presentation when compared to the non–damage control cohort, required more packed red blood cells and whole blood, and were more severely injured [Injury Severity Score (ISS 30 > ISS 17)] and had higher associated mortality (38.0% > 4.8%) (33). In

another contemporary analysis, damage control celiotomy performed for battlefield injury was associated with a 73% survival rate. Interestingly, these rates of mortality compare favorably with damage control surgery mortality outcomes of 28–60% quoted in the civilian trauma literature (30,32). In a related study by Edens, 12,536 trauma admissions yielded 101 emergency department thoracotomies (0.01%) (34). In patients undergoing resuscitative thoracotomy, penetrating trauma accounted for the majority of injuries (93%). There were no survivors after thoracotomies for blunt trauma ($n = 7$). Expanding the indication for resuscitative thoracotomy to abdomen (30%) and extremities (22%), 12% (12/101) of all patients requiring thoracotomy survived (34).

Recommendations

1. Damage control resuscitation should be considered for combat injury requiring massive transfusion.
2. Damage control surgery techniques, including extra-abdominal procedures, should be entertained for severe battlefield injury with unstable physiology.
3. The indication for resuscitative thoracotomy should be considered in all patients in extremis, excluding isolated brain injury.

Strength of recommendations: 1: B; 2: C; 3: B.

WHAT ARE THE CONTEMPORARY TECHNIQUES AND OUTCOMES OF COLON SURGERY PERFORMED ON THE BATTLEFIELD?

The practice of colon repair after injury has been intimately related to the lessons learned on the battlefield. In World War II, the propensity for complications and attributable mortality from failed primary colon repair led to a mandate from the British surgeon general to exteriorize all colon injury (35,36). This paradigm was pervasive for the next 50 years of surgical history. Civilian trauma surgeons in the 1990s challenged the veracity of this dogmatic approach and found that primary repair of colon injury was both safe and effective (37–39). However, there remains controversy as to whether the ballistic energy of the combat injury makes this type of enteric injury a different entity from that of the civilian environment. Data on colon injury and management from the Bosnia-Herzegovina conflict from 1992 to 1995 demonstrated no difference in the rate of complications between primary repair and colostomy. Complications, including abscess, leak, and fistula, occurred in 27% of the primary repair group versus 30% of the stoma group. There was a bias toward repair of right colon and exteriorization of left and sigmoid colon injuries in this analysis (40). Duncan et al. demonstrated an overall complication rate of 48% and a leak rate of 30% in a small population of combat injured marines with colon injury managed by primary repair (41). In a separate analysis of casualties from contemporary contingency operations, diversion was compared to primary repair/primary anastomosis. Primary repair was associated with a leak rate of only 10%, and once again, there was an attendant bias to divert colon injuries distal to the splenic

flexure and repair those proximal. Diversion was associated with a significantly lower incidence of complication. Despite the differences in complication between the treatment modalities, there was no attributable increase in sepsis or mortality in the patient population with complications (42). In a series of 65 patients with colon injury, Vertrees noted that primary repair was attempted in right ($n = 18$, 60%), transverse ($n = 11$, 85%), and left ($n = 9$, 38%) colon injuries. Delayed definitive treatment of colon injuries occurred in 42% of patients after damage control celiotomy. Failure of colon repair occurred in 16% of patients and was more likely with concomitant pancreatic, stomach, or renal injury. The associated complication rate for diversion was 30% but increased dramatically to 75% in patients with primary repair or delayed definitive reconstruction failure (43).

Recommendation

Colon diversion should be performed in patients with high-energy colon injury patients that would not tolerate complications. Strength of recommendation: C.

WHAT ARE THE CONTEMPORARY TECHNIQUES AND OUTCOMES OF VASCULAR SURGERY PERFORMED ON THE BATTLEFIELD?

Advances in vascular surgery have been made in times of war. Though conceptualized for over two centuries, the first successful arterial repair for injury was done in 1896 by Murphy (44–46). During World War I, German surgeons reported repair of over 100 arterial injuries and pioneered autogenous reconstruction of injured vessels. However, the proclivity for mass casualty, significant soft tissue injury, and protracted transport times made routine reconstruction impractical, and subsequently ligation of vessels became standard practice (44–46). DeBakey reported 2,471 arterial injuries treated by ligation in World War II with a 49% amputation rate (44–46). Hughes in Korea reported arterial repair as a standard of practice with a 13% amputation rate (47). Similar success were demonstrated by Rich and colleagues from the Vietnam conflict (6,7,45,46).

Improvements in the paradigm of casualty resuscitation during the current conflict have dramatically affected the capability of deployed surgeons to effect vascular repair after injury on the battlefield. Damage control techniques available to surgeons include temporary vascular shunts. Rasmussen et al. demonstrated that 57% of casualties had shunts placed at forward surgical facilities, and 86% of proximal shunts were patent on admission to the combat support hospital. This patency of flow allowed for ongoing resuscitation in the context of a perfused extremity (48). In two separate analyses, Fox et al. showed that damage control resuscitation and damage control surgery techniques applied in the context of vascular injury were associated with the ability to perform prolonged complex limb revascularizations with limb salvage rates of 95% (49,50). Clouse, Sohn, and Fox independently demonstrated acute limb salvage rates for revascularization in theater of 92–95% (51–53). Late complications associated with revascularization included thrombosis, infection, and compartment syndrome (49,51). The factor most significantly associated with

postrevascularization morbidity was the use of prosthetic graft implants. In this population, the incidence of graft loss was 80% (49,51,54).

The management of venous injuries on the battlefield included ligation in 63% and repair in 37%. All patients developed postoperative edema. Thrombosis of the repair was demonstrated in 16% of the repaired veins. There was no acute limb loss associated within venous ligation or venous graft failure (55).

Proximity injury in the civilian penetrating extremity trauma population has been classically managed expectantly after studies by Thal and Frykberg demonstrated no increased incidence of vascular lesions requiring surgical therapy (56–58). However, the high-energy nature of combat wounds lead investigators to reevaluate this diagnostic/management paradigm in the proximity combat penetrating extremity population. In a study of 99 patients who underwent angiography after evacuation for wound proximity, 47% had vascular abnormalities noted on angiography. Two-thirds of this group had a normal physical examination. Of this population with an abnormal angiogram, 52% required operative intervention (59). In a similar analysis by Fox and Gillespie, a similar study of cervical vascular proximity by computerized tomographic angiography detected occult injury in 30% of studies, of which 50% required interventional or surgical management (60).

Recommendations

1. Damage control techniques, including shunting, should be utilized to optimize revascularization outcomes.
2. In the combat environment, arterial reconstruction should be performed with autogenous material.
3. In the context of battlefield venous injury, venous ligation is safe and effective option for the management of venous vascular injury.
4. Proximity extremity injury should be evaluated by angiography to mitigate the risk of occult vascular injury.

Strength of recommendation: 1: B; 2: B; 3: B; 4: B.

WHAT ARE THE CONTEMPORARY TECHNIQUES AND OUTCOMES OF BURN SURGERY PERFORMED ON THE BATTLEFIELD?

The complexity of burn management in the combat environment is manifest across the spectrum of medical care from point of injury through resuscitation, intensive care through the continuum and ultimately definitive surgical care. Contemporary data from the battlefield demonstrates that 52–63% of burn injuries are battle injury (61,62). The majority of these burns are associated with explosive etiology. Early surgical care for burn injury is limited to escharotomy and debridement of devitalized tissue. The most challenging phase of the battlefield burn casualty is the intensive care evacuation process performed by the U.S. Air Force Critical Care Air Transport Team and the U.S. Army Burn Flight Team. Classically, burn resuscitation has been practiced on a paradigm based on weight and body surface area burned, according to the guidelines developed at the Parkland Memorial Hospital and the Brooke Army

Burn Center. Ennis et al. reported that a urine output–based resuscitation paradigm tracked by a flow sheet resulted in a decrease in the rate of resuscitation associated abdominal compartment syndrome from 16% to 5% with an attendant decrease in mortality (63). In a separate study of burn injuries from combat versus the civilian environment, Wolf and colleagues showed that the most important

effectors of burn related mortality were total body surface area burned, age ≥ 40 , and the presence of inhalation injury (62).

Recommendation

Burn casualties should be resuscitated based on urine output. Strength of recommendation: B.

Levels of Evidence

Issue	Recommendation	Level of evidence	Strength of recommendation	Ref.
What is the role of a trauma system in combat injury outcomes?	Trauma systems are responsible for improvements in outcome after combat injury and should be a key element of the battlefield medical system.	II	C	21
What are the impact damage control measures on the morbidity and mortality of combat injury?	1. Damage control resuscitation should be considered for combat injury requiring massive transfusion.	II	B	22–26
	2. Damage control surgery techniques, including extra-abdominal procedures, should be entertained for severe battlefield injury with unstable physiology.	II	C	27–33
	3. The indication for resuscitative thoracotomy should be considered in all patients in extremis, excluding isolated brain injury.	II	B	34
What are the contemporary techniques and outcomes of colon surgery performed on the battlefield?	Colon diversion should be performed in patients with high-energy colon injury patients that would not tolerate complications.	II–III	C	35–43
What are the contemporary techniques and outcomes of vascular surgery performed on the battlefield?	1. Damage control techniques, including shunting should be utilized to optimize revascularization outcomes.	II	B	48–50
	2. In the combat environment, arterial reconstruction should be performed with autogenous material.	II	B	51–54
	3. In the context of battlefield venous injury, venous ligation is safe and effective option for the management of venous vascular injury.	II	B	55
	4. Proximity extremity injury should be evaluated by angiography to mitigate the risk of occult vascular injury.	II	B	58–60
What are the contemporary techniques and outcomes of burn surgery performed on the battlefield?	Burn casualties should be resuscitated based on urine output.	II	B	63

REFERENCES

- Trunkey DD. History and development of trauma care in the United States. *Clin Orthop Relat Res* 2000; 374: 36–46.
- Trunkey DD. In search of solutions. *J Trauma* 2002; 53: 1189–91.
- DeBaey ME. History, the torch that illuminates: lessons from military medicine. *Mil Med* 1996; 161: 711–16.
- Hoff WS, Schwab CW. Trauma system development in North America. *Clin Orthop Relat Res* 2004; 422: 17–22.
- Rich NM. Vietnam missile wounds evaluated in 750 patients. *Mil Med* 1968; 133: 9–22.
- Rich NM, Baugh JH, Hughes CW. Acute arterial injuries in Vietnam: 1,000 cases. *J Trauma* 1970; 10: 359–69.
- Rich NM, Hughes CW. Vietnam vascular registry: a preliminary report. *Surgery* 1969; 65: 218–26.
- Demetriades D, Kimbrell B, Salim A, et al. Trauma deaths in a mature urban trauma system: is “trimodal” distribution a valid concept? *J Am Coll Surg* 2005; 201: 343–8.
- Jurkovich GJ, Mock C. Systematic review of trauma system effectiveness based on registry comparisons. *J Trauma* 1999; 47(3 Suppl): S46–55.
- Mann NC. Assessing the effectiveness and optimal structure of trauma systems: a consensus among experts. *J Trauma* 1999; 47(3 Suppl): S69–74.
- Mann NC, Mullins RJ. Research recommendations and proposed action items to facilitate trauma system implementation and evaluation. *J Trauma* 1999; 47(3 Suppl): S75–8.
- Mann NC, Mullins R, MacKenzie E, et al. Systematic review of published evidence regarding trauma system effectiveness. *J Trauma* 1999; 47(3 Suppl): S25–33.
- Mullins RJ. A historical perspective of trauma system development in the United States. *J Trauma* 1999; 47(3 Suppl): S8–14.
- Mullins RJ, Mann NC. Population-based research assessing the effectiveness of trauma systems. *J Trauma* 1999; 47(3 Suppl): S59–66.

15. Mullins RJ, Mann NC. Introduction to the academic symposium to evaluate evidence regarding the efficacy of trauma Systems. *J Trauma* 1999; 47(3 Suppl): S3-7.
16. Mullins RJ, Veum-Stone J, Hedges J, et al. Influence of a statewide trauma system on location of hospitalization and outcome of injured patients. *J Trauma* 1996; 40: 536-45; discussion 545-6.
17. Nathens AB, Jurkovich G, Rivara F, et al. Effectiveness of state trauma systems in reducing injury-related mortality: a national evaluation. *J Trauma* 2000; 48: 25-30; discussion 30-1.
18. O'Keefe GE, Jurkovich G, Copass M, et al. Ten-year trend in survival and resource utilization at a Level I trauma center. *Ann Surg* 1999; 229: 409-15.
19. Trunkey DD. Trauma care systems. *Emerg Med Clin North Am* 1984; 2: 913-22.
20. West JG, Williams M, Trunkey D, et al. Trauma systems. Current status—future challenges. *JAMA* 1988; 259: 3597-600.
21. Eastridge BJ, Jenkins D, Flaherty S, et al. Trauma system development in a theater of war: experiences from operation Iraqi freedom and operation enduring freedom. *J Trauma* 2006; 61: 1366-72; discussion 1372-3.
22. Cancio LC, Wade C, West S, et al. Prediction of mortality and of the need for massive transfusion in casualties arriving at combat support hospitals in Iraq. *J Trauma* 2008; 64(2 Suppl): S51-5; discussion S55-6.
23. Hess JR, Dutton R, Holcomb J, et al. Giving plasma at a 1:1 ratio with red cells in resuscitation: who might benefit? *Transfusion* 2008; 48: 1763-5.
24. Spinella PC, Perkins J, Grathwohl K, et al. Effect of plasma and red blood cell transfusions on survival in patients with combat related traumatic injuries. *J Trauma* 2008; 64(2 Suppl): S69-77; discussion S77-8.
25. Spinella PC, Perkins J, McLaughlin D, et al. The effect of recombinant activated factor VII on mortality in combat-related casualties with severe trauma and massive transfusion. *J Trauma* 2008; 64: 286-93; discussion 293-4.
26. Stinger HK, Spinella P, Perkins J, et al. The ratio of fibrinogen to red cells transfused affects survival in casualties receiving massive transfusions at an army combat support hospital. *J Trauma* 2008; 64(2 Suppl): S79-85; discussion S85.
27. Stone HH, Strom PR, Mullins PR. Management of the major coagulopathy with onset during laparotomy. *Ann Surg* 1983; 197: 532-5.
28. Johnson JW, Gracias V, Schwab C, et al. Evolution in damage control for exsanguinating penetrating abdominal injury. *J Trauma* 2001; 51: 261-9; discussion 269-71.
29. Rotondo MF, Bard MR. Damage control surgery for thoracic injuries. *Injury* 2004; 35: 649-54.
30. Rotondo MF, et al. "Damage control": an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993; 35: 375-82; discussion 382-3.
31. Rotondo MF, Zonies MF. The damage control sequence and underlying logic. *Surg Clin North Am* 1997; 77: 761-77.
32. Shapiro MB, et al. Damage control: Collective review. *J Trauma* 2000; 49: 969-78.
33. Eastridge BJ. Damage control surgery in a combat environment. *Arch Surg* 2008 to Blackbourne, Combat damage control surgery. *Crit Care Med*. 2008; 36(Suppl 7): S304-10.
34. Edens J. Emergency department thoracotomy in combat. *J Trauma* 2008 (Accepted).
35. Imes PR. Chemotherapy in traumatic surgery of the abdomen. *Ann Surg* 1946; 123: 44-7.
36. Imes PR. The emergency management of abdominal trauma. *Surg Clin North Am* 1956; 1289-94.
37. George SM Jr, Fabian TC, Mangiante EC. Colon trauma: further support for primary repair. *Am J Surg* 1988; 156: 16-20.
38. Fabian TC. Infection in penetrating abdominal trauma: risk factors and preventive antibiotics. *Am Surg* 2002; 68: 29-35.
39. Stone HH, Fabian TC. Management of perforating colon trauma: randomization between primary closure and exteriorization. *Ann Surg* 1979; 190: 430-6.
40. Hudolin T, Hudolin I. The role of primary repair for colonic injuries in wartime. *Br J Surg* 2005; 92: 643-7.
41. Duncan JE, Corwin C, Sweeney W, et al. Management of colorectal injuries during operation Iraqi freedom: patterns of stoma usage. *J Trauma* 2008; 64: 1043-7.
42. Steele SR, Wolcott K, Mullenix P, et al. Colon and rectal injuries during operation Iraqi freedom: are there any changing trends in management or outcome? *Dis Colon Rectum* 2007; 50: 870-7.
43. Vertrees A. Colon injury management in war. *Am Coll Surg* 2008; 207: 801-9.
44. Rich NM, Rhee P. An historical tour of vascular injury management: from its inception to the new millennium. *Surg Clin North Am* 2001; 81: 1199-215.
45. Rich N. Military surgery: "Bullets and blood vessels." *Surg Clin North Am* 1978; 58: 995-1003.
46. Rich NM. Vascular trauma. *Surg Clin North Am* 1973; 53: 1367-92.
47. Hughes CW. The primary repair of wounds of major arteries; an analysis of experience in Korea in 1953. *Ann Surg* 1955; 141: 297-303.
48. Rasmussen TE, Clouse W, Perkins D, et al. The use of temporary vascular shunts as a damage control adjunct in the management of wartime vascular injury. *J Trauma* 2006; 61: 8-12; discussion 12-15.
49. Fox CJ, Gillespie D, Cox E, et al. Damage control resuscitation for vascular surgery in a combat support hospital. *J Trauma* 2008; 65: 1-9.
50. Fox CJ, Gillespie D, Cox E, et al. The effectiveness of a damage control resuscitation strategy for vascular injury in a combat support hospital: results of a case control study. *J Trauma* 2008; 64(2 Suppl): S99-106; discussion S106-7.
51. Fox CJ, Gillespie D, O'Donnell S, et al. Contemporary management of wartime vascular trauma. *J Vasc Surg* 2005; 41: 638-44.
52. Clouse WD, Rasmussen T, Pexck M, et al. In-theater management of vascular injury: 2 years of the balad vascular Registry. *J Am Coll Surg* 2007; 204: 625-32.
53. Sohn VY, Arthurs Z, Herbert G, et al. Demographics, treatment, and early outcomes in penetrating vascular combat trauma. *Arch Surg* 2008; 143: 783-7.
54. Rasmussen TE, Clouse W, Jenkins D, et al. Echelons of care and the management of wartime vascular injury: a report from the 332nd EMDG/air force theater hospital, balad air base, Iraq. *Perspect Vasc Surg Endovasc Ther* 2006; 18: 91-9.
55. Quan RW, Gillespie D, Stuart R, et al. The effect of vein repair on the risk of venous thromboembolic events: a review of more than 100 traumatic military venous injuries. *J Vasc Surg* 2008; 47: 571-7.
56. Dennis JW, Frykberg E, Crump J, et al. New perspectives on the management of penetrating trauma in proximity to major limb arteries. *J Vasc Surg* 1990; 11: 84-92; discussion 92-3.
57. Frykberg ER, Crump J, Vines F, et al. A reassessment of the role of arteriography in penetrating proximity extremity trauma: a prospective study. *J Trauma* 1989; 29: 1041-50; discussion 1050-2.
58. Francis H III, Thal E, Weigelt J, et al. Vascular proximity: Is it a valid indication for arteriography in asymptomatic patients? *J Trauma* 1991; 31: 512-14.
59. Johnson ON III, Fox C, White P, et al. Physical exam and occult post-traumatic vascular lesions: implications for the evaluation and management of arterial injuries in modern

- warfare in the endovascular era. *J Cardiovasc Surg (Torino)* 2007; 48: 581–6.
60. Fox CJ, Gillespie D, Weber M, et al. Delayed evaluation of combat-related penetrating neck trauma. *J Vasc Surg* 2006; 44: 86–93.
61. Kauvar DS, Wolf S, Wade C, et al. Burns sustained in combat explosions in Operations Iraqi and Enduring Freedom (OIF/OEF explosion burns). *Burns* 2006; 32: 853–7.
62. Wolf SE, Kauvar D, Wade C, et al. Comparison between civilian burns and combat burns from Operation Iraqi Freedom and Operation Enduring Freedom. *Ann Surg* 2006; 243: 786–92; discussion 792–5.
63. Ennis JL, Chung J, Renz E, et al. Joint theater trauma system implementation of burn resuscitation guidelines improves outcomes in severely burned military casualties. *J Trauma* 2008; 64(2 Suppl): S146–51; discussion S151–2.

Evidence-Based Surgery: Traumatized Airway

Edgar J. Pierre and Amanda Saab

Clinical Questions		
Question	Answer	Grade
What are the LeFort fractures?	To ensure a positive outcome, a strong degree of suspicion based on mechanism of injury is mandated.	B
How would you secure the airway after a penetrating injury to the airway?	Avoid blind nasal intubation in facial trauma. Early oral intubation or tracheostomy.	B
Define neck injuries	Penetrating injuries are usually described according to the entrance site as one of three zones of the neck. An additional classification system divides the neck into anterolateral or posterior portions, divided by the sternocleidomastoid muscle.	B
How do you evaluate and diagnose penetrating neck injuries?	Following brief training (e.g., the Advanced Trauma Life Support course) physicians are capable of performing emergency cricothyroidotomy in the field with a high success rate and minimal complications, regardless of medical specialty.	B
What is the optimal management of the airway in someone with penetrating neck injury?	Concomitant cervical spine injury should not delay appropriate and timely treatment of facial fractures because adequate means of intraoperative stabilization are readily available. LMA have been shown to be effective in the management of difficult airway.	B

INTRODUCTION

Acute airway trauma is a rare yet potentially lethal injury. It is traditionally classified as blunt or penetrating according to the mechanism. Blunt trauma remains the more prevalent mechanism, although the incidence of penetrating trauma has been steadily increasing over the past 30 years (1). The majority of blunt trauma is due to motor vehicle collisions, closely followed by sport-related and domestic violence-related trauma. The source of most penetrating injuries is secondary to gunshot or stab wounds.

The primary goals of airway intervention are to relieve or prevent airway obstruction, secure the unprotected airway from aspiration, provide adequate gas exchange, and maintain cervical spine stabilization. Gaining control of the traumatized airway is the ultimate test to the of the provider's adeptness and clinical acumen as the provider must assume that the patient has a full stomach and an unstable cervical spine, two conditions that exacerbate an already difficult task. It requires knowledge of the hazards encountered secondary to the injury itself as well as those resulting from interventions by the anesthesiologist.

When a trauma patient arrives to the emergency room or resuscitation bay, the initial moments should be devoted to obtaining the most basic information about the overall condition: stable, unstable, moribund, or deceased. The primary survey of the Advanced Trauma Life Support protocol involves rapid evaluation and stabilization of the

functions that are crucial to survival: airway patency, breathing, circulation with hemorrhage control, evaluation of disability with brief neurologic exam, and exposure of the patient by removal of all articles of clothing.

During these initial moments of the encounter, the anesthesiologist must be attentive to any signs of airway trauma, as the most critical step in management of acute airway trauma is recognition of the condition. The physician should have a high index of suspicion in the setting of anterior cervical trauma. Symptoms such as hoarseness, dyspnea, dysphagia, dysphonia, and pain with phonation are frequently seen with laryngeal trauma, whereas crepitus, stridor, hemoptysis, anterior cervical edema, ecchymoses, and laceration are usually representative of laryngeal-tracheal injury (1–19). For patients with laryngeal-tracheal injury, airway control is fundamental and should be as rapid as possible.

Control of the traumatized airway can be obtained by either routine intubation or tracheostomy. The decision is ultimately the result of the location of the injury as well as the provider's comfort level with each method. Whereas most anesthesiologists are extremely comfortable with intubation via direct or fiber optic laryngoscopy, surgeons generally have more experience fashioning a surgical airway. At first glance, endotracheal intubation may seem to be the most helpful and efficient method of gaining airway control, however, a tracheostomy can be advantageous in certain situations. For injuries at or just below the

level of the larynx, a tracheostomy provides space with which to examine the site of injury both at the site and from above with direct laryngoscopy. Endotracheal intubation might render further examination of the injury difficult and might aggravate an existing laryngeal injury. At the Ryder Trauma Center, specific guidelines have been developed for the management of penetrating neck injuries. We suggest using awake fiber optic intubation, rapid sequence fiber optic intubation, rapid sequence induction, or awake orotracheal intubation depending on the severity or emergency need for an airway. If any of these methods fail, a surgical airway through a cricothyroidotomy should be established, recognizing the risk of laryngeal tracheal separation in patients with large injuries.

HOW WOULD YOU EVALUATE THE AIRWAY?

Trauma to the face and upper airway poses particular difficulties. Failure to identify an injury to the face or neck can lead to acute or subacute airway obstruction secondary to swelling and hematomas. In patients with severe facial injuries, early oral intubation is recommended before swelling and edema compromise the airway.

It is imperative that the trauma team remain cognizant of the fact that many patients who have sustained this type of injury often prefer to take the sitting position because it is easier for them to maintain a patent airway when seated as opposed to the supine position. Assuming no absolute contraindications to this position exist, these patients should be allowed and encouraged to remain seated until the trauma team is ready to manage the patient's airway definitively. Facial and pharyngeal injuries also pose a particular danger because their gory appearance (i.e., cribiform plate injuries with cerebrospinal fluid leak) may serve to distract from other critical injuries that often occur in this setting, such as cervical spine instability. Careful axial traction should be applied to stabilize the cervical spine during intubation.

Most facial injuries are obvious and can be recognized by hemorrhage, edema, erythema, and facial distortion. In a minority of cases, mainly isolated facial blunt trauma, edema and erythema may not appear in the very early stages. In this case, crepitus on palpation, hoarse voice, drooling, and refusal to obtain the supine posture should alert for facial injury and/or airway injury.

WHAT ARE THE LEFORT FRACTURES?

Significant injury to the upper airway is uncommon, with a reported incidence of 0.03–2.8% of all trauma patients. Most upper airway injuries are secondary to direct blunt or penetrating trauma (knife or gunshot) or severe flexion-extension injuries. A patient with blunt or penetrating injury of the midface, mandible, or oral cavity is at risk of brain damage or death from upper airway obstruction. The most common fractures involve the mandible and midface maxilla, referred to as the LeFort fractures.

Fragmentation of bone and teeth and disruption of adjacent soft tissues characterize severe injuries of the mandible. Floor of the mouth tears can extend to the pharynx, tonsil, submaxillary triangle, and hyoid bone.

Midface fractures, or LeFort fractures of the maxilla, often present difficult clinical problems. Motion of the

maxilla independent of the remainder of the face indicates a LeFort I fracture. In addition, the LeFort II fracture can extend through the orbital rim, medial orbital wall, ethmoid sinuses, and nose. Injury of the ethmoid sinus roof or cribiform plate may result in cerebrospinal fluid rhinorrhea, meningitis, or temporary or permanent loss of smell. LeFort III fracture is a transverse fracture above the malar bone and through the orbits. It is characterized by complete separation of the maxilla from the craniofacial skeleton, epistaxis, and a flat dish-face deformity.

Penetrating trauma to the face can be described by a number of facial zones divisions. The simplest one divides the face to midface and mandibular zones. Practically all stab wounds and most gunshot wounds (71%) are to the midface zone (13).

Recommendation: To ensure a positive outcome, a strong degree of suspicion based on mechanism of injury is mandated. Recommendation grade: B.

HOW WOULD YOU SECURE THE AIRWAY AFTER A PENETRATING INJURY TO THE AIRWAY?

Because of the extreme urgency in these situations, assessment of the airway should be almost entirely clinical. Important findings to note include anxiety, stridor, ability or inability to phonate, adequacy of air movement through the mouth and nares, presence of tracheal deviation, the use of accessory muscles of respiration, and movement of the diaphragm.

Findings such as intraoral hemorrhage, pharyngeal erythema, mandibular injuries, and change in voice are all indications for early intubation. Bilateral mandibular fractures and pharyngeal hemorrhage may lead to upper airway obstruction, particularly in a supine patient. Therefore, a patient found in the sitting or prone position because of airway compromise is best left in that position until the moment of anesthetic induction and intubation (2).

Because facial and pharyngeal injuries pose difficult (yet not impossible) intubation situations, it is imperative that intubation be attempted in a controlled environment that is equipped to execute the difficult airway algorithm. An oropharyngeal or nasopharyngeal airway may be required to temporarily maintain airway patency until these conditions are met (12). Rapid sequence intubation with cervical in-line immobilization is the preferred method of intubating the trachea of the trauma patients.

However, prolonged struggle to intubate may be a misuse of the Golden Hour, compromising the patient's respiratory status and elevating intracranial pressure. Cricothyroidotomy is a useful alternative. Perhaps early cricothyroidotomy, rather than repeated multiple attempts to intubate, would result in less hypoxia and improved patient outcome. Emergency tracheotomy is not considered an appropriate method to establish emergency definitive airway as the procedure is lengthy and carries significant rate of complications. In a series of 71 patients with laryngeal-tracheal trauma, 39 (54.9%) required an emergency airway. Forty-eight percent of patients underwent initial orotracheal intubation, whereas tracheostomy and cricothyroidotomy were performed in 4% each. Patients with blunt laryngotracheal trauma required an emergency airway in 78.9% of cases, whereas those with penetrating injuries required one in 46.2%. Intubation was successful in 14 of

the 15 patients in the blunt trauma group and 20 of the 24 patients in the penetrating trauma group (2).

Recommendation: Avoid blind nasal intubation in facial trauma. Early oral intubation or tracheostomy. Recommendation grade: B.

DEFINE NECK INJURIES

The neck is a very narrow corridor containing the main airway and digestive conduits, the cervical spinal cord, and its nerves. Because each of these components is vital to life, injury to the neck carries a high rate of mortality and morbidity (7). Injury to the neck is classified by both the mechanism and location. Obstructive injury to the airway is the second most common cause of death associated with trauma to the head and neck (3). Mild to moderate trauma may cause tissue edema, hematoma, or mucosal tears. Severe injuries can result in disruption of the airway, neurovascular bundle, and visceral rupture (6). Fortunately, injuries to the cervical aerodigestive tract are uncommon, ranging from 1.2% in blunt trauma to 10.2% in penetrating injuries to the neck (10).

The most important injuries in the neck include:

- Disruption of tracheal continuity (partial/total).
- Fractures of larynx/cricoid obstructing the airway.
- Major arterial/venous bleeding leading to hemorrhagic shock.
- Cervical spine injury causing apnea or neurogenic shock.
- Perforation of esophagus.

Penetrating neck trauma due to gunshot, knife, or other foreign body presents many challenges for surgical and anesthetic management. The neck zones contain the airway, vascular, and neurologic structures within a confined space and therefore poses potential for disastrous outcome when any of these structures are injured.

Penetrating injuries are usually described according to the entrance site as one of three zones of the neck. Zone I extends from the clavicles to the cricoid cartilage and injury to this zone carries a high mortality. In addition to neck organs it contains upper thoracic lung and blood vessels. Zone II lies between the cricoid cartilage and the angle of the mandible. It contains major cervical arteries and veins as well as extrathoracic air and food tracts. Despite being the most frequently injured area, the associated mortality is significantly lower due to facilitated surgical access. Zone III comprises the area between the base of skull and the angle of the mandible. This area is difficult to approach surgically (5).

An additional classification system divides the neck into anterolateral or posterior portions, divided by the sternocleidomastoid muscle. Naturally, injury to the anterolateral part is more dangerous because of the proximity to the trachea, larynx, and cervical vessels (5).

Blunt laryngotracheal injury may be caused by three mechanisms:

- Direct: vehicular dashboard, human assault (i.e., strangulation), sports injury (ball, baseball bat, etc.), fall from height, and hanging.
- Deceleration injury: Car accidents and fall from height can exert shearing injuries to fixed organs such as the cricoid cartilage or tracheal carina.

- Increased pressure: Sudden anteroposterior chest compression against closed glottis can cause abrupt increase in intrathoracic pressure. The result can be linear rupture of the posterior membranous trachea (7,9).

Coexisting Injuries

It is extremely important to realize that blunt neck trauma is associated with other injuries in a rate as high as 50% or higher. Spine, maxillofacial fractures, chest trauma, and closed head injuries are some of the associated injuries that are both common and obvious, distracting from the potentially lethal blunt neck injury (7).

Recommendation: Penetrating injuries are usually described according to the entrance site as one of three zones of the neck. An additional classification system divides the neck into anterolateral or posterior portions, divided by the sternocleidomastoid muscle. Recommendation grade: B.

HOW DO YOU EVALUATE AND DIAGNOSE PENETRATING NECK INJURIES?

The diagnosis of penetrating neck trauma is usually simple because the injury is obvious (3). On the contrary, diagnosis of blunt neck trauma depends on a high index of suspicion (3).

Clinical examination remains the most reliable sign of laryngotracheal injury. The only hard diagnostic sign to laryngotracheal trauma is air leaking through the neck wound, which is often difficult to definitively identify. Equally as critical is the prompt identification of subcutaneous emphysema through the detection of crepitus to palpation over the anterior face, neck, and upper chest. Patients with neck injury may also have dyspnea, hemoptysis, hoarseness, stridor, and crepitus on palpation (2,14). The symptoms associated with these injuries are secondary to the soft tissue swelling, including the sensation of choking, dyspnea, dysphagia, hoarseness, and stridor experienced by these patients (6).

The quality of the victim's voice (i.e., hoarseness) is unpredictable. However, a hoarse patient suffers major airway injury until proven otherwise. A hoarse voice should only be assumed to exist prior to the injury only if an awake and oriented patient can confirm this.

Trauma is a dynamic disease, especially in the acute phase. Because the patient's condition can change very quickly, frequent reassessment of the patient's state is essential. Frequent checks of the patient also help identify the propagation of edema and hematoma that can lead to an insidious airway obstruction.

Recommendation: Following brief training (e.g., the Advanced Trauma Life Support course) physicians are capable of performing emergency cricothyroidotomy in the field with a high success rate and minimal complications, regardless of medical specialty. Recommendation grade: B.

WHAT IS THE OPTIMAL MANAGEMENT OF THE AIRWAY IN SOMEONE WITH PENETRATING NECK INJURY?

The most urgent priority in neck trauma is securing the airway. The end result should be an orotracheal tube

with an inflated sealed cuff positioned entirely distal to a laryngotracheal perforation. Nevertheless, intubation of the trachea might be extremely difficult as pharyngeal or neck hematoma might obscure the vocal cords or distort the anatomy. Passing an endotracheal tube blindly is dangerous because it may follow or produce a false route. In the instance of a partial transection, an endotracheal tube advanced with zeal may cause complete laryngotracheal separation (4,9).

In light of the possible hazards, the obvious conclusion is to avoid tracheal intubation on the scene or emergency department, assuming a stable patient. The more common neck injuries, such as stab wounds and low-velocity gunshot wounds, do not mandate prehospital or emergency department intubation. In this case, intubation should be performed in operating room by the most experienced available anesthesiologist, equipped by appropriate instruments and availability of a surgical airway. On the contrary, high-velocity gunshots bullets and severe blunt neck injuries often mandate urgent airway control (14).

Traditionally, rapid sequence orotracheal intubation is necessary. Concomitant preparation for fiber optic assurance of the proper tube position as well as continuing preparations for establishment of surgical airway via cricothyroidotomy is mandatory. Emergency tracheotomy is not considered an appropriate method to establish emergency definitive airway because the procedure is lengthy and carries significant rate of complications.

An unstable patient with a slashed throat can be intubated through the incision as a life-saving act that may be the only practical alternative for if artificial airway establishment cannot be delayed until hospital arrival. In the past, cricothyroidotomy or tracheotomy was the procedure of choice even in hospitals (7).

Signs indicative of vascular injuries include hematoma, shock, and persistent bleeding (6). The hematoma can be limited without jeopardizing the airway. Bleeding and edema formation is obviously higher in patients treated with anticoagulants. In this case, a critical point might be reached in which the airway will be obstructed and the patient will deteriorate abruptly (6). It is reasonable to postpone tracheal intubation to the hospital because of the inability to predict the clinical course and the anticipated difficult tracheal intubation, such as a bulging hematoma and soft tissue swelling. Nevertheless, close monitoring of the patient as well as the size of hematoma is crucial. Preventive intubation should be done if the hematoma

enlarges or if the patient shows progressive signs of airway compromise. Low threshold for intubation is advocated if the evacuation time is long or if health provider skills are limited. In the prehospital, emergency department, and operating room, difficult intubation should be anticipated, and the technique is to be planned accordingly.

Once the airway is secured, a meticulous diagnostic workup is to be started to verify the exact location of injury and choose the appropriate surgical intervention. This workup will mostly include fiber optic examination of the pharynx, larynx, trachea, and esophagus. Other modalities can include chest and neck radiographs, computed tomography, angiography, and contrast swallow fluoroscopy.

Recommendation: Concomitant cervical spine injury should not delay appropriate and timely treatment of facial fractures because adequate means of intraoperative stabilization are readily available. Laryngeal Mask Airway (LMA) have been shown to be effective in the management of difficult airway. Recommendation grade: B.

SUMMARY

Penetrating trauma is usually obvious, whereas blunt trauma mandates a high index of suspicion to recognize its existence. Comprehensive injury understanding is mandatory to plan the best timing and method to secure the airway. If the airway is stable, it is advised that airway control will be carried out in operating room, by the most experienced anesthesiologist available, with the availability of a surgical airway. In any doubt it is better to maintain spontaneous ventilation.

KEY POINTS

- Facial and neck injuries carry significant risk for airway compromise.
- The traumatized airway can be associated with other life-threatening injuries and cervical spine involvement.
- Penetrating trauma is usually obvious, whereas blunt might be obscure.
- Repeated assessment is vital because airway obstruction might be insidious.
- Gunshot and mandibular penetrating injuries carries the highest risk for the need to emergency airway control.

Traumatized Airway Level of Evidence and Grades of Recommendation

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
What are the LeFort fractures?							
Kaufman	13	1999	III	Le fort Fractures	CS	NR	To ensure a positive outcome, a strong degree of suspicion based on mechanism of injury is mandated
How would you secure the airway after a penetrating injury to the airway?							
Walls	12	1997	Ia	Laryngeal-tracheal trauma	RCS	NR	Avoid blind nasal intubation in facial trauma
Dutton	2	2005	III	Anesthesia	RCS	NR	Early oral intubation or tracheostomy
Define neck injuries							
Santhanagoppalan	7	2000	III	Airway	RCS	NR	LMA have been shown to be effective in the management of difficult airway. We recommend that training in the use of these devices be made mandatory
Chen	3	1996	III	Airway	RCT	There was no significant difference in the prevalence of complications between gunshot, shotgun, and stab wounds	Gunshot wounds were more likely to require emergent airway establishment than shotgun wounds or stab wounds. A higher prevalence of globe injury among shotgun wounds than among gunshot wounds
Leibovici	6	1997	III	Airway	RCT	There was no evidence of higher success rate when the performers were surgeons, anesthesiologist, intensive care specialists (100% success), compared to that of all other specialties (83.33%)	These results show that following brief training (e.g., the Advanced Trauma Life Support course) physicians are capable of performing emergency cricothyroidotomy in the field with a high success rate and minimal complications, regardless of medical specialty
Marlow	10	1997	III	Airway	CS	NR	Avoid blind nasal intubation in facial trauma
Chesshire	5	2001	IV	Facial trauma	CS	NR	The possibility of occult hemorrhage due to other injuries must never be forgotten
Neal	9	1996	III	Fiber optic intubation	CS	NR	Intubation in the semi-prone position may be a useful technique in injuries of this type
How do you evaluate and diagnose penetrating neck injuries?							
Chen	3	1996	III	Airway	CRS		There was no significant difference in the prevalence of complications between gunshot, shotgun, and stab wounds ($p = 0.18$)
Dutton	2	2005	Ia	Airway	RCS	NR	Early oral intubation or tracheostomy
Keogh	14	2002	IV	Neck injury	CS	NR	Patients with a history of blunt neck trauma may initially appear stable, then quickly decompensate and require an emergency airway

(Continued)

Traumatized Airway Level of Evidence and Grades of Recommendation (Continued)

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Leibovici	6	1997	III	Airway	RCT	There was no evidence of higher success rate when the performers were surgeons, anesthesiologists, or intensive care specialists (100% success), compared to that of all other specialties (83.33%)	These results show that following brief training (e.g., the Advanced Trauma Life Support course) physicians are capable of performing emergency cricothyroidotomy in the field with a high success rate and minimal complications, regardless of medical specialty
What is the optimal management of the airway in someone with penetrating neck injury?							
Merritt	4	1997	III	Airway	CS	NR	Concomitant cervical spine injury should not delay appropriate and timely treatment of facial fractures because adequate means of intraoperative stabilization are readily available
Neal	9	1996	III	Fiberoptic intubation	CS	NR	Intubation in the semi-prone position may be a useful technique in injuries of this type
Keogh	14	2002	III	Neck Injury	CS	NR	Patients with a history of blunt neck trauma may initially appear stable, then quickly decompensate and require an emergency airway
Santhanagoppalan	7	2000	III	Airway	RCS	NR	LMA have been shown to be effective in the management of difficult airway. We recommend that training in the use of these devices be made mandatory
Leibovici	6	1997	III	Airway	CRS	NR	There was no evidence of higher success rate when the performers were surgeons, anesthesiologists, or intensive care specialists (100% success), compared to that of all other specialties (83.33%)

Abbreviations: CS, case series (retrospective); NR, not reported; RCS, retrospective cohort study; RCT, randomized control trial.

REFERENCES

- Kadish H, Schunk J, Woodward GA. Blunt pediatric laryngo-tracheal trauma: case reports and review of the literature. *Am J Emerg Med* 1994; 12: 207–11.
- Dutton RP, McCunn M. Anesthesia for trauma. In: Miller RD, ed. *Miller's Anesthesia*. Philadelphia: Churchill Livingstone, 2005: 2451–9.
- Chen AY, Stewart MG, Raup G. Penetrating injuries of the face. *Otolaryngol Head Neck Surg* 1996; 115: 464–70.
- Merritt RM, Williams MF. Cervical spine injury complicating facial trauma: incidence and management. *Am J Otolaryngol* 1997; 18: 235–8.
- Chesshire N, Knight DJW. The anaesthetic management of facial trauma and fractures. *BJA CEPD Rev* 2001: 1.
- Leibovici D, Friedman B, Gofrit ON, et al. Prehospital cricothyroidotomy by physician. *Am J Emerg Med* 1997; 15: 91–3.
- Santhanagoppalan K, Chestnutt N, McBride G. Intubating LMA guided awake fiberoptic intubation in severe maxillo-facial trauma. *Can J Anesth* 2000; 47: 989–91.
- Patteson SK, Epps JL, Hall J. Simultaneous oral and nasal tracheal intubation utilizing a fiberoptic scope in a patient with facial trauma. *J Clin Anesth* 1996; 8: 258–9.
- Neal MR, Groves J, Gell IR, et al. Awake fiberoptic intubation in the semiprone position following facial trauma. *Anaesthesia* 1996; 51: 1053–4.
- Marlow TR, Goltra DD, Schabel SI. Intracranial placement of a nasotracheal tube after facial fracture: a rare complication. *J Emerg Med* 1997; 15: 187–91.

11. Rosen CL, Wolfe RE, Chew SE, et al. Blind nasotracheal intubation in the presence of facial trauma. *J Emerg Med* 1997; 15: 141–5.
12. Walls MW. Blind nasotracheal intubation in the presence of facial trauma—is it safe? *J Emerg Med* 1997; 15: 243–4.
13. Kaufman HJ, Ciraulo DL, Burns P. Traumatic fracture of the hyoid bone: three case presentations of cardiorespiratory compromise secondary to missed diagnosis. *Am Surg* 1999; 65: 877–80.
14. Keogh IJ, Rowley H, Russel J. Critical airway compromise caused by neck hematoma. *Clin Otolaryngol* 2002; 27: 244–5.
15. Vassiliu P, Baker J, Henderson S, et al. Aerodigestive injuries of the neck. *Am Surg* 2001; 67: 75–9.
16. Desjardins G, Varon AJ. Airway management for penetrating neck injuries: the Miami experience. *Resuscitation* 2001; 48: 71–5.
17. Demetriades D, Velmahos GG, Asensio JA. Cervical pharyngotracheal and laryngotracheal injuries. *World J Surg* 2001; 25: 1044–8.
18. van As AB, van Deurzen DFP, Verleisdonk EJMM. Gunshots to the neck: selective angiography as part of conservative management. *Injury* 2002; 33: 453–6.
19. Hirshberg A, Wall MJ, Johnston RH, et al. Transcervical gunshot injuries. *Am J Surg* 1994; 167: 309–12.

Monitoring of the Trauma Patient

Eugene Y. Fukudome and Marc A. De Moya

Clinical Questions		
Question	Answer	Grade of recommendation
Are HR and BP adequate indicators of shock?	Trauma patients who have suffered significant blood loss may present in compensated shock with normal vital signs, therefore, HR and BP are not adequate indicators of shock.	B
Is there a biochemical parameter that best identifies shock and guides resuscitation?	Serum lactate, arterial base deficit, arterial pH, and bicarbonate can help identify occult hypoperfusion. Lactate may be the best biochemical parameter to follow over time. Therapy aimed at normalizing a biochemical parameter as a single endpoint of resuscitation has not been studied prospectively.	B
Does hemodynamic monitoring with a pulmonary artery catheter improve outcomes?	The use of pulmonary artery catheters does not improve outcomes.	A
	Pulmonary artery catheters may offer a benefit in severely injured patients or elderly trauma patients.	C
Do local tissue perfusion measures improve our ability to diagnose shock? Does their use improve outcomes?	There is no evidence that using local tissue perfusion as a guide for therapy improves outcomes.	A
Should the geriatric trauma patient have more invasive monitoring?	Elderly patients with severe injuries may benefit from invasive hemodynamic monitoring.	C
Abbreviations: BP, blood pressure; HR, heart rate.		

Traumatic injuries are the third leading cause of death among all age groups, and the leading cause of death among Americans younger than 44 years of age (1). On arrival to the hospital, immediately life-threatening injuries must be diagnosed and treated. Attention is then turned to resuscitation, the secondary survey, and diagnosis and management of all other injuries. The trauma surgeon must decide what type of monitoring will ensure accurate diagnosis of shock, adequate and timely resuscitation, and early identification of potential problems.

ARE HEART RATE AND BLOOD PRESSURE ADEQUATE INDICATORS OF SHOCK?

Shock is a state of supply-demand mismatch where end-organ perfusion is inadequate and metabolic requirements exceed oxygen delivery. The result is oxygen debt and anaerobic metabolism. Following trauma, shock is usually a result of hemorrhage, but the degree of blood loss may be difficult to estimate. Advanced shock is easily recognized because the patient will have hypotension and

tachycardia, however, identifying early shock can be challenging. "Compensated shock" or "occult hypoperfusion" may exist in a patient with normal heart rate (HR) and blood pressure (BP), and is easily missed. Physical exam findings of shock, such as moist clammy skin and peripheral vasoconstriction, are subjective and subtle. Animal studies of hemorrhage show that even if hemodynamic parameters return to normal, mesenteric oxygen delivery is compromised and anaerobic metabolism persists (2). Early identification and treatment of shock is essential because if untreated, shock leads to cellular dysfunction, organ failure, morbidity, and mortality.

The American College of Surgeons Committee on Trauma has defined four classes of shock. Although tachycardia is considered a better indicator of shock than BP (3), it is not present until class II shock where the patient may have lost 15–30% of his or her blood volume (4). Moreover, studies suggest that tachycardia is actually a poor predictor of shock (5), and 28.9% of hypotensive patients had an HR <90 (6). A study using base deficit as a marker for hypoperfusion also found a poor correlation between blood pressure and base deficit and found that hypotension was

reliably present only in patients with a large base deficit indicative of severe, advanced shock (7). Thus, even hemodynamically stable patients may have sustained significant hemorrhage and may suffer complications as a result (8). By the time a bleeding trauma patient develops hypotension (systolic BP <90 mmHg) from shock, the mortality rate may be higher than 50% (9). Even trauma patients with a systolic BP of 90–109 had increased morbidity and mortality compared to those with a systolic BP greater than 109 (10). Thus, hypotension and tachycardia in a trauma patient are late indicators of shock.

Answer: HR and BP are not adequate indicators of shock. Trauma patients with significant blood loss may present in compensated shock with normal vital signs. The trauma surgeon must seek other data in addition to HR and BP to determine if a patient has ongoing occult hypoperfusion that must be treated. Grade of recommendation: B.

IS THERE A BIOCHEMICAL PARAMETER THAT BEST IDENTIFIES SHOCK AND GUIDES RESUSCITATION?

Inadequate end-organ perfusion that defines a state of shock results in anaerobic metabolism. Instead of entering the Krebs cycle, pyruvate is converted to lactate (lactic acid), leading to metabolic acidosis with an increased anion gap, low serum bicarbonate, and low serum pH. Thus, abnormalities in these metabolic parameters indicate ongoing anaerobic metabolism and are associated with poor outcomes.

Elevated serum lactate levels have been shown to indicate the presence of hypoperfusion, even with normal vital signs, and elevated initial lactate levels were seen in trauma patients that developed complications (11). Clearance of lactate during the initial 24 hours after trauma correlated with improved survival, whereas persistently elevated lactate levels were common in patients with multisystem organ failure, pulmonary complications, and death (11). Higher rates of infection were also seen in trauma patients with persistently elevated lactate levels (12). Among surgical intensive care patients, elevated initial lactate levels (13) and failure to normalize lactate levels correlated with mortality (13,14). Pal and associates point out that although lactate levels are significantly higher in patients who died compared to patients who survived, the significant association does not mean that high lactate predicts death. In fact, because many trauma patients have elevated lactate and relatively few actually die, the positive predictive value of an elevated lactate for death is low (15).

Lactate levels must be interpreted with caution because conditions such as diabetic ketoacidosis, stimulation of glycolysis by catecholamines, and inhibition of pyruvate dehydrogenase by endotoxin may all cause elevated lactate levels in the absence of hypoperfusion. In other words, serum lactate may be sensitive for hypoperfusion, but not specific for it (16).

Base deficit is calculated from an arterial blood gas and is the amount of base required to return the pH of 1 L of blood back to a normal level. Thus, base deficit is a measure of uncompensated metabolic acidosis. Base deficit, like serum lactate, is also widely used as a marker for hypoperfusion and need for resuscitation in both medical and surgical patients. Several studies have examined the

use of base deficit in the evaluation of trauma patients. Injured patients with an abnormal base deficit on admission had poor outcomes, such as a greater need for blood transfusion and more organ failure (17) as well as higher mortality (18). Acute lung injury was more prevalent in trauma patients with an abnormal base deficit (19). Patients who failed to normalize their base deficit had higher rates of multiple organ failure and death (20–22). The main drawback of using base deficit relates to the fact that it is a global indicator of acidosis and adequately resuscitated trauma patients may have an abnormal base deficit due to renal failure, chronic obstructive pulmonary disease, or other causes (3). Nevertheless, base deficit appears to be superior to pH in distinguishing survivors and nonsurvivors (23), but may not offer any advantage over serum bicarbonate levels (24).

Interestingly, lactate and base deficit values often conflict with each other. Martin and colleagues retrospectively studied 12,197 simultaneously obtained data points of lactate and base deficit drawn from 1,298 patients and found that the values did not correlate 44% of the time (25). Further analysis of these data shows that admission lactate and base deficit were about equivalent in their association with mortality, however, later in a patient's hospital course, lactate was more strongly associated with mortality than base deficit. In fact, when lactate levels were normal, an abnormal base deficit did not correlate with mortality, but when base deficit levels were normal, elevated lactate did correlate with mortality (25). These results were similar to a prior study that also showed poor correlation between lactate and base deficit (13).

In summary, elevated biochemical parameters such as lactate and base deficit are associated with more complications and higher mortality because they indicate ongoing hypoperfusion and cellular injury. Persistently abnormal biochemical parameters are particularly ominous. To date, there have not been prospective studies that prove that using any of these biochemical parameters as a single endpoint of resuscitation improves survival.

Answer: Abnormal serum lactate, arterial pH, bicarbonate, and base deficit suggest occult hypoperfusion and a need for intervention, and failure to normalize these parameters correlate with poor outcome. Lactate may be the best biochemical parameter to follow over time. Therapy aimed at normalizing these parameters as a single endpoint of resuscitation have not been studied prospectively. Grade of recommendation: B.

DOES HEMODYNAMIC MONITORING WITH A PULMONARY ARTERY CATHETER IMPROVE OUTCOMES?

Advanced hemodynamic monitoring with a pulmonary artery catheter (PAC) is sometimes thought of as the gold standard for hemodynamic monitoring because PACs are able to directly measure and calculate parameters such as cardiac output. Although PACs are widely in use, they have been associated with complication about 10% of the time (26). Complications include catheter-associated blood stream infection, arrhythmia, insertion site complications, and pulmonary artery rupture, among others. Reports of increased mortality associated with PAC use (27) have prompted intense investigation to determine their utility.

PACs were found to offer no benefit in patients undergoing elective surgery (28–30), although these studies did not include trauma patients.

Other studies evaluating the use of PACs have included trauma patients. In an observational study of intensive care patients, Chittock et al. found that PACs may offer a benefit to the sickest subgroup of patients (31). However, a subsequent prospective randomized study (26), as well as a meta-analysis of 13 randomized clinical trials (32), both failed to reveal a benefit of PACs. The only trial that specifically studies trauma patients is a retrospective examination of the National Trauma Data Bank (NTDB) conducted by Friese and associates. They found that in a subgroup of severely injured patients, as well as elderly patients, PAC use was associated with improved survival (33). This finding requires further study in a prospective trial.

Others have used PACs not only as a monitoring device to detect suboptimal hemodynamics but as a device to achieve supranormal physiologic goals of resuscitation. Velmahos et al. placed PACs in severely injured trauma patients and found that there was no difference in mortality or organ failure produced by optimizing hemodynamics (34). A meta-analysis of trials examining the use of supraphysiologic resuscitation goals in medical, surgical, and trauma intensive care patients also did not find any improvement in mortality (35).

Answer: Hemodynamic monitoring with PACs may improve outcomes among severely injured patients and elderly trauma patients. Grade of recommendation: C. However, this benefit has not been demonstrated in a prospective trial. In a trauma patient who has a prolonged intensive care course, PACs do not appear to offer any additional benefit. The use of PACs to achieve supranormal resuscitation endpoints also does not appear to offer any benefit. Grade of recommendation: A.

DO LOCAL TISSUE PERFUSION MEASURES IMPROVE OUR ABILITY TO DIAGNOSE SHOCK? DOES THEIR USE IMPROVE OUTCOMES?

As already discussed, there is a lack of evidence that therapy guided by PACs improves outcomes among critically ill patients. One limitation of PACs is that they can only generate data that is global in nature. Patients may have ongoing hypoperfusion to key organs such as the intestines that are not detected by PACs and that lead to poor outcomes. There is growing interest in measuring perfusion to end organs to quantifying the adequacy of perfusion. Some authors hypothesize that resuscitation guided by correction of end-organ hypoperfusion may improve outcomes. Currently, clinicians assess perfusion to the skin (an end organ) by physical exam, but this method is subjective and may be inaccurately assessed by an inexperienced clinician. Objective measures of end-organ perfusion may overcome this limitation.

Several devices are available to measure local tissue perfusion. Gastric tonometry measures gastric intramucosal pH (ipH) via a probe attached to a nasogastric tube. Sublingual capnometry measures pCO₂ as a marker for hypoperfusion. Near infrared spectroscopy (NIRS) measures oxygen saturation of hemoglobin found in peripheral muscle tissue or subcutaneous tissue. All of these techniques

are based on the fact that during shock, blood flow is redistributed away from the organs that they are assessing (oral mucosa, gastric mucosa, and skeletal muscle).

Multiple studies using these techniques have demonstrated promising results. Patients in shock were noted to have low gastric ipH (36), high sublingual pCO₂ (37), and low peripheral tissue oxygen saturation measured by NIRS (38). Low ipH that failed to correct in 24 hours predicted mortality and poor outcomes in trauma patients (39,40) and was also the first sign of organ failure (40). Moreover, a high sublingual capnometry value predicted mortality among hypotensive trauma patients (41) and was a better predictor of mortality than arterial lactate in intensive care patients (42). NIRS also identified hypoperfusion and was a predictor for death and organ failure in trauma patients (43).

Although studies indicate that hypoperfusion could be detected by these techniques, and hypoperfusion was a marker for poor outcomes, it was not clear whether these devices offered a benefit over conventional methods of monitoring a patient and diagnosing hypoperfusion. Several recent studies have investigated this question. Ivatury and associates found that resuscitation using ipH as an endpoint offered no outcome advantage compared to resuscitation based on oxygen delivery index and oxygen consumption index (44). Gomersall and colleagues studied patients admitted to an intensive care unit with medical or surgical illnesses. They found that additional resuscitation that specifically corrected gastric ipH did not offer any benefit (45). Later, the Miami Trauma Clinical Trials Group specifically studied trauma patients in shock and also found that therapy guided by gastric ipH added no benefit (46).

Although the application of these devices in the hospital or trauma center has not been shown to improve outcomes, they may be beneficial elsewhere. In the battlefield, for example, it may be difficult to obtain an accurate blood pressure measurement by sphygmomanometry, and regional hypoperfusion detected by a portable device may be the only indicator of shock. Similarly, during a mass casualty, these devices may be a useful triage tool (37). Such applications require further validation.

Answer: Although several techniques are under development, at the present time there is no evidence that using local tissue perfusion as a guide for therapy improves outcomes. Grade of recommendation: A.

SHOULD THE GERIATRIC TRAUMA PATIENT HAVE MORE INVASIVE MONITORING?

The injured geriatric patient presents an additional challenge to those who care for trauma patients. Less force is required to produce an injury in an elderly patient, and seemingly trivial mechanisms may result in major injuries. In fact, 30% of people greater than 65 years of age fall each year, and 32% of these falls result in significant injury (47,48). The geriatric population in the United States is increasing, and reducing morbidity and mortality, preserving quality of life, and returning patients to their previous functional status are obvious goals of care.

Elderly patients have worse outcomes following traumatic injury compared with younger patients with similar

injury severity scores (49). Geriatric patients tend to have preexisting medical conditions, such as coronary artery disease, valvular heart disease, systemic hypertension, pulmonary disease, and renal insufficiency, and commonly take medications such as β -blockers, calcium channel blockers, diuretics, antiplatelet agents, and anticoagulants. As a result, elderly patients may not become tachycardic or may not be able to augment cardiac output in response to hypovolemia caused by hemorrhage. A blood pressure that is “normal” may actually represent hypotension in an elderly patient with uncontrolled baseline hypertension. In addition, elderly patients with congestive heart failure may have difficulty regulating their total body volume status and may develop pulmonary edema in response to modest volume resuscitation.

Early studies have lead to a hypothesis that geriatric trauma outcomes can be improved with hemodynamic monitoring and early aggressive treatment. Schultz et al. randomized 70 patients with hip fractures to either monitoring with a pulmonary artery catheter PAC or monitoring central venous pressure and found that the use of PACs decreased mortality to 2.9% compared to 29% in the control group (50). Scalea and colleagues implemented a policy of mandatory monitoring with a PAC and optimization of cardiac index and oxygen consumption index in geriatric blunt polytrauma patients with acidosis, initial

systolic BP less than 150 mmHg, multiple fractures, or head injury. They concluded that elderly patients with normal vital signs may have ongoing occult hypoperfusion, and when begun within the first one to two hours after arrival in a hospital, invasive monitoring and hemodynamic optimization improved survival (51). More recently, a retrospectively reviewed the NTDB indicated that PACs may be beneficial in elderly trauma patients (33).

Although these three studies support the use of invasive monitoring in elderly trauma patients, the results must be interpreted with caution due to limitations of the studies. The study conducted by Schultz et al. (50) did not employ any prospectively determined resuscitation endpoints for either the PAC or control group. Moreover, the patients studied were not polytrauma patients. The study by Scalea et al. (51) compared outcomes to historic controls, rather than randomizing patients to treatment and control groups. Last, the study by Friesse et al. (33) utilized the NTDB, which contains many missing data points, resulting in a high exclusion rate of subjects. The trial also used subgroup analysis. A prospective study will be necessary to validate these observations.

Answer: Elderly patients with severe injuries may benefit from invasive hemodynamic monitoring, but further studies in this area are required. Grade of recommendation: C.

Level of Evidence

Ref.	Level of evidence	Study design	Results
5	IIC	Retrospective review of 14,325 patients analyzing the association between variables such as HR and BP. Study conducted between July 1988–January 1997.	Tachycardia is not sensitive or specific for hypotension. 35% of hypotensive patients were not tachycardic, and 39% of patients with normal systolic BP had tachycardia.
7	IIC	Retrospective review of 115,830 trauma patients using the NTDB who had base deficit and BP measurements. The correlation between base deficit and systolic BP measured in the emergency department were analyzed.	Systolic BP measured in the emergency department and base deficit had a poor correlation. Patients with hypoperfusion as indicated by base deficit may not present with hypotension.
10	IIC	Retrospective review of 2,071 trauma patients with gastric, small bowel, or diaphragm injuries requiring emergency laparotomy. Patients were divided into three groups based on BP and outcomes were analyzed. Study conducted between 1980–2003.	Patients with a systolic BP between 90–109 had a 5% mortality, whereas patients with a systolic BP > 109 had a 1% mortality. The difference in mortality was significant.
13	IIC	Retrospective review of 137 SICU patients with serial lactate and base deficit measurements. Base deficit and lactate values were correlated with outcomes. Study conducted between September 1996–December 2001.	Initial lactate and 24-hour lactate best correlated with outcome and mortality. 24-hour base deficit correlated with mortality. Initial base deficit was not significantly associated with mortality.
25	IIC	Retrospective review of 1,298 ICU patients with simultaneously drawn base deficit and lactate values. Correlation between lactate, base deficit, and outcome were analyzed. Study conducted between June 1996–June 2004.	Lactate and base deficit did not correlate 44% of the time. Admission lactate and base deficit are equivalent in their association with mortality. When base deficit levels were normal, elevated lactate correlated with mortality.
26	Ib	Prospective, randomized trial. 1,041 ICU patients were randomized to management with (n = 519) and without (n = 522) a PAC. The major endpoint was hospital mortality. Other endpoints included length of stay, organ-days of support. Study conducted between October 2001–March 2004.	PAC use not associated with benefit or harm.
31	IIC	Retrospective review of 7,310 ICU patients. PAC use was correlated with outcomes. Study conducted between March 1988–March 1998.	No association between PAC use and mortality overall. PAC use was associated with a lower risk of death in the sickest subgroup of patients.

(Continued)

Level of Evidence (Continued)

Ref.	Level of evidence	Study design	Results
32	Ia	Meta-analysis of 13 randomized clinical trials (5,051 total patients). Relationship between PAC use and outcomes was analyzed.	PAC use not associated with benefit or harm.
33	Iic	Retrospective review of 53,312 trauma patients using the NTDB. Those who underwent PAC insertion (n = 1,933) were compared to those who did not (n = 51,379). Patients were grouped by age, injury severity score and initial base deficit, and the association between PAC use and mortality was studied within each group. Data collected between January 1994–December 2001.	PAC use associated with decreased mortality in three groups: (1) age 61–90 with base deficit –6 to –10; (2) age 61–90 and base deficit –11 and worse; (3) age 16–40 with base deficit –11 and worse. Hypothesis-generating study.
45	Ib	Prospective randomized trial. 210 ICU patients were randomized to two groups: intervention (n = 106) and control (n = 104). After resuscitation according to standard practice, the intervention group received additional therapy for ipH < 7.35. The major endpoint was mortality. Other endpoints included ICU, hospital, 30-day mortality, length of ICU and hospital stay.	No differences between the intervention and control group.
46	Ib	Prospective randomized trial. 151 severely injured patients were randomized to three groups: (1) routine management, n = 54 (2) gastric tonometry measurement with additional resuscitation for abnormal ipH, n = 50 (3) gastric tonometry-guided therapy according to predetermined protocol, n = 47. The major endpoint was mortality. Other endpoints included duration of mechanical ventilation, ICU stay, and hospital stay.	No differences between the three groups.

Abbreviations: BP, blood pressure; HR, heart rate; ICU, intensive care unit; NTDB, national trauma data bank; PAC, pulmonary artery catheter.

REFERENCES

- www.cdc.gov/ncipc/wisqars
- Chiara O, Pelosi P, Segala M, et al. Mesenteric and renal oxygen transport during hemorrhage and reperfusion: evaluation of optimal goals for resuscitation. *J Trauma* 2001; 51: 356–62.
- Cocchi MN, Kimlin E, Walsh M, et al. Identification and resuscitation of the trauma patient in shock. *Emerg Med Clin North Am* 2007; 25: 623–42.
- American College of Surgeons Committee on Trauma. Advanced Trauma Life Support Program for Doctors, 7th edition. Chicago: American College of Surgeons, 2004.
- Victorino GP, Battistella FD, Wisner DH. Does tachycardia correlate with hypotension after trauma? *J Am Coll Surg* 2003; 196: 679–84.
- Demetriades D, Chan LS, Bhasin P, et al. Relative bradycardia in patients with traumatic hypotension. *J Trauma* 1998; 45: 534–9.
- Parks JK, Elliott AC, Gentilello LM, et al. Systemic hypotension is a late marker of shock after trauma: a validation study of advanced trauma life support principles in a large national sample. *Am J Surg* 2006; 192: 727–31.
- Brown CV, Velmahos GC, Neville AL, et al. Hemodynamically “stable” patients with peritonitis after penetrating abdominal trauma: identifying those who are bleeding. *Arch Surg* 2005; 140: 767–72.
- Heckbert SR, Vedder NB, Hoffman W, et al. Outcome after hemorrhagic shock in trauma patients. *J Trauma* 1998; 45: 545–9.
- Edelman DA, White MT, Tyburski JG, et al. Post-traumatic hypotension: should systolic blood pressure of 90–109 mmHg be included? *Shock* 2007; 27: 134–8.
- Blow O, Magliore L, Claridge JA, et al. The golden hour and the silver day: detection and correction of occult hypoperfusion within 24 hours improves outcomes after major trauma. *J Trauma* 1999; 47: 964–9.
- Claridge JA, Crabtree TD, Pelletier SJ, et al. Persistent occult hypoperfusion is associated with a significant increase in infection rate and mortality in major trauma patients. *J Trauma* 2000; 48: 8–14.
- Husain FA, Martin MJ, Mullenix PS, et al. Serum lactate and base deficit as predictors of mortality and morbidity. *Am J Surg* 2003; 185: 485–91.
- McNelis J, Marini CP, Jurkiewicz A, et al. Prolonged lactate clearance is associated with increased mortality in the surgical intensive care unit. *Am J Surg* 2001; 182: 481–5.
- Pal JD, Victorino GP, Twomey P, et al. Admission serum lactate levels do not predict mortality in the acutely injured patient. *J Trauma* 2006; 60: 583–7.
- Morris CG, Low J. Metabolic acidosis in the critically ill: Part 2. Causes and treatment. *Anaesthesia* 2008; 63: 396–411.
- Davis JW, Parks SN, Kaups KL, et al. Admission base deficit predicts transfusion requirements and risk of complications. *J Trauma* 1996; 41: 769–74.
- Kincaid EH, Chang MC, Letton RW, et al. Admission base deficit in pediatric trauma: A study using the National Trauma Data Bank. *J Trauma* 2001; 51: 332–5.
- Eberhard LW, Morabito DJ, Matthay MA, et al. Initial severity of metabolic acidosis predicts the development of acute lung injury in severely traumatized patients. *Crit Care Med* 2000; 28: 125–31.
- Kincaid EH, Miller PR, Meredith JW, et al. Elevated arterial base deficit in trauma patients: a marker of impaired oxygen utilization. *J Am Coll Surg* 1998; 187: 384–92.
- Eachempati SR, Robb T, Ivatury RR, et al. Factors associated with mortality in patients with penetrating abdominal vascular trauma. *J Surg Res* 2002; 108: 222–6.
- Randolph LC, Takacs M, Davis KA. Resuscitation in the pediatric trauma population: admission base deficit remains an important prognostic indicator. *J Trauma* 2002; 53: 838–42.

23. Davis JW, Kaups KL, Parks SN. Base deficit is superior to pH in evaluating clearance of acidosis after traumatic shock. *J Trauma* 1998; 44: 114–18.
24. FitzSullivan E, Salim A, Demetriades D, et al. Serum bicarbonate may replace the arterial base deficit in the trauma intensive care unit. *Am J Surg* 2005; 190: 941–6.
25. Martin MJ, FitzSullivan E, Salim A, et al. Discordance between lactate and base deficit in the surgical intensive care unit: Which one do you trust? *Am J Surg* 2006; 191: 625–30.
26. Harvey S, Harrison DA, Singer M, et al. PAC-Man study collaboration. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. *Lancet* 2005; 366: 472–7.
27. Connors AF Jr, Speroff T, Dawson NV, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. SUPPORT Investigators. *JAMA* 1996; 276: 889–97.
28. Barone JE, Tucker JB, Rassias D, et al. Routine perioperative pulmonary artery catheterization has no effect on rate of complications in vascular surgery: a meta-analysis. *Am Surg* 2001; 67: 674–9.
29. Polanczyk CA, Rohde LE, Goldman L, et al. Right heart catheterization and cardiac complications in patients undergoing noncardiac surgery: an observational study. *JAMA* 2001; 286: 309–14.
30. Sandham JD, Hull RD, Brant RF, et al. Canadian Critical Care Clinical Trials Group. A randomized, controlled trial of the use of pulmonary-artery catheters in high-risk surgical patients. *N Engl J Med* 2003; 348: 5–14.
31. Chittock DR, Dhingra VK, Ronco JJ, et al. Severity of illness and risk of death associated with pulmonary artery catheter use. *Crit Care Med* 2004; 32: 911–15.
32. Shah MR, Hasselblad V, Stevenson LW, et al. Impact of the pulmonary artery catheter in critically ill patients: Meta-analysis of randomized clinical trials. *JAMA* 2005; 294: 1664–70.
33. Fries RS, Shafi S, Gentilello LM. Pulmonary artery catheter use is associated with reduced mortality in severely injured patients: A National Trauma Data Bank analysis of 53,312 patients. *Crit Care Med* 2006; 34: 1597–601.
34. Velmahos GC, Demetriades D, Shoemaker WC, et al. End-points of resuscitation of critically injured patients: normal or supranormal? A prospective randomized trial. *Ann Surg* 2000; 232: 409–18.
35. Heyland DK, Cook DJ, King D, et al. Maximizing oxygen delivery in critically ill patients: a methodologic appraisal of the evidence. *Crit Care Med* 1996; 24: 517–24.
36. Tang W, Weil MH, Sun S, et al. Gastric intramural PCO₂ as monitor of perfusion failure during hemorrhagic and anaphylactic shock. *J Appl Physiol* 1994; 76: 572–7.
37. Weil MH, Nakagawa Y, Tang W, et al. Sublingual capnometry: a new noninvasive measurement for diagnosis and quantitation of severity of circulatory shock. *Crit Care Med* 1999; 27: 1225–59.
38. Crookes BA, Cohn SM, Bloch S, et al. Can near-infrared spectroscopy identify the severity of shock in trauma patients? *J Trauma* 2005; 58: 806–13.
39. Chang MC, Cheatham ML, Nelson LD, et al. Gastric tonometry supplements information provided by systemic indicators of oxygen transport. *J Trauma* 1994; 37: 488–94.
40. Ivatury RR, Simon RJ, Havriliak D, et al. Gastric mucosal pH and oxygen delivery and oxygen consumption indices in the assessment of adequacy of resuscitation after trauma: a prospective, randomized study. *J Trauma* 1995; 39: 128–34.
41. Baron BJ, Dutton RP, Zehtabchi S, et al. Sublingual capnometry for rapid determination of the severity of hemorrhagic shock. *J Trauma* 2007; 62: 120–4.
42. Marik PE, Bankov A. Sublingual capnometry versus traditional markers of tissue oxygenation in critically ill patients. *Crit Care Med* 2003; 31: 818–22.
43. Cohn SM, Nathens AB, Moore FA, et al. StO₂ in Trauma Patients Trial Investigators. Tissue oxygen saturation predicts the development of organ dysfunction during traumatic shock resuscitation. *J Trauma* 2007; 62: 44–54.
44. Ivatury RR, Simon RJ, Islam S, et al. A prospective randomized study of end points of resuscitation after major trauma: global oxygen transport indices versus organ-specific gastric mucosal pH. *J Am Coll Surg* 1996; 183: 145–54.
45. Gomersall CD, Joynt GM, Freebairn RC, et al. Resuscitation of critically ill patients based on the results of gastric tonometry: a prospective, randomized, controlled trial. *Crit Care Med* 2000; 28: 607–14.
46. Miami Trauma Clinical Trials Group. Splanchnic hypoperfusion-directed therapies in trauma: a prospective, randomized trial. *Am Surg* 2005; 71: 252–60.
47. Sterling DA, O'Connor JA, Bonadies J. Geriatric falls: injury severity is high and disproportionate to mechanism. *J Trauma* 2001; 50: 116–19.
48. Callaway DW, Wolfe R. Geriatric trauma. *Emerg Med Clin North Am* 2007; 25: 837–60.
49. Smith DP, Enderson BL, Maull KI. Trauma in the elderly: determinants of outcome. *South Med J* 1990; 83: 171–7.
50. Schultz RJ, Whitfield GF, LaMura JJ, et al. The role of physiologic monitoring in patients with fractures of the hip. *J Trauma* 1985; 25: 309–16.
51. Scalea TM, Simon HM, Duncan AO, et al. Geriatric blunt multiple trauma: improved survival with early invasive monitoring. *J Trauma* 1990; 30: 129–34.

Resuscitation of the Trauma Patient

David R. King

Question Summary		
Question	Answer	Grade of recommendation
What type of fluid should be used for acute resuscitation of the trauma patient?	Isotonic crystalloid	A
How does one determine whether a traumatized patient requires fluid resuscitation?	Blood pressure less than 110 mmHg on presentation	C
What are the endpoints for termination of fluid resuscitation?	Clinical judgment	B
Does the concept of hypotensive (delayed) resuscitation have a role in trauma care?	Yes	A
Should blood or blood products be used as an initial resuscitation fluid, when available?	No	C
Do vasoactive drugs play a role in early resuscitation of the trauma patient?	No	C

INTRODUCTION

The Edwin Smith papyrus (1600 B.C.) describes administering fluid by mouth following traumatic injury (1). This may represent the earliest description of fluid resuscitation. Later, Cannon warns of the potential perils of aggressive fluid resuscitation, including exacerbating hemorrhage by (possibly) raising blood pressure and disrupting soft clots (2). Indeed, it seems that the debates surrounding fluid resuscitation predate this evidence-based textbook by centuries.

This chapter addresses several fundamental questions related to resuscitation of the trauma patient within an evidence-based construct. The particular questions are important, however, they clearly do not represent all possible resuscitation-related dilemma that may confront the surgeon/clinician. Therefore, the goal is to demonstrate and differentiate those maneuvers that are based in scientific evidence and discriminate them from those based solely in historical opinion. This is not to say that our surgical forefathers were wrong in their approaches and therapy (because in many cases they were right on target) but simply to articulate those therapies that have a scientific basis from those whose basis should be questioned and improved on if shown to be false.

METHODS

An OVID MEDLINE search was performed for all articles from 1950 to May 2008 using the terms "resuscitation" and

"trauma." The search was limited to clinical trials and randomized controlled trials on human subjects. Multiple languages were accepted if there was an English language translation available. Manuscripts were screened for appropriateness to the topics listed, and article references were examined for relevant similar articles using PubMed. A review as also performed of the Cochrane library using similar key terms. Manuscripts were discarded if there were significant methodological flaws or if the papers actually represented multiple case reports.

Several important questions were posed, and evidence was evaluated to address each question. Each question's levels of evidence were classified using the system of the Oxford Centre for Evidence Based Medicine.

QUESTION RESULTS

What Type of Fluid Should Be Used for Acute Resuscitation of the Trauma Patient?

Despite the trauma surgeon's fascination with lactated Ringer's solution, no evidence exists to suggest that this crystalloid solution has any survival benefit over others. Nearly every clinical trial demonstrates equivalence of a variety of resuscitation fluids, including lactated Ringer's, normal saline, and 3% or 7.5% hypertonic saline, hetastarch/pentastarch solutions, and gelatins (3–9,12–15,17,19,23–30). Resuscitation with normal saline may result in a hyperchloremic metabolic acidosis, however, the presence of said acidosis has never been demonstrated to worsen outcome (8,9).

The use of hetastarches and gelatins has no morbidity or mortality advantage, but less volume of these fluids is required to achieve similar resuscitation endpoints (4,12–15,17,19). Although this advantage may be of little significance in a resource-abundant civilian trauma center, there may be significant logistical advantages for the military, especially in far forward units where supplies are limited by weight and volume. Colloids, however, are dramatically more expensive than crystalloid solutions, and this may become important in all environments (9,30). Of note, newer generation hetastarches with improved C2/C6 ratios, 1:20 branching, and 0.75 degree of substitution have no demonstrable effect on the coagulation system (17). The use of 7.5% hypertonic saline has some theoretical advantages (potential for sodium to act as an osmotic dehydrating agent in the injured brain and prevent edema formation) over isotonic fluid resuscitation in the multi-trauma patient with a concurrent brain injury, however, results from multiple clinical trials are mixed with the majority of studies demonstrating equivalence with isotonic fluid resuscitation (4–6,11,13–15,24–26). The use of hypotonic fluids for trauma resuscitation has never been studied, therefore, a specific analysis on this type of fluid cannot be generated.

The use of hemoglobin-based oxygen carriers for trauma resuscitation remains a research interest only. Despite convincing animal studies demonstrating survival advantages, all trauma-related clinical trials with these agents result in higher mortality rates (18,31–34). There are currently not enough data to support their general use in trauma, although hemoglobin-based oxygen carriers remain the theoretical ideal resuscitation fluid.

Acute phase trauma resuscitation may be conducted safely with any isotonic crystalloid or colloid solution, as well as hypertonic saline. In general, crystalloid solutions remain preferred because of their low cost and similar outcomes compared to colloids. Level of evidence: Ia. Strength of recommendation: A.

How does One Determine Whether a Traumatized Patient Requires Fluid Resuscitation?

Shock is generally defined as inadequate tissue perfusion. In trauma, this condition is often recognized on the basis of vital signs and mental status. Shock should be regarded as present if any trauma patient presents with a systolic blood pressure less than 110mmHg and a heart rate greater than 100 beats/min (14,16,37). This is a significant departure from earlier classical teaching where blood pressure below 80 or 90mmHg and heart rates above 120beats/min was regarded as a reliable threshold for determination of shock. Altered mental status should also be regarded as a sign of shock until proven otherwise. If any of these parameters are present, fluid resuscitation should be instituted. One must understand that these parameters are meant to overtriage trauma patients such that few or no patients in hemorrhagic shock are inappropriately excluded from fluid resuscitation efforts.

Following trauma, any patient with a heart rate above 100beats/min or blood pressure lower than 110mmHg systolic indicates shock and should trigger aggressive fluid resuscitation efforts. Level of evidence: IIc. Strength of recommendation: C.

What are the Endpoints for Termination of Fluid Resuscitation?

Reliable and well-defined endpoints to resuscitation remain elusive. Multiple strategies have been proposed and tested, and none have proven to be better than clinical judgment based on vital signs, urine output, and simple laboratory tests such as base deficit (16,20,21). Oxygen delivery-based therapy and endpoints determined with a pulmonary artery catheter has excellent theoretical advantages; however, multiple clinical trials have shown no significant morbidity or mortality advantage (16,20). Tissue-level near-infrared spectroscopy, as well as intramuscular polarographic Clark-type electrode tissue pO_2 monitoring, has been shown to be useful in animal studies, whereas its role as a resuscitation endpoint in humans remains no better than clinical judgment (38–40). The available data suggest that resuscitation endpoints would be more usefully conceptualized as resuscitation spectrum, where fluid administration is not suddenly terminated once a specific criteria or point is reached, but rather slowly deescalated as the patient's clinical condition improves. Certain exceptions to ongoing resuscitation endpoints exist in the setting of penetrating torso trauma; this will be addressed separately. One should also be aware that overresuscitation may be equally as deleterious as underresuscitation. The surgeon should constantly reevaluate the trauma patient to prevent overuse of resuscitation fluid and the consequences associated with this practice.

Clinical judgment combined with simple laboratory testing remains the best approach to deciding when to deescalate fluid resuscitation. This should be approached as a continuum rather than a static point in care. Level of evidence: IIb. Strength of recommendation: B.

Does the Concept of Hypotensive (Delayed) Resuscitation Have a Role in Trauma Care?

Hypotensive resuscitation, or delayed fluid resuscitation, is a concept whereby fluid administration is intentionally withheld, slowed, or halted at some point before the standard endpoints of resuscitation are achieved. There is evidence of survival benefit with the use of a delayed resuscitation paradigm following penetrating torso injury (22), although no conclusive data exist for blunt or extremity injuries (10). Patients with a penetrating injury should have intravenous access established and fluid withheld until surgical intervention is available. A plethora of expert opinion has been generated from the battlefields of Iraq and Afghanistan. Most experts generally suggest that hypotensive resuscitation is appropriate for patients in shock until definitive surgical intervention is available. This opinion, however, remains unstudied in a randomized controlled fashion.

Hypotensive or delayed fluid resuscitation should be considered following penetrating torso injuries. No evidence exists to support that this strategy should be imposed on patients suffering from shock after blunt or extremity injuries. Level of evidence: Ib. Strength of recommendation: A.

Should Blood or Blood Products Be Used as an Initial Resuscitation Fluid When Available?

Some surgeons propose that in the setting of acute hemorrhage, one should replace lost intravascular volume with fresh whole blood or packed red blood cells. Unfortunately,

capillary refill across the interstitial space occurs rapidly, and this interstitial free water deficit must be restored to return the patient to fluid equilibrium. Additionally, although many patients present with acute blood loss, most will be successfully managed without blood transfusion. The use of blood and blood products also exposes the patient to risks associated with communicable diseases and transfusion reactions. No evidence exists demonstrating any clinical advantage to this practice because prehospital randomization of patients to crystalloid or red blood cells is logistically difficult. Some evidence exists in the early hospital-based resuscitation environment suggesting that patients who obviously have a large vascular injury and will require massive transfusion may benefit from early administration of blood and blood products (41–43). Even in these series, however, the initial fluid of choice was crystalloid solution before switching to blood.

Initial fluid resuscitation should begin with a crystalloid solution. There is no evidence to support initial resuscitation with blood products. Level of evidence: IIc. Strength of recommendation: C.

Do Vasoactive Drugs Play a Role in Early Resuscitation of the Trauma Patient?

The use of vasopressors in the acute resuscitation of trauma patients has regained substantial interest in recent years. Although multiple animal studies demonstrate dramatic survival advantage associated with early vasopressor use in trauma resuscitation, the clinical trial data squarely dispute these findings (35,36). The available clinical data suggest no morbidity or mortality advantage, and one recent trial demonstrated a significantly greater mortality in the vasopressor group (35).

Although the early use of vasopressors after trauma remains an intense research interest, this practice is not currently supported by the existing body of clinical data. Hypotensive blunt trauma patients should be managed with aggressive crystalloid resuscitation. Level of evidence: IIc. Strength of recommendation: C.

CLOSING COMMENTS

The practice of evidence-based medicine allows the surgeon to make decisions based in the best science possible. By definition, evidence applies to populations of patients who share common characteristics. I implore you, when your patient is failing to respond to conventional therapy, to reevaluate how that patient is *different* from the evidence-based study population. Often, what is good therapy for the population may not be entirely appropriate for a specific individual or group of individuals who make up a subset population. Sometimes these difficult patients provide insight and lead to the next great randomized controlled trial that alters the way we practice surgery. Perhaps such a study will be included in the next edition of this textbook.

REFERENCES

1. Rutkow IM. *Surgery: An Illustrated History*. St. Louis, MO: Mosby, 1993.
2. Cannon W, Fraser J, Cowell E. Preventive treatment of wound shock. *JAMA* 1918; 70: 618–21.
3. Vassar MJ, Perry CA, Gannaway WL, et al. 7.5% sodium chloride/dextran for resuscitation of trauma patients undergoing helicopter transport. *Arch Surg* 1991; 126: 1065–72.
4. Vassar MJ, Fischer RP, O'Brien PE, et al. A multicenter trial for resuscitation of injured patients with 7.5% sodium chloride. The effect of added dextran 70. The Multicenter Group for the Study of Hypertonic Saline in Trauma Patients. *Arch Surg* 1993; 128: 1003–111; discussion 1011–13.
5. Mattox KL, Maningas PA, Moore EE, et al. Prehospital hypertonic saline/dextran infusion for post-traumatic hypotension. The U.S.A. Multicenter Trial. *Ann Surg* 1991; 213: 482–91.
6. Wade CE, Grady JJ, Kramer GC. Efficacy of hypertonic saline dextran fluid resuscitation for patients with hypotension from penetrating trauma. *J Trauma* 2003; 54(5 Suppl): S144–8.
7. Tranbaugh RF, Lewis FR. Crystalloid versus colloid for fluid resuscitation of hypovolemic patients. *Adv Shock Res* 1983; 9: 203–16.
8. SAFE Study Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group; Australian Red Cross Blood Service; George Institute for International Health, Myburgh J, Cooper DJ, Finfer S, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med* 2007; 357: 874–84.
9. Finfer S, Bellomo R, Boyce N, et al. SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 2004; 350: 2247–56.
10. Dutton RP, Mackenzie CF, Scalea TM. Hypotensive resuscitation during active hemorrhage: Impact on in-hospital mortality. *J Trauma* 2002; 52: 1141–6.
11. York J, Arrillaga A, Graham R, et al. Fluid resuscitation of patients with multiple injuries and severe closed head injury: experience with an aggressive fluid resuscitation strategy. *J Trauma* 2000; 48: 376–9; discussion 379–80.
12. Shatney CH, Deepika K, Militello PR, et al. Efficacy of hetastarch in the resuscitation of patients with multisystem trauma and shock. *Arch Surg* 1983; 118: 804–9.
13. Bulger EM, Jurkovich GJ, Nathens AB, et al. Hypertonic resuscitation of hypovolemic shock after blunt trauma: a randomized controlled trial. *Arch Surg* 2008; 143: 139–48; discussion 149.
14. Rizoli SB, Rhind SG, Shek PN, et al. The immunomodulatory effects of hypertonic saline resuscitation in patients sustaining traumatic hemorrhagic shock: a randomized, controlled, double-blinded trial. *Ann Surg* 2006; 243: 47–57.
15. Cooper DJ, Myles PS, McDermott FT, et al. HTS Study Investigators. Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trial. *JAMA* 2004; 291: 1350–7.
16. Velmahos GC, Demetriades D, Shoemaker WC, et al. End-points of resuscitation of critically injured patients: normal or supranormal? A prospective randomized trial. *Ann Surg* 2000; 232: 409–18.
17. Allison KP, Gosling P, Jones S, et al. Randomized trial of hydroxyethyl starch versus gelatine for trauma resuscitation. *J Trauma* 1999; 47: 1114–21.
18. Sloan EP, Koenigsberg M, Gens D, et al. Diaspirin cross-linked hemoglobin (DCLHb) in the treatment of severe traumatic hemorrhagic shock: a randomized controlled efficacy trial. *JAMA* 1999; 282: 1857–64.
19. Younes RN, Yin KC, Amino CJ, et al. Use of pentastarch solution in the treatment of patients with hemorrhagic hypovolemia: Randomized phase II study in the emergency room. *World J Surg* 1998; 22: 2–5.
20. Miller PR, Meredith JW, Chang MC. Randomized, prospective comparison of increased preload versus inotropes in the resuscitation of trauma patients: effects on cardiopulmonary function and visceral perfusion. *J Trauma* 1998; 44: 107–13.
21. Durham RM, Neunaber K, Mazuski JE, et al. The use of oxygen consumption and delivery as endpoints for

- resuscitation in critically ill patients. *J Trauma* 1996; 41: 32–9; discussion 39–40.
22. Bickell WH, Wall MJ Jr, Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med* 1994; 331: 1105–9.
 23. Nagy KK, Davis J, Duda J, et al. A comparison of pentastarch and lactated Ringer's solution in the resuscitation of patients with hemorrhagic shock. *Circ Shock* 1993; 40: 289–94.
 24. Vassar MJ, Perry CA, Holcroft JW. Prehospital resuscitation of hypotensive trauma patients with 7.5% NaCl versus 7.5% NaCl with added dextran: a controlled trial. *J Trauma* 1993; 34: 622–32; discussion 632–3.
 25. Younes RN, Aun F, Accioly CQ, et al. Hypertonic solutions in the treatment of hypovolemic shock: a prospective, randomized study in patients admitted to the emergency room. *Surgery* 1992; 111: 380–5.
 26. Holcroft JW, Vassar MJ, Turner JE, et al. 3% NaCl and 7.5% NaCl/dextran 70 in the resuscitation of severely injured patients. *Ann Surg* 1987; 206: 279–88.
 27. Modig J. Advantages of dextran 70 over Ringer acetate solution in shock treatment and in prevention of adult respiratory distress syndrome. A randomized study in man after traumatic-haemorrhagic shock. *Resuscitation* 1983; 10: 219–26.
 28. Moss GS, Lowe RJ, Jilek J, et al. Colloid or crystalloid in the resuscitation of hemorrhagic shock: a controlled clinical trial. *Surgery* 1981; 89: 434–8.
 29. Lowe RJ, Moss GS, Jilek J, et al. Crystalloid versus colloid in the etiology of pulmonary failure after trauma—a randomized trial in man. *Crit Care Med* 1979; 7: 107–12.
 30. Wu JJ, Huang MS, Tang GJ, et al. Hemodynamic response of modified fluid gelatin compared with lactated Ringer's solution for volume expansion in emergency resuscitation of hypovolemic shock patients: preliminary report of a prospective, randomized trial. *World J Surg* 2001; 25: 598–602.
 31. Moore EE, Cheng AM, Moore HB, et al. Hemoglobin-based oxygen carriers in trauma care: Scientific rationale for the US multicenter prehospital trial. *World J Surg* 2006; 30: 1247–57.
 32. Natanson C, Kern SJ, Lurie P, et al. Cell-free hemoglobin-based blood substitutes and risk of myocardial infarction and death: a meta-analysis. *JAMA* 2008; 299: 2304–12.
 33. www.fda.gov/ohrms/dockets/ac/06/minutes/2006-4270M.htm
 34. Presentation at NIH/FDA HBOC Workshop, April 29–30, 2008.
 35. Sperry JL, Minei JP, Frankel HL, et al. Early use of vasopressors after injury: caution before constriction. *J Trauma* 2008; 64: 9–14.
 36. Lienhart HG, Wenzel V, Braun J, et al. Vasopressin for therapy of persistent traumatic hemorrhagic shock: the VITRIS. at study. *Anaesthesist* 2007; 56: 145–8, 150.
 37. Eastridge BJ, Salinas J, McManus JG, et al. Hypotension begins at 110 mm Hg: Redefining “hypotension” with data. *J Trauma* 2007; 63: 291–7; discussion 297–9.
 38. McKinley BA, Marvin RG, Cocanour CS, et al. Tissue hemoglobin O₂ saturation during resuscitation of traumatic shock monitored using near infrared spectrometry. *J Trauma* 2000; 48: 637–42.
 39. Crookes BA, Cohn SM, Bloch S, et al. Can near-infrared spectroscopy identify the severity of shock in trauma patients? *J Trauma* 2005; 58: 806–13; discussion 813–16.
 40. Ikossi DG, Knudson MM, Morabito DJ, et al. Continuous muscle tissue oxygenation in critically injured patients: a prospective observational study. *J Trauma* 2006; 61: 780–8; discussion 788–90.
 41. Spinella PC, Perkins JG, Grathwohl KW, et al. Effect of plasma and red blood cell transfusions on survival in patients with combat related traumatic injuries. *J Trauma* 2008; 64(2 Suppl): S69–77; discussion S77–8.
 42. Stinger HK, Spinella PC, Perkins JG, et al. The ratio of fibrinogen to red cells transfused affects survival in casualties receiving massive transfusions at an army combat support hospital. *J Trauma* 2008; 64(2 Suppl): S79–85; discussion S85.
 43. Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007; 63: 805–13.

Diagnosis of Injury in the Trauma Patient

Pedro G. R. Teixeira and Kenji Inaba

Summary of Clinical Questions		
Question	Answer	Grade of recommendation
1 What is the role of FAST in the initial assessment of hemodynamically stable blunt trauma patients?	As a result of its low sensitivity and negative predictive value for intraperitoneal free fluid and intra-abdominal injuries, FAST should not be used as the only diagnostic modality to exclude significant intra-abdominal injury in the initial assessment of the blunt trauma patient.	B
	Patients with suspected intra-abdominal injury should undergo clinical observation or further investigation, irrespective of the ultrasound findings.	B
2 What is the role of FAST in the initial assessment of hemodynamically unstable blunt trauma patients?	FAST is specific and has a high positive predictive value for the presence of hemoperitoneum.	B
	A positive FAST warrants laparotomy in hemodynamically unstable patients.	B
	Hemodynamically unstable patients with a negative FAST may benefit from diagnostic peritoneal aspirate to rule out an intra-abdominal source of bleeding.	C
3 What is the role of ultrasound in the initial assessment of penetrating trauma patients: cardiac view and abdominal view?	Ultrasound should be the initial diagnostic modality for patients with penetrating precordial wounds.	A
	A positive ultrasound for fluid in the pericardial sac warrants immediate surgical intervention.	B
	The FAST is not a reliable imaging modality in penetrating trauma for ruling out significant intra-abdominal injury.	B
	Patients with penetrating injuries to the abdomen with a negative FAST require further investigation.	C
4 What is the current evidence to support the use of US for the diagnosis of pneumothorax in the resuscitation area?	Ultrasound is as or more sensitive than plain chest radiography and can be utilized to diagnose pneumothorax in injured patients.	A
5 Routine AP pelvis plain radiographs: are these mandatory?	Clinical assessment is sensitive for the identification of significant pelvic fractures in hemodynamically stable, evaluable trauma patients and routine pelvic plain films are unnecessary in this population.	B
6 What is the role of CT angiography in peripheral vascular injuries?	Multidetector helical CT angiography is sensitive for the identification of peripheral vascular injuries and can be used as the initial diagnostic modality for the assessment of suspected vascular injuries in the extremities.	B
Abbreviations: AP, ATLS protocol; CT, computed tomography; FAST, focused abdominal sonography for trauma; US, ultrasonography.		

Diagnostic imaging remains critical in the management of the acutely injured trauma patient, especially in this era of nonoperative management. As diagnostic technology evolves, constant reassessment is required to ensure that the sensitivity and specificity parameters of any diagnostic test are

well understood and that the target population is well defined so as to minimize cost, radiation burden, patient movement, and time.

For unstable patients, imaging is used to search for areas of hemorrhage, concurrent with resuscitative efforts.

In these patients, the primary goal is to diagnose and stop ongoing bleeding. The diagnosis of specific injuries can occur during exploration or can be delayed until all life-threatening injuries have been addressed. For stable patients, imaging is also essential for the diagnosis and characterization of specific injuries. For both stable and unstable patients, prompt and accurate diagnosis is essential. Blood loss is a major cause of early deaths after injury (1) and remains the primary cause of preventable and potentially preventable deaths at mature trauma centers (2,3). Once stabilized, missed injuries become a significant problem and contribute to an increase in morbidity and mortality.

Ultrasonography (US), plain radiographs, and computerized tomography (CT) are widely available imaging modalities that have been fully incorporated into the armamentarium of the trauma surgeon and are an essential component of trauma management algorithms. This chapter reviews the evidence base to support the use of these modalities for the initial assessment of the injured patient.

Focused abdominal sonography for trauma (FAST) is a standardized ultrasound examination that aims to identify the presence of free fluid in the pericardium and peritoneal cavity. As an initial diagnostic adjunct, the ultrasound has several advantages: It is noninvasive, repeatable, accessible, portable, rapid, and cost-effective. However, ultrasound is highly operator dependent, and several patient-related factors, such as subcutaneous emphysema, morbid obesity, severe chest wall injury, narrow subcostal area, and a large hemothorax, may limit adequate image acquisition.

WHAT IS THE ROLE OF FAST IN THE INITIAL ASSESSMENT OF THE HEMODYNAMICALLY STABLE BLUNT TRAUMA PATIENT?

Physical examination alone is unreliable for the diagnosis of intra-abdominal injuries in patients who have sustained blunt abdominal trauma (5,6). Diagnostic imaging is therefore relied on to diagnose or rule out intra-abdominal injuries. The ideal screening examination for intra-abdominal injuries would have a high degree of sensitivity, which would allow for the safe exclusion of significant injuries while maintaining an acceptable specificity, effectively decreasing the number of patients requiring definitive imaging.

Early reports suggesting a high sensitivity for the identification of intraperitoneal free fluid generated great enthusiasm for the use of FAST as a screening modality in the work-up of blunt trauma patients (7–10). The majority of the studies reporting high sensitivities for FAST, however, are limited by major methodological issues: A definitive reference gold standard was not applied to all patients and in the majority of studies, long-term follow-up was not available (11–17). This may contribute to an underestimation of false negative results. More important, recent studies and systematic reviews have challenged the value of the FAST examination in the initial evaluation of blunt trauma patients, specifically because of its inability to rule out significant intra-abdominal injuries. Increasing concerns that FAST may miss clinically significant injuries have contributed to an increasing awareness about the limitations of this imaging modality as a screening method for blunt abdominal trauma.

It has been demonstrated that 18–26% of the patients with intra-abdominal injuries had no detectable free intraperitoneal fluid (18,19) and that up to 29% of abdominal injuries may be missed if ultrasound is the only diagnostic adjunct utilized in blunt trauma patients (18).

In a well-designed prospective study with uniform application of CT scan as the standard reference in all enrolled patients, Miller and colleagues found that the FAST examination had a 42% sensitivity for intraperitoneal fluid in hemodynamically stable patients. They concluded that the ultrasound should not be the sole screening method for the evaluation of blunt abdominal trauma. Likewise, Richards and colleagues found emergent ultrasound to be only 60% sensitive for the detection of intraperitoneal fluid (20). In a comprehensive review, Stengel et al. identified sufficient Level IIb and IIIb data to support a grade B recommendation regarding the use of ultrasound in the initial assessment of patients with blunt abdominal trauma. The concerning finding of this study was that significant bias existed in most of the studies included in the review, which contributed to an overestimation of the diagnostic power of ultrasound. The review concluded that FAST lacked sensitivity and negative predictive value for the identification of intra-abdominal injuries in the pooled data and therefore constituted a poor screening method for this patient population. In this study, a negative ultrasound could not reliably rule out significant injury, missing 1 in every 10 abdominal injuries.

Likewise, the review of currently available evidence by Griffin et al. concluded that FAST cannot reduce CT scan utilization without negatively affecting outcomes (21). Finally, a Cochrane review analyzing ultrasound-based treatment algorithms suggested that the use of ultrasound in the evaluation of trauma patients had minimal impact on management decisions (22).

Recommendation: As a result of its low sensitivity and negative predictive value for intraperitoneal free fluid and intra-abdominal injuries, FAST should not be used as the only diagnostic modality to exclude significant intra-abdominal injury in the initial assessment of the blunt trauma patient (grade B). Patients with suspected intra-abdominal injury should undergo clinical observation or further investigation, irrespective of ultrasound findings (grade B).

WHAT IS THE ROLE OF FAST IN THE INITIAL ASSESSMENT OF THE HEMODYNAMICALLY UNSTABLE BLUNT TRAUMA PATIENT?

The FAST examination has largely supplanted diagnostic peritoneal lavage as the primary diagnostic adjunct for the identification of free intra-abdominal fluid in hemodynamically unstable patients. A positive FAST in the setting of hemodynamic instability mandates immediate surgical intervention to rule out intra-abdominal bleeding as the source of the instability. A positive FAST in hemodynamically unstable blunt injured patients correlated to a therapeutic laparotomy in 64–83% of the cases (23–25). For the hypotensive blunt trauma patient, a negative ultrasound is less useful. Recent studies report a significant number of false negative results in this setting. Lee et al. demonstrated that 37% of the patients with a negative FAST exam on initial investigation required therapeutic

laparotomy (23). In another study, Holmes et al. also found that 32% of the unstable patients with a negative ultrasound had intra-abdominal injuries.

One option to mitigate this lack of sensitivity for intra-abdominal bleeding in the unstable blunt trauma patient is the diagnostic peritoneal aspirate (DPA). Hypothesizing that intraperitoneal blood of sufficient volume to cause hypotension would be accurately detected by DPA, Kuncir and colleagues prospectively compared FAST to DPA using laparotomy, CT scan, and autopsy findings as reference standards (26). In this study, DPA was found to be more sensitive and specific for the identification of intra-abdominal bleeding at 89% and 100% respectively, than ultrasound at 50% and 95%.

Recommendation: The FAST exam is specific and has a high positive predictive value for the presence of hemoperitoneum (grade B). A positive FAST warrants laparotomy in hemodynamically unstable patients (grade B). Hemodynamically unstable patients with a negative FAST may benefit from DPA to rule out an intra-abdominal source of bleeding (grade C).

WHAT IS THE ROLE OF ULTRASOUND IN THE INITIAL ASSESSMENT OF PENETRATING TRAUMA PATIENTS: CARDIAC VIEW AND ABDOMINAL VIEW?

Time is of the essence in the management of cardiac injuries. Early diagnosis and treatment are critical factors for survival. The physical examination and percutaneous pericardiocentesis however, are inaccurate for the diagnosis of cardiac injury.

The cardiac component of the FAST examination, which is the assessment of the pericardial sac for the presence of fluid, is an immediately available, repeatable, and noninvasive diagnostic option. In a well-designed prospective study, Rozycki et al. investigated the role of ultrasound as the primary imaging modality used to determine the need for surgical intervention in patients with suspected cardiac injuries (27). The ultrasound was 100% accurate in detecting hemopericardium, with no false positive or false negative results. These findings were subsequently replicated in four further prospective studies (10,28–30). One of these was a prospective multicenter study with five participating Level I trauma centers demonstrating that ultrasound was reliable for the identification of hemopericardium in high-risk patients with penetrating torso injuries, with a 100% sensitivity and 97% specificity (28). The high survival rate among patients with hemopericardium observed in this study (96.5%) suggests that the use of ultrasound for investigating penetrating thoracic injuries contributed to the prompt and accurate diagnosis of cardiac injuries.

The utility of the abdominal windows of the FAST examination in penetrating injuries is less clear. For patients sustaining penetrating abdominal trauma and have a clear indication for laparotomy, such as peritonitis or hemodynamic instability, the FAST results will not alter management. For the patient without a clear indication for laparotomy being considered for nonoperative management, likewise, FAST will not impact clinical decision making. Even if positive for fluid, a positive FAST is no longer a contraindication to a nonoperative management strategy

because there may be a solid organ injury that has resulted in hemoperitoneum and the positive FAST but not require laparotomy (31,32). If the FAST is negative, in the setting of penetrating abdominal injuries it is not reliable for the exclusion of clinically significant intra-abdominal injuries. Udobi et al. investigated 75 hemodynamically stable patients sustaining penetrating abdominal trauma and demonstrated that the ultrasound lacked sensitivity, identifying only 46% of the patients with intra-abdominal injury (33). The authors suggested that penetrating trauma is more localized and significant injuries may exist without the presence of significant amounts of intra-abdominal fluid. These findings were corroborated by three other prospective studies that found the FAST exam to be poorly sensitive (48–71%) for intra-abdominal injuries (34–36). In the study by Soffer et al., the majority of positive laparotomies could be predicted by clinical criteria such that the ultrasound resulted in a change of management in only 1.7% of the patients in their series (36).

Recommendation: Ultrasound should be the initial diagnostic modality for patients with penetrating precordial wounds (grade A), and a positive ultrasound for fluid in the pericardial sac warrants immediate surgical intervention (grade B). The FAST exam is not a reliable imaging modality in penetrating trauma for ruling out significant intra-abdominal injury (grade B). Patients with penetrating injuries to the abdomen with a negative FAST require further investigation (grade C).

WHAT IS THE CURRENT EVIDENCE TO SUPPORT THE USE OF US FOR THE DIAGNOSIS OF PNEUMOTHORAX IN THE RESUSCITATION AREA?

Traditionally, the diagnosis of pneumothorax is established using plain radiography. The gold standard imaging modality is CT, which is a highly sensitive and specific method for the detection of pneumothorax (37).

Plain radiography however has several limitations. Because the air accumulates preferentially in the anteromedial and subpulmonic region in patients in the supine position, radiographic images obtained in supine trauma patients may miss pneumothoraces, although the clinical significance of these occult pneumothoraces is questionable (38,39). The process of obtaining the plain radiographs, however, is time consuming, involves radiation, and suffers from a delay to obtain the images—all of which may be obviated with the advantages of ultrasound. The technique for diagnosing pneumothoraces using ultrasound has been described (40–43), and several series describing the diagnosis of pneumothorax with ultrasound have been published (40,44,45).

Rowan et al. demonstrated in a small prospective study that US was more sensitive and accurate than plain chest x-ray in the detection of pneumothorax and had a sensitivity comparable to CT scan (46). Two further prospective studies using CT scan as a reference standard have demonstrated a higher sensitivity for ultrasound compared to plain chest x-ray (92–98% versus 52–76%) (47,48). Two large prospective studies comparing ultrasound to plain chest radiography demonstrated that the ultrasound had a sensitivity of 92–95% and specificity of 97–100% in identifying pneumothorax (49,50). Using a composite gold standard

for pneumothorax that included chest x-ray and CT scan results as well as a positive air leak on chest tube insertion, Kirkpatrick et al. demonstrated a 59% sensitivity and 99% specificity for pneumothorax detection by hand-held ultrasound (51). Zhang et al. demonstrated in a prospective study that ultrasound outperformed plain x-ray for the detection of pneumothorax (86% versus 28%, $p < 0.001$), allowed a significantly faster detection of pneumothorax (2.3 ± 2.9 versus 19.9 ± 10.3 , $p < 0.001$), and had stronger agreement with CT scan findings (52). Despite its ability to specifically diagnose pneumothoraces, the role of thoracic US in a diagnostic algorithm has not yet been clarified because most patients at risk for a pneumothorax will get a chest x-ray.

Recommendation: Ultrasound is as or more sensitive than plain chest radiography and can be used to diagnose pneumothorax in injured patients (grade B).

ROUTINE PELVIS PLAIN FILMS: ARE THESE MANDATORY FILMS?

According to the Advanced Trauma Life Support protocol, chest and pelvis plain films are adjuncts to the primary survey (53). Pelvic fractures are common, occurring in 9–13% of patients admitted to a high-volume academic Level I trauma center and account for significant morbidity and mortality (54,55).

Early identification of pelvic fractures is critical because they can be a source of significant bleeding and are commonly associated with other intra-abdominal injuries. In hemodynamically unstable patients and in non-evaluable patients where there is suspicion of a pelvic injury, plain pelvic radiography can provide clinically useful information. Once other bleeding sources have been ruled out, in unstable patients with pelvic fractures, angiography and embolization remain a valid treatment option, particularly with specific fracture patterns such as the disruption of the sacroiliac joint, which has been identified as an independent predictor of positive pelvic angiography (55).

Most blunt trauma patients, however, do not have pelvic fractures, and the policy of routinely obtaining pelvic x-rays would expose a large number of patients to unnecessary radiation and result in increased costs and time. It has been suggested that the routine pelvic x-ray may not be necessary in all injured patients and a selective policy of obtaining these films based on clinical parameters and risk stratification can be safely adopted (56–62).

Gross et al. analyzed a set of criteria to rule out the presence of pelvic fracture: Glasgow Coma Score (GCS) ≥ 14 , no complaint of pelvic pain, no pelvic tenderness on physical examination, no distracting injury, and no intoxication. They were able to demonstrate that in patients that met all these criteria, a clinically significant pelvic fracture could be safely ruled out (59). Gonzalez and colleagues demonstrated that in patients who were awake and alert, the physical exam was a reliable screening method to identify pelvic fractures, with 93% sensitivity and none of the pelvic fractures missed by clinical examination required surgical intervention (56). These findings corroborated the earlier data presented by Salvino et al., who demonstrated that routine pelvic plain films performed for patients without

clinical findings had an extremely low yield of 1%, and no clinically significant fracture was identified by plain films that had not been suspected on clinical grounds (60). Yugueros and colleagues demonstrated that a normal physical exam missed only 2 in 57 pelvic fractures in hemodynamically stable blunt trauma patients with a GCS ≥ 10 and without spinal injury. Both missed fractures required no specific treatment.

Other authors have demonstrated that for hemodynamically stable patients in whom the mechanism of injury warrants investigation with CT scan, the plain pelvic film does not provide any additional decision-making information and therefore does not impact patient management (63–66).

Recommendation: Clinical assessment is sensitive for identification of significant pelvic fractures in hemodynamically stable, evaluable trauma patients and routine pelvic plain films are unnecessary in this population (grade B).

WHAT IS THE ROLE OF CT-ANGIOGRAPHY IN PERIPHERAL VASCULAR INJURIES?

Traditionally, catheter-based angiography has been considered the gold standard for the diagnosis of extremity vascular injuries. This invasive diagnostic modality, however, is associated with complications related to the access site (thrombosis, dissection, and pseudo-aneurysm formation) (67–69) and to the use of contrast, such as nephropathy and allergic reactions. Catheter angiography is also a time-consuming procedure that involves the mobilization of an interventional radiology team, which in many institutions is not in-house and may result in a significant delay.

The evolution of computed tomographic technology, with the advent of newer generation multidetector scanners, has expanded the application of this technology to include the assessment of vascular structures (70,71). Multidetector computed tomographic angiography (CTA) provides high-resolution vascular imaging, with minimal motion artifact and three-dimensional reconstruction capabilities. Albrecht and colleagues demonstrated in a well-designed prospective study that compared to digital subtraction angiography, 16-slice multidetector CTA was highly sensitive and specific for the detection of nontraumatic stenoses of the aortoiliac and lower extremity arteries (72).

The emergence of the CTA as an alternative to formal catheter-based angiography in trauma has multiple advantages. It is a noninvasive method, no arterial catheterization is required, significantly lower volumes of contrast are necessary, and it can be performed as part of the CT scan sequence in multisystem trauma patients.

CTA technology has been assessed as the primary imaging modality for the initial assessment of the peripheral vasculature in injured patients (73). Busquets et al. reviewed 95 cases of extremity injuries assessed with CTA and demonstrated that all injuries identified on CTA (25 cases) were confirmed by arteriography and/or surgery and no injury was missed (74). Iezzi and colleagues found the CTA to be 96% sensitive and 90% specific for traumatic arterial injuries of the lower extremities (75), corroborating the findings previously reported by Inaba and colleagues, who demonstrated that multislice helical CTA was 100%

sensitive and 100% specific in detecting clinically significant arterial injuries (76). Rieger et al. demonstrated that CTA was sufficient for a reliable diagnosis in 95% of the patients with extremity trauma and permitted adequate imaging not only of the main arteries but also of their major branches (77). Finally, Soto et al. demonstrated that CTA was sufficient to correctly guide treatment in 94% of

134 patients with suspected arterial injuries in the proximal portions of the extremities (78).

Recommendation: Multidetector helical CTA is sensitive for the identification of peripheral vascular injuries and can be used as the initial diagnostic modality for the assessment of suspected vascular injuries in the extremities (grade B).

Levels of Evidence

Questions	Author	Ref.	Year	Reference standards	Level of evidence	Design	Endpoint	Interpretation/Comments
1	Stengel	22	2005	—	IIIa	Systematic review (Cochrane Review)	Evaluation of the efficiency and effectiveness of ultrasound-based algorithms	The utilization of ultrasound in the evaluation of trauma patients had minimal impact on management decision.
1, 2	Stengel	79	2001	—	IIIa	Systematic review (meta-analysis)	Evaluation of US as the primary assessment modality in blunt abdominal trauma	Pooled data demonstrated that ultrasound had low sensitivity and NPV for intra-abdominal injury. Initial ultrasound would not be suitable as the only diagnostic modality to exclude significant intra-abdominal injury.
1	Griffin	21	2007	—	IIIa	Systematic review	Evaluation of FAST as screening test to reduce the use of CT scan	Failed to demonstrate that FAST-based protocols can reduce CT scan utilization without negatively affecting outcomes.
1, 2	Kirkpatrick	80	2005	Laparotomy, CT scan, observation	IIIb	Prospective diagnostic study	Intraperitoneal free fluid	274 patients with blunt abdominal trauma. Formal FAST: sensitivity 69%, specificity 97%, PPV 83%, NPV 93%, accuracy 92%. Hand-held FAST: sensitivity 77%, specificity 99%, PPV 96%, NPV 94%, accuracy 95%.
							Intra-abdominal injury	Formal FAST: sensitivity 52%, specificity 97%, PPV 83%, NPV 86%, accuracy 86%. Hand-held FAST: sensitivity 63%, specificity 99%, PPV 96%, NPV 89%, accuracy 90%.
1, 2	Miller	81	2003	CT scan	IIb	Prospective diagnostic study	Intraperitoneal free fluid	356 hemodynamically stable patients with blunt abdominal injury. FAST sensitivity 42%, specificity 98%, PPV 67%, NPV 93%, accuracy 92%.
1, 2	Richards	20	2002	Laparotomy, CT scan, DPL observation	IIIb	Prospective diagnostic study	Intraperitoneal free fluid	3264 patients with blunt abdominal trauma. FAST sensitivity 60%, specificity 98%, PPV 82%, NPV 95%.
2	Holmes	25	2004	Laparotomy, CT scan, observation	IIIb	Retrospective diagnostic study	Intra-abdominal injury and hemoperitoneum	447 hypotensive blunt injured patients. Sensitivity 79%, specificity 95%, PPV 86%, NPV 93%.
2	Farahmand	24	2005	Laparotomy, CT scan, observation	IIIb	Retrospective diagnostic study	Intra-abdominal injury and hemoperitoneum	130 hypotensive blunt injured patients. Sensitivity 85%, specificity 96%, PPV 94%, NPV 90%, accuracy 91%.

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Levels of Evidence (Continued)

Questions	Author	Ref.	Year	Reference standards	Level of evidence	Design	Endpoint	Interpretation/Comments
2	Kuncir	26	2007	Laparotomy, CT scan, autopsy	IIb	Prospective diagnostic study	Diagnosis of intra-abdominal bleeding as the source of hemodynamic instability	62 hemodynamically unstable blunt injured patients. All underwent FAST and DPA. FAST: sensitivity 50%, specificity 95%. DPA: sensitivity 89%, specificity 100%.
3	Rozycki	27	1996	Sternotomy, observation	Ib	Prospective diagnostic study	Identification of intrapericardial fluid	247 consecutive patients with penetrating chest injuries (121 gunshot wound, 126 SW). Sensitivity 100%, specificity 100%, PPV 100%, NPV 100%.
3	Rozycki	10	1998	Sternotomy, observation	IIIb	Prospective diagnostic study	Identification of intrapericardial fluid	313 nonconsecutive patients with penetrating precordial or transthoracic injuries. Sensitivity 100%, specificity 99%, PPV 92%, NPV 100%.
3	Rozycki	28	1999	Sternotomy, observation	IIIb	Prospective multicenter diagnostic study	Identification of intrapericardial fluid	261 nonconsecutive patients (175 SW, 83 gunshot wound, 3 Shot gun wounds). Sensitivity 100%, specificity 97%, PPV 81%, NPV 100%. Lack of follow-up of all patients after discharge.
3	Patel	29	2003	Sternotomy, observation	IIIb	Retrospective diagnostic study	Identification of intrapericardial fluid	478 penetrating thoracic trauma patients. Sensitivity 100%, specificity 99%, PPV 87%, NPV 100%.
3	Tayal	30	2004	Sternotomy, observation	IIIb	Prospective diagnostic study	Identification of intrapericardial fluid	32 patients with penetrating anterior chest trauma. Sensitivity 100%, specificity 100%, PPV 100%, NPV 100%.
3	Udobi	33	2001	Laparotomy, CT scan, observation	IIIb	Prospective diagnostic study	Intra-abdominal injury	75 consecutive stable patients with penetrating trauma to the abdomen. Sensitivity 46%, specificity 94%, PPV 90%, NPV 68%, accuracy 68%.
3	Boulanger	34	2001	Laparotomy, DPL, CT scan	IIIb	Prospective diagnostic study	Intra-abdominal injury	66 patients with penetrating abdominal injuries. Sensitivity 67%, specificity 98%, PPV 92%, NPV 89%, accuracy 89%.
3	Soffer	36	2004	Laparotomy, CT scan, observation	IIIb	Prospective diagnostic study	Intra-abdominal injury	177 patients with penetrating torso trauma. Sensitivity 48%, specificity 98%, PPV 89%, NPV 82%, accuracy 83%.
3	Kirkpatrick	35	2004	Laparotomy, CT scan, observation, autopsy	IIIb	Prospective diagnostic study	Intra-abdominal injury	38 patients with penetrating abdominal trauma. Formal FAST: sensitivity 50%, specificity 100%, PPV 100%, NPV 86%, accuracy 89%. Hand-held FAST: sensitivity 92%, specificity 100%, PPV 100%, NPV 96%, accuracy 97%.

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Levels of Evidence (Continued)

Questions	Author	Ref.	Year	Reference standards	Level of evidence	Design	Endpoint	Interpretation/Comments
4	Rowan	46	2002	CT scan	IIIb	Prospective blinded diagnostic study	Pneumothorax detection	27 nonconsecutive patients. US sensitivity 100%, specificity 94%, PPV 92%, NPV 100%. Plain chest x-ray: 36% sensitivity, 100% specificity, PPV 100%, NPV 70%.
4	Blaivas	47	2005	CT scan	IIIb	Prospective single-blinded diagnostic study with convenience sampling	Pneumothorax detection	176 patients. US: sensitivity 98%, specificity 99%, PPV 98%, NPV 99%. Chest x-ray: sensitivity 76%, specificity 100%, PPV 100%, NPV 90%.
4	Dulchavsky	49	2001	Plain chest x-ray	IIIb	Prospective diagnostic study	Pneumothorax detection	382 stable surgical patient (95% trauma). Sensitivity 95%, specificity 100%. The use of chest x-ray as gold standard is a weakness.
4	Knudtson	50	2004	Plain chest x-ray	IIIb	Prospective diagnostic study	Pneumothorax detection	328 patients. Sensitivity 92%, specificity 99%, PPV 92%, NPV 99%, accuracy 99%. The use of chest x-ray as gold standard is a weakness.
4	Kirkparick	51	2004	Composite standard (plain chest x-ray, CT scan, or positive air leak on chest tube insertion)	IIIb	Prospective diagnostic study	Pneumothorax detection	225 patients. US: sensitivity 59%, specificity 99%, PPV 92%, NPV 94%.
4	Zhang	52	2006	CT scan or positive air leak on chest tube insertion	IIIb	Prospective blinded diagnostic study	Pneumothorax detection and pneumothorax size estimation	135 consecutive patients. US: sensitivity 86%, specificity 97%, PPV 89%, NPV 96%. Chest x-ray: sensitivity 28%, specificity 100%, PPV 100%, NPV 84%. Size determination of pneumothorax in agreement with CT scan findings.
4	Soldati	48	2006	CT scan	IIb	Prospective blinded diagnostic study	Pneumothorax detection and pneumothorax size estimation	186 consecutive patients. US: sensitivity 98%, specificity 100%, PPV 100%, NPV 99%. Chest x-ray: sensitivity 54%, specificity 100%, PPV 100%, NPV 83%. Size determination of pneumothorax in agreement with CT scan findings.
4	Soldati	82	2008	CT scan	Ib	Prospective multicenter blinded diagnostic study	Pneumothorax detection and pneumothorax size estimation	109 consecutive patients. US: sensitivity 92%, specificity 99%, PPV 96%, NPV 99%. Chest x-ray: sensitivity 52%, specificity 100%, PPV 100%, NPV 94%. Size determination of pneumothorax in agreement with CT scan findings.

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Levels of Evidence (Continued)

Questions	Author	Ref.	Year	Reference standards	Level of evidence	Design	Endpoint	Interpretation/Comments
5	Gonzalez	56	2002	Pelvic x-ray, CT scan	IIb	Prospective diagnostic study	Identification of pelvic fracture by clinical exam	2,176 consecutive blunt trauma patients presenting with GCS ≥ 14 . Physical exam sensitivity: 93%.
5	Salvino	60	1992	Pelvic x-ray, CT scan	IIb	Prospective diagnostic study	Identification of pelvic fracture by clinical exam	810 consecutive blunt trauma patients presenting with GCS ≥ 13 . Physical exam sensitivity 92%, specificity 96%, PPV 56%, NPV 99%.
5	Yugueros	61	1995	Pelvic x-ray	IIb	Prospective diagnostic blinded study	Identification of pelvic fracture by clinical exam	608 consecutive blunt trauma patients older than 13 years, with GCS ≥ 10 , hemodynamically stable and without spinal injury. Sensitivity 96%, specificity 95%, NPV 99%, accuracy 95%.
6	Busquets	74	2007	Surgery, conventional arteriography, observation	IV	Retrospective diagnostic study	Vascular injury identification	97 injured patients with extremity injuries. All 25 injuries identified on CT-angio confirmed by arteriography and/or surgery. No missed injuries.
6	Peng	73	2008	Surgery, conventional arteriography, observation	IV	Retrospective diagnostic study	Vascular injury identification	38 injured patients undergoing CT-angio of the extremities. No missed injuries.
6	Iezzi	75	2007	Surgery, conventional arteriography, observation	IIIb	Retrospective diagnostic study	Vascular injury identification	47 patients with suspected arterial injury in the lower extremities undergoing CT-angio. Sensitivity 96%, specificity 90%, accuracy 94%.
6	Inaba	76	2006	Composite standard (surgery, duplex ultrasound, conventional angiography, and clinical follow-up)	IIIb	Retrospective diagnostic study	Vascular injury identification	59 patients with suspected arterial injury in the lower extremities undergoing CT-angio. Sensitivity 100%, specificity 100%.
6	Rieger	77	2006	Surgery, conventional arteriography, observation	IIIb	Retrospective diagnostic study	Vascular injury identification	87 patients with suspected arterial injury in the extremities. Sensitivity 99%, specificity 87%.
6	Soto	78	2001	Surgery, conventional arteriography, observation	IIIb	Prospective diagnostic study	Vascular injury identification	139 patients (142 arterial segments with clinical suspicion of injury were imaged). Sensitivity 95%, specificity 99%.
6	Soto	83	1999	Angiography	IIIb	Prospective diagnostic study	Vascular injury identification	43 patients with suspected arterial injury in the extremities. CT-angios interpreted by two independent readers. Reader 1: sensitivity 90%, specificity 100. Reader 2: sensitivity 100%, specificity 100%.

Abbreviations: AP, ATLS protocol; CT, computed tomography; DPA, diagnostic peritoneal aspirate; DPL, diagnostic peritoneal lavage; FAST, focused abdominal sonography for trauma; NPV, negative predictive value; PPV, positive predictive value; SW, stab wound; US, ultrasonography.

REFERENCES

1. Sauaia A, Moore FA, Moore EE, et al. Epidemiology of trauma deaths: a reassessment. *J Trauma* 1995; 38: 185–93.
2. Gruen RL, Jurkovich GJ, McIntyre LK, et al. Patterns of errors contributing to trauma mortality: lessons learned from 2,594 deaths. *Ann Surg* 2006; 244: 371–80.
3. Teixeira PG, Inaba K, Hadjizacharia P, et al. Preventable or potentially preventable mortality at a mature trauma center. *J Trauma* 2007; 63: 1338–46; discussion 1346–7.
4. Meyer DM, Jessen ME, Grayburn PA. Use of echocardiography to detect occult cardiac injury after penetrating thoracic trauma: a prospective study. *J Trauma* 1995; 39: 902–7; discussion 907–9.
5. Rodriguez A, DuPriest RW Jr, Shatney CH. Recognition of intra-abdominal injury in blunt trauma victims. A prospective study comparing physical examination with peritoneal lavage. *Am Surg* 1982; 48: 457–9.
6. Schurink GW, Bode PJ, van Luijt PA, et al. The value of physical examination in the diagnosis of patients with blunt abdominal trauma: a retrospective study. *Injury* 1997; 28: 261–5.
7. Boulanger BR, McLellan BA, Brenneman FD, et al. Emergent abdominal sonography as a screening test in a new diagnostic algorithm for blunt trauma. *J Trauma* 1996; 40: 867–74.
8. Healey MA, Simons RK, Winchell RJ, et al. A prospective evaluation of abdominal ultrasound in blunt trauma: is it useful? *J Trauma* 1996; 40: 875–83; discussion 883–5.
9. Rozycki GS, Ochsner MG, Jaffin JH, et al. Prospective evaluation of surgeons' use of ultrasound in the evaluation of trauma patients. *J Trauma* 1993; 34: 516–26; discussion 526–7.
10. Rozycki GS, Ballard RB, Feliciano DV, et al. Surgeon-performed ultrasound for the assessment of truncal injuries: lessons learned from 1540 patients. *Ann Surg* 1998; 228: 557–67.
11. Sirlin CB, Brown MA, Andrade-Barreto OA, et al. Blunt abdominal trauma: clinical value of negative screening US scans. *Radiology* 2004; 230: 661–8.
12. Nural MS, Yordan T, Guven H, et al. Diagnostic value of ultrasonography in the evaluation of blunt abdominal trauma. *Diag Interv Radiol* 2005; 11: 41–4.
13. Brown MA, Casola G, Sirlin CB, et al. Blunt abdominal trauma: screening us in 2,693 patients. *Radiology* 2001; 218: 352–8.
14. Bakker J, Genders R, Mali W, et al. Sonography as the primary screening method in evaluating blunt abdominal trauma. *J Clin Ultrasound* 2005; 33: 155–63.
15. Dolich MO, McKenney MG, Varela JE, et al. 2,576 ultrasounds for blunt abdominal trauma. *J Trauma* 2001; 50: 108–12.
16. Lingawi SS, Buckley AR. Focused abdominal US in patients with trauma. *Radiology* 2000; 217: 426–9.
17. Bode PJ, Edwards MJ, Kruit MC, et al. Sonography in a clinical algorithm for early evaluation of 1671 patients with blunt abdominal trauma. *Am J Roentgenol* 1999; 172: 905–11.
18. Chiu WC, Cushing BM, Rodriguez A, et al. Abdominal injuries without hemoperitoneum: a potential limitation of focused abdominal sonography for trauma (FAST). *J Trauma* 1997; 42: 617–23; discussion 623–5.
19. Yoshii H, Sato M, Yamamoto S, et al. Usefulness and limitations of ultrasonography in the initial evaluation of blunt abdominal trauma. *J Trauma* 1998; 45: 45–50; discussion 50–51.
20. Richards JR, Schleper NH, Woo BD, et al. Sonographic assessment of blunt abdominal trauma: a 4-year prospective study. *J Clin Ultrasound* 2002; 30: 59–67.
21. Griffin XL, Pullinger R. Are diagnostic peritoneal lavage or focused abdominal sonography for trauma safe screening investigations for hemodynamically stable patients after blunt abdominal trauma? A review of the literature. *J Trauma* 2007; 62: 779–84.
22. Stengel D, Bauwens K, Sehoul J, et al. Emergency ultrasound-based algorithms for diagnosing blunt abdominal trauma. *Cochrane Database Syst Rev* 2005; CD004446.
23. Lee BC, Ormsby EL, McGahan JP, et al. The utility of sonography for the triage of blunt abdominal trauma patients to exploratory laparotomy. *Am J Roentgenol* 2007; 188: 415–21.
24. Farahmand N, Sirlin CB, Brown MA, et al. Hypotensive patients with blunt abdominal trauma: performance of screening US. *Radiology* 2005; 235: 436–43.
25. Holmes JF, Harris D, Battistella FD. Performance of abdominal ultrasonography in blunt trauma patients with out-of-hospital or emergency department hypotension. *Ann Emerg Med* 2004; 43: 354–61.
26. Kuncir EJ, Velmahos GC. Diagnostic peritoneal aspiration—the foster child of DPL: a prospective observational study. *Int J Surg* 2007; 5: 167–71.
27. Rozycki GS, Feliciano DV, Schmidt JA, et al. The role of surgeon-performed ultrasound in patients with possible cardiac wounds. *Ann Surg* 1996; 223: 737–44; discussion 744–6.
28. Rozycki GS, Feliciano DV, Ochsner MG, et al. The role of ultrasound in patients with possible penetrating cardiac wounds: a prospective multicenter study. *J Trauma* 1999; 46: 543–51; discussion 551–2.
29. Patel AN, Brenning C, Cotner J, et al. Successful diagnosis of penetrating cardiac injury using surgeon-performed sonography. *Ann Thorac Surg* 2003; 76: 2043–6; discussion 2046–7.
30. Tayal VS, Beatty MA, Marx JA, et al. FAST (focused assessment with sonography in trauma) accurate for cardiac and intraperitoneal injury in penetrating anterior chest trauma. *J Ultrasound Med* 2004; 23: 467–72.
31. DuBose J, Inaba K, Teixeira PG, et al. Selective non-operative management of solid organ injury following abdominal gunshot wounds. *Injury* 2007; 38: 1084–90.
32. Demetriades D, Hadjizacharia P, Constantinou C, et al. Selective nonoperative management of penetrating abdominal solid organ injuries. *Ann Surg* 2006; 244: 620–8.
33. Udobi KF, Rodriguez A, Chiu WC, et al. Role of ultrasonography in penetrating abdominal trauma: a prospective clinical study. *J Trauma* 2001; 50: 475–9.
34. Boulanger BR, Kearney PA, Tsuei B, et al. The routine use of sonography in penetrating torso injury is beneficial. *J Trauma* 2001; 51: 320–5.
35. Kirkpatrick AW, Sirois M, Ball CG, et al. The hand-held ultrasound examination for penetrating abdominal trauma. *Am J Surg* 2004; 187: 660–5.
36. Soffer D, McKenney MG, Cohn S, et al. A prospective evaluation of ultrasonography for the diagnosis of penetrating torso injury. *J Trauma* 2004; 56: 953–7; discussion 957–9.
37. Wall SD, Federle MP, Jeffrey RB, et al. CT diagnosis of unsuspected pneumothorax after blunt abdominal trauma. *Am J Roentgenol* 1983; 141: 919–21.
38. Chan O, Hiorns M. Chest trauma. *Eur J Radiol* 1996; 23: 23–34.
39. Tocino IM, Miller MH, Fairfax WR. Distribution of pneumothorax in the supine and semirecumbent critically ill adult. *Am J Roentgenol* 1985; 144: 901–5.
40. Goodman TR, Traill ZC, Phillips AJ, et al. Ultrasound detection of pneumothorax. *Clin Radiol* 1999; 54: 736–9.
41. Lichtenstein D, Meziere G, Biderman P, et al. The comet-tail artifact: an ultrasound sign ruling out pneumothorax. *Intensive Care Med* 1999; 25: 383–8.
42. Lichtenstein DA, Menu Y. A bedside ultrasound sign ruling out pneumothorax in the critically ill. *Lung sliding*. *Chest* 1995; 108: 1345–8.
43. Wernecke K, Galanski M, Peters PE, et al. Pneumothorax: evaluation by ultrasound—preliminary results. *J Thorac Imaging* 1987; 2: 76–8.
44. Targhetta R, Bourgeois JM, Balmes P. Echography of pneumothorax. *Rev Mal Respir* 1990; 7: 575–9.
45. Targhetta R, Bourgeois JM, Chavagneux R, et al. Diagnosis of pneumothorax by ultrasound immediately after ultrasonically guided aspiration biopsy. *Chest* 1992; 101: 855–6.

46. Rowan KR, Kirkpatrick AW, Liu D, et al. Traumatic pneumothorax detection with thoracic US: Correlation with chest radiography and CT—initial experience. *Radiology* 2002; 225: 210–14.
47. Blaivas M, Lyon M, Duggal S. A prospective comparison of supine chest radiography and bedside ultrasound for the diagnosis of traumatic pneumothorax. *Acad Emerg Med* 2005; 12: 844–9.
48. Soldati G, Testa A, Pignataro G, et al. The ultrasonographic deep sulcus sign in traumatic pneumothorax. *Ultrasound Med Biol* 2006; 32: 1157–63.
49. Dulchavsky SA, Schwarz KL, Kirkpatrick AW, et al. Prospective evaluation of thoracic ultrasound in the detection of pneumothorax. *J Trauma* 2001; 50: 201–5.
50. Knudtson JL, Dort JM, Helmer SD, et al. Surgeon-performed ultrasound for pneumothorax in the trauma suite. *J Trauma* 2004; 56: 527–30.
51. Kirkpatrick AW, Sirois M, Laupland KB, et al. Hand-held thoracic sonography for detecting post-traumatic pneumothoraces: the Extended Focused Assessment with Sonography for Trauma (EFAST). *J Trauma* 2004; 57: 288–95.
52. Zhang M, Liu ZH, Yang JX, et al. Rapid detection of pneumothorax by ultrasonography in patients with multiple trauma. *Crit Care* 2006; 10: R112.
53. American College of Surgeons Committee on Trauma. ATLS—Advanced Trauma Life Support for Doctors. 2004.
54. Demetriades D, Karaiskakis M, Toutouzas K, et al. Pelvic fractures: epidemiology and predictors of associated abdominal injuries and outcomes. *J Am Coll Surg* 2002; 195: 1–10.
55. Salim A, Teixeira PG, DuBose J, et al. Predictors of positive angiography in pelvic fractures: a prospective study. *J Am Coll Surg* 2008; 207: 656–52.
56. Gonzalez RP, Fried PQ, Bukhalo M. The utility of clinical examination in screening for pelvic fractures in blunt trauma. *J Am Coll Surg* 2002; 194: 121–5.
57. Duane TM, Tan BB, Golay D, et al. Blunt trauma and the role of routine pelvic radiographs: a prospective analysis. *J Trauma* 2002; 53: 463–8.
58. Ersoy G, Karcioğlu O, Enginbas Y, et al. Should all patients with blunt trauma undergo “routine” pelvic X-ray? *Eur J Emerg Med* 1995; 2: 65–8.
59. Gross EA, Niedens BA. Validation of a decision instrument to limit pelvic radiography in blunt trauma. *J Emerg Med* 2005; 28: 263–6.
60. Salvino CK, Esposito TJ, Smith D, et al. Routine pelvic x-ray studies in awake blunt trauma patients: a sensible policy? *J Trauma* 1992; 33: 413–16.
61. Yugueros P, Sarmiento JM, Garcia AF, et al. Unnecessary use of pelvic x-ray in blunt trauma. *J Trauma* 1995; 39: 722–5.
62. Koury HI, Peschiera JL, Welling RE. Selective use of pelvic roentgenograms in blunt trauma patients. *J Trauma* 1993; 34: 236–7.
63. Guillaumondegui OD, Pryor JP, Gracias VH, et al. Pelvic radiography in blunt trauma resuscitation: a diminishing role. *J Trauma* 2002; 53: 1043–7.
64. Hilty MP, Behrendt I, Benneker LM, et al. Pelvic radiography in ATLS algorithms: a diminishing role? *World J Emerg Surg* 2008; 3: 11.
65. Kessel B, Sevi R, Jeroukhimov I, et al. Is routine portable pelvic x-ray in stable multiple trauma patients always justified in a high technology era? *Injury* 2007; 38: 559–63.
66. Obaid AK, Barleben A, Porral D, et al. Utility of plain film pelvic radiographs in blunt trauma patients in the emergency department. *Am Surg* 2006; 72: 951–4.
67. AbuRahma AF, Robinson PA, Boland JP, et al. Complications of arteriography in a recent series of 707 cases: factors affecting outcome. *Ann Vasc Surg* 1993; 7: 122–9.
68. Rose SC, Moore EE. Emergency trauma angiography: accuracy, safety, and pitfalls. *Am J Roentgenol* 1987; 148: 1243–6.
69. Sclafani SJ, Cooper R, Shaftan GW, et al. Arterial trauma: diagnostic and therapeutic angiography. *Radiology* 1986; 161: 165–72.
70. Willmann JK, Baumert B, Schertler T, et al. Aortoiliac and lower extremity arteries assessed with 16-detector row CT angiography: prospective comparison with digital subtraction angiography. *Radiology* 2005; 236: 1083–93.
71. Hiatt MD, Fleischmann D, Hellinger JC, et al. Angiographic imaging of the lower extremities with multidetector CT. *Radiol Clin North Am* 2005; 43: 1119–27, ix.
72. Albrecht T, Foert E, Holtkamp R, et al. 16-MDCT angiography of aortoiliac and lower extremity arteries: comparison with digital subtraction angiography. *Am J Roentgenol* 2007; 189: 702–11.
73. Peng PD, Spain DA, Tataria M, et al. CT angiography effectively evaluates extremity vascular trauma. *Am Surg* 2008; 74: 103–7.
74. Busquets AR, Acosta JA, Colon E, et al. Helical computed tomographic angiography for the diagnosis of traumatic arterial injuries of the extremities. *J Trauma* 2004; 56: 625–8.
75. Iezzi R, Cotroneo AR, Pascali D, et al. Multi-slice CT (MSCT) angiography for assessment of traumatic lesions of lower limbs peripheral arteries. *Emerg Radiol* 2007; 14: 389–94.
76. Inaba K, Potzman J, Munera F, et al. Multi-slice CT angiography for arterial evaluation in the injured lower extremity. *J Trauma* 2006; 60: 502–6; discussion 506–7.
77. Rieger M, Mallouhi A, Tauscher T, et al. Traumatic arterial injuries of the extremities: Initial evaluation with MDCT angiography. *Am J Roentgenol* 2006; 186: 656–64.
78. Soto JA, Munera F, Morales C, et al. Focal arterial injuries of the proximal extremities: Helical CT arteriography as the initial method of diagnosis. *Radiology* 2001; 218: 188–94.
79. Stengel D, Bauwens K, Sehouli J, et al. Systematic review and meta-analysis of emergency ultrasonography for blunt abdominal trauma. *Br J Surg* 2001; 88: 901–12.
80. Kirkpatrick AW, Sirois M, Laupland KB, et al. Prospective evaluation of hand-held focused abdominal sonography for trauma (FAST) in blunt abdominal trauma. *Can J Surg* 2005; 48: 453–60.
81. Miller MT, Pasquale MD, Bromberg WJ, Wasser TE, Cox J. Not so FAST. *J Trauma* 2003; 54: 52–9; discussion 59–60.
82. Soldati G, Testa A, Sher S, et al. Occult traumatic pneumothorax: diagnostic accuracy of lung ultrasonography in the emergency department. *Chest* 2008; 133: 204–11.
83. Soto JA, Munera F, Cardoso N, et al. Diagnostic performance of helical CT angiography in trauma to large arteries of the extremities. *J Comput Assist Tomogr* 1999; 23: 188–96.

An Evidence-Based Approach to Damage Control Laparotomy for Trauma

Bruce Crookes

Question Summary		
Question	Answer	Grade
Does a damage control approach improve mortality?	The application of damage control techniques does appear to have decreased mortality rates, although the absolute mortality reduction is difficult to quantify, due to improvements in critical care and resuscitation.	C
How do we preoperatively identify the damage control patient?	A damage control approach should be taken with any patient in the ED who has any of the following characteristics: 1. An RTS ≤ 5 2. Patients who require $\geq 2,000$ ml of crystalloids for resuscitation in the ED 3. Patients who require ≥ 2 units of PRBCs for resuscitation in the ED 3. Patients who have a pH ≤ 7.2	C
How do we intraoperatively identify the damage control patient?	In the operating room, a damage control technique should be employed when and if the following criteria apply: Patients who require $\geq 4,000$ ml of PRBCs for their resuscitation Patients who have had an ED or OR thoracotomy Patients who have a pH ≤ 7.2 Patients who have a temperature of $\leq 34^{\circ}\text{C}$ If the patient has an inaccessible major venous injury If the surgeon cannot achieve hemostasis owing to a recalcitrant coagulopathy If the definitive operative repair is a time-consuming procedure in the patient with suboptimal response to resuscitation If the patient requires the management of an extra-abdominal life-threatening injury If the patient will require a reassessment of intra-abdominal contents If the surgeon cannot reapproximate the abdominal fascia due to splanchnic reperfusion-induced visceral edema.	D
When should we terminate an initial damage control operation?	Damage control operations should be rapidly terminated, and the patient should be transferred to the intensive care unit, when the patient meets any of the following criteria: Core temperature $\leq 34^{\circ}\text{C}$ pH ≤ 7.2 PT $\geq$ twice normal PTT $\geq$ twice normal	B
What is the best method to temporarily close the abdomen that prevents long-term morbidity?	Temporary closure of the open abdomen is best accomplished with a combination of a vacuum type device and a fascial tensioning system. Abdominal closure is best accomplished by hospital day 8 to reduce morbidity.	C
What is the morbidity rate from a damage control approach?	Expected complication rate from damage control ranges from 25% to 40% of patients, with the most common complications being intra-abdominal abscesses and enterocutaneous fistulae. Methods to avoid these complications are unclear from the literature.	C
Abbreviations: ED, emergency department; OR, operating room; PRBCs, packed red blood cells; PT, prothrombin time; PTT, partial thromboplastin time; RTS, revised trauma score.		

Over the course of the past 15 years, the term “damage control” has become common vernacular among trauma surgeons, general surgeons, and orthopedists. Initially conceptualized as a temporizing measure to stabilize the victims of penetrating trauma, it is now a widely applied care

algorithm that has become a standard of care within the trauma community.

The term “damage control” has its origin within the U.S. Navy, where it was intended to describe a technique in which the damaged hull of a ship undergoes rapid

assessment and stabilization, so that it may return to the controlled environment of port (1). Although the original application of the term to surgery is attributed to Rotondo et al. (2) in 1993, the origins of the surgical technique can be traced back to Pringle (3), who first applied hepatic placking to arrest live hemorrhage. Most authors, however, attribute the formalization of the technique to Stone (4), who in 1983 described the technique of laparotomy truncation in the setting of exsanguinating hepatic hemorrhage. Stone and his associates terminated the initial laparotomy of patients with hepatic injury once the patient became coagulopathic. Stone's work was replicated by several other authors, most typically in the setting of hepatic injury (5–10).

With an increase in semiautomatic weapons use in the late 1980s, trauma surgeons began to see a marked increase in homicide rates (11). Now faced with an average of 2.7 shots per body (11–12), traumatologists saw a concomitant increase in mortality as a result of these devastating injuries. From this crucible of interpersonal violence arose the sentinel report by Rotondo et al. (2), and the term “damage control” was applied to trauma surgery for the first time. Damage control is now readily practiced in trauma centers around the world (13) and, most recently, has been extensively applied to foreign conflicts (14).

The damage control sequence is commonly employed to avoid the “lethal triad” of hypothermia (defined as a core body temperature of $<35^{\circ}\text{C}$), coagulopathy, and acidosis. Although there is no formal definition of the damage control technique, its steps are commonly acknowledged to include the following, three step sequence (15–18):

1. Operating Room (Part I)
 - Rapid control of hemorrhage
 - Control or containment of contamination
 - Restoration of vascular flow when required
 - Intra-abdominal packing
 - Temporary abdominal closure
2. Intensive Care Unit
 - Core rewarming
 - Optimization of hemodynamics
 - Correction of coagulopathy
 - Ventilatory support
 - Secondary survey and injury identification
3. Operating Room (Part II)
 - Pack removal
 - Definitive repair of injuries
 - Abdominal wall closure

The purpose of this chapter is to provide an evidence-based review of the literature with respect to the indications for the implementation of damage control techniques, the morbidity and mortality associated with the use of damage control, as well as the optimal technique for temporary closure of the abdominal wall.

DOES A DAMAGE CONTROL APPROACH IMPROVE MORTALITY?

Early reports of damage control procedures denoted mortality rates ranging from 39% to 63% (19–22). In a collective review of 961 damage control patients, published in 1994, Rotondo et al. (15) delineated a cumulative mortality rate of 58% from all of the known, published damage control series.

More recent series, however, seem to have shown a continued improvement in mortality rates. Johnson et al. (23) performed a retrospective cohort series comparing their damage control experience with that at their center from 10 years earlier. Although the historical control group had a mortality rate of 58%, Johnson and colleagues had a mortality of 10% for their more recent series. The authors postulated that this was due to improved intensive care unit (ICU) care, increased experience with the open abdomen, and improved temperature control. Sutton et al. reported an initial mortality rate of 27%, and found no long-term deaths if the patient survived the initial hospitalization (24). In a large case series of 344 patients, Miller et al.'s (25) series had a similar mortality rate of 25%. Arthurs et al. (26) examined the application of a damage control technique to soldiers who suffered multisystem penetrating pelvic injuries, with a resultant mortality of 28%.

Asensio et al. (27) examined the mortality rate in damage control patients before and after the institution of intraoperative guidelines, and found a consistent mortality rate of 24% pre- and postimplementation. Interestingly, the combination of a vascular injury and rectal injury resulted in a mortality of 36%, and was found to be the most deadly injury complex. Nicholas et al. (28) used a retrospective cohort analysis to find that in penetrating abdominal trauma, an increasing application of damage control techniques resulted in a statistically significantly higher survival rate (73.3%). Unfortunately, it carried with it a significant morbidity load, including sepsis, intra-abdominal abscess, and gastrointestinal fistula rate.

Finally, Finlay et al. (29) used a damage control technique to control hemorrhage in general surgical patients. They then predicted their outcome by P-POSSUM and POSSUM scoring and found that the observed mortality rate (7.1%) was significantly reduced.

Recommendation: The application of damage control techniques does appear to have decreased mortality rates, although the absolute mortality reduction is difficult to quantify due to improvements in critical care and resuscitation. Strength of recommendation: C.

HOW DO WE PREOPERATIVELY IDENTIFY THE DAMAGE CONTROL PATIENT?

The decision to employ a damage control technique initiates a sequence of events that require an intense utilization and commitment of resources: The patient must now undergo at least two operations, the ICU must assume the responsibility for a complex and time-consuming resuscitation, and the surgeon and the operating room staff are obligated to return to the operating room within the next several days after the injury. Thus, the decision to convert to a damage control approach is crucial.

Clearly, the majority of trauma patients will not require a damage control technique. Multiple authors have attempted to characterize patients who would benefit from a damage control approach, most employing objective markers, including mechanism of injury, injury severity score, temperature, pH, coagulopathy, lactate levels, and the number of units of blood transfused.

Ansensio et al. (30) retrospectively evaluated 548 patients for prehospital characteristics that predicted

“exsanguination syndrome.” Using a logistic regression model, they identified several independent risk factors for survival on presentation to the emergency department (ED): penetrating trauma, spontaneous ventilation, and the absence of an ED thoracotomy. As a result, the authors of this article recommend that patients arriving in the ED with a Revised Trauma Score (RTS) ≤ 5 , patients requiring $\geq 2,000$ ml of crystalloids, ≥ 2 units of packed red blood cells (PRBCs) for resuscitation, and those who have a pH of ≤ 7.2 are in the early stages of the exsanguination syndrome and are excellent candidates for a damage control approach.

Recommendation: A damage control approach should be taken with any patient in the ED who has any of the following characteristics:

- An RTS ≤ 5
- Requires $\geq 2,000$ ml of crystalloids for resuscitation in the ED
- Requires ≥ 2 units of PRBCs for resuscitation in the ED
- A pH of ≤ 7.2

Strength of evidence: C.

HOW DO WE INTRAOPERATIVELY IDENTIFY THE DAMAGE CONTROL PATIENT?

Once the patient is in the operating room, how does one know when to convert to a “damage control” technique?

Rotondo et al. (2) began to employ a damage control technique once a patient had received more than 10 units of PRBCs before the termination of the laparotomy, but did not evaluate the effectiveness of this transfusion requirement as a trigger point for conversion to damage control. Cué et al. (31) noted that coagulopathy began to occur in patients who had received more than 15 units of PRBCs during their initial resuscitation and operation, and recommended abdominal packing prior to reaching that transfusion threshold. Burch et al. (32) performed a retrospective review of 200 patients who were treated over 7.5 years using damage control techniques. This group used a logistic regression analysis to show that the two most powerful predictors of mortality were the rate of red cell transfusion (units per hour) and pH. When plotted as a scatter plot, these two variables correctly identified patient death within 48 hours of injury 77% of the time. Asensio et al. (30) identified the following values as predictive of survival once a trauma patient was in the operating room (OR): ISS ≤ 20 , spontaneous ventilation in the ED, OR blood product replacement of $< 4,000$ ml, no ED or OR thoracotomy, and the absence of abdominal vascular injury. His group recommended that damage control techniques be employed when transfusion volumes were $> 4,000$ ml PRBCs (or $> 5,000$ ml if both PRBCs and whole blood were used), total OR volume of resuscitation is $> 12,000$ ml (crystalloid and blood products), or a pH of ≤ 7.2 and a temperature of $\leq 34^\circ\text{C}$ in a patient with a blood loss of $\geq 5,000$ ml.

Sharp et al. (33), in a case series of 39 patients, identified several intraoperative risk factors for mortality, including a pH ≤ 7.18 , a temperature of $\leq 33^\circ\text{C}$, a prothrombin time ≥ 16 , a partial thromboplastin time of ≥ 50 , and transfusion of 10 units or more as being predictive of outcome. Patients

with four to five risk factors had a 100% mortality rate, although this represents a small subset of the overall study (three patients). Those who had two to three risk factors had a 83% mortality rate, and those with zero to one risk factor had a 18% mortality rate.

Other nontraditional endpoints may be helpful in identifying the physiologically unstable patient, including end-tidal CO_2 – arterial CO_2 differences ($\text{Pa} - \text{ET}\text{CO}_2$) and thenar eminence mixed tissue oxygen saturation (StO_2). In a database of 501 trauma patients, Tyburski et al. (34) found that patients with a ($\text{Pa} - \text{ET}\text{CO}_2$) difference > 10 mmHg that was persistent (i.e., initial OR, postresuscitation, and final OR) predicted a 100% mortality. Minimum thenar eminence StO_2 may also be predictive of the need for massive transfusion and may ultimately provide a surrogate marker for the need for damage control (35).

Several reviews of damage control indicate that a damage control technique should be employed in the following circumstances (13,15,18,36):

1. Inability to achieve hemostasis owing to a recalcitrant coagulopathy
2. Inaccessible major venous injury
3. Time-consuming procedure in the patient with suboptimal response to resuscitation
4. Management of extra-abdominal life-threatening injury
5. Reassessment of intra-abdominal contents
6. Inability to reapproximate abdominal fascia due to splanchnic reperfusion-induced visceral edema

Although these indications represent the application of good sound surgical judgement, evidence-based guidelines to support their implementation are lacking at present.

Recommendation: In the OR, a damage control technique should be employed when and if the following criteria apply:

- Patients who require $\geq 4,000$ ml PRBCs for their resuscitation
- Patients who have had an ED or OR thoracotomy
- Patients who have a pH ≤ 7.2
- Patients who have a temperature of $\leq 34^\circ\text{C}$
- If the patient has an inaccessible major venous injury
- If the surgeon cannot achieve hemostasis owing to a recalcitrant coagulopathy
- If the definitive operative repair is a time-consuming procedure in the patient with suboptimal response to resuscitation
- If the patient requires the management of an extra-abdominal life-threatening injury
- If the patient will require a reassessment of intra-abdominal contents
- If the surgeon cannot reapproximate the abdominal fascia due to splanchnic reperfusion-induced visceral edema

Strength of recommendation: D.

WHEN SHOULD WE TERMINATE THE INITIAL DAMAGE CONTROL OPERATION?

In Rotondo et al.’s (2) initial description of the technique, the authors retrospectively included those patients who

had penetrating injury resulting in exsanguination from an abdominal source who had received more than 10 units of PRBCs prior to completion of the laparotomy.

It would seem obvious that the need to terminate an operation would be based on the factors of coagulopathy, acidosis, or hypothermia. Ferrara et al. (37) examined a series of 45 trauma patients who required massive transfusions. They found that nonsurvivors were more likely to have had penetrating injuries (88% versus 55%), have received more transfusions (26.5 versus 18.6), had lower pH (7.04 versus 7.18), had lower core temperatures (31 versus 34°C), and had a higher incidence of clinical coagulopathy (73% versus 23%). Severe hypothermia occurred in 80% of nonsurvivors versus 6% of survivors.

Cosgrif et al. (38) used a logistic regression analysis to develop a predictive model for the development of coagulopathy. Factors that predicted the presence of coagulopathy included an ISS >25, a pH <7.10, and a temperature <34°C. If all four of these variables were present, 98% of patients had a coagulopathy (defined as a prothrombin time and partial thromboplastin time greater than two times normal). Clearly, prolonging an operation in the setting of these factors would be unwise.

Garrison et al. (39) examined a series of 70 consecutive patients who underwent a damage control operation to control hemorrhage, comparing survivors and nonsurvivors. Significant differences included ISS (29 versus 38), initial pH (7.3 versus 7.1), platelet count (229,000 versus 179,000), prothrombin time (14 versus 22 seconds), partial thromboplastin time (42 versus 69 seconds), and duration of hypotension (50 versus 90 minutes).

Recommendation: Damage control operations should be rapidly terminated and the patient should be transferred to the "ICE" when he or she meets any of the following criteria:

- Core temperature $\leq 34^{\circ}\text{C}$
- pH ≤ 7.2
- Prothrombin time $\geq$ twice normal
- Partial thromboplastin time $\geq$ twice normal

Strength of recommendation: B.

WHAT IS THE BEST METHOD TO TEMPORARILY CLOSE THE ABDOMEN THAT PREVENTS LONG-TERM MORBIDITY?

Historically, multiple methods have been described to temporarily close the open abdomen, ranging from simple towel clips, to the Bogota bag, to PTFE patches, to the Wittman patch, to vacuum closures (40). As damage control laparotomies have become more prevalent, there has also been an evolution in the methods used to close the abdomen. Offner et al. (41) retrospectively compared methods used to temporarily close the open abdomen, including primary fascial closure, towel clips, and the Bogota bag. The group found that primary fascial closure lead to a statistically higher incidence of abdominal compartment syndrome, acute respiratory distress syndrome, and multisystem organ failure.

Barker et al. reported a case series of 717 general surgical and trauma patients who had a vacuum-type closure

of their abdominal wall, in which the overall complication rate was 15.5% (14.7% in trauma patients) (40). In this series, 68.1% of the patients underwent a primary fascial closure of their abdomen. Garner et al. (42) achieved a 90% (13 out of 14 patients) primary closure rate when the incision was managed with a vacuum closure dressing. Smith et al. (43) reported on a four-year experience of treating open abdomens with a vacuum dressing and reported a 4.3% rate of intra-abdominal abscesses and a 4.3% rate of enterocutaneous fistulae.

Cothren et al. (44) used a modified closure technique, combining a vacuum dressing with persistent fascial tension (using #1 polydioxanone suture) to accomplish a 100% fascial closure rate. Using a similar technique, Miller et al. (45) closed 88% of patients with an open abdomen with a mean time to closure of 9.5 days. One patient who was successfully closed developed an incisional hernia. Fantus et al. (46) report a 100% fascial closure rate in a small case series of patients who were treated with a Wittman patch with a vacuum dressing.

Miller et al. (45) has published the largest series in the literature (344 patients), which examined closure technique of the open abdomen. His group found that complications began to escalate after eight days from the initial operative intervention to fascial closure. Patients undergoing primary closure had significantly fewer complications than those patients undergoing temporary abdominal closure (skin closure only, split thickness skin graft, and/or absorbable mesh) or prosthetic closures, despite equivalent mean ISS scores between the groups.

Recommendation: Temporary closure of the open abdomen is best accomplished with a combination of a vacuum-type device and a fascial tensioning system. Abdominal closure is best accomplished by hospital day 8 to reduce morbidity. Strength of recommendation: C.

WHAT IS THE MORBIDITY RATE FROM A DAMAGE CONTROL APPROACH?

Carillo et al. report a morbidity rate of 56% in their case series of 14 patients (20). Sharp et al. (33) denoted a complication rate of 27% of survivors. Nicholas et al. (28) denoted that an increase in the use of damage control techniques resulted in higher rates of sepsis, intra-abdominal abscesses, and gastrointestinal fistulas. Zonies et al. (15) delineated a 40% morbidity rate when all damage control series were summated. Morris et al. (19) found an overall complication rate of 1.09 complications per patient, with 8 positive blood cultures, 6 intra-abdominal abscesses, and abdominal compartment syndrome in 16 patients.

Abikhaled et al. (47) compared groups of damage control patients who were packed, noting that patients who were packed for more than 72 hours had statistically significant lower rates of abscess rate and mortality. The duration of packing, however, may be more indicative of ongoing physiologic instability rather than serving as a conduit for higher mortality.

Sutton published a prospective series of 56 consecutive trauma patients who underwent a damage control approach and found that 76% were readmitted at least once, with the most common reasons for readmission being infection (n = 19), ventral hernia repair (n = 17), and fistula

management (n = 14). Interestingly, if the patient survived the initial hospitalization to discharge, there was a 0% mortality rate (24). For patients who are discharged with a ventral incisional hernia, it appears that abdominal wall reconstruction is feasible within six months of discharge, with no increase in complications (48).

Recommendation: Expected complication rate from damage control ranges from 25% to 40% of patients, with the most common complications being intra-abdominal abscesses and enterocutaneous fistulae. Methods to avoid these complications are unclear from the literature. Strength of recommendation: C.

Level of Evidence

Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint	Comments
2	1993	III	22 DL, 24 DC	RCS	Unknown	Mortality	No major survival difference between the DC and DL groups (55% DC versus 58% DL) when examined overall. Subgroup analysis, however, of those with penetrating vascular injury showed a survival advantage for DC (77% versus 11%)
19	1993	IV	107 patients undergoing staged celiotomy with packing	CS		Mortality and morbidity	54.2% of patients survived to reconstruction. 117 complications (8 patients with positive blood cultures, 6 patients with abdominal abscesses, ACS developed in 16 patients)
20	1993	IV	14 patients undergoing damage control	CS		Mortality	Overall mortality rate of 16.6%, morbidity rate of 56%
21	1992	IV	11 patients undergoing abdominal packing after control of intra-abdominal hemorrhage	CS		Mortality	7 of 11 patients survived, with all patients being brought back to the OR within 48 hrs
22	1994	IV	124 patients undergoing damage control operations for trauma	CS		Mortality	Overall survival rate of 58%
23	2001	III	24 patients undergoing damage control compared with a historical control group treated with damage control from 10 years earlier	RCS			Continued application of damage control techniques lead to improved survival. These findings may have been due to improvements in ICU care, temperature control, and better techniques for managing the open abdomen
24	2006	IV	56 consecutive damage control patients at a single institution	CS	2 years	Mortality and morbidity	Overall mortality rate of 27%, with 0% subsequent mortality in patients surviving to discharge from the hospital. Readmissions were for infection (n = 19), ventral hernia repair (n = 17), and fistula management (n = 14)
25	2005	IV	344 damage control patients: Group I: primary fascial closure, Group II: temporizing (skin only, STSG, and/or absorbable mesh), Group III: prosthetic closure	CS		Mortality and morbidity	Primary closure accomplished in 65% of patients; no difference in ISS between groups, but primary closure had statistically significant decrease in complication rates. Overall mortality was 25%
26	2006	IV	28 patients with damage control techniques used for multisystem pelvic injuries	CS		Mortality	28 patients, with 21% mortality. The subset of patients with a combined rectal and vascular injury had a mortality of 36%
27	2004	IV	139 damage control patients; Group I 86 patients prior to institution of guidelines to convert to damage control approach, Group II 53 patients after guidelines instituted	RCS		Mortality and morbidity	No difference in mortality. Group I patients spent more time in the OR, used more units of PRBCs and FFP, and had a higher EBL. Abdominal closure rate was significantly higher in Group II patients (93% versus 22%)

(Continued)

Level of Evidence (Continued)

Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint	Comments
28	2003	IV	250 consecutive patients requiring a laparotomy of penetrating abdominal trauma, retrospectively compared with a historical cohort from 1988	RCS		Mortality and morbidity	Increasing use of damage control (17.9% versus 7.0%) lead to increased survival (73.3% versus 23.8%), but increase rate of complications (sepsis, intra-abdominal abscess, and gastrointestinal fistulae)
29	2004	IV	14 general surgical patients	CS		Mortality	Observed mortality rate (7.1%) was significantly decreased from that predicted by POSSUM (64.5%) and P-POSSUM (49.6%) scoring systems
30	2001	II	548 patients meeting one or more criteria: EBL >2,000 cc during laparotomy, required >1.5 l of PRBCs during resuscitation, or "diagnosis of exsanguination". Analysis of death versus survival in the ED and death versus survival in the OR	RCS		Mortality	Death versus survival in the ED: independent risk factors for survival: penetrating trauma, spontaneous ventilation, and no ED thoracotomy. Death versus survival in the OR: ISS ≤20, spontaneous ventilation in the ED, OR PRBC replacement of <4 L, no ED or OR thoracotomy, absence of abdominal vascular injury
31	1990	IV	35 patients undergoing intra-abdominal packing for control of bleeding	CS		Mortality	Packing was effective if instituted prior to transfusion of >15 units PRBCs, and was contraindicated before repair of retrohepatic caval injuries or hepatic venous injuries; selective hepatic artery ligation should be avoided if packing alone stops bleeding; abdominal closure with a synthetic mesh decreases the incidence of wound infection; patients should be returned to the operation room for repacking if 24 hr postoperative blood requirements exceed 10 units
32	1992	IV	200 trauma patients with "terminated" laparotomies	CS	Unreported; until hospital discharge	Mortality	No control for the technique of damage control; overall mortality 49% survival to planned reoperation 33% overall survival to hospital discharge
33	1992	IV	39 damage control patients	CS		Mortality	44% overall mortality rate (23% exsanguinated, 8% died from traumatic brain injury, 8% of MOS, 5% of late complications). Intraoperative risk factors included pH ≤7.18, temperature of ≤33°C, PT ≥16, PTT ≥50 and transfusion of 10 units PRBCs. Patients with 4–5 risk factors had a 100% mortality rate, 2–3 had an 83% mortality rate, and 0–1 had an 18% mortality rate. 27% of survivors had complications. In 77% packing helped achieve hemostasis
34	2003	IV	501 trauma patients	CS		Mortality	Pa - ETCO ₂ differences of >10 mmHg at all phases of resuscitation (initial OR, postresuscitation, and final OR) was 100% predictive of mortality
35	2008	II	383 patients total, with subset examination of 114 massive transfusion patients	PCS		Massive transfusion (≥10 units of PRBCs within 24 hrs of hospital admission)	Patients who require massive transfusion can be predicted early. Persistent low StO ₂ identifies those patients who are destined to have poor outcomes
37	1990	IV	45 patients requiring massive transfusions	CS		Mortality	Severe hypothermia (T <34°C) occurred in 36% of survivors, and 80% of non-survivors

(Continued)

Level of Evidence (Continued)

Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint	Comments
38	1997	I	58 patients >15 yrs who received >15 units/24 hrs	PCS	Irrelevant	Coagulopathy (PT twice normal controls and PTT greater than twice normal controls)	27 patients (47%) developed a life-threatening coagulopathy. Four risk factors were pH <7.0, temperature <34°C, ISS >25, and systolic blood pressure <70 mmHg. If ISS >25 + SBP <70 mmHg = 39% risk of coagulopathy, ISS >25 + temp <34°C = 49%, ISS <25 + pH <7.1 = 49%; if all four were present, risk was 98%
39	1996	IV	70 consecutive patients undergoing damage control operations to control hemorrhage	CS		Coagulopathy	Packing controlled hemorrhage in 53% of patients, significant differences between survivors and nonsurvivors included ISS (29 versus 38), initial pH (7.3 versus 7.1), platelet count (229,000 versus 179,000), PT (14 versus 22), PTT (42 versus 69), and duration of hypotension (50 versus 90 min)
40	2007	IV	258 surgical patients (116 trauma, 142 vascular surgery) with 717 vacuum closures	CS		Abdominal closure or complications	Total abdominal complication rate of 15.5% (14.7% for trauma), fistulae (5%), intra-abdominal abscesses (3.5%), bowel obstruction (1.2%), ACS (1.2%), evisceration (0.4%). 68.1% were primarily closed, with 31.9% requiring delayed closure. Overall mortality rate was 26.0%
41	2001	III	52 patients who required a damage control laparotomy	RCS		ACS, ARDS, MOF	Patients with primary fascial closure had an 80% incidence of ACS and a 90% incidence of ARDS and MOF. Skin closure was associated with a 24% incidence of ACS, and a 36% incidence of ARDS/MOF. Bogota bag closure had an 18% incidence of ACS, and a 47% incidence of ARDS/MOF
42	2001	IV	14 trauma patients	CS		Abdominal closure or complications	90% (13 out of 14 patients) had their open abdomens closed when a vacuum dressing was employed
43	1997	IV	93 patients with open abdomens, all treated with vacuum dressings	CS		Complications	4.3% rate of enterocutaneous fistulae, 4.3% rate of intra-abdominal abscesses. Overall hospital mortality was 32%
44	2006	IV	14 patients	CS		Fascial closure	14 patients who underwent a temporary abdominal closure followed to fascial closure (obtained in 100%)
45	2004	IV	53 patients with open abdomens, 45 surviving to abdominal closure	CS		Mortality and morbidity	Closure rate with a combination of a vacuum device and fascial tension lead to 88% abdominal closure rate, with mean time to closure of 9.5 days. Incisional hernia rate was 2.3%
46	2006	IV	11 patients	CS		Fascial closure	10 patients primarily closed with a combination of a vacuum dressing and a Wittman patch. There was one death in the series, unrelated to the method of abdominal closure
47	1997	IV	35 patients, treated with abdominal packing, and surviving to reoperation	CS		Complications	Patients packed for less than 72 hrs had a lower rate of abscesses, sepsis, and mortality than those packed for more than 72 hrs; differences in abscess rates and mortality were statistically significant
48	2006	IV	84 damage control patients: 31 died, 33 had immediate closure, and 20 had delayed closure	CS		Mortality and morbidity	No statistically significant difference in complication rates in patients closed before or after 6 months

Abbreviations: ACS, abdominal compartment syndrome; ARDS, acute respiratory distress syndrome; CS, case series (retrospective); DC, damage control; DL, definitive laparotomy; EBL, estimated blood loss; ED, emergency department; FFP, fresh frozen plasma; ISS, injury severity score; MOF, multiple organ failure; MOS, multi-system organ failure; NR, not reported; OR, operating room; PCS, prospective cohort study; PRBCs, packed red blood cells; PT, prothrombin time; PTT, partial thromboplastin time; RCS, retrospective cohort study; RCT, randomized controlled trial; RTW, return to work; STSG, split thickness skin graft.

REFERENCES

1. Surface Ship Survivability. Naval War Publication 3-20.31. Washington, DC: Department of Defense, 1996.
2. Rotondo M, Schwab C, McGonigal M, et al. "Damage control": an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993; 35: 375-82; discussion 382-3.
3. Pringle J. Notes on the arrest of hepatic hemorrhage due to trauma. *Ann Surg* 1908; 48: 541-9.
4. Stone H, Strom P, Mullins R. Management of the major coagulopathy with onset during laparotomy. *Ann Surg* 1983; 197: 532-5.
5. Carmona R, Peck D, Lim R. The role of packing and planned reoperation in severe hepatic trauma. *J Trauma* 1984; 24: 779-84.
6. Ivatury R, Nallathambi M, Gunduz Y, et al. (Liver packing for uncontrolled hemorrhage: a reappraisal. *J Trauma* 1986; 26: 744-53.
7. Svoboda J, Peter E, Dang C, et al. Severe liver trauma in the face of coagulopathy. A case for temporary packing and early reexploration. *Am J Surgery* 1982; 144: 717-21.
8. Feliciano D, Mattox K, Jordan G. Intra-abdominal packing for control of hepatic hemorrhage: a reappraisal. *J Trauma*, 1981; 21: 285-90.
9. Calne R, McMaster P, Pentlow B. The treatment of major liver trauma by primary packing with transfer of the patient for definitive treatment. *B J Surg* 1979; 66: 338-9.
10. Lucas C, Ledgerwood A. Prospective evaluation of hemostatic techniques for liver injuries. *J Trauma* 1976; 16: 442-51.
11. McGonigal M, Cole J, Schwab C, et al. Urban firearm deaths: A five-year perspective. *J Trauma* 1993; 35: 532-6; discussion 536-7.
12. Schwab C. Violence: America's uncivil war—presidential address, Sixth Scientific Assembly of the Eastern Association for the Surgery of Trauma. *J Trauma* 1993; 35: 657-65.
13. Shapiro M, Jenkins D, Schwab C, et al. Damage control: Collective review. *J Trauma* 2000; 49: 969-78.
14. Fox C, Gillespie D, Cox E, et al. The effectiveness of a damage control resuscitation strategy for vascular injury in a combat support hospital: results of a case control study. *J T Inj Infec Crit Care* 2008; 64(Suppl): S99-S107.
15. Rotondo M, Zonies D. The damage control sequence and underlying logic. *Surg Clin N Am* 1997; 77: 761-77.
16. Lee J, Peitzman A. Damage-control laparotomy. *Curr Opin Crit Care* 2006; 12: 346-50.
17. Scalea T. What's new in trauma in the past 10 years. *Intl Anesthes Clin* 2002; 40: 1-17.
18. Moore E, Burch J, Franciose R, et al. Staged physiologic restoration and damage control surgery. *World J Surg* 1998; 22: 1184-90; discussion 1190-1.
19. Morris J, Eddy V, Blinman T, et al. The staged celiotomy for trauma. Issues in unpacking and reconstruction. *Ann Surg* 1993; 217: 576-84; discussion 584-6.
20. Carrillo C, Fogler R, Shaftan G. Delayed gastrointestinal reconstruction following massive abdominal trauma. *J Trauma* 1993; 34: 233-5.
21. Talbert S, Trooskin S, Scalea T, et al. Packing and re-exploration for patients with nonhepatic injuries. *J Trauma* 1992; 33: 121-4; discussion 124-5.
22. Hirshberg A, Wall M, Mattox K. Planned reoperation for trauma: a two year experience with 124 consecutive patients. *J Trauma* 1994; 37: 365-9.
23. Johnson J, Gracias V, Schwab C, et al. Evolution in damage control for exsanguinating penetrating abdominal injury. *J Trauma* 2001; 51: 261-9; discussion 269-71.
24. Sutton E, Bochicchio G, Bochicchio K, et al. Long term impact of damage control surgery: a preliminary prospective study. *J Trauma Inj Infec Crit Care* 2006; 61: 831-6.
25. Miller R, Morris J, Diaz J, et al. Complications after 344 damage-control open celiotomies. *J Trauma Inj Infec Crit Care* 2005; 59: 1365-74.
26. Arthurs Z, Kjorstad R, Mullenix P, et al. The use of damage-control principles for penetrating pelvic battlefield trauma. *Am J Surg* 2006; 191: 604-9.
27. Asensio J, Petrone P, Roldán G, et al. Has evolution in awareness of guidelines for institution of damage control improved outcome in the management of the posttraumatic open abdomen? *Arch Surgery* 2004; 139: 209-14; discussion 215.
28. Nicholas J, Rix E, Easley K, et al. Changing patterns in the management of penetrating abdominal trauma: the more things change, the more they stay the same. *J Trauma Inj Infec Crit Care* 2003; 55: 1095-110.
29. Finlay I, Edwards T, Lambert A. Damage control laparotomy. *Br JSurg* 2004; 91: 83-5.
30. Asensio J, McDuffie L, Petrone P, et al. Reliable variables in the exsanguinated patient which indicate damage control and predict outcome. *Am J Surg* 2001; 182: 743-51.
31. Cué J, Cryer H, Miller F, et al. Packing and planned reexploration for hepatic and retroperitoneal hemorrhage: critical refinements of a useful technique. *J Trauma* 1990; 30: 1007-11; discussion 1011-13.
32. Burch J, Ortiz V, Richardson R, et al. Abbreviated laparotomy and planned reoperation for critically injured patients. *Ann Surg* 1992; 215: 476-83; discussion 483-4.
33. Sharp K, Locicero R. Abdominal packing for surgically uncontrollable hemorrhage. *Ann Surg* 1992; 215: 467-74; discussion 474-5.
34. Tyburski J, Carlin A, Harvey E, et al. End-tidal CO₂-arterial CO₂ differences: a useful intraoperative mortality marker in trauma surgery. *J Trauma Inj Infec Crit Care* 2003; 55: 892-7.
35. Moore F, Nelson T, Mckinley B, et al. Massive transfusion in trauma patients: tissue hemoglobin oxygen saturation predicts poor outcome. *J Trauma Inj Infec Crit Care* 2008; 64: 1010-23.
36. Loveland J, Boffard K. Damage control in the abdomen and beyond. *Br J Surg* 2004; 91: 1095-101.
37. Ferrara A, MacArthur J, Wright H, et al. Hypothermia and acidosis worsen coagulopathy in the patient requiring massive transfusion. *Am J Surg* 1990; 160: 515-18.
38. Cosgriff N, Moore E, Sauaia A, et al. Predicting life-threatening coagulopathy in the massively transfused trauma patient: Hypothermia and acidosis revisited. *J Trauma* 1997; 42: 857-61; discussion 861-2.
39. Garrison J, Richardson J, Hilakos A, et al. Predicting the need to pack early for severe intra-abdominal hemorrhage. *J Trauma* 1996; 40: 923-7; discussion 927-9.
40. Barker D, Green J, Maxwell R, et al. Experience with vacuum-pack temporary abdominal wound closure in 258 trauma and general and vascular surgical patients. *J Am Coll Surg* 2007; 204: 784-92.
41. Offner P, de Souza A, Moore E, et al. Avoidance of abdominal compartment syndrome in damage-control laparotomy after trauma. *Arch Surg* 2001; 136: 676-81.
42. Garner G, Ware D, Cocanour C, et al. Vacuum-assisted wound closure provides early fascial reapproximation in trauma patients with open abdomens. *Am J Surg* 2001; 182: 630-8.
43. Smith L, Barker D, Chase C, et al. Vacuum pack technique of temporary abdominal closure: A four-year experience. *Am Surg* 1997; 63: 1102-7; discussion 1107-8.
44. Cothren C, Moore E, Johnson J, et al. One hundred percent fascial approximation with sequential abdominal closure of the open abdomen. *Am J Surg* 2006; 192: 238-42.

45. Miller P, Meredith J, Johnson J, et al. Prospective evaluation of vacuum-assisted fascial closure after open abdomen. *Ann Surg* 2004; 239: 608–16.
46. Fantus R, Mellett M, Kirby J. Use of controlled fascial tension and an adhesion preventing barrier to achieve delayed primary fascial closure in patients managed with an open abdomen. *Am J Surg* 2006; 192: 243–7.
47. Abikhalel J, Granchi T, Wall M, et al. (Prolonged abdominal packing for trauma is associated with increased morbidity and mortality. *Am Surg* 1997; 63: 1109–12; discussion 1112–13.
48. Ekeh A, McCarthy M, Woods R, et al. Delayed closure of ventral abdominal hernias after severe trauma. *Am J Surg* 2006; 191: 391–5.

Evidence-Based Surgery: Coagulopathy in the Trauma Patient

Joseph J. DuBose and Peter M. Rhee

Clinical Questions		
Question	Answer	Grade of recommendation
Do massive transfusion protocols work?	Protocols improve blood product utilization and outcomes	B
Is there an ideal FFP:PRBCs ratio for administration of FFP?	Early empiric use of FFP at ratios of 1:1 or 1:2 are beneficial	B
Is there a role for whole blood transfusion in trauma?	Whole blood transfusion may be life-saving in austere settings	C
Is factor VIIa a useful adjunct to massive transfusion in trauma?	The role of rFVIIa remains not well defined. The largest PRCT on the topic has been closed due to futility. Until the full report from this study is release, the off-label use of this adjunct for trauma should be considered carefully	B
What is the best tool to determine coagulopathy associated with trauma and guide therapy?	No Level I, II, or III evidence exists. Traditional laboratory parameters remain standard. Thromboelastography use is under investigation	C
Abbreviations: FFP, fresh frozen plasma; PRBCs, packed red blood cells; PRCT, prospective randomized control trial; rFVIIa, recombinant factor VIIa.		

INTRODUCTION

Laboratory abnormalities of coagulation may be present in over one-fourth of patients presenting to trauma centers after injury (1). Coagulopathy in this setting has been shown to be a significant independent predictor of adverse outcome (1,2) and remains one of the leading causes of death following trauma. The etiology of these abnormalities are often multifactorial, including hemorrhage with loss of coagulation factors, dilution of coagulation factors due to fluid resuscitation, release of tissue thromboplastin, hypothermia, medications, and preexisting medical conditions (3–9). Regardless of the precipitating causes, the end result remains the depletion of functional coagulation factors sufficient to affect hemostasis.

The early recognition and effective treatment of coagulation abnormalities following injury remains one of the most significant challenges facing trauma providers. Accordingly, the investigation of this phenomenon continues to warrant considerable research. Recent investigations have suggested that protocolized approaches to the correction of coagulopathy may be beneficial; including the earlier and more aggressive utilization of fresh frozen plasma (FFP). The role of recombinant factor VII and other coagulation adjuncts are also under active examination. Even the optimal modality by which to identify and define coagulopathy remains an active field of investigation. Efforts to establish evidence-based practices from the findings of

this research are paramount in the establishment of effective diagnostic and treatment guidelines to combat the coagulopathy associated with trauma.

DO MASSIVE TRANSFUSION PROTOCOLS WORK?

The need for massive transfusion, commonly defined ≥ 10 packed red blood cells (PRBCs) over 24 hours is associated with high mortality (10–15). Survivors of massive transfusion, however, may achieve excellent clinical outcomes (16). Even among trauma victims requiring over 50 units of PRBCs, a surprising number will return to a high level of function (11,12). Therefore, massive ongoing bleeding requiring transfusions of PRBCs often requires empiric FFP, platelets, and factor replacement.

Although the optimal approach to the correction of coagulopathy in victims of trauma remains ill-defined, the theoretical benefits of standardized protocols for massive transfusion are attractive (17). The effective implementation of these practices may improve patient outcomes and decrease hospital costs (16,18,19). They may also improve the optimal utilization of blood products, an increasingly precious resource.

Retrospective models obtained from data on military casualties have suggested the benefit of predefined ratios for the transfusion of blood components (20,21). Computer models, developed using retrospective data, have also

suggested that optimal ratios for blood product administration following trauma may exist (22,23). Individual and institutional practices of massive transfusion, however, vary widely (24,25). Although protocolized approaches are used by some academic centers, scientific investigation of their benefit is lacking (25). At present, there exist no Level I data examining the effects of predefined massive transfusion protocols on morbidity or mortality after trauma.

In one recent Level III study, however, Cotton et al. (26) examined the effects of a massive transfusion protocol for trauma. In this retrospective examination, the investigators compared the outcomes of protocol use with a cohort of historical patient controls. After controlling for age, gender, mechanism of injury, trauma and injury severity scoring (TRISS), and 24-hour blood product usage these investigators found that among 211 trauma patients requiring massive transfusion (≥ 10 units of PRBCs), there was a 74% reduction in the odds of mortality among individuals transfused using a protocol. They also noted that blood product consumption was significantly reduced in the protocol group. Although this study suggests the promise that massive transfusion protocols may hold in improving both patient outcome and blood product utilization, further prospective investigations are required.

The ideal quantity of FFP that should be administered during trauma resuscitation has only recently been examined closely. In a 2005 survey of 100 trauma surgeons, Coimbra and colleagues (24) found that most used FFP not as part of a protocol but based on the type and location of injury, initial international normalized ratio (INR), and targeted INR values. The findings of contemporary investigations, however, suggest that the benefit of FFP may be better realized when it is utilized empirically and as part of a predetermined protocol (21–23,26–29).

Recommendation: The use of protocolized approaches to massive transfusions may improve patient outcomes and decrease blood product consumption. A lack of Level I evidence precludes grade A treatment recommendations by current standards. Existing surgical literature, however, suggests that protocolized approaches to massive transfusion reduce blood product consumption and may improve patient outcomes, including survival.

HOW SHOULD FFP BE UTILIZED IN TRAUMA RESUSCITATION? IS THERE AN IDEAL RATIO FOR ADMINISTRATION?

FFP is produced from whole blood separation or apheresis and is most commonly frozen within eight hours to preserve the activity of the labile coagulation factors it contains for up to one year. Subsequent thawing of this component therapy for use requires approximately 30 minutes. Responding to an increasing awareness that early administration may be of great importance following trauma, many larger centers now maintain a ready thawed plasma supply for immediate use.

In the aforementioned study by Cotton and colleagues, the use of a trauma transfusion protocol, including a fixed FFP ratio, was shown to be associated with improved mortality and lower overall blood consumption compared to

historical controls (26). Historical controls have also been used in the development of computer models designed to predict the optimal ratio of FFP:PRBCs that should be administered, as well as the appropriate timing for administration. In one such model, Hirshberg and colleagues (22) found that the optimal replacement ratio was 2:3. Based on the findings of another pharmacokinetic simulation developed by Ho et al. (23), the investigators recommended that if FFP transfusion can be initiated before plasma factor concentration drops below 50% of normal, an FFP:PRBCs transfusion ratio of 1:1 would prevent further dilution. Once excessive deficiency of factors has progressed to cause unabated bleeding, however, the authors concluded that up to 1.5 units of FFP per unit of PRBCs may be required. Another study by Gonzalez et al. (28) suggested that administration of FFP in advance of the onset of severe coagulopathy is likely to prove beneficial. In a review of the results of their own protocol use at Methodist Hospital in Houston, this group found that 1:1 ratio utilization after arrival to the intensive care unit (ICU) did not completely correct coagulopathy in trauma patients requiring massive transfusion. They hypothesized that more aggressive pre-ICU intervention to correct coagulopathy would improve effectiveness in decreasing PRBC requirements and the mortality associated with an elevated INR on arrival to the ICU.

Borgman et al. (21) conducted a retrospective examination of patients with combat-related trauma requiring massive transfusion (≥ 10 units PRBCs in 24 hours). After dividing these patients into three categories based on the ratio of FFP to PRBC they had received, the investigators conducted an analysis of outcomes. Using logistic regression, they noted that plasma to RBC ratio was independently associated with improved survival, with this benefit proving most pronounced for the highest ratio category examined (1:1.4). They also found that the beneficial effect of higher ratios was primarily due to decreased death from hemorrhage.

In the largest human study to date, Teixeira et al. (30) conducted a retrospective examination of FFP to PRBC ratios used in massively transfused patients. This group found that among 383 patients, higher ratios were an independent predictor of survival. Their findings also suggested that more aggressive early use of FFP improved subsequent outcome following massive transfusion.

Recommendation: Using predetermined protocols, the early empiric use of high FFP:PRBC ratios in the resuscitation of trauma patients anticipated to require massive transfusions may be beneficial. Although an absence of Level I evidence does not permit the adoption of grade A recommendations, several Level III studies have suggested the benefit of this practice. At present, the early implementation of massive transfusion protocols utilizing a 1:1 or 1:2 ratio of plasma to RBCs for all patients with coagulopathy following trauma should be strongly considered. This topic does, however, warrant additional examination in well-designed prospective randomized trials.

IS THERE A ROLE FOR WHOLE BLOOD TRANSFUSION IN THE TRAUMA SETTING?

Since the fractionation of blood was first introduced in the 1940s, concerns about logistics, safety, and relative efficacy

of whole blood versus component therapy have argued against the use of whole blood in most settings. Whole blood transfusion by healthy donors, however, has continued to be used safely and effectively for selective patient populations (31,32) and in austere environments (33). The largest contemporary experience with whole blood transfusion has occurred following the depletion of component products in theaters of armed conflict (34–39). One of the largest reports of such experiences was that reported by Spinella et al. (34), who during Operation Iraqi Freedom were required to use whole blood transfusion in 87 combat casualties over the span of one year. These practices, often called walking donor transfusion, may have important civilian applications in situations in which local blood supply could be overwhelmed by demand due to natural or manmade disaster (40). To date, however, only case series of this practice exist.

Recommendation: Although no Level I, II or III evidence exists to support this practice, whole blood transfusion remains a potentially life-saving method of resuscitation in austere environments without access to component therapy.

IS FACTOR VII A USEFUL ADJUNCT TO MASSIVE TRANSFUSION FOR TRAUMA?

Initially introduced for use in uncontrollable bleeding in hemophilia patients, factor VII use following trauma in a nonhemophiliac was first reported in an Israeli soldier in 1999 (41). Several subsequent investigators have investigated the use of this adjunct in various patient populations, including trauma (42–45). The rationale for the use of factor VII in hemorrhage is that it should induce coagulation primarily at those sites where tissue factor is also present; however, concerns regarding potential thromboembolic complications have been raised.

The use of recombinant factor VIIa (rFVIIa) has been examined in a pair of randomized control trials examining its efficacy and safety after injury due to both penetrating and blunt mechanisms. In these investigations, Boffard and colleagues (46) examined the transfusion requirements and incidence of thromboembolic events following rFVIIa use in patients requiring more than 6 units of PRBCs over four hours following these mechanisms of injury. On 30-day follow-up, the investigators found that the use of rFVIIa in patients with severe bleeding after blunt mechanism of injury resulted in a significant reduction in both total PRBC transfusions required and the need for massive transfusion among individuals surviving 48 hours from the administration of the first dose. Trends toward similar results were also seen among victims of penetrating trauma, although these did not reach statistical significance. Nonsignificant trends in reduced mortality and critical complications were also observed. The incidence of thromboembolic events was distributed evenly between patients receiving rFVIIa and placebo controls. Although this study was not designed or powered to detect a survival difference, it demonstrated the safety of rFVIIa use among trauma patients with severe bleeding and provided evidence that the use of this adjunct decreased transfusion requirements among survivors of severe bleeding following blunt injury.

Several smaller, Class III studies have also suggested the potential benefit of rFVIIa. In a post hoc analysis of the data from the Boffard trial, Rizoli et al. (47) found that among coagulopathic trauma patients requiring the transfusion of at least 8 units of PRBCs, the use of rFVIIa was associated with a significantly lower requirement for overall PRBCs, FFP, platelets, and massive transfusions. The study also noted that the administration of rFVIIa in this population was not associated with the occurrence of increased thromboembolic events but did result in a significant reduction in multiorgan failure and acute respiratory distress syndrome. In another study conducted by Rizoli and colleagues (48), the investigators found that in a retrospective review of patients requiring ≥ 8 units PRBCs over the first 12 hours of admission, rFVIIa use was associated with improved survival at 24 hours compared to controls. A limited report by Bartsch et al. (49) also suggested that rFVIIa may have a role in patients with traumatic intracranial bleeding. The findings of a more contemporary PRCT conducted by Mayer and colleagues (50), however, called the use of rFVIIa for stroke into question. This group found that the use of 80 mcg/kg doses of rFVIIa did not improve survival or functional outcome of patients with acute intracerebral hemorrhage due to nontraumatic causes.

The safety of rFVIIa use in specific populations of severe hemorrhage has also been investigated. Retrospective studies have suggested that the use of rFVIIa is not associated with increased thromboembolic or other complications following use for patients with traumatic brain injury (51) or in austere combat environments (52,53). When used in the early care of combat casualties, in fact, two retrospective studies have suggested that rFVIIa decreases PRBC transfusion requirements (53) and improves both 24-hour and 30-day mortality (53). Several retrospective reports have, however, demonstrated that the risk of thromboembolic complications following rFVIIa use are very real, particularly in the setting of off-label utilization (54,55).

Additionally, a large, prospective multinational study designed to better determine the safety and efficacy of rFVIIa among bleeding trauma patients has recently concluded. This examination is titled the clinical trial on the effect of rFVIIa on traumatic blood loss, or the CONTROL study. With plans to enroll 1,500 patients, this investigation was designed with sufficient power to detect potential survival benefit associated with rFVIIa use. In June 2008, the study was halted due to futility. As of this writing, the full results of the study have not been reported. In light of the resulting futility disclosure, however, the role of rFVIIa use in the correction of coagulopathy following trauma remains not well defined.

Recommendation: Initial Level II evidence suggested that the use of rFVIIa was not associated with increased risk of thromboembolic events and would significantly reduce the PRBCs required and need for massive transfusion among severely bleeding trauma patients after blunt mechanisms of injury. No PRCT has shown a mortality benefit from use of this adjunct. The largest PRCT multicenter trial examining the use of rFVIIa was recently closed due to futility. In light of this development, the role of rFVIIa remains ill-defined, and the off-label use of this medication should be considered carefully.

WHAT IS THE BEST TOOL TO DETERMINE COAGULOPATHY AND GUIDE THERAPY?

Coagulopathy remains one of the most common causes of death among victims of severe trauma. Several studies have shown that early coagulopathy, which may occur even prior to the initiation of resuscitation (2,56) is associated with adverse outcomes (1,2,56). A consistent definition of coagulopathy, as well as the best measures by which to rapidly identify and guide the early reversal of this phenomena, however, remain active topics of investigation.

Several groups have recently attempted to define predictive factors associated with the onset of coagulopathy following trauma (15,57–61). If an accurate predictive model could be appropriately validated, and the onset of severe coagulation dysfunction be reliably predicted, then sufficient early intervention practices might improve outcomes in these patients. Yucel and colleagues (57) proposed such a scoring system in the form of the Trauma Associated Severe Hemorrhage Score. In a retrospective study using potential clinical and laboratory variables from a large trauma registry to predict the probability of massive transfusion, they found that a scoring system using seven variables reliably predicted the need for PRBC transfusion of at least 10 units. These included systolic blood pressure, hemoglobin, intra-abdominal fluid, complex long bone and/or pelvic fractures, heart rate, base deficit, and gender. Kuhne et al. (58) have proposed a similar model, utilizing the Emergency Transfusion Score (ETS), which includes the parameters of low blood pressure, free fluid on ultrasound, clinical instability of the pelvic ring, age, admission from the scene, and trauma mechanism. In a prospective evaluation of the ETS, this group found that this scoring system had a sensitivity of 97.5% in predicting the need for massive transfusion (≥ 10 units PRBCs) but a specificity of only 68%. The use of these types of scoring systems has not, to date, been subjected to well-designed prospective validation. In addition, whereas they may predict the need for massive transfusion, they provide no information by which to guide subsequent therapy during resuscitation and correction of coagulopathy.

Laboratory evaluation has traditionally been used to define coagulopathy and guide correction of this complication of trauma. Initial and serial measurements of prothrombin time (PT), partial thromboplastin time (PTT), INR, platelet number and function, and d-dimer measurements remain the standard of care following trauma. Available retrospective studies have all used variants of these measures in the identification of early coagulopathy in this setting (1,2,59–76). The relative predictive value of abnormalities is not, however, well defined. In one retrospective series reported by MacLeod et al., the investigators found that 28% of trauma patients had an abnormal PT, compared with 8% of patients with an abnormal PT (1). These investigators found, however, that an abnormal PTT was associated with an odds ratio of death of 4.26, compared with 1.54 for an abnormal PT. In a computer model developed by Hirshberg et al. (22), it has been suggested that prolongation of PT may be the sentinel event of dilutional coagulopathy. Other investigators have examined the role of testing of protein C levels (62,77), activated coagulation time (78), fibrinogen degradation (79), and INR (80) in

evaluating coagulation abnormalities following trauma. To date, the ability of laboratory abnormalities to reliably predict coagulopathy and provide meaningful guidance in treatment has not been subjected to examination in well-designed prospective trials.

The ideal laboratory testing would optimally depend on simple and reliable point of care testing that would allow providers to rapidly identify and appropriately treat the coagulopathy associated with trauma. Unfortunately, current standard testing of coagulative function requires time and may not accurately reflect the dynamic changes in the coagulation status that occur during active resuscitation. *In vivo* coagulation is defined by the interaction of platelets and coagulation factor enzymes. Measurements of PT and PTT, however, are performed on platelet-poor plasma and do not reliably reflect cellular interactions of normal clotting function. Standard platelet and fibrinogen assays provide numerical values by which to assess coagulation, but these also fail to provide adequate information on function. Formal assessment of bleeding time provides better information about function, but this type of evaluation is cumbersome, and there is no evidence that abnormalities in this testing occur sufficiently in advance of other indicators of bleeding to allow actions to be taken to alter outcome favorably (81). In addition, bleeding time does not provide adequate information that may be used to guide component therapy in the correction of coagulation defects.

Importantly, traditional laboratory testing also does not account for the role of hypothermia in coagulopathy. Even moderate reductions in body temperature have been associated with slowing of enzyme activity, as well as both decreased platelet adhesion and function (82,83). The majority of currently available parameters by which to assess coagulation are performed in the laboratory only after warming and do not reflect the true *in vivo* coagulative function of a patient with hypothermia following injury (3).

The development of the thromboelastograph (TEG) analyzer represents a promising alternative to traditional evaluation of coagulopathy. The use of this device provides functional bedside evaluation of overall coagulation in whole blood at the same temperature as the patients. Requiring only a small aliquot for effective testing, the TEG is capable of assessing clotting time, clot formation, clot strength, and clot lysis. Interpretation of alterations in each of these parameters has the potential to provide both early and effective diagnosis of coagulation abnormalities. The TEG may also be used to guide subsequent correction of identified defects of coagulation using component therapy and other systemic adjuncts.

Despite its theoretical advantages over traditional laboratory evaluations of coagulation, however, TEG has failed to emerge as the standard of care for assessment of coagulopathy. As a point of care test, whole blood samples must be run within three to four minutes of collection, necessitating the presence of machines in multiple critical areas of the hospital as opposed to central laboratory collection. Centrally located machines can be utilized, but the transport of specimens subsequently necessitates that citrated blood be used for testing. As Zambruni et al. (84) have demonstrated, the accuracy of TEG may be significantly altered by the presence of citrate in these samples. Other limitations of TEG include potential differences in

patient age and gender and recent reports concerning blood collection sites, sample stability, and repeat sampling (15,85–91). Despite these limitations, the possible applications of TEG in the care of trauma patients remain promising. Several animal and human case series have suggested this potential in various settings, including following trauma (4,71,92–99). To date, however, there are no Class I, II, or III studies demonstrating its clinical effectiveness in identifying or guiding the correction of coagulation abnormalities associated with trauma.

Recommendation: At present, there are no Class I, II, or III studies on which to develop high-quality recommendations regarding the best tool to diagnose the presence of coagulopathy and guide subsequent therapy. Although the use of the TEG has garnered some enthusiasm and has several theoretical benefits as a diagnostic tool in trauma, it remains an unproven entity. Based on available Level IV data, traditional laboratory assessments of coagulopathy that include evaluation of PTT and PT/INR remain the grade C recommended standard of care.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Massive transfusion protocols	2008	26	III	B	Protocolized approaches to massive transfusion may be beneficial.
PRBCs:FFP Ratio	2003–2008	21–23, 26, 28, 30	III	B	Early empiric use of FFP at ratios of 1:1 or 1:2 appear to be beneficial.
Whole blood transfusion	2000–2008	34–40	IV	C	Whole blood use may save lives in austere settings where component therapy is unavailable.
Factor VIIa for trauma	2005	46	II	B	The role of rFVIIa use in trauma remains not well defined.

Abbreviations: FFP, fresh frozen plasma; PRBCs, packed red blood cells; rFVIIa, recombinant factor VIIa.

REFERENCES

- MacLeod JB, Lynn M, McKenney MG, et al. Early coagulopathy predicts mortality in trauma. *J Trauma* 2003; 55: 39–44.
- Brohi K, Singh J, Heron M, et al. Acute traumatic coagulopathy. *J Trauma* 2003; 54: 1127–30.
- Kettner SC, Sitzwohl C, Zimpfer M, et al. The effect of graded hypothermia (36 degrees C–32 degrees C) on hemostasis in anesthetized patients without surgical trauma. *Anesth Analg* 2003; 96: 1772–6.
- Kheirabadi BS, Crissey JM, Deguzman R, et al. In vivo bleeding time and in vitro thrombelastography measurements are better indicators of dilutional hypothermic coagulopathy than prothrombin time. *J Trauma* 2007; 62: 1352–9; discussion 1359–61.
- Weeks DL, Jahr JS, Lim JC, et al. Does hextend impair coagulation compared to 6% hetastarch? An ex vivo thrombelastography study. *Am J Ther* 2008; 15: 225–30.
- Boldt J, Haisch G, Suttner S, et al. Effects of a new modified, balanced hydroxyethyl starch preparation (hextend) on measures of coagulation. *Br J Anaesth* 2002; 89: 722–8.
- Felfernig M, Franz A, Braunlich P, et al. The effects of hydroxyethyl starch solutions on thrombelastography in preoperative male patients. *Acta Anaesthesiol Scand* 2003; 47: 70–3.
- Via D, Kaufmann C, Anderson D, et al. Effect of hydroxyethyl starch on coagulopathy in a swine model of hemorrhagic shock resuscitation. *J Trauma* 2001; 50: 1076–82.
- Kretschmer V, Daraktchiev A, Bade S, et al. Does hemodilution enhance coagulability? *Anesthesiol Intensivmed Notfallmed Schmerzther* 2004; 39: 751–6.
- Huber-Wagner S, Qvick M, Mussack T, et al. Massive blood transfusion and outcome in 1062 polytrauma patients: a prospective study based on the trauma registry of the German trauma society. *Vox Sang* 2007; 92: 69–78.
- Vaslef SN, Knudsen NW, Neligan PJ, et al. Massive transfusion exceeding 50 units of blood products in trauma patients. *J Trauma* 2002; 53: 291–5; discussion 295–6.
- Velmahos GC, Chan L, Chan M, et al. Is there a limit to massive blood transfusion after severe trauma? *Arch Surg* 1998; 133: 947–52.
- Phillips TF, Soulier G, Wilson RF. Outcome of massive transfusion exceeding two blood volumes in trauma and emergency surgery. *J Trauma* 1987; 27: 903–10.
- Wudel JH, Morris JA Jr, Yates K, et al. Massive transfusion: outcome in blunt trauma patients. *J Trauma* 1991; 31: 1–7.
- Schreiber MA, Perkins J, Kiraly L, et al. Early predictors of massive transfusion in combat casualties. *J Am Coll Surg* 2007; 205: 541–5.
- Cinat ME, Wallace WC, Nastanski F, et al. Improved survival following massive transfusion in patients who have undergone trauma. *Arch Surg* 1999; 134: 964–8; discussion 968–70.
- Counts RB, Haisch C, Simon TL, et al. Hemostasis in massively transfused trauma patients. *Ann Surg* 1979; 190: 91–9.
- Schwab CW, Shayne JP, Turner J. Immediate trauma resuscitation with type O uncrossmatched blood: a two-year prospective experience. *J Trauma* 1986; 26: 897–902.
- Johansson PI. The blood bank: from provider to partner in treatment of massively bleeding patients. *Transfusion* 2007; 47: 176S–181S; discussion 182S–183S.
- Stinger HK, Spinella PC, Perkins JG, et al. The ratio of fibrinogen to red cells transfused affects survival in casualties receiving massive transfusions at an army combat support hospital. *J Trauma* 2008; 64: S79–S85; discussion S85.
- Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007; 63: 805–13.

22. Hirshberg A, Dugas M, Banez EI, et al. Minimizing dilutional coagulopathy in exsanguinating hemorrhage: a computer simulation. *J Trauma* 2003; 54: 454–63.
23. Ho AM, Dion PW, Cheng CA, et al. A mathematical model for fresh frozen plasma transfusion strategies during major trauma resuscitation with ongoing hemorrhage. *Can J Surg* 2005; 48: 470–8.
24. Coimbra R, Hoyt DB, Anjaria DJ, et al. Reversal of anticoagulation in trauma: a North American survey on clinical practices among trauma surgeons. *J Trauma* 2005; 59: 375–82.
25. Malone DL, Hess JR, Fingerhut A. Massive transfusion practices around the globe and a suggestion for a common massive transfusion protocol. *J Trauma* 2006; 60: S91–S96.
26. Cotton BA, Gunter OL, Isbell J, et al. Damage control hematology: the impact of a trauma exsanguination protocol on survival and blood product utilization. *J Trauma* 2008; 64: 1177–82; discussion 1182–3.
27. Geeraedts LM Jr, Demiral H, Schaap NP, et al. “Blind” transfusion of blood products in exsanguinating trauma patients. *Resuscitation* 2007; 73: 382–8.
28. Gonzalez EA, Moore FA, Holcomb JB, et al. Fresh frozen plasma should be given earlier to patients requiring massive transfusion. *J Trauma* 2007; 62: 112–19.
29. Ho AM, Karmakar MK, Dion PW. Are we giving enough coagulation factors during major trauma resuscitation? *Am J Surg* 2005; 190: 479–84.
30. Teixeira PGR, Inaba K, Shulman I, et al. Impact of plasma transfusion in massively transfused trauma patients. *J Trauma* 2009; 66: 693–7.
31. Barret JP, Desai MH, Herndon DN. Massive transfusion of reconstituted whole blood is well tolerated in pediatric burn surgery. *J Trauma* 1999; 47: 526–8.
32. Erber WN, Tan J, Grey D, et al. Use of unrefrigerated fresh whole blood in massive transfusion. *Med J Aust* 1996; 165: 11–13.
33. Horzic M, Bunoza D, Maric K, et al. A prospective study of the application of transfusions in a field hospital during the war in Croatia. *Mil Med* 1996; 161: 89–91.
34. Spinella PC, Perkins JG, Grathwohl KW, et al. Fresh whole blood transfusions in coalition military, foreign national, and enemy combatant patients during operation Iraqi Freedom at a U.S. combat support hospital. *World J Surg* 2008; 32: 2–6.
35. Malsby R III, Frizzi J, Ray P, et al. Walking donor transfusion in a far forward environment. *South Med J* 2005; 98: 809–10.
36. Grosso SM, Keenan JO. Whole blood transfusion for exsanguinating coagulopathy in a US field surgical hospital in postwar Kosovo. *J Trauma* 2000; 49: 145–8.
37. Repine TB, Perkins JG, Kauvar DS, et al. The use of fresh whole blood in massive transfusion. *J Trauma* 2006; 60: S59–S69.
38. Kauvar DS, Holcomb JB, Norris GC, et al. Fresh whole blood transfusion: a controversial military practice. *J Trauma* 2006; 61: 181–4.
39. Spinella PC, Perkins JG, Grathwohl KW, et al. Risks associated with fresh whole blood and red blood cell transfusions in a combat support hospital. *Crit Care Med* 2007; 35: 2576–81.
40. Hrezo RJ, Clark J. The walking blood bank: an alternative blood supply in military mass casualties. *Disaster Manag Response* 2003; 1: 19–22.
41. Kenet G, Walden R, Eldad A, et al. Treatment of traumatic bleeding with recombinant factor VIIa. *Lancet* 1999; 354: 1879.
42. McMullin NR, Kauvar DS, Currier HM, et al. The clinical and laboratory response to recombinant factor VIIa in trauma and surgical patients with acquired coagulopathy. *Curr Surg* 2006; 63: 246–51.
43. Hendriks HG, Meijer K, de Wolf JT, et al. Effects of recombinant activated factor VII on coagulation measured by thromboelastography in liver transplantation. *Blood Coagul Fibrinolysis* 2002; 13: 309–13.
44. Pusateri AE, Park MS. Mechanistic implications for the use and monitoring of recombinant activated factor VII in trauma. *Crit Care* 2005; 9 Suppl 5: S15–S24.
45. McRoberts RJ, Beard D, Walsh TS. A study of blood product use in patients with major trauma in Scotland: analysis of a major trauma database. *Emerg Med J* 2007; 24: 325–9.
46. Boffard KD, Riou B, Warren B, et al. Recombinant factor VIIa as adjunctive therapy for bleeding control in severely injured trauma patients: two parallel randomized, placebo-controlled, double-blind clinical trials. *J Trauma* 2005; 59: 8–15; discussion 15–18.
47. Rizoli SB, Boffard KD, Riou B, et al. Recombinant activated factor VII as an adjunctive therapy for bleeding control in severe trauma patients with coagulopathy: subgroup analysis from two randomized trials. *Crit Care* 2006; 10: R178.
48. Rizoli SB, Nascimento B Jr, Osman F, et al. Recombinant activated coagulation factor VII and bleeding trauma patients. *J Trauma* 2006; 61: 1419–25.
49. Bartsch C, Freedman J, Bowman K, et al. Coagulopathic patients with traumatic intracranial bleeding: defining the role of recombinant factor VIIa. *J Trauma* 2007; 63: 725–32.
50. Mayer SA, Brun NC, Bergtrup K, et al. Efficacy and safety of recombinant activated factor VII for acute cerebral hemorrhage. *N Engl J Med* 2008; 358: L2127–L2137.
51. Kluger Y, Riou B, Rossaint R, et al. Safety of rFVIIa in hemodynamically unstable polytrauma patients with traumatic brain injury: post hoc analysis of 30 patients from a prospective, randomized, placebo-controlled, double-blind clinical trial. *Crit Care* 2007; 11: R85.
52. Spinella PC, Perkins JG, McLaughlin DF, et al. The effect of recombinant activated factor VII on mortality in combat-related casualties with severe trauma and massive transfusion. *J Trauma* 2008; 64: 286–93; discussion 293–4.
53. Perkins JG, Schreiber MA, Wade CE, et al. Early versus late recombinant factor VIIa in combat trauma patients requiring massive transfusion. *J Trauma* 2007; 62: 1095–9; discussion 1099–101.
54. Thomas GO, Dutton RP, Hemlock B, et al. Thromboembolic complications associated with factor VIIa administration. *J Trauma* 2007; 62: 564–9.
55. O’Connell KA, Wood JJ, Wise RP, et al. Thromboembolic adverse events after use of recombinant human coagulation factor VIIa. *JAMA* 2006; 295: 293–398.
56. Maegele M, Lefering R, Yucel N, et al. Early coagulopathy in multiple injury: an analysis from the German trauma registry on 8724 patients. *Injury* 2007; 38: 298–304.
57. Yucel N, Lefering R, Maegele M, et al. Trauma associated severe hemorrhage (TASH)-score: probability of mass transfusion as surrogate for life threatening hemorrhage after multiple trauma. *J Trauma* 2006; 60: 1228–36; discussion 1236–7.
58. Kuhne CA, Zettl RP, Fischbacher M, et al. Emergency transfusion score (ETS): a useful instrument for prediction of blood transfusion requirement in severely injured patients. *World J Surg* 2008; 32: 1183–8.
59. Davis JW, Parks SN, Kaups KL, et al. Admission base deficit predicts transfusion requirements and risk of complications. *J Trauma* 1996; 41: 769–74.
60. McLaughlin DF, Niles SE, Salinas J, et al. A predictive model for massive transfusion in combat casualty patients. *J Trauma* 2008; 64: S57–S63; discussion S63.
61. Park MS, Salinas J, Wade CE, et al. Combining early coagulation and inflammatory status improves prediction of mortality in burned and nonburned trauma patients. *J Trauma* 2008; 64: S188–S194.
62. Brohi K, Cohen MJ, Ganter MT, et al. Acute traumatic coagulopathy: initiated by hypoperfusion: modulated through the protein C pathway? *Ann Surg* 2007; 245: 812–18.

63. Murshid WR, Gader AG. The coagulopathy in acute head injury: comparison of cerebral versus peripheral measurements of haemostatic activation markers. *Br J Neurosurg* 2002; 16: 362–9.
64. Kumura E, Sato M, Fukuda A, et al. Coagulation disorders following acute head injury. *Acta Neurochir (Wien)* 1987; 85: 23–8.
65. Cortiana M, Zagara G, Fava S, et al. Coagulation abnormalities in patients with head injury. *J Neurosurg Sci* 1986; 30: 133–8.
66. Becker S, Schneider W, Kreuz W, et al. Post-trauma coagulation and fibrinolysis in children suffering from severe cerebrocranial trauma. *Eur J Pediatr* 1999; 158 Suppl 3: S197–S202.
67. Nekludov M, Bellander BM, Blomback M, et al. Platelet dysfunction in patients with severe traumatic brain injury. *J Neurotrauma* 2007; 24: 1699–706.
68. Vecht CJ, Sibinga CT, Minderhoud JM. Disseminated intravascular coagulation and head injury. *J Neurol Neurosurg Psychiatry* 1975; 38: 567–71.
69. Davis JW, Davis IC, Bennink LD, et al. Placement of intracranial pressure monitors: are “normal” coagulation parameters necessary? *J Trauma* 2004; 57: 1173–7.
70. Scherer RU, Spangenberg P. Procoagulant activity in patients with isolated severe head trauma. *Crit Care Med* 1998; 26: 149–56.
71. Lawrie AS, Cardigan RA, Williamson LM, et al. The dynamics of clot formation in fresh-frozen plasma. *Vox Sang* 2008; 94: 306–14.
72. Abdel-Wahab OI, Healy B, Dzik WH. Effect of fresh-frozen plasma transfusion on prothrombin time and bleeding in patients with mild coagulation abnormalities. *Transfusion* 2006; 46: 1279–85.
73. Garcia-Avello A, Lorente JA, Cesar-Perez J, et al. Degree of hypercoagulability and hyperfibrinolysis is related to organ failure and prognosis after burn trauma. *Thromb Res* 1998; 89: 59–64.
74. Gando S, Tedo I, Kubota M. Posttrauma coagulation and fibrinolysis. *Crit Care Med* 1992; 20: 594–600.
75. Avikainen V. Coagulation disorders in severely and critically injured patients. *Ann Chir Gynaecol* 1977; 66: 269–77.
76. Leslie SD, Toy PT. Laboratory hemostatic abnormalities in massively transfused patients given red blood cells and crystalloid. *Am J Clin Pathol* 1991; 96: 770–3.
77. Brohi K, Cohen MJ, Davenport RA. Acute coagulopathy of trauma: mechanism, identification and effect. *Curr Opin Crit Care* 2007; 13: 680–5.
78. Aucar JA, Norman P, Whitten E, et al. Intraoperative detection of traumatic coagulopathy using the activated coagulation time. *Shock* 2003; 19: 404–7.
79. Martini WZ, Chinkes DL, Pusateri AE, et al. Acute changes in fibrinogen metabolism and coagulation after hemorrhage in pigs. *Am J Physiol Endocrinol Metab* 2005; 289: E930–E934.
80. Yuan S, Ferrell C, Chandler WL. Comparing the prothrombin time INR versus the APTT to evaluate the coagulopathy of acute trauma. *Thromb Res* 2007; 120: 29–37.
81. Rodgers RP, Levin J. A critical reappraisal of the bleeding time. *Semin Thromb Hemost* 1990; 16: 1–20.
82. Wolberg AS, Meng ZH, Monroe DM III, Hoffman M. A systematic evaluation of the effect of temperature on coagulation enzyme activity and platelet function. *J Trauma* 2004; 56: 1221–8.
83. Watts DD, Trask A, Soeken K, et al. Hypothermic coagulopathy in trauma: effect of varying levels of hypothermia on enzyme speed, platelet function, and fibrinolytic activity. *J Trauma* 1998; 44: 846–54.
84. Zambruni A, Thalheimer U, Leandro G, et al. Thromboelastography with citrated blood: comparability with native blood, stability of citrate storage and effect of repeated sampling. *Blood Coagul Fibrinolysis* 2004; 15: 103–7.
85. Pivalizza EG, Pivalizza PJ, Gottschalk LI, et al. Celite-activated thrombelastography in children. *J Clin Anesth* 2001; 13: 20–3.
86. Manspeizer HE, Imai M, Frumento RJ, et al. Arterial and venous thrombelastograph variables differ during cardiac surgery. *Anesth Analg* 2001; 93: 277–81.
87. Gorton HJ, Warren ER, Simpson NA, et al. Thromboelastography identifies sex-related differences in coagulation. *Anesth Analg* 2000; 91: 1279–81.
88. Camenzind V, Bombeli T, Seifert B, et al. Citrate storage affects thrombelastograph analysis. *Anesthesiology* 2000; 92: 1242–9.
89. Vig S, Chitolie A, Bevan DH, et al. Thromboelastography: a reliable test? *Blood Coagul Fibrinolysis* 2001; 12: 555–61.
90. Rajwal S, Richards M, O'Meara M. The use of recalcified citrated whole blood—a pragmatic approach for thromboelastography in children. *Paediatr Anaesth* 2004; 14: 656–60.
91. Bailey LA, Sistino JJ, Uber WE. Is platelet function as measured by thrombelastograph monitoring in whole blood affected by platelet inhibitors? *J Extra Corpor Technol* 2005; 37: 43–7.
92. Plotkin AJ, Wade CE, Jenkins DH, et al. A reduction in clot formation rate and strength assessed by thrombelastography is indicative of transfusion requirements in patients with penetrating injuries. *J Trauma* 2008; 64: S64–S68.
93. Levrat A, Gros A, Rugeri L, et al. Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients. *Br J Anaesth* 2008; 100: 792–7.
94. Rugeri L, Levrat A, David JS, et al. Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography. *J Thromb Haemost* 2007; 5: 289–95.
95. Bowbrick VA, Mikhailidis DP, Stansby G. Influence of platelet count and activity on thromboelastography parameters. *Platelets* 2003; 14: 219–24.
96. Coakley M, Reddy K, Mackie I, et al. Transfusion triggers in orthotopic liver transplantation: a comparison of the thromboelastometry analyzer, the thromboelastogram, and conventional coagulation tests. *J Cardiothorac Vasc Anesth* 2006; 20: 548–53.
97. Essell JH, Martin TJ, Salinas J, et al. Comparison of thromboelastography to bleeding time and standard coagulation tests in patients after cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 1993; 7: 410–15.
98. Zuckerman L, Caprini JA, Lipp V, et al. Disseminated intravascular multiple systems activation (DIMSA) following thermal injury. *J Trauma* 1978; 18: 432–9.
99. Kaufmann CR, Dwyer KM, Crews JD, et al. Usefulness of thrombelastography in assessment of trauma patient coagulation. *J Trauma* 1997; 42: 716–20; discussion 720–2.

Traumatic Brain Injury

Ara J. Feinstein and Kenneth D. Stahl

Clinical Questions		
Question	Answer	Grade of recommendation
Do evidence-based guidelines improve outcome?	Yes, outcomes and mortality may be improved.	B
Does repeat head CT determine the need for intervention?	Only patients with deteriorating exam or severe injury require repeat CT.	B
Does progesterone improve outcome?	Yes, it improves both mortality and functional outcome.	A
When and how should DVT prophylaxis be utilized?	LMWH, VCF, and SCDs are all effective in TBI patients. Timing of LMWH is unknown.	B
Is seizure prophylaxis beneficial?	Yes, up to 7 days after TBI. It is not beneficial after 7 days.	B
What is the optimal transfusion trigger?	Transfusion triggers should be the same as other ICU patients.	C
Abbreviations: CT, computed tomography; DVT, deep vein thrombosis; ICU, intensive care unit; LMWH, low molecular weight heparin; SCD, sequential compression device; TBI, traumatic brain injury; VCF: vena cava filter.		

Traumatic brain injury (TBI) continues to be a major cause of death and disability. The Centers for Disease Control reported 1,565,000 TBIs in the United States leading to 51,000 deaths in 2003, most due to falls and motor vehicle crashes (1). TBI is viewed as a dual cerebral insult composed of primary and secondary processes (2). The primary injury occurs at the time of impact with immediate damage to brain cells. These subsequently become progressively vulnerable to further damage due to secondary cerebral changes, such as intracranial hypertension, decrease in cerebral perfusion pressure, and cerebral hypoxia (3). Treatment of these patients is often complicated by concomitant injuries that affect the ability of the clinician to effectively manage TBI. In an effort to improve outcome, questions arise regarding monitoring, treatment guidelines, and pharmacologic management of these patients.

DOES ADHERENCE TO EVIDENCE-BASED GUIDELINES IMPROVE OUTCOME IN TBI?

The Brain Trauma Foundation first published the Guidelines for the Management of Severe Traumatic Brain Injury in 2000 and it was most recently updated in 2007 (4). These guidelines utilize current evidence-based methodology to make specific recommendations for the uniform management of patients with severe TBI. Despite a comprehensive evaluation of the literature, the guidelines only make one Level I recommendation. Level II and Level III recommendations rely largely on measuring and treating elevated intracranial pressure (ICP) to reduce the secondary insult.

Despite this lack of rigorous trials, the implementation of the guidelines continues to increase. Hesdorffer et al. surveyed 173 Level I and 215 Level II trauma centers (5). They saw a significant increase in the number of centers following guidelines from previous surveys conducted in 1991 and 2000. Level I centers were more likely to adhere to guidelines than were Level II centers.

Several studies have examined if adherence to the guidelines as a whole improves outcomes. Rusnack and colleagues prospectively evaluated 405 nonrandomized TBI patients and assessed whether adherence to individual Brain Trauma Foundation guidelines changed outcomes (6). Overall adherence to guidelines did not change mortality. Implementing the recommendations on monitoring, hyperventilation, steroid use, and seizure prophylaxis decreased intensive care unit (ICU) length of stay.

Fakhry et al. retrospectively examined the records of 830 TBI patients, dividing them into time periods of pre-guidelines, low compliance, and high compliance (7). Mortality was decreased in the high compliance group. There was a significant decrease in ICU days, hospital days, and hospital charges after implementation of protocols.

Palmer et al. retrospectively and prospectively examined 93 patients before and after implementation of Brain Trauma Foundation guidelines (8). Patients treated after guidelines were implemented had significantly higher hospital charges. Outcomes may have been improved, but the statistics are lacking.

Clayton et al. retrospectively examined the records of 843 TBI patients admitted before and after the institution of an evidence-based medicine protocol similar to the Brain Trauma Foundation guidelines for treatment of head injury (9). Implementation of the protocol was associated with a significant reduction in hospital mortality from 24.55% to 20.8%.

Together, these retrospective cohort studies agree that the implementation of guidelines improved some clinical outcome measures including mortality and thus constitute Level 3A evidence.

Answer: Evidence-based guidelines are based on limited data and rely largely on strategies to manage ICP and cerebral perfusion pressure (CPP) to reduce the secondary insult after TBI. Retrospective studies indicate implementation of these guidelines may decrease mortality, hospital stay, and improve clinical outcomes (Grade C recommendation). It is unclear whether they increase or decrease hospital costs.

Refer to Brain Trauma Foundation Guidelines (4).

DOES REPEAT HEAD COMPUTED TOMOGRAPHY AFTER TBI DETERMINE THE NEED FOR CLINICAL INTERVENTION?

Head computed tomography (CT) is an invaluable tool in the evaluation of patients with suspected TBI. Any patient with blunt trauma and a Glasgow coma score (GCS) of less than 15 undergoes head CT at most institutions. Repeat head CT scans are routinely performed to evaluate progression of intracranial bleeding or the need for neurosurgical intervention regardless of clinical course. Repeat head CT scans are associated with increased cost and the difficulty of moving severely injured ICU patients. Several retrospective studies have called this practice into question, suggesting that these scans are not helpful in the absence of clinical deterioration (10–15) (Level IIIA evidence).

Sifri and colleagues prospectively evaluated 130 patients with minor head injury (GCS >12 and loss of consciousness or amnesia) and intracranial bleeding on initial CT scan that did not require immediate intervention (16). Ninety-nine of these patients had no deterioration of their exam prior to the second CT. Twelve patients had worsening of their bleed on repeat CT, but none of these required neurosurgical intervention. In contrast, of the 31 patients who had deterioration of their neurologic exam prior to the second CT, 14 had worse scans and 2 required surgical intervention. After the initial CT, a stable neurologic exam has a negative predictive value of 100% in predicting the lack of neurosurgical intervention.

Brown et al. prospectively studied 100 TBI patients with an abnormal initial head CT that did not require immediate neurosurgical intervention (17). Sixty-eight of these patients underwent 90 repeat CT scans. Eighty-one of these scans were performed without neurological change, and none of these patients required medical or surgical intervention for TBI despite worsening on 19 (23%) scans. Of the nine CT scans done in the setting of a deteriorating mental status, six (67%) were worse, requiring two surgical and one medical intervention.

In a subsequent study, Brown et al. prospectively examined 274 patients with an abnormal head CT not requiring immediate intervention (18). Patients were stratified into mild (GCS 13–15), moderate (GCS 9–12), and severe (GCS ≤8). Only two patients had changes on repeat CT that required intervention in the absence of clinical deterioration. Both were in the severe injury group.

Oertel et al. prospectively studied 142 patients (mean GCS 8) who underwent repeat head CT after brain trauma

(19). Fifteen of these patients required craniotomy after the second head CT. No data are given if the patients' neurological exam deteriorated in the interval between the first and second scan, and the GCS of this subgroup is not given.

Together, these prospective cohort studies constitute Level 2A evidence.

Answer: Patients with an abnormal initial head CT, a deteriorating neurologic exam, or the presence of severe injury (GCS ≤8) warrant a repeat head CT to guide therapy (Grade B recommendation).

DOES PROGESTERONE IMPROVE OUTCOME AFTER TBI?

Animal studies suggest there may be a benefit to progesterone in the setting of TBI (20–25). Progesterone appears to exert its beneficial effects by protecting or rebuilding the blood-brain barrier, decreasing development of cerebral edema, down-regulating the inflammatory cascade, and limiting cellular necrosis and apoptosis (26). A pilot study showed that adequate plasma levels of progesterone could be achieved in TBI patients (27). This was followed by two recent randomized, double-blind, placebo-controlled trials that evaluated the safety and efficacy of progesterone in clinical TBI.

Wright et al. enrolled 100 TBI patients from a single trauma center with a GCS of 4 to 12 (28). Subjects were randomized on a 4:1 basis to receive either intravenous progesterone or placebo. Seventy-seven patients received progesterone, 23 received placebo. Patients randomized to progesterone had a significantly lower 30-day mortality rate than controls. In moderately injured patients (GCS 9–12), those randomized to progesterone had significantly higher incidence of moderate or good recovery compared to controls at 30 days. There were no increased adverse events in the progesterone group.

Xiao and colleagues enrolled and randomized 159 patients with a GCS ≤8. Eighty-two received progesterone and 77 received placebo. (29) The mortality rate of the progesterone group was significantly lower than that of the placebo group at six-month follow-up. Both the Glasgow Outcome Score and modified Functional Independence Measure Score were significantly improved at three and six months with progesterone when compared to placebo.

Although these findings are derived from relatively small, single-center studies, the quality of the studies is high. Further large, multicenter trials are needed, but together these studies represent Level 1B evidence.

Answer: In patients with moderate to severe head injury GCS ≤12, progesterone appears to improve mortality and improve functional outcome (Grade A recommendation).

WHEN AND HOW SHOULD DVT PROPHYLAXIS BE UTILIZED IN TBI?

Risk factors for the development of deep vein thrombosis (DVT) and associated pulmonary embolism (PE) in hospitalized patients include (among others) prior DVT, age >40 years, major surgery lasting >30 minutes, obesity, multiple trauma, cerebral vascular accident, spine injury

with immobilization, and long bone fractures (30). Accordingly, patients sustaining multiple trauma are known to have several risk factors for DVT and PE, and patients with TBI are at an even greater risk (31). The association of multiple trauma and DVT varies from 7% to 58% depending on patient demographics, nature of injuries, and method of detection. The greatest risk categories are age >40 (odds ratio 2.01), lower extremity fracture (odds ratio 1.97) and TBI with the abbreviated injury scale (AIS) ≥ 3 (odds ratio 1.24). The absolute rate of DVT in patients with head injuries who have received no prophylactic treatment has been quoted as 20% (32). The rate of PE in most series has been reported to be 1.5–5%. The mortality of post-traumatic PE as a complication of DVT development in injured patients approaches 50% (33).

Various DVT prophylactic treatments have been studied for use individually and in combination after trauma. These include sequential lower extremity compression devices (SCDs), unfractionated heparin (UFH), low molecular weight heparin (LMWH), warfarin, and vena cava filter (VCF) (33). Level II recommendations support LMWH as the most effective method of prophylaxis to prevent DVT in trauma patients *without* TBI (34). Prophylactic therapy for DVT and PE in patients with intracranial hemorrhage injuries (IHIs) must always be balanced against the risk of expansion of intracranial hematoma and rebleeding (35). Prophylactic treatment regimens must be individualized based on injury patterns and risks of each patient.

A randomized, double-blind trial in elective neurosurgery patients using LMWH (enoxaparin) started the morning after surgery showed it was effective at preventing DVT (32% DVT placebo group versus 17% DVT LMWH group) and mortality from PE (two deaths in the placebo group from PE and none in the LMWH group). It was also safe, with no difference in bleeding (3% in each) between the two groups (36). Extrapolation of data from elective neurosurgical patients to TBI patients must be done with caution because the latter frequently have intracranial hemorrhage that is at a greater risk of expansion (37).

In a prospective nonrandomized study Norwood and coworkers analyzed the use and safety of LMWH (enoxaparin) in patients with IHIs following blunt trauma (38). The medication was started 24 hours after injury or craniotomy except in patients with concomitant splenic injury being conservatively managed. Head CT scans were carried out on admission, 24 hours after admission, and at various times during hospitalization. Although only 4% of patients managed nonoperatively had expansion of their hematoma while on enoxaparin, 9.1% of patients receiving surgical intervention suffered postoperative bleeding. This bleeding rate caused the study authors to change their protocol so the drug was started later (24 hours after surgical intervention). Venous color flow duplex studies were performed within 24 hours of hospital discharge on 101/150 patients that found a 2% DVT incidence in enoxaparin-treated patients (which they compare to historic controls), and no patient in the study group was documented to have suffered a PE.

The timing for dosing of enoxaparin is important as shown by Dickinson et al., who terminated their attempt at DVT prophylaxis in elective neurosurgical cases due to an increased incidence of postoperative intracranial

hemorrhage when enoxaparin was injected at induction of anesthesia (39).

A broad study of the use of certoparin, another LMWH preparation, by Kleindienst and co-workers included 344 patients with IHI (40). They administered LMWH within 24 hours of admission or 12 hours before and restarted 24 hours after surgery if the head CT scan showed no expansion of intracranial bleeding. They report an expansion of intracranial hemorrhage in nine patients (3.2%) of whom eight (2.8%) required reoperation. They attribute four of nine bleeding incidents to protocol violations and reported no increase in morbidity or mortality from rebleeding in these patients. They report a 0.2% incidence of DVT and 0.1% incidence of PE in their study group.

A retrospective evaluation of UFH use for DVT prophylaxis in patients sustaining severe closed head injuries (AIS >3) was carried out by Kim and colleagues (41). They compared two groups of patients who received UFH early after injury (<72 hours) versus late after injury (>72 hours) and did not exclude patients with splenic and hepatic lacerations managed conservatively. They demonstrated no increase in risk of increased intracranial bleeding in either group but also no difference in rate of DVT, PE, or death between the two groups. No conclusions as to the efficacy of UFH as a prophylactic agent for DVT can be drawn from this study, but it does suggest that prophylactic doses of heparin can be safely administered to patients with IHI.

The two available mechanical methods of prophylaxis are SCDs and VCFs. These are most useful in patients who cannot be anticoagulated because of their clinical circumstances. SCD use is aimed at preventing DVT; VCF does not prevent DVT but is designed to prevent propagation of DVT to PE. Use of SCDs in DVT prophylaxis for patients with multiple trauma including head injuries is supported by Level III data in the EAST Practice Management Guidelines Work Group and have no direct deleterious effect on IHI expansion (34). The effectiveness of VCF in the prevention of PE has been well established in patients who cannot be anticoagulated. It should be noted, however, that filter placement in patients without anticoagulation has been shown to increase the risk of DVT and can result in vena cava thrombosis (42).

Answer: Use of SCDs in TBI patients is supported by multiple Level II studies (Grade B recommendation). Use of LMWH is supported by Level III data (Grade B recommendation). The data conflict on the timing of initiation of LMWH therapy after injury. Level III data support the use of VCF for prophylaxis against PE in patients who cannot be anticoagulated due to IHI (Grade B recommendation).

IS STANDARD USE OF ANTIEPILEPTIC DRUGS FOR SEIZURE PROPHYLAXIS BENEFICIAL IN PATIENTS WITH TBI?

Post-traumatic seizure activity occurs both early and late after injury. Brain seizure activity is known to dramatically increase cerebral metabolic requirements, glucose metabolism (43), and ICP (44). Therefore, suppression of post-TBI seizure activity, should it occur, would seem to be a logical part of an overall brain protective strategy.

Antiepileptic drug (AED) regimens have been used in a variety of ways in TBI depending on local practice habits (45). If untreated, the overall risk of seizure activity following TBI in patients with no previous history of epilepsy is 2–5%, however, this varies widely depending on the age, wounding mechanism, and severity of TBI (46). In a population-based study of 4,541 adults and children with TBI, Annegers et al. reported a standardized seizure incidence ratio of 1.5 in mild TBI, 2.9 in moderate TBI, and 17.0 in patients with severe TBI (47). Patients who suffer penetrating head injuries account for a higher percentage of cases in combat casualty literature (48), which reports post-TBI seizure activity as high as 53% (49).

The presence of early seizures (<7 days) after TBI has not been substantiated to correlate with an increased mortality in trauma patients (50) but is predictive of the development of late seizure activity (46). As such, patients who suffer post-TBI seizures have been shown to have significantly worse long-term functional outcomes compared to patients who do not suffer seizure activity (51).

In a systematic review of Class I and Class II data, phenytoin was effective when used as prophylaxis against early post-TBI seizures given for seven days following TBI (52). Phenytoin demonstrated a significant benefit (3.4% early seizure rate when given AED versus 13.3% in placebo group) in suppressing post-TBI seizures in patients with severe brain injuries. They further evaluated adverse events and drug complications and found that there were few serious side effects from AED usage. From these data, the authors make practice recommendations for adult patients with severe TBI (defined as prolonged loss of consciousness, amnesia, intracranial hematoma or brain contusion on CT scan, and/or depressed skull fracture). These include prophylactic treatment with phenytoin, beginning with an IV loading dose as soon as possible after injury to decrease the risk of early (<7 days) post-TBI seizures.

The same study reviewed current data on the use of AED in late (>7 days) post-TBI seizures (52). From their review, they concluded that the data do not support use of phenytoin for more than seven days because there was no difference in late post-TBI seizures in the AED treated (10.0%) group versus placebo (8.4%) group. From these data, the authors make additional practice guideline recommendations that prophylactic treatment with phenytoin, carbamazepine, or valproate should not routinely be used beyond the first seven days after injury in an attempt to decrease the risk of post-TBI seizures.

Answer: There is a significantly lower risk of early (<7 days) postinjury seizures in patients with severe head injuries who are treated with phenytoin when compared to matched controls. There are no data to support treatment with AED for late (>7 days) postinjury seizure prophylaxis (Level II recommendations).

IN PATIENTS WITH TBI, IS THERE AN OPTIMAL HEMOGLOBIN LEVEL TO MINIMIZE SECONDARY BRAIN INSULT?

Secondary insult is common after TBI. In a recent study of the epidemiology of TBI in Australia and New Zealand,

28.5% of patients with TBI sustained secondary brain insults with severe consequences (53). Numerous studies have also stressed the negative impact on functional outcome and survivorship in patients who sustain secondary cerebral insults after TBI (54). Optimizing oxygen-carrying capacity should be part of an overall strategy to minimize cerebral hypoxia and thus secondary injury. However, there are numerous morbidities and even an increase in mortality associated with transfusion of donor blood, especially blood that has been stored for more than 14 days. There is especially a concern for the increased risk of immunosuppression and infection following transfusion in multiply injured patients (55).

In patients with TBI, a review of the neurosurgical literature suggests that hemoglobin levels should be maintained in the range of ~10 g/dl to enhance oxygen-carrying capacity to the injured brain (56). Based on this information, it has been shown that about 25% of patients undergoing craniotomy for intracranial hemorrhage receive transfusions of packed red blood cells intraoperatively, and 75% are transfused at some point in their ICU stay (57). However, this transfusion threshold has not been established in an evidence-based approach and recent reviews suggest that there are demonstrable negative systemic consequences of transfused blood (58,59). Transfusion requirements to optimize outcomes in injured patients and critical care populations have been studied in numerous centers and generally suggest lower hemoglobin levels. Hemoglobin levels of 7 g/dl correlate with better survivorship and lower complication rates (60). Any temptation to transfuse patients after TBI to a predetermined hemoglobin level in an effort to avoid secondary cerebral insults must be tempered by this knowledge of increased risk of adverse outcomes related to transfusions.

In a review of secondary brain insult factors, Jeremitsky and co-workers documented 11 harbingers of poor outcomes 24 hours after TBI (50). The five most important were: acidosis (BE >−4), coagulopathy (INR >2), hypotension (MAP <70 mmHg), hypothermia (T <35°C), and hypoxia (PaO₂/FIO₂ <200). It has been logically suggested that vigorous steps to avoid these secondary factors in patients with TBI as part of an overall brain protective strategy should correlate with better outcomes (61).

The beneficial effects of packed red blood cells transfusion on local cerebral tissue oxygen tension is described by Smith and colleagues who showed that 26/35 (74.3%) patients achieved an increase of 5.1 ± 9.4 mmHg (49% change from baseline) in brain tissue partial pressure of oxygen (PbtO₂) within one hour of an increase of transfusion (62). They also noted 9/35 (25.7%) of their patients experienced an actual decrease in PbtO₂ under the same circumstances. This is consistent with data that suggest the decreased deformability of stored packed red blood cells used in transfusion may actually worsen tissue perfusion and ischemia (63).

In a retrospective review of anemia and transfusion in TBI, Carlson et al. evaluated the hospital records of 169 patients with admission GCS ≤8 (64). They correlated lowest hematocrit, persistence of anemia, and use of transfusion with outcomes. Their data (analyzed with linear regression models) show that transfusion was independently associated with poor outcome and number of days with a hematocrit below 30 was actually associated with

improved neurologic outcomes. They concluded that the longer patients remained with a low hematocrit, the more likely they were to avoid transfusion and subsequent poor outcomes. They suggest TBI patients should have the same transfusion trigger as the rest of the ICU patient population.

Answer: Current literature does not support a recommendation for an absolute hemoglobin threshold that independently predicts better outcomes in patients who sustain TBI. Overuse of transfused blood should be avoided to minimize the deleterious effects of banked blood (Grade C recommendation).

Levels of Evidence

Trial Ref.	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Median follow-up	Minor end point	Major end point	Interpretations/Comments
DVT Prophylaxis								
34	2002	I	Systematic review				DVT prevention	LMWH has efficacy in DVT prophylaxis in trauma
34	2002	III	Systematic review				PE prevention	VCF should be considered in TBI patients were LMWH is contraindicated to prevent PE
36	1998	I	Randomized double-blind trial	SCD with and without LMWH (enoxaparin)	60 days		Increase intracranial bleeding or objective documentation of DVT/PE prevention	LMWH is effective in DVT prevention and safe in elective neurosurgical patients but there is a only marginal transfer of these data to patients with TBI
38	2002	III	Prospective nonrandomized observational study	LMWH given 24 hours after admission or 24 hours after surgery to patients with TBI	Variable, until hospital discharge or death		Expansion of IHI or prevention of DVT/PE	Study group small and nonrandomized. Variable study protocol changed during study due to bleeding complication. Trend toward safety of LMWH in TBI patients with CT scan follow-up
40	2003	III	Retrospective nonrandomized observational analysis	LMWH (certoparin, anti-factor Xa) given within 24 hours of TBI or surgery if CT scan confirms no expansion of IHI	Variable, until patient discharge or death		Prevention of DVT/PE with no evidence of HIT or major bleeding	Use of LMWH deemed safe when guided by CT scans showing no expansion of intracranial hemorrhage
41	2002	III	Retrospective observational study of 64 patients with TBI and AIS >3	Groups divided into early (<72 h) versus late (>72 h) administration of UFH	12 months or until discharge or death			No significant difference between two groups if DVT prevention (4% early versus 6% late) with no major increases in intracranial bleeding. Groups too small to draw major conclusions

(Continued)

Levels of Evidence (Continued)

Trial Ref.	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Median follow-up	Minor end point	Major end point	Interpretations/Comments
Seizure Prophylaxis								
47	2000	II	Population cohort based retrospective review of outcomes	4,541 patients with mild to severe TBI and no prior history of epilepsy compared to cohort of population without TBI	From injury to last known follow-up with medical professional. Excluded patients who died within 30 days of injury		Unprovoked seizure activity following TBI	There is an increased risk of seizures following TBI that varies with the severity of the injury and time from injury
51	1999	II	Retrospective cohort observational study of post-TBI patients who had or had not suffered seizures in the postinjury period	490 patients with TBI and postinjury executive dysfunction were retrospectively analyzed for presence or absence of seizure activity	≥5 years from time of injury		Analysis of functional outcomes as measure on the glasgow outcome scale	Young children were more prone to early seizures and adolescents and adults to late seizure. Presence of late seizures worsened functional outcomes as measured on the glasgow outcome scale
52	2007	II	Systematic review of existing literature	Review of data Levels I–IV from the decade of 1996–2006				Summary of pooled dated suggests benefits to AED in early (<7 days) post injury seizure prophylaxis
Transfusion								
56	2004	III	Systematic review					Neurosurgical textbook review of literature
50	2003	III	Retrospective observational study	Retrospective review of 81 patients with GCS ≤8 and transport times <2 hours to Level I trauma center	Death or hospital discharge		Length or stay correlates with presence of secondary brain injury factors	Identified secondary brain injury factors as most likely to correlate with poor outcomes that most needed correction in the first 24 hours of admission (hypotension and hypothermia independently correlated with mortality)
62	1999	II	Randomized metacenter randomized equivalency trial	Compared liberal transfusion protocol (Hg level 10–12) versus restrictive transfusion protocol (Hg 7–9)	30 day	Death from all causes at 60 days	Death from all causes at 30 days	Restrictive transfusion policy is at least as effective as and possibly superior to a liberal transfusion strategy in critically ill patients. This study included but did not limit patients with neurological abnormalities and is only used as an example of effects of transfusion

(Continued)

Levels of Evidence (Continued)

Trial Ref.	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Median follow-up	Minor end point	Major end point	Interpretations/Comments
64	2006	III	Retrospective outcome based record review of patient with severe TBI mean ISS 25.7	Review of 169 patients who survived at least 24 hours after severe TBI and length of time with HCT <30	8.5 months		Condition at hospital discharge	Because of the complexity of biological factors associated with transfused blood, TBI patients with days with HCT <30 showed better neurological outcomes by logistic regression analysis

Abbreviations: AED, antiepileptic drug; AIS, ; CT, computed tomography; DVT, deep vein thrombosis; GCS, glasgow coma score; HCT, hematocrit; HIT, heparin induced thrombocytopenia; ISS, injury severity score; IHI, intracranial hemorrhage injury; LMWH, low molecular weight heparin; PE, pulmonary embolism; SCD, sequential compression device; TBI, traumatic brain injury; UFH, unfractionated heparin; VCF, vena cava filter.

REFERENCES

- Rutland-Brown W, Langlois JA, Thomas KE, et al. Incidence of traumatic brain injury in the United States, 2003. *J Head Trauma Rehab* 2006; 21: 544–8.
- Sarrafzadeh AS, Peltonen EE, Kaisers U, et al. Secondary insults in severe head injury: do multiply injured patients do worse? *Crit Care Med* 2001; 29: 1116–23.
- Carlson A, Schermer C, Lu S. Retrospective evaluation of anemia and transfusion in traumatic brain injury. *J Trauma* 2006; 61: 567–71.
- Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. *J Neurotrauma* 2007; 24(Suppl 1): S1–S106. www.braintrauma.org
- Hesdorffer DC, Ghajar J. Marked improvement in adherence to traumatic brain injury guidelines in United States trauma centers. *J Trauma* 2007; 63: 841–7.
- Rusnak M, Janciak I, Majdan M, et al. Australian Severe TBI Study Investigators. Severe traumatic brain injury in Austria VI: Effects of guideline-based management. *Wien Klin Wochenschr* 2007; 119: 64–71.
- Fakhry SM, Trask AL, Waller MA, et al. IRTC Neurotrauma Task Force. Management of brain-injured patients by an evidence-based medicine protocol improves outcomes and decreases hospital charges. *J Trauma* 2004; 56: 492–9.
- Palmer S, Bader MK, Qureshi A, et al. The impact on outcomes in a community hospital setting of using the AANS traumatic brain injury guidelines. *American Association of Neurological Surgeons. J Trauma* 2001; 50: 657–64.
- Clayton TJ, Nelson RJ, Manara AR. Reduction in mortality from severe head injury following introduction of a protocol for intensive care management. *Br J Anaesth* 2004; 93: 761–7.
- Smith JS, Chang EF, Rosenthal G, et al. The role of early follow-up computed tomography imaging in the management of traumatic brain injury patients with intracranial hemorrhage. *J Trauma* 2007; 63: 75–82.
- Velmahos GC, Gervasini A, Petrovick L, et al. Routine repeat head CT for minimal head injury is unnecessary. *J Trauma* 2006; 60: 494–9.
- Dharap SB, Khandkar AA, Pandey A, et al. Repeat CT scan in closed head injury. *Injury* 2005; 36: 412–16.
- Schuster R, Waxman K. Is repeated head computed tomography necessary for traumatic intracranial hemorrhage? *Am Surg* 2005; 71: 701–4.
- Kaups KL, Davis JW, Parks SN. Routinely repeated computed tomography after blunt head trauma: does it benefit patients? *J Trauma* 2004; 56: 475–80.
- Chao A, Pearl J, Perdue P, et al. Utility of routine serial computed tomography for blunt intracranial injury. *J Trauma* 2001; 51: 870–5.
- Sifri ZC, Homnick AT, Vaynman A, et al. A prospective evaluation of the value of repeat cranial computed tomography in patients with minimal head injury and an intracranial bleed. *J Trauma* 2006; 61: 862–7.
- Brown CV, Weng J, Oh D, et al. Does routine serial computed tomography of the head influence management of traumatic brain injury? A prospective evaluation. *J Trauma* 2004; 57: 939–43.
- Brown CV, Zada G, et al. Indications for routine repeat head computed tomography (CT) stratified by severity of traumatic brain injury. *J Trauma* 2007; 62: 1339–44.
- Oertel M, Kelly DF, McArthur D, et al. Progressive hemorrhage after head trauma: predictors and consequences of the evolving injury. *J Neurosurg* 2002; 96: 109–16.
- Gilmer LK, Roberts KN, Scheff SW. Efficacy of progesterone following a moderate unilateral cortical contusion injury. *J Neurotrauma* 2008; 25: 593–602.
- Roof RL, Hoffman SW, Stein DG. Progesterone protects against lipid peroxidation following traumatic brain injury in rats. *Mol Chem Neuropathol* 1997; 31: 1–11.
- Roof RL, Duvdevani R, Heyburn JW, et al. Progesterone rapidly decreases brain edema: treatment delayed up to 24 hours is still effective. *Exp Neurol* 1996; 138: 246–51.
- Roof RL, Duvdevani R, Braswell L, et al. Progesterone facilitates cognitive recovery and reduces secondary neuronal loss caused by cortical contusion injury in male rats. *Exp Neurol* 1994; 129: 64–9.
- Pettus EH, Wright DW, Stein DG, et al. Progesterone treatment inhibits the inflammatory agents that accompany traumatic brain injury. *Brain Res* 2005; 1049: 112–19.
- Wright DW, Bauer ME, Hoffman SW, et al. Serum progesterone levels correlate with decreased cerebral edema after traumatic brain injury in male rats. *J Neurotrauma* 2001; 18: 901–9.

26. Stein DG, Wright DW, Kellermann AL. Does progesterone have neuroprotective properties? *Ann Emerg Med* 2008; 51: 164–72.
27. Wright DW, Ritchie JC, Mullins RE, et al. Steady-state serum concentrations of progesterone following continuous intravenous infusion in patients with acute moderate to severe traumatic brain injury. *J Clin Pharmacol* 2005; 45: 640–8.
28. Wright DW, Kellermann AL, Hertzberg VS, et al. ProTECT: a randomized clinical trial of progesterone for acute traumatic brain injury. *Ann Emerg Med* 2007; 49: 391–402.
29. Xiao G, Wei J, Yan W, et al. Improved outcomes from the administration of progesterone for patients with acute severe traumatic brain injury: a randomized controlled trial. *Crit Care* 2008; 12: R61.
30. Velmahos GC, Kern J, Chan LS, et al. Prevention of venous thromboembolism after injury: An evidence-based report—Part II: Analysis of risk factors and evaluation of the role of vena caval filters. *J Trauma* 2000; 49: 140–4.
31. Burke DT. Venous thrombosis in traumatic brain injury. *J Head Trauma Rehab* 1999; 14: 515–19.
32. Wen D, Hall W. Complications of subcutaneous low-dose heparin therapy in neurosurgical patients. *Surg Neurol* 1998; 50: 521–5.
33. Knudson MM, Ikossi DG, Khaw L, et al. Thromboembolism after trauma an analysis of 1602 episodes from the American College of Surgeons National Trauma Data Bank. *Ann Surg* 2004; 240: 490–8.
34. Rogers FB, Cipolle MD, Velmahos G, et al. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST Practice Management Guidelines Work Group. *J Trauma* 2002; 53: 142–64.
35. Hammond F, Meighben M. Venous thromboembolism in the patient with acute traumatic brain injury: screening, diagnosis, prophylaxis and treatment issues. *J Head Trauma Rehab* 1998; 13: 36–50.
36. Agnelli G, Pilvella F, Buonchristiani P, et al. Exoxaparin plus compression stockings compared with compression stockings alone in the prevention of venous thromboembolism after elective neurosurgery. *N Engl J Med* 1998; 339: 80–5.
37. Bratton SL, Chestnut RM, Ghajar H, et al. Deep vein thrombosis prophylaxis. *J Neurotrauma* 2007; 24(S1): S32–S36.
38. Norwood SH, McAuley CE, Berne JD, et al. Prospective evaluation of the safety of enoxaparin prophylaxis for venous thromboembolism in patients with intracranial hemorrhagic injuries. *Arch Surg* 2002; 137: 696–702.
39. Dickinson LD, Miller LD, Patel CP, et al. Enoxaparin increases the incidence of postoperative intracranial hemorrhage when initiated preoperatively for deep vein thrombosis prophylaxis in patients with brain tumors. *Neurosurgery* 1998; 43: 1074–81.
40. Kleindienst A, Harvey HB, Mater E, et al. Early antithrombotic prophylaxis with low molecular weight heparin in neurosurgery. *Acta Neurochir (Wien)* 2003; 145: 1085–91.
41. Kim J, Gearhart MM, Zurick A, et al. Preliminary report on the safety of heparin for deep venous thrombosis after severe head injury. *J Trauma* 2002; 53: 38–43.
42. Patton JH, Fabian TC, Croce MA, et al. Prophylactic Greenfield filters: acute complications and long-term follow-up. *J Trauma* 1996; 41: 231–7.
43. Darbina O, Rissob JJ, Carreb E, et al. Metabolic changes in rat striatum following convulsive seizures. *Brain Res* 2005; 1050: 124–9.
44. Shah AK, Fuerst D, Sood S, et al. Seizures lead to elevation of intracranial pressure in children undergoing invasive EEG monitoring. *Epilepsia* 2007; 48: 1097–103.
45. Chang BS, Lowenstein DH. Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: Antiepileptic drug prophylaxis in severe traumatic brain injury: Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2003; 60: 10–16.
46. Wang HC, Chang WN, Chang HW, et al. Factors predictive of outcome in posttraumatic seizures. *J Trauma* 2008; 64: 883–8.
47. Annegers J, Hauser W, Coan S, et al. A population-based study of seizures after traumatic brain injuries. *N Engl J Med* 1998; 338: 20–4.
48. Campion H, Bellamy R, Roberts C, et al. A profile of combat injury. *J Trauma* 2003; 54: S13–S19.
49. Annegers J, Coan S. The risks of epilepsy after traumatic brain injury. *Seizure* 2000; 9: 453–7.
50. Jeremitsky E, Omert L, Dunham CM, et al. Harbingers of poor outcome the day after severe brain injury: hypothermia, hypoxia, and hypoperfusion. *J Trauma* 2003; 54: 312–19.
51. Asikainen I, Kaste M, Sarna S. Early and late posttraumatic seizures in traumatic brain injury rehabilitation patients: brain injury factors causing late seizures and influence of seizures on long-term outcome. *Epilepsia* 1999; 40: 584–9.
52. Bratton SL, Chestnut RM, Ghajar J, et al. Antiseizure prophylaxis. *J Neurotrauma* 2007; 24(S1): S83–S86.
53. Myburgh JA, Cooper JD, Finfer SR, et al. Epidemiology and 12-month outcomes from traumatic brain injury in Australia and New Zealand. *J Trauma* 2008; 64: 854–62.
54. Chestnut RM, Marshall LF, Flauber MR, et al. The role of secondary brain injury in determining outcome from severe head injury. *J Trauma* 1993; 34: 216–22.
55. Goodnough LT. Risks of blood transfusion. *Crit Care Med* 2003; 31: S678–S686.
56. Winn HR. *Youmans Neurological Surgery*, 5th edition. Philadelphia: Saunders, 2004.
57. Couture DE, Ellegala DB, Dumont AS, et al. Blood use in cerebrovascular neurosurgery. *Stroke* 2002; 33: 994–7.
58. Van der Watering LMG, Hermans J, Houbiers JGA. Beneficial effects of leukocyte depletion of transfused blood on postoperative complications in patients undergoing cardiac surgery: A randomized clinical trial. *Circ* 1998; 97: 562–8.
59. Vincent JL, Baron JF, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. *JAMA* 2002; 288: 1499–507.
60. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *N Engl J Med* 1999; 340: 409–17.
61. Dearden NM. Mechanisms and prevention of secondary brain damage during intensive care. *Clin Neuropathol* 1998; 17: 221–8.
62. Smith MJ, Stiefel MF, Magge S, et al. Packed red blood cell transfusion increases local cerebral oxygenation. *Crit Care Med* 2005; 35: 1104–8.
63. Marik PE, Sibbald WF. Effects of stored blood transfusion on oxygen delivery in patients with sepsis. *JAMA* 1993; 269: 3024–9.
64. Carlson AP, Schermer CR, Lu SW. Retrospective evaluation of anemia and transfusion in traumatic brain injury. *J Trauma* 2006; 61: 567–71.

Spine and Spinal Cord Injuries

Yoram Klein and Shaul Sagiv

Clinical Questions		
Question	Answer	Grade of recommendation
What is the impact of airway maneuvers on cervical spine movement?	Relative segmental spine movement might happen, and can be minimized with in-line immobilization	B
What is the preferred way to achieve tracheal intubation in patients with suspected CSI?	Both direct oral and fiber optic awaked nasotracheal intubation are safe and effective. Oral intubation is preferred in emergency situations	B C
What criteria should be used to clear the cervical spine in a trauma patient?	The Nexus or the Canadian c-spine criteria can be used for clinical clearance of the spine	B
What is the imaging modality of choice for evaluation of the spine?	CT	B
Should high-dose corticosteroids be used in trauma patients with SCI?	No	B
What is the optimal timing to operate a patient with spinal injury?	No advantage for early operation except for decompression in evolving neurological deterioration	D
Abbreviations: CSI, cervical spinal cord injury; CT: computed tomography; SCI, spinal cord injury.		

INTRODUCTION

Spine injuries are common in the modern urban trauma setting. Although rare, spinal cord injury (1.3% of all trauma patients) carries an extremely high rate of morbidity and mortality. There are about 11,000 new traumatic spinal cord injuries (SCIs) each year. The SCI population in the United States is about 240,000 and the cost of treating them is billions of dollars (1).

Although surgical techniques have dramatically improved and the ability to get spinal stability and alignment enable earlier rehabilitation of the patients, the neurological recovery and the 10-year survival of this population has not changed significantly over the years.

The etiologies of SCI are:

1. due to high-energy motor vehicle collisions (MVCs); most are thoracic and lumbar
2. high fall injuries; most are in the thoracolumbar zone
3. sports injuries, from diving or other head collisions; most are cervical
4. violence/penetrating trauma
5. other miscellaneous causes

Three other statistical points worth mentioning:

1. Male to female ratio for these injuries is 4:1, without any racial predisposition.

2. In sports accidents-related SCI, 92% resulted in quadriplegia as compared to 54% in MVC-related SCI.
3. The 10-year survival rate of patients beyond 30 years with SCI is about 50%.

PATHOPHYSIOLOGY

Most SCIs are the result of contusion or traction forces rather than transection. These cause ischemia and hypoxia of the cord, which might lead to secondary tissue degeneration. Most of the damage to neural tissue is related to the primary injury, although some additional injury can be attributed to continuous cord compression or traction.

NEUROLOGICAL ASSESSMENT

An initial neurological examination of the SCI patient is essential for evaluation of the functional level and the prognosis. The examination should include sensory, motor, and proprioception evaluation together with perianal sensation, rectal sphincter tone, and bulbocavernous reflex.

A simple and acceptable classification of SCI is the Frankel classification (2):

- A. Complete absence of motor and sensory function.
- B. Sensation present but no motor function.

- C. Sensation + motor function 2–3/5.
- D. Sensation present with motor function of 4/5.
- E. Normal sensory and motor function.

To assess the patient, certain conditions must be defined:

1. Complete SCI: There is no motor or sensory function caudal to the level of injury and the bulbocavernosus reflex is present.
2. Spinal shock: Defined as a complete SCI with absent bulbocavernosus reflex. It should not be confused with neurogenic shock that is a hemodynamic condition characterized by hypotension and bradycardia.

Only after the reappearance of the bulbocavernosus reflex can we reevaluate the neurologic status of the patient and classify him or her to one of the incomplete or complete SCI syndromes.

3. Incomplete spinal cord injuries (ICSCIs): There is some motor or sensory function below the level of injury. There are a few formal types of ICSCI:
 - Central cord syndrome is the most common ICSCI and is presented as quadriplegia, with perianal and sacral sparing. About 75% of the patients will have partial recovery of the motor function.
 - Brown-Sequard syndrome is an unilateral SCI (usually due to penetration) characterized by motor deficit ipsilateral to the injury combined with contralateral sensory deficit. Most of these patients gain partial recovery with bowel and bladder continence and usually walking ability.
 - Anterior cord syndrome is a this relatively common ICSCI characterized by complete motor and sensory loss with some remnant of trunk and lower extremity deep sensation and proprioception. The prognosis of this syndrome is poor, and only 10% of them show some motor recovery.
 - Posterior cord syndrome is a rare ICSCI and is characterized by loss of proprioception and deep sensation but intact motor functioning. The patients usually ambulate in a “tabes dorsalis gait”.

INITIAL MANAGEMENT

As with every other severe trauma patient, initial management includes securing a patent airway, control of adequate oxygenation, and management of hemodynamics and perfusion.

Airway Management

Head injury with depressed level of consciousness is the most common indication for definitive airway control in trauma patients. Unfortunately, cervical spine injury is more common among these patients. The overall incidence of cervical spinal cord injury (CSI) is found to be around 2%, and patients with a Glasgow Coma Score (GCS) of less than 8 have an incidence of more than 10% (3).

Although extremely rare, worsening of cervical spinal cord damage due to airway control maneuver is a dreaded complication.

WHAT IS THE IMPACT OF AIRWAY MANEUVERS ON CERVICAL SPINE MOVEMENT?

Numerous studies have tried to define the spinal movement during airway management in patients with intact and injured cervical spine. Nevertheless, the evidence is limited due to the heterogeneity of the measurement techniques and the controversy about the clinical importance of the biomechanical findings. Both basic and advanced airway maneuver were found to cause movement in different segments of the cervical spine. Even presumably safe maneuvers, such as chin lift and jaw thrust, were found to cause movements that theoretically might jeopardize the cord. Advanced airway intervention, such as blind nasotracheal intubation and direct laryngoscopy and orotracheal intubation (DLOI) were also found to cause relative segmental cervical spine movement (to a lesser extent than the pre-intubation maneuver) in patients with normal and injured cervical spine. The most accentuated movements were found to be at the atlanto-occipital and atlantoaxial joints, but other portions of the cervical spine were affected as well (4,5). No significant different in movement was found between curved or straight laryngoscope blades (6).

Although the measured movements can be considered within the physiological margins in the intact cervical spine, the injured spine might be still compromised by these maneuvers. This is the reason for the application of spine immobilization during airway intervention. The most common immobilization technique is the manual in-line stabilization that was found to be most effective in limiting segmental movement to 1–3mm in various airway maneuvers (7,8).

Summary and recommendations: There are no Level I clinical data. The accumulated experimental data suggest that airway management in the trauma patient with suspected CSI might inflict relative spinal segmental movement. Manual in-line stabilization of the neck during the airway intervention can safely be applied and significantly limit the allegedly dangerous spine motion. Recommendation grade: B.

WHAT IS THE PREFERRED WAY TO ACHIEVE TRACHEAL INTUBATION IN PATIENTS WITH SUSPECTED CSI?

There are several options for achieving definitive airway control in a trauma patient with suspected CSI. Traditionally, DLOI was considered unsafe for patients with unstable CSI, and so blind nasotracheal intubation and surgical cricothyroidotomy were recommended as better options in that scenario. In the past decade, many series demonstrated the safety of DLOI. Although all series were retrospective, one fact aroused from them very clearly: Neurologic deterioration after orotracheal intubation is an extremely rare event even in patients with unstable CSI. In a review article from 2006, Crosby summarized the results of 12 retrospective series examining the outcome of tracheal intubations in patients with CSI, most of them unstable. The accumulated number of DLOI was 395; only two experienced neurological deterioration that was not attributed to the airway intervention (9).

Regardless the evident safety of DLOI, awake nasotracheal intubation is an option that many anesthesiologists

choose as the proffered technique for definitive airway control in patients with suspected CSI (10). This maneuver can be done blindly or, more commonly in recent years, with a fiber optic endoscope. Minimal spine movement, the ability to continue the neurological examination after the intubation, and maintaining airway protective reflexes are some of the advantages of this procedure. The potential disadvantages are the slow learning curve that causes many caregivers to be uncomfortable with the procedure (11) and the potential for desaturation that might aggravate secondary cord injury (12). No significant differences in success rate or safety were found between flexible and rigid endoscopes in establishing controlled airway in patients with a compromised cervical spine (13).

Summary and recommendations: Both DLOI and fiber optic awake nasotracheal intubation are safe and effective options for securing the airway in a trauma patient with suspected CSI. Recommendation grade: B. No data exist to support one technique over the other. Because no special equipment or advanced expertise is needed for DLOI, it is probably preferred in emergency situations whereas the fiber optic option is preferred for more elective procedures. Recommendation grade: C.

Breathing and Circulation

SCIs might inflict respiratory failure and hemodynamic compromise. On the other hand, hypoxemia and hypotension might increase the chance for secondary cord injury and worsening the neurological outcome. Cervical spinal cord injury might cause respiratory muscle paresis and paralysis, causing decreased ventilatory efficiency, hypoxemia, and hypoventilation. Patients with cervical SCI are at significant risk for ventilatory failure. This risk varies based on the level and completeness of injury. Ventilatory support is needed for the majority of patients with C5 and higher injuries and virtually all patients with C3 and higher injuries in the acute phase. Adequate fluid resuscitation and hemodynamic improvement was found to correlated to better neurological outcome (14). High SCI (usually above the level of T6) can be associated with disruption of the sympathetic chain that will cause hypotension and bradycardia. This condition, called neurogenic shock, is caused by unopposed parasympathetic vasodilation and bradycardia. Its incidence in recent retrospective cohort study was found to be 19.3% (15). In most patients, perfusion pressure can be maintained with fluid administration. Despite a lack of evidence-based literature on the subject, if systolic blood pressure of at least 90 mmHg, mean arterial pressure of 85 mmHg, and normal perfusion status are not achieved, early administration of vasoactive drug should be considered (16).

Diagnostic Options in Patients with Suspected Spine Injury

Imaging of the suspected injured spine has been the focus of many studies and analyses. Readily available computerized imaging has revolutionized the evaluation of the spine. On the other hand, large-scale studies demonstrated the safety of clearing the spine without any imaging in certain circumstances.

WHAT CRITERIA SHOULD BE USED TO CLEAR THE CERVICAL SPINE IN A TRAUMA PATIENT?

Two major research projects have been published in an attempt to establish a set of criteria by which a significant CSI can be safely ruled out based on clinical evaluation alone. Other smaller prospective studies basically reached the same conclusion. The NEXUS study enrolled 34,069 patients. There were five criteria for the definition a low probability of CSI: no midline cervical tenderness, no focal neurological deficit, normal alertness, no intoxication, and no painful, distracting injury. The decision instrument missed 8 of the 818 patients who eventually were diagnosed with CSI [sensitivity, 99.0%; 95% confidence interval (CI), 98.0–99.6%]. The negative predictive value was 99.8 percent (95% CI, 99.6 to 100%), the specificity was 12.9%, and the positive predictive value was 2.7% (17). The Canadian study enrolled 8,924 adults with blunt trauma to the head and neck, with normal vital signs and GCS of 15. Among the study population there were 151 (1.7%) patients diagnosed with clinically important CSI. The decision to order C-spine radiography was based on three questions: (1) Is there any high-risk factor present that mandates radiography (i.e., age 65 years, dangerous mechanism, or paresthesias in extremities)? (2) Is there any low-risk factor present that allows safe assessment of range of motion (i.e., simple rear-end MVC, sitting position in emergency department, ambulatory at any time since injury, delayed onset of neck pain, or absence of midline C-spine tenderness)? (3) Is the patient able to actively rotate neck 45° to the left and right? The results were 100% sensitivity (95% CI, 98–100%) and 42.5% specificity (95% CI, 40–44%) for identifying clinically important C-spine injuries (18). In 2003, a prospective comparison of the two criteria sets was published. There were 169 important CSIs among the 8,283 study patients. The Canadian C-spine rule was more sensitive than the NEXUS (99.4% versus 90.7%, $p < 0.001$), more specific (45.1% versus 36.8%, $p < 0.001$), and resulted in lower radiography rates (19).

Summary and recommendations: Both the NEXUS or the Canadian C-spine rule set of criteria can be safely used to clinically clear the C-spine in adult, asymptomatic patients with blunt trauma. Patients that meet the low-risk criteria do not need any further radiographic investigation. Recommendation grade: A.

WHAT IS THE IMAGING MODALITY OF CHOICE FOR EVALUATION OF THE SPINE?

Active flexion-extension cervical spine radiography has been suggested as adjacent to normal static radiographs in cases of continued neck tenderness or stiffness after a blunt trauma. However, despite its evident safety, it became a rare choice due to its high rate of technical inadequacy and the fact that it adds little information to computed tomography (CT) or magnetic resonance imaging (MRI), which became more available in recent years (20,21).

Traditionally, evaluation of the thoracic, lumbar, and sacral spine was done with plain radiographs augmented with CT in cases of evident fracture or technical inadequacy. In recent years the availability of the high-resolution fast multisliced CT scanner makes it the screening modality

of choice. With most victims of high-energy blunt trauma needing torso CT, regenerating the spine images has been found to be more effective than plain radiographs with proven cost reduction (22,23).

A known low-sensitivity, together with the cumbersome task of obtaining at least three views (lateral, anterior-posterior, and open mouth—odontoid) have led many trauma centers to choose cervical spine CT with coronal reconstruction as the primary screening modality for suspected CSI in the multiple trauma patients. The superiority of this approach was shown in a meta-analysis published in 2005. Despite some methodological flaws and the fact that no randomized controlled study was included, the authors presented pooled sensitivity for plain radiography of 52% (95% CI: 47, 56), versus pooled sensitivity for CT of 98% (95% CI: 96, 99) (24). The American College of Orthopaedic Surgeons now recommends routine cervical spine screening via CT scan instead of plain radiography (25). The three-view radiographic study should be performed only when CT is not readily available and should not be considered a substitute for CT. Lateral cervical plain radiographs in the resuscitation area cannot rule out unstable CSI, so the information gained will not change the management of the patient. This is why we do not recommend this study.

The assumption that CSI increases the risk for other thoracolumbar spine injuries has been proven in a large retrospective study based on the nationwide trauma database. The occurrence of thoracolumbar spine fracture was doubled from 6.9% to 13.06% if a concomitant cervical spine fracture was found (26).

MRI is the most sensitive imaging method for evaluation of the neck structure including soft tissue (ligaments, discs, etc.) and neural structures. This is why it is an appealing modality for diagnosis of a suspected injured spine. However, its relatively low availability and the technical problems of scanning trauma patients in the acute phase preclude its routine use in the initial evaluation. MRI is usually reserved for cases of spinal-related signs and symptoms that are not explained by findings in the CT (i.e., continued neck pain or motion limitation or unexplained clinical neurological finding).

Summary and recommendations: In patients where spine clearance cannot be achieved with clinical examination, CT of the cervical spine with reconstructions is the screening modality of choice. Views reconstructed from the thoracic and abdominal CT are adequate for the evaluation of the thoracic and lumbar spine. MRI should be preserved to selected cases of clinical/radiological discrepancy or inadequate CT. Recommendation grade: B.

Medical Management of Spinal Cord Damage

Inflicting direct forces such as laceration, compression, and distraction on the spinal cord create primary damage and cell death on impact. A secondary insult can occur within minutes as a result of hypoxia or hypoperfusion. The resulting inflammatory process, combined with other metabolic derangements, might further increase neural and glia cell apoptosis. These events will eventually lead to a worse neurological outcome. The relative contribution of the secondary insult to the final neurological outcome is not known but estimated to be no higher than 10% (27), and it is still the focus of numerous research projects.

Several studies focus on the effort to promote neural tissue recovery and regeneration. Autologous incubated macrophages, oscillating field stimulation, autologous bone marrow cell transplantation with granulocyte macrophage colony stimulating factor and autologous olfactory ensheathing cell transplantation are all in various stages of clinical studies after showing promising results in animal models. However none have yet produced any evidence to support use in any human clinical condition (28–31).

Several compounds that may attenuate secondary cord injury are being clinically tested. The most prominent are minocycline and GTPase ras homology protein inhibitor. Again, evidence for their routine use is yet to be found (32,33).

GM-1 ganglioside was thought to have neuroprotective properties via several mechanisms that participate in the secondary injury cascade. Despite promising initial results, a large multicenter study demonstrated no effectiveness for the drug, and therefore its use cannot be recommended (34).

SHOULD HIGH-DOSE CORTICOSTEROIDS BE USED IN TRAUMA PATIENTS WITH SCI?

Few issues in medicine have stirred up as much controversy and dispute as the issue of corticosteroids administration in SCI. The complexity of interpretation of evidence-based data and its influence on medicolegal considerations are demonstrated in a survey of 60 Canadian neurosurgeons and orthopedic spine surgeons about their practice. Approximately 75% of the responders routinely prescribe steroids for acute SCI, but 70% of them do so due to fear from litigation or peer criticism. Only 17% of them believe that steroids actually improve their patient's neurological outcome (35). The first study on administration of methylprednisolone (MP) was published in 1984 (36). In 1992, the National Spinal Cord Injury Study (NASCIS II) was published with high-profile professional and popular media coverage. It was a prospective, randomized, double-blind, controlled, multicenter trial with 487 patients randomized to high-dose MP, naloxone, or placebo. A one-year follow-up study summarized results. No significant neurological improvement was achieved, and an insignificant trend toward increased complication rate (mainly infection) was demonstrated. A post hoc analysis found that patients who received high-dose MP within eight hours of their injury showed a statistically significant although questionable improvement in motor and sensory scores at six months (37). The next pivotal study randomized 499 patients and compared 24 and 48 hours MP administration with no significant outcome differences. Again, post hoc analyses showed that the 48-hour MP group had a slightly better motor outcome if the drug was given 3–8 hours after the trauma. The sensory scores were equal between the groups. As in all other similar studies, an increased infectious complications rate was evident (38). In general, the same results were also obtained subsequently, including several prospective randomized studies.

Summary and recommendations: Current data do not support the routine use of high-dose MP in patients with SCI, because accumulative results suggest questionable

minimal functional recovery and a clear increase in complications. Recommendation grade: B.

SURGICAL INTERVENTION: TIMING

What Is the Optimal Timing to Operate a Patient with Spinal Injury?

The effect of early surgery on neurological outcomes remains a debatable topic. Vaccaro et al. (39) designed a prospective randomized controlled study to determine whether functional outcome is improved in patients with traumatic cervical SCI who underwent early surgery (<72 hours after injury) compared with those who underwent late surgery (>5 days after injury). They revealed no significant neurological benefit for the early surgical intervention.

Fehlings et al. (40) conducted a meta-analysis study, which provide the following recommendations: (1) Urgent decompression is recommended in case of bilateral locked facets and incomplete tetraplegia, or neurological deterioration; (2) urgent decompression in any acute CSI is a reasonable practice option.

The dilemma of timing is much more complicated in multitrauma patients with an associated spinal injury. Dai et al. (41) retrospectively summarized their experience with 147 patients, who sustained blunt high-energy multitrauma with thoracolumbar fractures. Although it is not the preferable study design in terms of evidence-based medicine, it is worthwhile to learn its results and conclusions. There was no statistically significant correlation between the timing of thoracolumbar surgery and the complications rate. Neither the severity of the injury nor the timing of surgery had any significant effect on the recovery rate.

The term “damage control” is a leading concept in traumatology. It should be considered by the surgeon when he or she decides if and when to operate on the patient.

Summary and recommendations: To date, there are no defined standards regarding the timing of decompression and stabilization in acute SCI. The literature does infer urgent spinal cord decompression in the face of evolving neurological deficit. The question of surgery timing in multiple trauma patients with spinal injury remains open for debate because prospective studies are unlikely to be initiated. Recommendation grade: D.

Level of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Choice of airway control method	2006	9	Ib	B	Both direct oral and fiber optic awaked nasotracheal intubation are safe and effective
Clinical clearance of the cervical spine	2003	19	Ib	A	The Nexus or the Canadian c-spine criteria can be used for clinical clearance of the spine
Imaging modality of choice of the spine	2005	24	Ia	B	CT is the modality of choice for radiological evaluation of the injured spine
High-dose steroids for SCI	1997	39	Ia	B	There is no proven functional benefit. There is significant increase in infection rate

Abbreviations: CT, computed tomography; SCI, spinal cord injury.

REFERENCES

- Aashjian RZ, Majercik S, Biffl WL, et al. Halo-vest immobilization increases early morbidity and mortality in elderly odontoid fractures. *J Trauma* 2006; 60: 199–203.
- Browner BD, Jupiter JB, Levine AM, et al. *Skeletal Trauma: Fractures, Dislocations, Ligamentous Injuries*. Philadelphia: WB Saunders, 1998.
- Demetriades D, Charalambides K, Chahwan S, et al. Non-skeletal cervical spine injuries: Epidemiology and diagnostic pitfalls. *J Trauma* 2000; 48: 724–7.
- Aprahamian C, Thompson BM, Finger WA, et al. Experimental cervical spine injury model: evaluation of airway management and splinting techniques. *Ann Emerg Med* 1984; 13: 584–7.
- Sawin PD, Todd MM, Traynelis VC, et al. Cervical spine motion with direct laryngoscopy and orotracheal intubation: an in vivo cinefluoroscopic study of subjects without cervical abnormality. *Anesthesiology* 1996; 85: 26–36.
- Gerling MC, Davis DP, Hamilton RS, et al. Effects of cervical spine immobilization technique and laryngoscope blade selection on an unstable cervical spine in a cadaver model of intubation. *Ann Emerg Med* 2000; 36: 293–300.
- Lennarson PJ, Smith D, Todd MM, et al. Segmental cervical spine motion during orotracheal intubation of the intact and injured spine with and without external stabilization. *J Neurosurg (Spine 2)* 2000; 92: 201–6.
- Brimacombe J, Keller C, Kunzel KH, et al. Cervical spine motion during airway management: a cinefluoroscopic study of the posteriorly destabilized third cervical vertebrae in human cadavers. *Anesth Analg* 2000; 91: 1274–8.
- Crosby ET. Airway management in adults after cervical spine trauma. *Anesthesiology* 2006; 104: 1293–318.
- Rosenblatt WH, Wagner PJ, Ovassapian A, et al. Practice patterns in managing the difficult airway by anesthesiologists in the United States. *Anesth Analg* 1998; 87: 153–7.
- Ezri T, Szmuk P, Warters RD, et al. Difficult airway management practice patterns among anesthesiologists practicing in the United States: Have we made any progress? *J Clin Anesth* 2003; 15: 418–22.
- Fuchs G, Schwarz G, Baumgartner A, et al. Fiberoptic intubation in 327 patients with lesions of the cervical spine. *J Neurosurg Anesth* 1999; 11: 11–16.
- Cohn AI, Zornow MH. Awake endotracheal intubation in patients with cervical spine disease: a comparison of the

- Bullard laryngoscope and the fiberoptic bronchoscope. *Anesth Analg* 1995; 81: 1283–6.
14. Vale FL, Burns J, Jackson AB, et al. Combined medical and surgical treatment after acute spinal cord injury: results of a prospective pilot study to assess the merits of aggressive medical resuscitation and blood pressure management. *J Neurosurg* 1997; 87: 239–46.
 15. Guly HR, Bouamra O, Lecky FE. Trauma Audit and Research Network. The incidence of neurogenic shock in patients with isolated spinal cord injury in the emergency department. *Resuscitation* 2008; 76: 57–62.
 16. Hadley MN, Walters BC, Grabb PA, et al. Blood pressure management after acute spinal cord injury. *Neurosurgery* 2002; 50(suppl): 58–26.
 17. Hoffman JR, Mower WR, Wolfson AB, et al. Validity of a set of clinical criteria to rule out injury to the cervical spine in patients with blunt trauma. National Emergency X-Radiography Utilisation Study Group. *N Engl J Med* 2000; 343: 94–9.
 18. Stiell IG, Wells GA, Vandemheen KL, et al. The Canadian C-spine rule for radiography in alert and stable trauma patients. *JAMA* 2001; 286: 1841–8.
 19. Stiell IG, Clement CM, McKnight RD, et al. The Canadian C-spine rule versus the NEXUS low-risk criteria in patients with trauma. *N Engl J Med* 2003; 349: 2510–18.
 20. Wang JC, Hatch JD, Sandhu HS, et al. Cervical flexion and extension radiographs in acutely injured patients. *Clin Orthop* 1999; 365: 111–16.
 21. Insko EK, Gracias VH, Gupta R, et al. Utility of flexion and extension radiographs of the cervical spine in the acute evaluation of blunt trauma. *J Trauma* 2002; 53: 426–9.
 22. Sheridan R, Peralta R, Rhen J, et al. Reformatted visceral protocol helical computed tomographic scanning allows conventional radiographs of the thoracic and lumbar spine to be eliminated in the evaluation of blunt trauma patients. *J Trauma* 2003; 55: 655–69.
 23. Brandt MM, Wahl WL, Yeom K, et al. Computed tomographic scanning reduces cost and time of complete spine evaluation. *J Trauma* 2004; 56: 1022–6.
 24. Holmes JF, Akkinepalli R. Computed tomography versus plain radiography to screen for cervical spine injury: a meta-analysis. *J Trauma* 2005; 58: 902–5.
 25. Mulkens TH, Marchal P, Daineffe S, et al. Comparison of low-dose with standard-dose multidetector CT in cervical spine trauma. *Am J Neuroradiol* 2007; 28: 1444–50.
 26. Winslow JE III, Hensberry R, Bozeman WP, et al. Risk of thoracolumbar fractures doubled in victims of motor vehicle collisions with cervical spine fractures. *J Trauma*. 2006; 61: 686–7.
 27. Young W, Yen V, Blight A. Extracellular calcium ion activity in experimental spinal cord contusion. *Brain Res* 1982; 235: 105–13.
 28. Knoller N, Auerbach G, Fulga V, et al. Clinical experience using incubated autologous macrophages as a treatment for complete spinal cord injury: Phase I study results. *J Neurosurg Spine* 2005; 3: 173–81.
 29. Shapiro S, Borgens R, Pascuzzi R, et al. Oscillating field stimulation for complete spinal cord injury in humans: a Phase I trial. *J Neurosurg Spine* 2005; 2: 3–10.
 30. Yoon SH, Shim YS, Park YH, et al. Complete spinal cord injury treatment using autologous bone marrow cell transplantation and bone marrow stimulation with granulocyte macrophage-colony stimulating factor: phase I/II clinical trial. *Stem Cells* 2007; 25: 2066–73.
 31. Féron F, Perry C, Cochrane J, et al. Autologous olfactory ensheathing cell transplantation in human spinal cord injury. *Brain* 2005; 128: 2951–60.
 32. Yune TY, Lee JY, Jung GY, et al. Minocycline alleviates death of oligodendrocytes by inhibiting pro-nerve growth factor production in microglia after spinal cord injury. *J Neurosci* 2007; 27: 7751–61.
 33. Fournier AE, Takizawa BT, Strittmatter SM. Rho kinase inhibition enhances axonal regeneration in the injured CNS. *J Neurosci* 2003; 23: 1416–23.
 34. Geisler FH, Coleman WP, Grieve G, et al. The Sygen multicentre acute spinal cord injury study. *Spine* 2001; 26: 87–98.
 35. Hurlbert RJ, Moulton R. Why do you prescribe methylprednisolone for acute spinal cord injury? *Can J Neurol Sci* 2002; 29: 236–9.
 36. Bracken MB, Collins WF, Freeman DF, et al. Efficacy of methylprednisolone in acute spinal cord injury. *JAMA* 1984; 251: 45–52.
 37. Bracken MB, Shepard MJ, Collins WF, et al. Methylprednisolone or naloxone treatment after acute spinal cord injury: 1-year follow-up data. *J Neurosurg* 1992; 76: 23–31.
 38. Bracken MB, Shepard MJ, Holford TR, et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. *JAMA* 1997; 277: 1597–604.
 39. Vaccaro AR, Daugherty RJ, Sheehan TP, et al. Neurologic outcome of early versus late surgery for cervical spinal cord injury. *Spine* 1997; 22: 2609–13.
 40. Fehlings MG, Perrin RG. The role and timing of early decompression for cervical spinal cord injury: update with a review of recent clinical evidence. *Injury* 2005; 36(Suppl 2): S13–S26.
 41. Dai LY, Tao WF, Zhou O. Thoracolumbar fractures in patients with multiple injuries: diagnosis and treatment—a review of 147 cases. *J Trauma* 2004; 56: 348–55.

Facial Injuries

Antonio Jorge V. Forte, Renato da Silva Freitas and Joseph H. Shin

Clinical Questions		
Question	Answer	Grade of recommendation
What is the proper method and timing of closing and caring for facial lacerations and injuries after closure?	Repair should be performed within 6 hours with either absorbable or nonabsorbable sutures. Postoperative care with polyurethane dressing and botulinum toxin improve outcome.	A
What is the proper timing of repair of facial fractures, especially in the setting of neurologic trauma/other injuries?	Early repair in the neurologically stable patient appear to outweigh any possible issues related to delay.	B
Are antibiotics indicated in the management of facial lacerations or facial fractures and if so, when?	Prophylactic antibiotics in nonbite wounds is not necessary. In fractures, perioperative antibiotic use reduces the incidence of infection. Postoperative antibiotic do not seem to reduce infection rate.	A
Which treatment is better for mandible fractures: closed or open reductions?	Performance of open reduction and internal fixation with appropriate size fixation is critical in the development of the best possible result and patient outcome.	A

INTRODUCTION

Facial injuries are among the most common emergencies seen in an acute care setting. They range from simple soft tissue lacerations to complex facial fractures with associated significant craniomaxillofacial injuries and soft tissue loss. The management of these injuries generally follows standard surgical management priorities but is rendered more complex by the nature of the numerous areas of overlap in management areas, such as airway, neurologic, ophthalmologic, and dental. Also, the significant psychological nature of injuries affecting the face and the resultant aftermath of scarring can have devastating and long-lasting consequences. Despite the fact that these injuries are exceedingly common, they are cared for by a large group of different specialists and as such have a remarkably heterogeneous presentation and diverse treatment schema. Nonetheless, guiding principles in the care of these injuries will provide the basis for the best possible outcomes. The following questions will guide general management and provide a framework for understanding the principles in the acute care of patients with facial injuries and trauma.

WHAT IS THE PROPER TIMING AND METHOD OF CLOSING AND SUBSEQUENT CARE FOR FACIAL LACERATIONS AND INJURIES AFTER CLOSURE?

Despite the extremely common presentation of such injuries, there remains little standardization on repairing and then

caring for the wounds or lacerations. There is great variation in the repair of lacerations as well as the different materials used to repair them. This is again because of the numerous different specialties involved in the care of the injuries and their desires to provide the best possible outcome with regard to scarring. Pediatricians, emergency department personnel, and surgeons may not all agree on the best modalities for repair. Placement as well as type of dressing are also controversial.

The timing of facial skin laceration closure is the same as that of any open wound. The presence of contaminating factors in the management of wound would generally not allow closure after six hours and would favor delayed closure (1). However, clinical practice is slightly more variable with facial lacerations because of the uniquely sensitive nature of facial scarring. Although we generally ascribe to experimental data regarding timing of closure, in practice the six-hour rule is often overlooked with an attempt to be vigorous in cleaning the wound. The presence of exceptionally rich blood supply in the face is also deemed of benefit in extending the six-hour rule.

Regarding suturing technique, Gandham and Menon published a prospective and randomized clinical trial in 2003 in which 37 patients were followed for a period of 18 months. That study compared the cosmetic appearance of skin lacerations closed by either traditional or dynamic sliding loop suture technique. Two independent observers blinded to the technique used a Visual Analogue Cosmetic Scale to assess the aesthetic result. The study found that there

is no statistically shown difference between the cosmetic appearance of wounds sutured using either technique (2).

In 2005, Singer et al. published a single-center, prospective, randomized clinical trial that compared the short-term wound infection and dehiscence rates, as well as the cosmetic outcome after three months of traumatic facial lacerations closed with either a single or a double layer of sutures. The study included 65 patients, whose wounds were simple, linear, nonbite, and nongaping (<10mm in width). Wounds were evaluated at time of closure, five days later, and again three months later. Both the patient and a researcher that was blinded to the number of suture layers assessed cosmesis at the three-month follow-up. The authors demonstrated that skin closure with a single layer of suture was seven minutes shorter. However, no statistical difference was found between groups regarding aesthetic result. Therefore, cosmetic outcome was not improved by the addition of a second layer of deep sutures to simple interrupted percutaneous sutures for treatment of short facial lacerations (3).

With reference to the material that should be used for facial laceration closure, Luck et al. showed in 2008 that there is no difference in cosmetic outcome when either absorbable catgut suture or nonabsorbable nylon is used in pediatric patients. They conducted a prospective randomized study that included 47 patients divided in two groups: catgut group and nylon group. The authors show that there is no statistically significant difference in the rates of infection, wound dehiscence, keloid formation, and parental satisfaction. In addition, three different observers who used the cosmesis visual analog scale graded the aesthetic result and no difference between study groups was demonstrated (4).

Zempsky et al. suggest that another alternative for facial lacerations in pediatric patients include closure with either 3M Steri Strip or Dermabond. They conducted a prospective, randomized trial that consisted of 100 children divided in two groups, one treated with Steri Strips and the other given Dermabond. Pain was measured using a 100mm pain visual analog scale. After two months, patients' wounds were photographed in a standardized fashion and analyzed by two cosmetic surgeons blinded to the method of repair using a 100mm visual analog scale. There was no statistical difference in pain after closure, wound complications on short-term follow-up, or cosmetic score between groups after two months. The authors conclude that the use of Steri Strips for skin closure is less expensive and provides a clinically equivalent result when compared to Dermabond (5).

Even though the benefits of moist wound healing have been suggested, there's also the concern related to wound's microflora increase. Thomas et al. conducted a prospective, randomized clinical trial in 2000 that tried to determine the clinical effectiveness of a hydroactive dressing as well as its impact on the microflora. Acute facial lacerations in 60 patients were primarily closed, and patients were randomly given either a dry gauze dressing or a hydroactive polyurethane dressing. Original wound photographs were obtained using a linear scale. Cosmetic outcome was measured at 5, 28, and 56 days. At day 5, wounds treated with the polyurethane dressing presented a statistically significant better contour, less erythema, and less subjective potential for scarring when compared to the control (dry

gauze) group, in addition to being more comfortable. However, once the dressings were removed, no significant difference in any parameter was noted on days 28 and 56. Finally, the microbiological results demonstrated that hydroactive dressing does not increase the density of the flora nor favors any specific bacterial growth (6).

Botulinum toxin has also been studied as a therapeutic option to improve the quality of wound healing after facial laceration closure. Gassner et al. address this issue by designing a blinded, prospective, randomized clinical trial that was published in 2006. The rationale behind this hypothesis is that botulinum toxin-induced immobilization of muscle activity around the healing wound reduces the muscle tension that act on the wound edges, thereby decreasing the repeated microtrauma and the chance for hypertrophic and hyperpigmented scars. The study analyzed 31 patients who suffered traumatic forehead lacerations or underwent forehead mass excision, divided in two groups: One received vials with 0.2ml normal saline, and the other received vials containing 0.2ml normal saline and 15U botulinum toxin A. Both groups received one vial per 2cm of wound length. Photographs at the time of closure and during follow-up visits at one week and six months were taken and assessed by two experienced facial surgeons who used a cosmetic visual analog scale. The authors found that the cosmetic improvement in the group treated with botulinum toxin when compared to the placebo group after six months was statistically significant and that this modality of chemoimmobilization is safe in the hands of experienced professionals (7).

Answer: There is significant variation in the management of facial lacerations and wounds. In general, there appears to be little difference noted in terms of the ultimate outcome of the treatment of lacerations and injuries depending on type of suture or method of suturing. Early expeditious repair should be undertaken within six hours if at all feasible or practical. Either absorbable or nonabsorbable sutures may be considered as equal if performed with a small enough diameter and with good technique. Removal and timing of removal is generally best done between five and seven days. The advent of skin glues such as cyanoacrylates have obviated the need for this in some cases and can be equally efficacious and provide satisfactory results. Postoperative care with polyurethane dressing has also been demonstrated to improve outcomes, as well as the potential use of botulinum toxin for the management of wounds. This last treatment is controversial and still considered experimental. Grade recommendation: A.

WHAT IS THE PROPER TIMING OF REPAIR OF FACIAL FRACTURES, ESPECIALLY IN THE SETTING OF NEUROLOGIC TRAUMA/OTHER INJURIES?

Facial injuries, in particular facial fractures, have long been noted to be associated with concomitant head and cerebral injuries. It has been generally accepted that the outcome of facial fractures is improved by early repair as demonstrated in orthopedic literature. Delay of fracture fixation clearly impedes the restoration of both function as well as aesthetic results by allowing fibroblast migration and potentially increasing scarring, leading to a poor result.

In 1990, Derdyn and colleagues published a retrospective study that involved 4,000 head injury patients with history of loss of consciousness and analyzed 49 patients with a combination of displaced facial fractures and significant cerebral trauma. The timing of facial fracture repair was divided in early (0–3 days), middle (4–7 days), and late (after 7 days). Outcome was divided in two modalities: good recovery with minimal disability and moderate to severe disability or death. The researchers found that the level of facial fracture affected survival, because patients with upper and middle-level facial injuries statistically do more poorly than those with lower level lesions. They also affirm that additional multisystem trauma worsens prognosis, as well as the presence of intracranial hemorrhage or shift of midline cerebral structures. Furthermore, no patient operated in any period showed a statistically significant reduction in Glasgow Coma Scale (GCS) score, and no significant difference in the number of postoperative complication was noted between groups undergoing early, middle, and late surgery. Therefore, the authors suggest that if a patient has a GCS score of 6 or higher, without evidence of intracranial bleeding, midline cranial shift, or basal cistern effacement, and an intracranial pressure (ICP) of less than 15mmHg without obvious cerebrospinal fluid leak, the patient should be considered a good candidate for early facial fracture reduction. Otherwise, surgical treatment should be performed late, once ICP permits, even in patients with a low likelihood for neurologic recovery, to avoid the grotesque deformity (8).

Similarly, Janus et al. in 2008 retrospectively reviewed 34 charts of patients who underwent midface fracture repair at a Level I trauma center. Early repair was defined as postinjury day 1–5; the rest was classified as late (postinjury day 6). There was no statistically significant difference between the two groups with respect to operative time, median number of screws used for repair, complication rate, and estimated operative blood loss (though there was a trend toward increased blood loss in the early treatment group). The authors also suggest that midface fractures should be repaired before 14 days, because after this period bone begins to heal and manipulation becomes more difficult (9).

Answer: Despite the significant correlation between facial injuries as well as head injuries and other traumatic conditions, it appears at this time that there is support for performing early and timely repair of facial fractures as soon as it is feasible. This support, though retrospective, demonstrates that there is little to gain from significant delay in fracture management and that there is no increase in complications from early (postinjury day 0–5) repair. The benefits of early repair in the neurologically stable patient appear to outweigh any possible issues related to delay. Grade recommendation: B.

ARE ANTIBIOTICS INDICATED IN THE MANAGEMENT OF FACIAL LACERATIONS OR IN FACIAL FRACTURES, AND IF SO, WHEN?

Antibiotics are used widely in surgery and the management of facial injuries. Growing awareness of the efficacy

of antibiotic use in a perioperative setting must be balanced with the emerging threat of complications of prolonged use, the most serious of which is the development of antibiotic-resistant organisms. The profusion of opinion on the use of antibiotics is complicated again by the heterogeneous and varied presentations of the injuries as well as those presenting with dental and oral injuries with their exceedingly high risk of subsequent infection.

It has generally been accepted that in the patients with simple lacerations do not require either pretreatment or post-treatment antibiotic use. In 1995, Cummings et al. conducted a meta-analysis of prophylactic antibiotics in nonbite wounds managed in emergency departments. Of nine randomized trials with 1,734 study patients, there was no evidence of any benefit to the use of antibiotics as protection against infection, even among patients treated with a penicillinase-resistant antibiotic. In fact, patients treated with antibiotics appeared to have a slightly greater incidence of infection as opposed to the untreated controls (10).

The management of facial fractures and the use of antibiotics in these cases are more complicated. The presence of colonization and bacterial load in the paranasal sinuses, normal flora in the nasal and respiratory tract and in the oral mucosa represent possible sources for bacterial contamination and the potential for a subsequent infection. Therefore, the use of perioperative antibiotic treatment in these cases has a justifiable basis. Chole and Yee studied 101 patients with facial fractures in a prospective and randomized clinical trial that investigated the role of the administration of cefazolin 1g intravenously one hour prior to surgery and eight hours later. These included mandible, maxillary, and LeFort fractures as well. They concluded that perioperative antibiotic use reduces the incidence of postoperative infection (11).

In a prospective study that included 90 patients, Heit and colleagues compared, the efficacy and cost of 1g daily of ceftriaxone and 2 million units of penicillin G every four hours in patients with compound mandible fractures undergoing surgery. Two patients in each group developed infections. They conclude that ceftriaxone is equally effective and carries a lower cost than penicillin G without any increase in systemic toxicity. They also suggest that adding metronidazole to the regimen may extend anaerobic coverage (12).

Abubaker and Rollert conducted a prospective, randomized, double-blind clinical study in 2001 evaluating the use of antibiotics postoperatively following mandibular fracture treatment. Thirty patients were randomly assigned into two groups, and each group received penicillin G, 2million U intravenously, every 4 hours through the preoperative period, intraoperative period, and for 12 hours postoperatively. In addition, the study group received penicillin VK, 500mg every six hours for five days postoperatively, and the control group received oral placebo using the same schedule for the same duration. Patients were evaluated for signs of infection after one, two, four, and six weeks. The study reports that in uncomplicated mandibular fractures, the use of postoperative antibiotic prophylaxis does not seem to reduce infection rate. However, one important limitation of this study was its relatively small sample size (13).

In 2006, Miles and colleagues decided to determine the benefit of postoperative antibiotic treatment of mandible fractures. They studied 291 patients who underwent open reduction and internal fixation of mandibular fractures in a prospective and randomized trial. The study group received 2.4 mIU of intramuscular penicillin G benzathine, or if allergic, a five- to seven-day regimen of oral clindamycin. No antibiotics were given postoperatively to the control group. The follow-up period was five to eight weeks. The authors did not find statistically significant effectiveness in the use of postoperative antibiotics when addressing open mandibular fractures with open reduction and internal fixation techniques. They conclude that there is no benefit to the use of postoperative antibiotics in the patient with the open mandible fracture (14).

Finally, Andreasen et al. published a systematic review in 2006 that searched for evidence for prophylactic administration of antibiotics to treatment of maxillofacial fractures in the literature. They affirm that one-day administration of antibiotics is as effective as a seven-day course. Additionally, the authors believe that due to the very low infection incidence in maxillary, zygoma, and condylar fractures, antibiotic treatment does not seem necessary (15).

Answer: In general, antibiotic use is best reserved for those indications in which there is an established infection. There is little to no role for antibiotics use in a prophylactic manner for facial injuries, such as simple lacerations or general uncomplicated nonbite injuries. There does appear to be a more compelling role for antibiotic use preoperatively/perioperatively in patients with fractures of the maxilla or mandible. This follows more traditional guidelines. As it is so in such cases, the postoperative use of antibiotics, even in mandibular fractures with oral contamination, does not generally seem warranted. However, variability in this practice pattern is more common. Grade recommendation: A.

WHICH TREATMENT IS BETTER FOR MANDIBLE FRACTURES: CLOSED OR OPEN REDUCTIONS?

Despite many years experience with the management of mandible fractures with both a closed approach (maxillo-mandibular fixation, MMF) and the use of open reduction and internal fixation (ORIF), there remains significant controversy about management by proponents of each depending on the situation as well as the type of fixation. The benefit of ORIF is clear as it has been shown that early mobilization and return to functionality is of vital importance to the patient. MMF still has a very important role in those patients who cannot tolerate a longer operation, potentially in complex fractures that require a combination of techniques, or potentially in injuries affecting the condyle.

Eckelt et al. coordinated a prospective, randomized, multicenter study in 2006 that included 66 patients with mandibular condylar process displaced fractures divided in two groups according to their modality of treatment: open or closed reductions. Patients had a follow-up at six weeks and at six months. There was no statistically significant difference in either clinical complications or accuracy of

fracture reduction based on radiographs. However, patients who underwent open reduction presented statistically significant improvement of mandible mobility and subjective functional index, as well as statistically significant reduction in disturbance of function, disturbance of occlusion, subjective pain, and discomfort (16).

Collins and colleagues published in 2004 a prospective randomized clinical trial that studied 90 patients with mandible fractures comparing the outcomes of using 2 mm locking plates versus 2 mm nonlocking plates. The theoretical advantages of locking plates include less screw loosening, greater stability across fracture site, less precision required, and less alteration in osseous and occlusal relationship. Difference in overall complication rates according to plate used was not statistically significant, and operative time was the same (17).

Furr et al. retrospectively reviewed medical records of 273 patients with mandibular fractures treated surgically over a five-year period. They found a statistically significant positive relationship between tobacco, alcohol, drug use, and long-term complications. Patients who underwent plating were more prone to develop long-term complications than those who did not. Ultimately, though, there was no statistically significant relationship between the rate of complications and patient demographics, fracture site, delay to repair, length of hospitalization, and use of antibiotics (18).

Kaplan et al. conducted a prospective, randomized, single-blinded study to compare outcomes of patients who underwent open reduction and internal fixation of displaced mandible fractures followed by either immediate mobilization or two weeks of mandibular-maxillary fixation. Twenty-nine patients were followed and examined at six weeks, three months, and six months after surgery. The rates of infection, wound breakdown, and inferior alveolar nerve paresthesia, as well as the dentition quality and the quality of occlusion, did not show any statistically significant difference between patients after immediate mobilization or patients who underwent mandibular-maxillary fixation (19).

Kuriakose et al. reviewed 168 consecutive cases of mandibular fracture that were treated with either rigid plates or mini-plates. Even though both plating systems restored appropriate occlusion, the authors noticed that an oral approach was adopted in most cases of the mini-plate group, whereas an extraoral approach was required for the rigid plate group, which had a significantly higher rate of weakness of the marginal mandibular branch of the facial nerve. However, infection, rate of plate removal, and overall complication rates were statistically significantly higher in the mini-plate group. Moreover, better treatment outcome for angle and comminuted fractures was noted with rigid plates (20).

Answer: The data with regard to the management of facial fractures and optimal types of fracture fixation is too extensive a topic to be covered in this chapter. Several principles can be understood from this perspective, however. Technological advances in composition of rigid fixation with titanium alloys as well as the development of the self-drilling, self-tapping screws as well as the locking plate have greatly expanded the armamentarium of the surgeon caring for the patient with facial fractures. That being said, the fundamental treatment plan requiring occlusal stability

is unchanged. The use of MMF is well tolerated, especially in the medically compromised patient. However, when possible, the performance of open reduction and internal fixation with appropriate size fixation is critical in the development of the best possible result and patient outcome. Early motion and rehabilitation will allow greater functional improvement and allow for maximal patient benefit, especially with regard to feeding and nutrition. Six weeks of rigid fixation and liquid diet has significant impact of the patient's overall weight and return to function. Therefore, optimal timing of surgery and use of optimal rigid fixation when possible is indicated. Grade recommendation: A.

CONCLUSION

The management of facial injuries is often complex because of the different anatomic areas involved as well as the multiple specialties necessary to care for these separate issues. Ultimately the outcome for these patients can be most rewarding, as it may be excellent depending on proper management. Management includes appropriate timing as well as the optimal methods and materials in both early and late care as well as in operative treatment. The foregoing principles have been demonstrated to be effective guidelines in the care of patients with facial injuries.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Method and timing of closing and caring for facial lacerations	2000, 2006, 2008	4, 6, 7	IIA	A	Repair should be with either absorbable or nonabsorbable sutures. Postoperative care with polyurethane dressing and botulinum toxin improve outcome.
Timing of facial fracture repair	1990	8	IIIB	B	If a patient is neurologically stable, early facial fracture reduction should be considered.
Use of antibiotics for facial lacerations and fractures	1987, 1995, 2001, 2006	10, 11, 13, 14	IIA	A	Prophylactic antibiotics in nonbite wounds is not necessary. In fractures, perioperative antibiotic use reduces the incidence of infection. Postoperative antibiotic do not seem to reduce infection rate.
Surgical treatment of mandible fractures	2006	16	IIA	A	Patients who underwent open reduction presented improvement of mandible mobility, reduction in disturbance of function, disturbance of occlusion, subjective pain and discomfort.

REFERENCES

1. Edlich RF, Rogers W, Kaufman D, et al. Studies in the management of the open contaminated wound: I optimal timing for closure of the contaminated open wound; II comparison of resistance to infection of open and closed wound during healing. *Am J Surg* 1969; 117: 323–9.
2. Gandham SG, Menon D. Prospective randomized trial comparing traditional suture technique with the dynamic sliding loop suture technique in the closure of skin lacerations. *Emerg Med J* 2003; 20: 33–6.
3. Singer AJ, Gulla J, Hein M, et al. Single-layer versus double-layer closure of facial lacerations: a randomized controlled trial. *Plast Reconstr Surg* 2005; 116: 363–8.
4. Luck RP, Flood R, Eyal D, et al. Cosmetic outcomes of absorbable versus nonabsorbable sutures in pediatric facial lacerations. *Pediatr Emerg Care* 2008; 24: 137–42.
5. Zempsky WT, Parrotti D, Grem C, et al. Randomized controlled comparison of cosmetic outcomes of simple facial lacerations closed with Steri Strip Skin Closures or Dermabond tissue adhesive. *Pediatr Emerg Care* 2004; 20: 519–24.
6. Thomas DW, Hill CM, Lewis MA, et al. Randomized clinical trial of the effect of semi-occlusive dressings on the microflora and clinical outcome of acute facial wounds. *Wound Repair Regen* 2000; 8: 258–63.
7. Gassner HG, Brissett AE, Otley CC, et al. Botulinum toxin to improve facial wound healing: a prospective, blinded, placebo-controlled study. *Mayo Clin Proc* 2006; 81: 1023–8.
8. Derdyn C, Persing JA, Broaddus WC, et al. Craniofacial trauma: an assessment of risk related to timing of surgery. *Plast Reconstr Surg* 1990; 86: 238–45.
9. Janus SC, MacLeod SP, Odland R. Analysis of results in early versus late midface fracture repair. *Otolaryngol Head Neck Surg* 2008; 138: 464–7.
10. Cummings P, Del Beccaro MA. Antibiotics to prevent infection of simple wounds: a meta-analysis of randomized studies. *Am J Emerg Med* 1995; 13: 396–400.
11. Chole RA, Yee J. Antibiotic prophylaxis for facial fractures. A prospective, randomized clinical trial. *Arch Otolaryngol Head Neck Surg* 1987; 113: 1055–7.
12. Heit JM, Stevens MR, Jeffords K. Comparison of ceftriaxone with penicillin for antibiotic prophylaxis for compound

- mandible fractures. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997; 83: 423–6.
13. Abubaker AO, Rollert MK. Postoperative antibiotic prophylaxis in mandibular fractures: a preliminary randomized, double-blind, and placebo-controlled clinical study. *J Oral Maxillofac Surg* 2001; 59: 1415–19.
 14. Miles BA, Potter JK, Ellis E III. The efficacy of postoperative antibiotic regimens in the open treatment of mandibular fractures: a prospective randomized trial. *J Oral Maxillofac Surg* 2006; 64: 576–82.
 15. Andreasen JO, Jensen SS, Schwartz O, et al. A systematic review of prophylactic antibiotics in the surgical treatment of maxillofacial fractures. *J Oral Maxillofac Surg* 2006; 64: 1664–8.
 16. Eckelt U, Schneider M, Erasmus F, et al. Open versus closed treatment of fractures of the mandibular condylar process—a prospective randomized multi-centre study. *J Craniomaxillofac Surg* 2006; 34: 306–14.
 17. Collins CP, Pirinjian-Leonard G, Tolas A, et al. A prospective randomized clinical trial comparing 2.0-mm locking plates to 2.0-mm standard plates in treatment of mandible fractures. *J Oral Maxillofac Surg* 2004; 62: 1392–5.
 18. Furr AM, Schweinfurth JM, May WL. Factors associated with long-term complications after repair of mandibular fractures. *Laryngoscope* 2006; 116: 427–30.
 19. Kaplan BA, Hoard MA, Park SS. Immediate mobilization following fixation of mandible fractures: a prospective, randomized study. *Laryngoscope* 2001; 111: 1520–4.
 20. Kuriakose MA, Fardy M, Sirikumara M, et al. A comparative review of 266 mandibular fractures with internal fixation using rigid (AO/ASIF) plates or mini-plates. *Br J Oral Maxillofac Surg* 1996; 34: 315–21.

Ocular Trauma: An Evidence-Based Approach to Evaluation and Management

Heidi I. Becker and Kelly M. Green

Question Summary for Ocular Trauma		
Question	Answer	Grade
Do steroids or orbital surgery improve visual outcomes in traumatic optic neuropathy?	Retrospective case series do not support the use of steroids or orbital surgery.	C
Does enucleation have a role in the prevention or treatment of sympathetic ophthalmia?	Case series do not support the use of enucleation solely to prevent or treat SO.	C
Does patching speed resolution of simple corneal abrasions?	Several randomized clinical trials showed no benefit from patching.	A
Do topical NSAIDs provide pain control in simple corneal abrasions?	Topical NSAIDs reduce pain without affecting time to heal.	A
What medications prevent rebleeds in traumatic hyphemas?	Steroids and antifibrinolytics decrease rebleeds.	A
When is surgical intervention indicated after traumatic hyphema?	In non-sickle cell patients, 60 mmHg for 2 days, any corneal blood staining.	D
Do prophylactic intravitreal antibiotics reduce post-traumatic endophthalmitis?	In cases of intraocular foreign bodies.	B
Can CT accurately detect clinically occult ruptured globes?	No, but certain findings may heighten clinical suspicion.	B
<i>Abbreviations:</i> CT, computed tomography; NSAIDs, nonsteroidal anti-inflammatory drugs; SO, sympathetic ophthalmia.		

INTRODUCTION

Eye injuries are varied and represent a small percentage of trauma cases. Trauma patients often have limited follow-up at the tertiary care centers where they are referred for acute care. Researchers have therefore found it challenging to address the paucity of high-quality randomized clinical trials guiding treatment of ocular injuries because of difficulty with recruitment and follow-up. Ophthalmologists and their acute care colleagues have in many cases relied more on historical standard of care guidelines than evidence-based guidelines to treat the variety of ocular conditions that arise in the setting of trauma.

Although the nature of ocular injuries has not changed dramatically in the past few decades, the medical and particularly the surgical tools available for treating such conditions have evolved significantly. In some cases, the literature has not kept pace with the technology. For example, the guidelines for surgical intervention rather than medical treatment for traumatic hyphema are largely based on the outcomes of studies performed prior to the introduction of refined microsurgical techniques (1,2).

The goal of this chapter, therefore, is to clarify the current state of the literature addressing the evaluation and treatment of eye injury after trauma. The recommendations arising from this review are intended to guide clinicians and also identify potential areas of research.

DO STEROIDS OR ORBITAL DECOMPRESSION SURGERY IMPROVE FINAL VISUAL ACUITY IN CASES OF TRAUMATIC OPTIC NEUROPATHY?

Traumatic optic neuropathy (TON) occurs with blunt force frontal trauma and also in the setting of orbital hemorrhage or fractures. Patients present with decreased visual acuity, afferent pupillary defects, and decreased color vision in the affected eye. The optic nerve usually appears normal acutely.

Interest in treating patients with TON with high-dose corticosteroids arose in the wake of studies supporting steroid use in the setting of spinal cord trauma. A randomized controlled trial was begun in the 1990s to determine if high-dose corticosteroid treatment or orbital decompression improved final visual acuity in cases of blunt force TON (3). The trial, however, was converted to an observational case control study after it became clear that insufficient numbers of patients would make the study difficult to complete even after years of recruitment. Selection bias thus arose in this retrospective study that relied on individual ophthalmologists, orbital surgeons, and neuro-ophthalmologists to report their management and outcomes in absence of a standardized protocol. Patients included in the study were diagnosed within seven days of injury and had at least one month of follow-up.

The research found that neither optic canal decompression surgery nor corticosteroid treatment had a significant impact on final visual acuity and that improvement in visual acuity occurred in many patients whether they were simply observed, treated with surgery, corticosteroids, or both surgery and corticosteroids. The study was limited by its retrospective and observational nature.

More recently, a Cochrane Review examined the literature on TON and found that the literature lacks randomized clinical trials and is limited to retrospective case series such as the study by Levin et al. The Cochrane Review concludes that the current evidence does not support treating TON with either steroids or surgery (4,5).

Recommendation: TON cases should be observed rather than treated with corticosteroids or orbital decompression surgery.

DOES ENUCLEATION HAVE A ROLE IN THE PREVENTION OR TREATMENT OF SYMPATHETIC OPHTHALMIA?

Sympathetic ophthalmia (SO) is a potentially devastating complication of ocular trauma first described during ancient times and further characterized during the Civil War era. Bilateral granulomatous panuveitis arises after penetrating injury or surgery to one or both eyes. The majority of cases arise within three months of the initial insult with 90% manifesting within one year of injury (6). Modern incidence varies in reports from 0.03 per 100,000 to 0.2–0.5% after penetrating injury, a substantial drop from the 16% incidence reported during the Civil War (6). The decrease in incidence is believed to reflect improved surgical techniques for primary closure of ruptured globes and also due to better understanding and recognition of other etiologies of bilateral inflammatory ocular disease, such as Vogt-Koyanagi-Harada disease.

Enucleation (complete removal of the eye and a portion of the optic nerve) of the injured eye within two weeks of the onset of SO has been advocated to improve final visual acuity. The recommended timing of enucleation is based on retrospective data from a clinicopathologic study done in the 1980s. The pathology specimens from patients with a diagnosis of SO at a single center from 1913 to 1978 were reviewed along with the patients' clinic charts. Penetrating injury accounted for just over half of the cases of SO, whereas intraocular surgery was associated with 40.4% of cases. The authors found that enucleation within two weeks of the onset of symptoms of SO correlated with visual acuity of 20/70 or better in 74% of patients, whereas acuity in patients who were enucleated later in the course of disease fared significantly worse (7).

A second, smaller series similarly examined the timing of enucleation and its effect on visual outcomes as well as the impact of steroid use on final visual acuity. Reynard et al. retrospectively reviewed the pathology specimens and clinical charts of 30 cases of SO. The authors compared the visual outcomes of patients treated with early (defined as less than two weeks after onset of SO) enucleation and later enucleation. Visual outcomes of patients treated with topical or systemic corticosteroids were also compared with those of patients who did not receive steroids. The visual outcomes as well as disease severity as graded histologically by the authors were significantly better

in patients treated with early enucleation. Patients treated with steroids also had better outcomes than those who did not receive immunosuppressive therapy irrespective of enucleation status (8).

A prospective series published in 2000 examined the more recent incidence and clinical histories of newly diagnosed cases SO in the United Kingdom and Ireland. This series relied on individual ophthalmologists to report cases to the authors over a 12-month period. The authors found a low incidence of SO of 0.03/100,000 and found that of the 17 cases that met their inclusion criteria, over half arose after intraocular surgery rather than trauma. The mean age of 56 years of age and equal gender distribution also reflected the association with surgery rather than trauma. The authors found that enucleation was performed less frequently than in prior reports and that in one case, a diagnosis of SO was made months after enucleation for recurrent choroidal melanoma. Patients who were enucleated required no less immunosuppression than those who retained both eyes. With immunosuppressive therapy, such as corticosteroids, cyclosporine, and azathioprine, visual prognosis at one year from time of diagnosis was quite good, with over 75% of patients reported to have vision of 20/40. The case series was limited by its small size and might not have similar findings if conducted in a different population where trauma is more prevalent (9).

With current surgical techniques and timely repair, in many cases an injured eye retains reasonable visual function after penetrating injury. In the unlikely event that SO arises, prompt treatment is indicated. If the inciting eye is blind, painful, or is unlikely to regain vision, enucleation may be considered. However, preserving vision in the sympathizing eye requires treatment with steroids or steroid-sparing agents (6). With the current array of immunosuppressive agents, the inciting eye may also retain reasonable vision, and the literature does not support prophylactic or therapeutic enucleation for SO.

Recommendation: The literature regarding SO is limited to case series and clinicopathologic reports. As it stands, the literature does not support prophylactic or therapeutic enucleation for SO.

DOES PATCHING IMPROVE OUTCOMES OF CORNEAL ABRASIONS?

Traumatic corneal abrasions are painful deepithelializations caused by superficial trauma to the ocular surface. Corneal abrasions usually heal well in immunocompetent patients, but they are painful and have the potential to develop into infectious ulcers. Pain control and supportive measures, such as patching the eye shut to speed healing, are two areas of interest in the literature.

Turner and Rabiou provide a thorough review of the literature addressing patching. They reviewed 11 papers describing randomized clinical trials from 1960 to 2002. The authors comment the trials reviewed were of varying quality in terms of randomization and blinding. A meta-analysis of the major outcome of time-to-heal for simple, traumatic corneal abrasions less than 10mm² showed no improvement in healing time with patching (10).

Recommendation: Patching does not reduce pain or speed healing in simple corneal abrasions and does not have a role in the treatment of simple corneal abrasions.

DO TOPICAL NSAIDS PROVIDE PAIN CONTROL IN SIMPLE CORNEAL ABRASIONS?

Pain management for corneal abrasions has also received considerable attention in the literature. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) have been used successfully to treat postoperative pain from corneal deepithelializations after refractive surgery. Several investigators have examined NSAID use for pain management in the setting of simple corneal abrasions. A meta-analysis in 2005 used stringent inclusion criteria to review the randomized trials in the literature. Eleven randomized clinical trials were identified by the authors, of which five met inclusion criteria for analysis. Three of the five used similar pain rating scales, and the data from these studies were used for primary analysis. After meta-analysis of the three randomized controlled trials with similar pain rating scales, the authors found a significant improvement in pain control in patients using topical NSAIDs (11). Although the meta-analysis did not address whether the use of NSAIDs slowed healing of the corneal abrasions, one well-designed study that assessed time to heal along with pain control showed no significant delay in healing time in NSAID treated patients over placebo-treated controls (12).

Recommendation: Topical NSAIDs reduce pain without affecting time to heal of simple corneal abrasions.

WHAT MEDICATIONS (SYSTEMIC OR TOPICAL) PREVENT REBLEEDS OF TRAUMATIC HYPHEMAS?

Hyphema (bleeding in the anterior chamber) may arise spontaneously, after eye surgery, after penetrating trauma, and most classically, after blunt force trauma. Traumatic hyphemas are more common in young males and arise most often after assault and athletic accidents (13). Sequelae of hyphema include corneal blood staining, increased intraocular pressure and resultant optic atrophy, and peripheral anterior synechiae, all of which can decrease final visual acuity. Although corneal blood staining may be transient, children can develop amblyopia and permanent loss of vision even as the blood clears. Final visual acuity may also be limited by other pathology, such as macular holes or traumatic optic neuropathy related to the original trauma rather than the hyphema.

Secondary hemorrhages (rebleeds) are associated with higher rates of ocular hypertension, corneal blood staining, and optic atrophy. Visual outcomes after hyphema are worse in cases of secondary hemorrhage, and preventing rebleeding remains a key goal. Those at higher risk for rebleeding include patients with bleeding diatheses or on blood thinners, patients with sickle cell disease or trait, and more darkly pigmented patients irrespective of sickle cell status. A substantial body of literature addresses the medical, environmental, and surgical treatment of hyphema with the goal of reducing the incidence of rebleeding.

Walton et al. provided an extensive review and meta-analysis of this literature in 2002. In several randomized

controlled clinical trials, systemic medications such as corticosteroids and the antifibrinolytic agents ϵ -aminocaproic acid (Amicar) and tranexamic acid (Cyklokapron) decreased the incidence of rebleeds over placebo-treated controls. These studies, however, did not show improved final visual acuity over placebo-treated controls. These drugs, which have undesirable side effects, are therefore not uniformly used. The antifibrinolytics can cause undesirable side effects of nausea, vomiting, and orthostatic hypotension. They also must be renally dosed in cases of renal impairment, can precipitate renal failure in hemophiliacs, and are considered FDA pregnancy category C. Topical steroids and topical ϵ -aminocaproic acid also reduce the incidence of rebleeding, although the latter drug is not available in the United States (14).

Recommendation: The literature supports the use of steroids and antifibrinolytics to reduce rebleeds. Topical steroids and antifibrinolytics also reduce rebleeds. The decision to use systemic therapy versus or in addition to topical treatment should be influenced by the overall clinical picture and the patient's ability to tolerate the undesirable side effects of systemic therapy.

IS SURGICAL INTERVENTION INDICATED TO REDUCE COMPLICATIONS FROM TRAUMATIC HYPHEMAS?

If pressure is uncontrolled or corneal blood staining is noted, the hyphema should be surgically removed from the anterior chamber. The studies that guide the timing and technique of surgical intervention were performed in the 1970s and found significantly worse visual outcomes in patients treated surgically versus medically (15,16). Although the literature supports a conservative approach to surgical intervention (intraocular pressure above 60 mmHg for 2 days in non-sickle cell patients, for example), the tools and techniques available to the eye surgeon have evolved significantly since these studies. As suggested by other authors, earlier surgical intervention may be warranted, but the studies to support it are yet to be performed (13,14).

Recommendation: The literature does not advocate earlier surgical intervention to reduce complications from hyphemas, but the association of surgical intervention with worse visual outcomes arises from outdated data.

DO INTRAVITREAL ANTIBIOTICS PREVENT POST-TRAUMATIC BACTERIAL ENDOPTHALMITIS? DOES THEIR USE AFFECT FINAL OUTCOMES IN EYES THAT ARE ALREADY INFECTED?

Penetrating ocular trauma can not only destroy vital intraocular structures but also cause bacterial endophthalmitis, particularly in settings of contaminated wounds and intraocular foreign bodies. Treating bacterial endophthalmitis involves injection of intravitreal antibiotics and usually includes sampling the vitreous or anterior chamber fluid for cultures.

Whereas the current standard of care for ruptured globes includes prompt surgical repair and systemic and topical antibiotics, some have questioned whether prophylactic injection with intraocular antibiotics could reduce the

risk of developing endophthalmitis in eyes without signs of clinical infection.

A case control study in 2000 examined the effect of prophylactic intravitreal vancomycin and ceftazidime on the rate of endophthalmitis in patients treated for open globe injuries. Exclusion criteria included full hyphema, endophthalmitis, history of eye surgery within three months of presentation, delayed presentation (greater than 72 hours), delayed intraocular foreign body removal (greater than one week), and patients in whom visualization of the needle for intravitreal injection would have been difficult. Thirty-two patients were prospectively randomized to receive intravitreal injections at the time of primary repair and 38 were repaired without intravitreal injections. The method of randomization was not described. All patients received systemic and topical antibiotics and topical steroids. Some patients received systemic steroids. In cases of intraocular foreign bodies diagnosed at presentation, the foreign bodies were removed within one week of presentation. Patients were followed up for three months. Although the main outcome of clinically diagnosed endophthalmitis occurred more frequently in the control patients, the difference in the rate of endophthalmitis between controls and treated patients was not statistically significant. The *p* value became significant, however (0.03), if two patients in the treated group with initially undetected retained intraocular foreign bodies (eyelashes recovered at time of vitrectomy for endophthalmitis) were excluded from the statistical analysis (17).

A larger, multicenter, double-blind randomized controlled trial was undertaken by Sohelian and colleagues. The authors randomized 346 eyes of 346 patients with open globes undergoing repair to receive either balanced salt solution or gentamicin and clindamycin by intraocular injection after open globe repair. Exclusion criteria included vision of no light perception, "severe" hyphema, endophthalmitis at time of presentation, and opaque cornea. Monocular patients and children less than three years of age were also excluded. Patients received injections at the end of primary repair. Time to primary repair was reported, but time to removal of intraocular foreign body was not. Patients with trauma to the anterior segment were injected into the anterior chamber and patients with posterior damage received intravitreal injections. Endophthalmitis was diagnosed based on either clinical impression or positive vitreous cultures taken at the time of primary repair. The study found a trend toward lower rates of endophthalmitis in patients treated with prophylactic

intraocular antibiotics and patients with intraocular foreign bodies had statistically significant lower rates of post-traumatic endophthalmitis when treated with prophylactic antibiotics (*p* = 0.04) (18).

Recommendation: Prophylactic intravitreal antibiotics reduce the risk of endophthalmitis in open globes with intraocular foreign bodies. Open globes without intraocular foreign bodies may also benefit from prophylactic antibiotics.

CAN CT SCAN ACCURATELY DETECT CLINICALLY OCCULT RUPTURED GLOBES?

In cases of a full-thickness corneoscleral laceration or obvious uveal prolapse, little question exists as to the presence of a ruptured globe. However, in other cases, such as those with dense or diffuse subconjunctival hemorrhage and hyphema, it can be difficult to determine the integrity of the globe even with detailed slit lamp examination. An unconscious or uncooperative patient presents additional challenges. If the status of the globe cannot be determined clinically, surgical exploration to rule out the presence of an occult open globe is considered the gold standard.

Because computed tomography (CT) scans are commonly used in the evaluation of the trauma patient, some have questioned whether these scans may be able to aid the clinician in determining the status of the globe in unclear cases. In a retrospective review of the CT scans of 48 eyes that underwent exploration for occult ruptured globe, Arey et al. found that certain CT findings increased the likelihood of ruptured globe. Three masked observers, two neuroradiologists and one ophthalmologist, identified several findings on CT that increased the likelihood of the surgeon encountering a ruptured globe at surgery. The positive predictive value of the CT scan ranged from 86% to 100%, but the negative predictive value was much lower at 42–50%. Although a CT scan can be a useful adjunct in evaluating patients for open globes and may increase the pretest probability of encountering a ruptured globe at surgery, it cannot replace surgical exploration (19).

Recommendation: CT scan is an important study to obtain in settings of ocular trauma to evaluate for intraocular foreign bodies and associated orbital, facial, and head trauma. The findings on CT scan may heighten clinical suspicion for an occult ruptured globe, but CT cannot detect open globes accurately enough to preclude surgical exploration in unclear cases.

Level of Evidence for Ocular Trauma

Subject	Year	Ref.	Level	Strength	Findings
Steroids or orbital surgery for traumatic optic neuropathy	1999, 2007	3–5	IIIB	C	There is not support for either steroids or surgery in TON.
Enucleation for sympathetic ophthalmia	1980, 1983	6–9	IIIB	C	Case series do not support the use of enucleation solely to prevent or treat SO.
Patching for corneal abrasions	2006	10	IA	A	Several randomized clinical trials showed no benefit from patching.
NSAIDs for corneal abrasions	2001, 2005	11, 12	IA	A	Topical NSAIDs reduce pain without affecting time to heal.
Prevention of secondary hemorrhage in hyphema	2002	13, 14	IA	A	Steroids and antifibrinolytics decrease rebleeds.
Surgery for hyphema	1972, 1974	15, 16	III	D	In non-sickle cell patients, 60 mmHg for 2 days, any corneal blood staining.
Prophylactic intraocular antibiotics for endophthalmitis	2003, 2007	17, 18	IB	B	In cases of intraocular foreign bodies.
CT for detection of occult open globes	2007	19	IIB	B	No, but certain findings may heighten clinical suspicion.

Abbreviations: CT, computed tomography; NSAIDs, nonsteroidal anti-inflammatory drugs; SO, sympathetic ophthalmia; TON, traumatic optic neuropathy.

REFERENCES

- Read J. Traumatic hyphema: surgical vs medical management. *Ann Ophthalmol* 1975; 7: 659–62, 664–6, 668–70.
- Kunimoto DY, Kanitkar KD, Makar M, et al. The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease, 4th ed. Philadelphia: Lippincott Williams and Wilkins, 2004; 22.
- Levin LA, Beck RW, Joseph MP, et al. The treatment of traumatic optic neuropathy: the international optic nerve trauma study. *Ophthalmology* 1999; 106: 1268–77.
- Yu-Wai-Man P, Griffiths PG. Steroids for traumatic optic neuropathy. *Cochrane Database Syst Rev* 2007; CD006032.
- Yu-Wai-Man P, Griffiths PG. Surgery for traumatic optic neuropathy. *Cochrane Database Syst Rev* 2005; CD005024.
- Chu DS, Foster CS. Sympathetic ophthalmia. *Int Ophthalmol Clin* 2002; 42: 179–85.
- Lubin JR, Albert DM, Weinstein M. Sixty-five years of sympathetic ophthalmia: a clinicopathologic review of 105 cases (1913–1978). *Ophthalmology* 1980; 87: 109–21.
- Reynard M, Riffenburgh RS, Maes EF, et al. Effect of corticosteroid treatment and enucleation on the visual prognosis of sympathetic ophthalmia. *Am J Ophthalmol* 1983; 96: 290–4.
- Kilmartin DJ, Dick AD, Forrester JV. Prospective surveillance of sympathetic ophthalmia in the UK and the Republic of Ireland. *Br J Ophthalmol* 2000; 84: 259–63.
- Turner A, Rabiou M. Patching for corneal abrasion. *Cochrane Database Syst Rev* 2006; CD004764.
- Calder L, Balasubramanian S, Fergusson D. Topical non-steroidal anti-inflammatory drugs for corneal abrasions: meta-analysis of randomized trials. *Acad Emerg Med* 2005; 12: 467–73.
- Goyal R, Shankar J, Fone DL, et al. Randomised controlled trial of ketorolac in the management of corneal abrasions. *Acta Ophthalmol Scand* 2001; 79: 177–9.
- Campagna J. Traumatic hyphema: current strategies. *Focal Points Clin Mod: Am Acad Ophthalmol* 2007; 25: 10.
- Walton W, Von Hagen S, Grigorian R, et al. Management of traumatic hyphema. *Surv Ophthalmol* 2002; 47: 297–334.
- Rakusin W. Traumatic hyphema. *Am J Ophthalmol* 1972; 74: 284–92.
- Read J, Goldberg MF. Comparison of medical treatment for traumatic hyphema. *Trans Am Acad Ophthalmol Otolaryngol* 1974; 78: 799–815.
- Narang S, Gupta V, Gupta A, et al. Role of prophylactic antibiotics in open globe injuries. *Ind J Ophthalmol* 2003; 51: 39–44.
- Soheilian M, Rafati N, Mohebbi MR, et al. Prophylaxis of acute post-traumatic bacterial endophthalmitis. *Arch Ophthalmol* 2007; 125: 460–5.
- Arey ML, Mootha W, Whittemore AR, et al. Computer tomography in the diagnosis of occult open-globe injuries. *Ophthalmology* 2007; 114: 1448–52.

Neck Trauma

Marc A. de Moya

Summary of Key Questions and Answers		
Question	Answer	Grade
Is physical exam adequate to rule out significant aerodigestive or vascular injury in penetrating trauma?	Physical exam is adequate to rule out significant airway and vascular injuries. Caution is required when ruling out a digestive tract injury based on physical exam, and observation may be warranted.	B
Are both esophagoscopy and fluoroscopic studies required to rule out esophageal injuries?	Contrast esophagography, if completely negative, may effectively rule out an esophageal injury; however, esophagoscopy should be added in those cases that the esophagography is equivocal.	C
How reliable is CT scan for ruling out a vascular or aerodigestive tract injury?	16-slice CT scan can accurately identify vascular injuries and trajectory of bullets.	B
	Reformatted images are helpful in detecting tracheobronchial injuries. CT scan cannot be used to rule out an esophageal injury.	C
Can color flow Doppler rule out a vascular injury?	Duplex ultrasound may be used to rule out an arterial injury in Zone II, however is limited in Zones I or III.	C
What are the risk factors for BCVI?	Cervical spine fractures, carotid canal fractures, seat belt sign, unilateral neurologic deficits, near hanging, LeFort II or III	C
Is selective exploration safe for penetrating neck trauma?	Mandatory exploration and selective explorations have equivalent outcomes.	C
How should BCVI injuries be treated?	Systemic anticoagulation with either IV heparin (PTT 40–50 s) or antiplatelet therapy decreases stroke rate in Grades II, III, IV injuries.	C
Abbreviations: BCVI, blunt carotid/vertebral arterial injury; CT, computed tomography; PTT, partial thromboplastin time.		

INTRODUCTION

The neck is an area that has spawned much debate and research in trauma over the last several decades. It is a region packed with vital structures vulnerable to both blunt and penetrating mechanisms. Penetrating neck injuries, defined as penetration of the platysma, account for approximately 5–10% of all injuries (1). Blunt neck injuries, including aerodigestive, vascular, and nerve injuries, affect approximately 0.7–4.2% of all significant blunt trauma patients. This excludes the most common neck structure injured, the cervical spine. This chapter focuses on a few of the most commonly asked questions regarding the evaluation and treatment of aerodigestive and vascular injuries in the neck.

In 1969, Cook County investigators divided the neck into three zones (2). Roon and Christensen recapitulated this classification in 1979 (3) in an effort to standardize therapy and research efforts. Zone I refers to the area from the clavicles to the cricoid cartilage. Zone II refers to the area from the cricoid cartilage to the angle of the mandible, and Zone III refers to the area from the angle of the

mandible to the base of the skull. However, since the first description of these zones, much has changed in how we approach, image, and treat patients with neck trauma.

Mandatory exploration of the neck was the standard of care soon after World War II but led to a negative exploration rate of approximately 56% (4). In the 1960s, routine operative explorations were challenged in the abdomen by Dr. Carter Nance and I. Cohn Jr. (5) and in the neck by Drs. Shirkey, Beall, and Deakey (6). This initial push for nonoperative management eventually led to more careful selection of operative candidates. Clinicians began to use the hard signs of vascular injury to select operative candidates: (1) active external hemorrhage, (2) expanding hematomas, (3) bruit or thrill over the wound, (4) pulse deficit, and (5) a central neurologic deficit. Hard signs of tracheobronchial injuries include (1) bubbling from the wound, (2) massive subcutaneous emphysema, or (3) hemoptysis. Some consider crepitation/dysphagia/hematemesis as soft signs of digestive tract injuries. Hard signs of digestive tract injuries usually do not manifest themselves immediately but are more insidious, leading to neck cellulitis/sepsis.

In an effort to decrease the number of negative neck explorations, more emphasis has been placed on the physical exam, new imaging technology, and close observation. As technology has improved, so has the ability to see otherwise occult injuries, raising questions of treatment. There are seven questions that are addressed here, forming a foundation for the current assessment and treatment algorithms for neck trauma. The following recommendations are focused on the most recent literature.

ASSESSMENT OF NECK TRAUMA

How Good Is the Physical Exam to Rule Out a Significant Aerodigestive or Vascular Injury?

The initial evaluation of a patient with a suspected neck trauma is the physical exam. Clinicians have been unsure of how reliable the physical exam is as a predictor of a significant aerodigestive or vascular injury. Atteberry et al. in 1994 studied 28 patients with penetrating Zone II neck injuries (7). They compared the physical exam to angiographic, operative, and ultrasonic findings. There were no missed injuries, albeit a short follow-up period. The same group performed a follow-up study with a larger series in 2000 after having instituted strict physical exam driven protocols for neck trauma (8). This follow-up study with 145 patients over an eight-year period confirmed their earlier study. Again, the false negative rate was approximately 0.3%, which was quoted to be equivalent to false negative rates of angiograms. The false positive rate was 10%. In 1997, Demetriades et al. (9) reviewed their experience of 223 patients and claimed that the negative predictive value of physical exam was 100%. Of particular concern is the lack of significant signs following stab wounds to the cervical esophagus.

In penetrating neck trauma, cervical esophageal injuries occur in 0.5–7% of cases. Meyer et al. reported clinical exam findings indicative of an esophageal injury in approximately 68% of patients with penetrating neck injuries (10). Weigelt et al. discovered that up to 50% of esophageal injuries were missed in those stabbed, based on clinical exam. Conversely, they describe a 100% sensitivity in physical exam for gunshot wound victims (11). The early clinical findings described for an esophageal injury include crepitance (12), hematemesis, anterior tracheal deviation, or hoarseness. If the diagnosis is delayed, complications as a result of contamination arise, including abscess, sepsis, mediastinitis, or neck cellulitis.

The role of physical exam in blunt neck trauma is not as clear. In those with angiographically confirmed carotid/vertebral injuries. Some report up to approximately 60% of angiographically confirmed carotid/vertebral injuries lack any hard signs of injury. Therefore, the physical exam in blunt trauma is not consistently accurate in detecting vascular injuries. Injury secondary to blunt trauma has been reported but is exceedingly rare. Tracheobronchial injuries have similar findings as penetrating traumatic injuries with an equivalent sensitivity.

Recommendations: Physical exam is adequate to rule out significant airway and vascular injuries. Caution is required when ruling out a digestive tract injury based on physical exam and observation may be warranted (Recommendation grade: B).

Are Both Esophagoscopy and Swallow Studies Necessary to Rule Out Esophageal Injuries?

Esophageal injuries can occur in both blunt and penetrating trauma, however, it is exceedingly rare to have a blunt cervical esophageal injury. The lack of more obvious signs, particularly in stab wounds, has led clinicians to use other diagnostic methods to rule out/in an esophageal injury. The early treatment of esophageal injuries significantly decreases complications and costs (13–15). A delay in treatment may lead to stricture, dysfunction, and infectious complications.

The diagnostic modalities that one may choose from include an esophogram, flexible esophagoscopy, or rigid esophagoscopy. Some have found that esophograms were 90% accurate, whereas esophagoscopy was 86% accurate (16). Weigelt et al. reported a 100% sensitivity for the combination of esophagrams followed by rigid esophagoscopy if the esophagram was equivocal in 118 patients with penetrating neck trauma (11). Srinivasan et al. (17), in a retrospective study of 55 patients, discovered that flexible endoscopy yielded a sensitivity of 100% and specificity of 92.4%. However, this series had a small number of esophageal injuries and overall a small number of patients.

Recommendations: Contrast esophagography if completely negative may effectively rule out an esophageal injury, however, esophagoscopy should be added in those cases that the esophagography is equivocal (Recommendation grade: C).

How Reliable Is CT Scan for Ruling Out a Vascular or Aerodigestive Tract Injury?

Since the advent of the modern computed tomography (CT) scan, diagnostic accuracy has significantly improved, achieving better patient selection and also detecting smaller injuries. Once the trauma community began to challenge the notion of mandatory explorations, the reliance on better imaging modalities has evolved. Gracias et al. (18), reported if the trajectory of the injury was distant from vital structures, no further imaging was necessary. Mazolewhi et al. examined the role of CT angiography and found that when compared to operative findings, the CT was 100% sensitive and 91% specific in a group of 14 patients (19). Eastman et al. (20) compared 146 high-risk patients with both CT angiograms and digital subtraction angiograms. Of the 46 positive findings on digital subtraction, 1 false negative CT angiogram was discovered. This injury was a Grade I vertebral artery injury. They concluded that the sensitivity, specificity, positive predictive value, negative predictive, and accuracy was 97.7%, 100%, 100%, 99.3%, and 99.3%, respectively. One other study similar to the parallel CT angiogram versus digital subtraction angiogram design was performed by Malhotra et al. in 2007. Malhotra and colleagues did not agree with the Eastman trial and found the sensitivity, specificity, and positive and negative predictive values to be 74%, 86%, 65%, and 90%, respectively (21). However, if the initial values are eliminated from the study, the sensitivity and specificity values approach the Eastman values. In the discussion, the authors suggest that the early data may have been affected by the initial learning curve. Nevertheless, this study provides a warning that the initial optimism for CT angio needs to be tempered and critically analyzed further. Sliker et al. (22), compared the use of a

whole body CT protocol to a dedicated CT angiogram for visualization of neck injuries and found them to be equivalent. Both modalities had high sensitivities and specificities for ruling out a cerebrovascular injury. Munera et al. (23) and Nunez et al. (24) demonstrated that the CT scan was also sensitive in detecting nonvascular injuries. Inaba et al. (25) report on 106 patients with penetrating neck trauma. No injuries requiring intervention were missed by CT scan, and it appeared that this potentially reduced the number of unnecessary explorations.

Recommendations: Sixteen-slice CT scans can accurately identify vascular injuries and trajectory of bullets (Recommendation grade: B). Reformatted images are helpful in detecting tracheobronchial injuries (Recommendation grade: C). CT scans cannot be used to rule out an esophageal injury (Recommendation grade: C).

What Is the Role of Color Flow Doppler Imaging to Determine Vascular Injury?

Color flow Doppler imaging is noninvasive and readily available. In some series, the sensitivity when compared to digital subtraction angiography reaches 90–95% (26). Demetriades (27) and Ginzburg have both published duplex sensitivities and specificities approaching 100%. However, the limitations of ultrasound include the inability to detect nonocclusive injuries with preserved flow, such as intimal flaps and pseudo-aneurysms. The technique also fails to detect high internal carotid injuries, which is in fact the most common area injured in blunt trauma patients.

Recommendations: Duplex ultrasound may be used to rule out an arterial injury in Zone II, however is limited in Zones I or III (Recommendation grade: C).

What Are the Risk Factors for Blunt Carotid/Vertebral Arterial Injuries?

Although the signs and symptoms of significant neck trauma secondary to penetrating mechanisms tend to be fairly straightforward, those for blunt trauma are more obsequious. In Miller et al., approximately 34% of carotid artery injuries were diagnosed by ischemic changes confirmed by either CT angiogram or digital subtraction angiogram. Thirty-eight percent of the carotid artery injuries were diagnosed based on the suspicion given injury patterns and mechanism. In Fabian's 1996 study (42) of 87 blunt carotid/vertebral arterial injuries (BCVIs), his group suggested in their discussion that the higher incidence of BCVIs in their trial was as a result of "aggressive neurosurgical screening." Based on this and other suggestions, the "at-risk" group was more actively sought after. The Denver group screened all those patients with mechanisms compatible with severe cervical hyperextension/rotation or hyperflexion, displaced midface or complex mandibular fractures, closed head injury consistent with diffuse axonal injury, near hanging, seat belt sign across the neck, basilar skull fractures (particularly involving the carotid canal), and cervical body fractures. In addition to this list, some have advocated the presence of a Horner's syndrome to suggest enough force to produce a BCVI. Although in a recent study by Malhotra et al. (21) discovered that the presence of a Horner's syndrome was rarely associated (<10%)

with BCVI, suggesting that it may not be necessary to add to the list of risk factors. These recent studies are based on studies from almost 30 years ago that analyzed the associated injuries and found a high incidence associated with complex facial trauma, direct neck blows, cervical spine fractures, and near hanging (29–31).

Recommendations: Cervical spine fractures, carotid canal fractures, seat belt sign, unilateral neurologic deficits, near hanging, LeFort II or III (Recommendation grade: C).

TREATMENT OF NECK TRAUMA

Should Penetrating Neck Injuries Be Selectively Observed or Always Explored?

In 1956, Fogelman and Stewart demonstrated that mandatory exploration was associated with few complications and a diminished mortality (32). Since that time, several authors have challenged the concept of mandatory explorations. This challenge comes around as a result of improved technologies and more careful critical analysis of physical exam. Mandatory exploration produced a negative exploratory rate of approximately 50–60% (33–35). Over the past decade, larger prospective observational trials have demonstrated success with a more selective approach. Biffl et al. (36) describes a series of 128 asymptomatic patients with normal physical exams, only 1 patient had a missed injury. This injury was from an ice pick. He went on to describe that only 15% of the patients required adjuvant tests. Nason and colleagues (38) found that 67% of those mandatorily explored had a negative exploration, and all Zone II injuries were symptomatic. Velmahos et al. (39) described in a large retrospective series 3% of explorations were unnecessary, and in the monitored group 9% had missed injuries, however, interpretation of the high missed injury rate was difficult. The only randomized clinical trial comparing mandatory exploration to selective observation was Golueke et al. (40), in which there was no difference in hospital stay, morbidity, or mortality in 160 patients.

Recommendations: Mandatory exploration and selective explorations have equivalent outcomes (Recommendation grade: C).

How Should BCVI Be Treated?

Much has been written concerning carotid injuries, but little is known about how to best treatment the spectrum of carotid and vertebral injuries. The overall incidence of BCVIs is between 0.33% and 1% of all traumas. In 1994, a Western Trauma Association multi-institutional trial described 60 carotid artery injuries (41). The overall mortality was 43%, and moderate to bad neurologic complications were present in over 22%. In 1996, Fabian et al. (42), described treatment and outcomes of 87 blunt carotid artery injuries over an 11-year period. The use of heparin with a goal partial thromboplastin time of 40–50 seconds seemed to independently improve outcomes. In 1999, Biffl et al. (43), developed a grading system for studying and categorizing blunt carotid injuries. Grade I = <25% luminal stenosis, Grade II = >25% luminal stenosis or intimal flap, Grade III = pseudo-aneurysm, Grade IV = complete occlusion, and Grade V = transection with active extravasation. They studied 76 patients with 109 blunt carotid injuries and determined that based on their protocol they had favorable

outcomes with the use of systemic anticoagulation, however, they lacked any controls. In 2001, Miller et al. (44) described 139 BCVIs in 96 patients. Seventy-five were carotid artery injuries, and 64 were vertebral artery injuries. Overall stroke rate for carotid injuries was 31%, and the overall stroke rate for vertebral injuries was 14%. Those patients with carotid injuries who received systemic anticoagulation had a significant decrease in stroke rate (6.8% versus 64%). Those with vertebral artery injuries who received systemic anticoagulation also benefited from systemic anticoagulation with a decreased stroke rate (2.6% versus 54%).

Recommendations: Systemic anticoagulation with either IV heparin (PTT 40-50s) or antiplatelet therapy decreases stroke rate in Grades II, III, IV injuries. Grade: C.

REFERENCES

- Demetriades D, Asensio JA, Velmahos G, et al. Complex problems in penetrating neck trauma. *Surg Clin North Am* 1996; 6: 661-83.
- Monson DO, Saletta JD, Freeark RJ. Carotid vertebral trauma. *J Trauma* 1969; 9: 987-99.
- Roon AJ, Christensen N. Evaluation and treatment of penetrating cervical injuries. *J Trauma* 1979; 19: 391-7.
- Elerding SC, Manart FD, Moore EE. A reappraisal of penetrating neck injury management. *J Trauma* 1980; 20: 695-7.
- Nance FC, Cohn I Jr. Surgical judgement in the management of stab wounds of the abdomen. A retrospective and prospective analysis based on a study of 600 stabbed patients. *Ann Surg* 1969; 170: 569-645.
- Shirkey AL, Beall AC Jr, Debakey ME. Surgical management of penetrating wounds of the neck. *Arch Surg* 1963; 86: 955-63.
- Atteberry LR, Dennis JW, Menawat SS, et al. Physical examination alone is safe and accurate for evaluation of vascular injuries in penetrating Zone II neck trauma. *J Am Coll Surg* 1994; 179: 57-62.
- Sekharan J, Dennis JW, Veldenz HC, et al. Continued experience with physical examination alone for evaluation and management of penetrating Zone 2 neck injuries: results of 145 cases. *J Vasc Surg* 2000; 32: 483-9.
- Demetriades D, Theodorou D, Cornwell E III, et al. Evaluation of penetrating injuries of the neck: prospective study of 223 patients. *World J Surg* 1997; 21: 41-8.
- Meyer JP, Barrett JA, Schuler JJ, et al. Mandatory vs selective exploration for penetrating neck trauma. A prospective assessment. *Arch Surg* 1987; 122: 592.
- Weigelt JA, Thal ER, Snyder WH III, et al. Diagnosis of penetrating cervical esophageal injuries. *Am J Surg* 1987; 154: 619.
- Goudy SL, Miller FB, Bumpous JM. Neck crepitance: evaluation and management of suspected upper aerodigestive tract injury. *Laryngoscope* 2002; 112: 791-5.
- Symbas PN, Hatcher CR Jr, Vlasits SE. Esophageal gunshot injuries. *Ann Surg* 1980; 191: 703-7.
- Shama DM, Odell J. Penetrating neck trauma with tracheal and esophageal injuries. *Br J Surg* 1984; 71: 534-6.
- Asensio JA, Chahwan S, Fornao W, et al. Penetrating esophageal injuries: multicenter study of the American Association for the surgery of trauma. *J Trauma* 2001; 50: 289.
- Noyes LD, McSwain NE Jr, Markowitz IP. Panendoscopy with arteriography versus mandatory exploration of penetrating wounds of the neck. *Ann Surg* 1986; 204: 21-31.
- Srinivasan R, Haywood T, Horwitz B, et al. Role of flexible endoscopy in the evaluation of possible esophageal trauma after penetrating injuries. *Am J Gastroenterol* 2000; 95: 1725-9.
- Gracias VH, Reilly PM, Philpott J, et al. Computed tomography in the evaluation of penetrating neck trauma: a preliminary study. *Arch Surg* 2001; 136: 1231-5.
- Mazolewski PJ, Curry JD, Browder T, et al. Computed tomographic scan can be used for surgical decision making in Zone II penetrating neck injuries. *J Trauma* 2001; 51: 315-19.
- Eastman AL, Chason DP, Perez CL, et al. Computed tomographic angiography for the diagnosis of blunt cervical vascular injury: is it ready for primetime? *J Trauma* 2006; 60: 925-9.
- Malhotra AK, Camacho M, Ivatury RR, et al. Computed tomographic angiography for the diagnosis of blunt carotid/vertebral artery injury: a note of caution. *Ann Surg* 2007; 246: 632-42.
- Sliker CW, Shanmuganathan K, Mirvis SE. Diagnosis of blunt cerebrovascular injuries with 16-MDCT: accuracy of whole-body MDCT compared with neck MDCT angiography. *AJR Am J Rad* 2008; 190: 790-9.
- Munera F, Soto JA, Nuniz D. Penetrating injuries of the neck and the increasing role of CTA. *Emerg Radiol* 2004; 10: 303-9.
- Nunez DB Jr, Torres-Leon M, Munera F. Vascular injuries of the neck and thoracic inlet: helical CT-angiographic correlation. *Radiographics* 2004; 24: 1087-98.
- Inaba K, Munera F, McKenney M, et al. Prospective evaluation of screening multislice helical computed tomographic angiography in the initial evaluation of penetrating neck injuries. *J Trauma* 2006; 61: 144-9.
- Kuzniec S, Kauffman P, Molnar LJ, et al. Diagnosis of limb and neck arterial trauma using duplex ultrasonography. *Cardiovasc Surg* 1998; 6: 358-66.
- Demetriades D, Theodorov D, Cornwell E III, et al. Penetrating injuries to the neck in patients in stable condition: physical examination, angiography or color flow imaging. *Arch Surg* 1995; 130: 971-5.
- Ginzburg E, Montavo B, Leblang S, et al. The use of duplex ultrasound in penetrating neck trauma. *Arch Surg* 1996; 131: 691-3.
- Stringer WL, Kelly DL. Traumatic dissection of the extracranial internal carotid artery. *Neurosurgery* 1980; 6: 123.
- Perry MO, Snyder WH, Tahl ER. Carotid artery injuries caused by blunt trauma. *Ann Surg* 1980; 192: 74.
- Davis JW, Holbrook TL, Hoyt DB, et al. Blunt carotid artery dissection: incidence, associated injuries, screening, and treatment. *J Trauma* 1990; 30: 1514.
- Fogelman M, Stewart R. Penetrating wounds of the neck. *Am J Surg* 1956; 91: 581-96.
- Saletta JD, Lowe RJ, Lim LT, et al. Penetrating trauma of the neck. *J Trauma* 1976; 16: 579-87.
- Elerding SC, Manart FD, Moore EE. A reappraisal of penetrating neck injury management. *J Trauma* 1980; 20: 695-7.
- Bishara RA, Pasch AR, Douglas DD, et al. The necessity of mandatory exploration of penetrating Zone II neck injuries. *Surgery* 1986; 100: 655-60.
- Biffl WL, Moore EE, Rehse DH, et al. Selective management of penetrating neck trauma based on cervical level of injury. *Am J Surg* 1997; 174: 678-82.
- Sriussadaporn S, Pak-Art R, Tharavej C, et al. Selective management of penetrating neck injuries based on clinical presentations is safe and practical. *Int Surg* 2001; 86: 90-3.
- Nason RW, Assuras GN, Gray PR, et al. Penetrating neck injuries: analysis of experience from a Canadian trauma centre. *Can J Surg* 2001; 44: 122-6.

39. Velmahos GC, Souter I, Degiannis E, et al. Selective surgical management in penetrating neck injuries. *Can J Surg* 1994; 37: 487–91.
40. Golueke PF, Goldstein AS, Sclafani SJ, et al. Routine versus selective exploration of penetrating neck injuries: a randomized prospective study. *J Trauma* 1984; 24: 1010–14.
41. Cogbil TH, Moore EE, Meissner M, et al. The spectrum of blunt injury to the carotid artery: a multicenter perspective. *J Trauma* 1994; 37: 473–9.
42. Fabian TC, Patton JH, Croce MA, et al. Blunt carotid injury: importance of early diagnosis and anticoagulant therapy. *Ann Surg* 1996; 223: 513–25.
43. Biffl WL, Moore EE, Offner PJ, et al. Blunt carotid arterial injuries: implications of a new grading scale. *J Trauma* 1999; 47: 845.
44. Miller PR, Fabian TC, Bee TK, et al. Blunt cerebrovascular injuries: diagnosis and treatment. *J Trauma* 2001; 51: 279–86.

Emergency Thoracotomy

Joseph J. DuBose and Mark Gunst

Clinical Questions		
Question	Answer	Grade of recommendation
Duration of prehospital CPR for penetrating thoracic injuries after which EDT futile?	According to retrospective data, EDT after more than 15 minutes of prehospital CPR is futile.	C
Should EDT be performed after blunt mechanism of injury in patients requiring prehospital CPR?	Limiting EDT use to patients with penetrating injuries results in better survival rates.	C
Is EDT effective at reducing mortality in patients with extrathoracic injuries?	EDT may facilitate salvage in a very select group of agonal patients with vascular injuries to the abdomen, neck, or extremities.	C
Do protocolized approaches to the performance of EDT influence outcomes?	A protocol confining EDT use to penetrating injuries with signs of life may improve survival rates.	C
Should the pericardium be opened in all cases of emergency thoracotomy?	Pericardiotomy should be performed following penetrating thoracic injury for evacuation of tamponade, direct control of cardiac hemorrhage, and optimal delivery of cardiac compressions.	C
Abbreviations: CPR, cardiopulmonary resuscitation; EDT, emergency department thoracotomy.		

INTRODUCTION

Emergency department thoracotomy (EDT) is used as a life-saving maneuver in an attempt to facilitate resuscitation of patients in cardiovascular collapse following trauma. Despite the aggressive nature of this operation, it has been difficult to effectively evaluate the impact that EDT has on outcomes and resource utilization. Additionally, the definition of “signs of life” and specific indications and protocols for EDT are inconsistent across trauma centers and in the published literature. The conditions under which the procedure is performed largely preclude validation in clinical trials. Research on this topic has therefore been limited to retrospective reviews and a number of small case series. In the era of evidence-based medicine, there is little evidence on which to establish concrete practice guidelines for this procedure (1–12).

In the absence of conclusive evidence to guide management, the burden for determining the appropriate use of EDT continues to rely on the clinical judgment of trauma providers. Although institutional protocols have been advocated (13), the utility of EDT continues to require a risk-benefit analysis on a case-by-case basis. The likelihood of a favorable outcome must be balanced against the misuse of limited resources, potential for occupational exposure to bloodborne pathogens, and the monetary cost of performing a potentially futile procedure. Appropriate patient

selection, therefore, requires thorough knowledge of the available literature and appropriate application to each unique scenario.

IS THERE A LENGTH OF PREHOSPITAL CPR TIME BEYOND WHICH THE PERFORMANCE OF EMERGENCY THORACOTOMY FOR PENETRATING TRAUMA SHOULD BE CONSIDERED FUTILE?

Several large, retrospective reviews have suggested that the most favorable outcomes following EDT occur in patients with penetrating thoracic injuries and signs of life on arrival to the hospital (7,8,14,15). Additionally, other reports have shown that EDT may benefit select patients who require prehospital cardiopulmonary resuscitation (CPR) after penetrating injuries. In a 26-year review of 959 patients who underwent EDT, Powell and colleagues (7) found that among 26 survivors requiring prehospital CPR, 21 (81%) were neurologically functional at discharge. Patients with cardiac stab wounds and pericardial tamponade were the most likely to benefit from EDT, even if they arrived in asystole. Among these five survivors, four (80%) patients requiring CPR for less than 15 minutes experienced good functional outcomes. In contrast, of those patients with a penetrating injury who required more than 15 minutes of prehospital CPR, none survived.

In another review of EDT use, Rhee et al. (8) noted an overall survival following EDT after penetrating injury of 8.8% (273 of 3,173). These investigators found that survival following these mechanisms was associated with shorter intervals between the loss of signs of life and the performance of thoracotomy. As the authors pointed out, however, uniform definitions of signs of life across the literature confounded their review.

Answer: Based on available literature, the most favorable outcomes following EDT are achieved in patients with penetrating thoracic injuries and who have required CPR for less than 15 minutes. Patients with tamponade following cardiac stab wounds appear to be the most likely to benefit in this scenario. Conclusive evidence of an association between a specific duration of prehospital CPR and optimal outcome, however, has not been identified. Recommendation grade: C.

SHOULD EDT BE PERFORMED ON BLUNT TRAUMA PATIENTS WHO LOSE VITALS IN THE PREHOSPITAL SETTING?

Favorable outcomes are relatively poor following EDT after blunt trauma. The largest retrospective reviews have documented that an average of 1.4% of these patients will survive, 2% of those presenting in shock, and less than 1% if no vital signs are present on arrival (2,4,8). Out of 38 patients injured by blunt mechanisms who required CPR after a witnessed arrest, Fialka and colleagues reported 4 EDT survivors (10.5%) following CPR for a mean of 13 minutes (16). Powell et al. (7), however, identified no survivors among those who had undergone EDT after more than 5 minutes of CPR. Of the survivors in this latter series, neurologic outcomes were universally poor.

Answer: Based on the retrospective data available, EDT after blunt trauma is associated with a very low survival and poor neurologic outcome. Although rare survivors are reported, there is no evidence to effectively guide appropriate selection for EDT after blunt injury. Limiting EDT use to patients with penetrating injuries may result in a more appreciable survival rate and more efficient use of resources. Recommendation grade: C.

IS EDT EFFECTIVE AT REDUCING MORTALITY IN PATIENTS WITH EXTRATHORACIC INJURIES?

Some authors have suggested that EDT may improve survival of select patients with extrathoracic injuries (10,17,18). Several small retrospective reports demonstrate that EDT with rapid cross-clamping of the thoracic aorta may allow temporary control of nonthoracic sources of exsanguinating arterial hemorrhage in agonal patients. In a review of 50 patients who underwent EDT for intra-abdominal hemorrhage, Seamon and colleagues (10) documented survival with good neurologic outcomes in 8 (16%) patients. All of these survivors presented with hemorrhagic shock secondary to major abdominal vascular (75%) or severe liver injuries (25%). The authors attributed the survival of these individuals to the ability of EDT to establish subdiaphragmatic arterial control and facilitate effective

internal cardiac compressions until massive transfusion and definitive hemorrhage control could be accomplished at laparotomy.

Sheppard et al. (18) have specifically examined the utility of EDT in agonal patients with nontorso injuries. Among 959 patients who underwent EDT over a 26-year period, they found that 27 (3%) of them followed penetrating nontorso injuries. All of these patients who had sustained penetrating head injuries died. Of the remaining patients with penetrating injuries to the neck or extremities, three (11%) survived to leave the hospital with good neurologic function, and one sustained a mild neurologic deficit.

Answer: The utility of emergency thoracotomy for patients with nonthoracic injuries has not been well examined. Very small retrospective reports have suggested that the use of this procedure may facilitate salvage in a very select group of agonal patients with exsanguinating vascular injuries to the abdomen, neck, or extremities. Recommendation grade: C.

DO PROTOCOLIZED APPROACHES TO THE PERFORMANCE OF EDT INFLUENCE OUTCOMES?

Based on consideration of the reported survival rates, risks, and costs associated with EDT use, some authors have proposed the adoption of institutional protocols to guide the most effective utilization of this intervention (13). The potential impact of such protocols, however, has not been well defined. Aihara and colleagues (13) described their experience before and after the implementation of an EDT protocol. Their protocol called for EDT only in the event of pericardial tamponade secondary to penetrating chest trauma on patients with obtainable vital signs and unaltered sensorium in the field or on arrival to the emergency room. Compared to the six years prior to implementation, protocol utilization resulted in an increase in survival rate from 4% to 20%. Furthermore, the total number of EDTs declined from 32.2 cases per year to 8.1 cases per year. The authors suggested that establishing an institutional protocol may improve survival and minimize potential exposure risk to staff.

Answer: There are no conclusive data that support institutional EDT protocols. One small, single-center retrospective report has suggested that a protocol confining EDT use to penetrating cardiac injuries with signs of life may improve patient survival and decrease the potential for staff exposure. Recommendation grade: C.

SHOULD THE PERICARDIUM BE OPENED IN ALL CASES OF EDT?

Large retrospective reviews have suggested that the greatest survival benefit following EDT may occur in patients sustaining penetrating cardiac injuries, particularly stab wounds. Among these patients, the rapid release of pericardial tamponade and direct control of the source of hemorrhage is paramount to survival. Small retrospective series suggest that pericardial tamponade may be present in as many as 50% of penetrating injuries and approximately 20% of patients undergoing EDT after blunt mechanisms (19). Among survivors of EDT, pericardial tamponade has been

documented in as many as 87.5% (20). Rapid pericardiotomy via EDT not only facilitates effective evacuation of these intrapericardial collections but also provides access to sources of cardiac hemorrhage and facilitates effective internal cardiac compressions.

Answer: Although limited to retrospective reports, EDT may have the greatest survival rate for those patients

with pericardial tamponade resulting from a penetrating cardiac injury. Therefore, pericardiotomy should be performed as a routine component of EDT following penetrating thoracic injury. Furthermore, this maneuver may allow direct control of cardiac hemorrhage and will facilitate optimal delivery of cardiac compressions. Recommendation grade: C.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
EDT following CPR for penetrating thoracic trauma	2000–2004	7, 8	III	C	According to retrospective reviews, EDT after more than 15 minutes of prehospital CPR is futile.
EDT following CPR for blunt trauma	2000–2004	2, 4, 7, 8	III	C	Retrospective reviews suggest that EDT survival after blunt trauma is <1%.
EDT for extra-thoracic injuries	2002–2008	10, 17, 18	IV	D	Very small series have demonstrated EDT survivors following vascular injuries to abdomen, neck, and extremities.
Institutional protocols for EDT	2001	13	IV	D	Protocols dictating EDT use for only penetrating injuries will increase EDT survival and decrease overall number of EDT performed.
Pericardiotomy during EDT	1991–2002	19, 20	III	C	Expedient relief of tamponade is a common finding among EDT survivors.

Abbreviations: CPR, cardiopulmonary resuscitation; EDT, emergency department thoracotomy.

REFERENCES

- Arreola-Risa C, Rhee P, Boyle EM, et al. Factors influencing outcome in stab wounds of the heart. *Am J Surg* 1995; 169: 553–6.
- Cothren CC, Moore EE. Emergency department thoracotomy for the critically injured patient: objectives, indications, and outcomes. *World J Emerg Surg* 2006; 1: 4.
- Hall BL, Buchman TG. A visual, timeline-based display of evidence for emergency thoracotomy. *J Trauma* 2005; 59: 773–7.
- Hunt PA, Greaves I, Owens WA. Emergency thoracotomy in thoracic trauma—a review. *Injury* 2006; 37: 1–19.
- Karmy-Jones R, Nathens A, Jurkovich GJ, et al. Urgent and emergent thoracotomy for penetrating chest trauma. *J Trauma* 2004; 56: 664–8; discussion 668–9.
- Mejia JC, Stewart RM, Cohn SM. Emergency department thoracotomy. *Semin Thorac Cardiovasc Surg* 2008; 20: 13–18.
- Powell DW, Moore EE, Cothren CC, et al. Is emergency department resuscitative thoracotomy futile care for the critically injured patient requiring prehospital cardiopulmonary resuscitation? *J Am Coll Surg* 2004; 199: 211–15.
- Rhee PM, Acosta J, Bridgeman A, et al. Survival after emergency department thoracotomy: Review of published data from the past 25 years. *J Am Coll Surg* 2000; 190: 288–98.
- Seamon MJ, Fisher CA, Gaughan J, et al. Prehospital procedures before emergency department thoracotomy: “Scoop and run” saves lives. *J Trauma* 2007; 63: 113–20.
- Seamon MJ, Fisher CA, Gaughan JP, et al. Emergency department thoracotomy: Survival of the least expected. *World J Surg* 2008; 32: 604–12.
- Soreide K, Petrone P, Asensio JA. Emergency thoracotomy in trauma: rationale, risks, and realities. *Scand J Surg* 2007; 96: 4–10.
- Soreide K, Soiland H, Lossius HM, et al. Resuscitative emergency thoracotomy in a Scandinavian trauma hospital—is it justified? *Injury* 2007; 38: 34–42.
- Aihara R, Millham FH, Blansfield J, et al. Emergency room thoracotomy for penetrating chest injury: effect of an institutional protocol. *J Trauma* 2001; 50: 1027–30.
- Baxter BT, Moore EE, Moore JB, et al. Emergency department thoracotomy following injury: critical determinants for patient salvage. *World J Surg* 1988; 12: 671–5.
- Working Group, Ad Hoc Subcommittee on Outcomes, American College of Surgeons Committee on Trauma. Practice management guidelines for emergency department thoracotomy. *J Am Coll Surg* 2001; 193: 303–9.
- Fialka C, Sebok C, Kemetzhof P, et al. Open-chest cardiopulmonary resuscitation after cardiac arrest in cases of blunt chest or abdominal trauma: a consecutive series of 38 cases. *J Trauma* 2004; 57: 809–14.
- Asensio JA, Arroyo H Jr, Veloz W, et al. Penetrating thoracoabdominal injuries: ongoing dilemma—which cavity and when? *World J Surg* 2002; 26: 539–43.
- Sheppard FR, Cothren CC, Moore EE, et al. Emergency department resuscitative thoracotomy for nontorso injuries. *Surgery* 2006; 139: 574–6.
- Grove CA, Lemmon G, Anderson G, et al. Emergency thoracotomy: appropriate use in the resuscitation of trauma patients. *Am Surg* 2002; 68: 313–16; discussion 316–17.
- Lewis G, Knottenbelt JD. Should emergency room thoracotomy be reserved for cases of cardiac tamponade? *Injury* 1991; 22: 5–6.

Trauma to the Chest Wall

Joseph J. DuBose and Lydia Lam

Clinical Questions		
Question	Answer	Grade of recommendation
What is the best imaging modality for lung injury?	Although no Level I data exists, chest x-ray remains the initial imaging modality of choice. CT has the greatest sensitivity and specificity for detection of commonly encountered injuries.	C
What is the optimal method for pain control in patients with chest wall trauma?	Thoracic epidural use should be strongly considered in patients with thoracic pain refractory to narcotic-based regimens	B
What is the optimal initial method for control of lung hemorrhage?	No significant level of evidence exists. Familiarity with various techniques is advised.	D
What is the most efficient ventilatory weaning modality after acute lung injury?	Pressure supported or T-tube spontaneous breathing trials are superior to synchronized mechanical ventilation weaning.	A
What is the optimal method of resolving persistent air leaks?	There is an absence of Level I data. The role of VATS has not yet been validated.	D
What is the optimal management of retained hemothorax?	Early VATS may decrease hospital stay and cost. Further examination of VATS and pleural fibrinolytics in the post-traumatic setting is needed.	B
Abbreviations: CT, computed tomography; VATS, video-assisted thoracoscopic surgery.		

Trauma to the chest wall and lungs is frequently associated with significant morbidity and mortality (1–5). The identification and treatment of these injuries remains a demanding task that requires both the effective use of diagnostic tools and the timely employment of therapeutic interventions. Many issues surrounding the optimization of outcomes following these injuries, however, are either not well defined or remain controversial. What are the most reliable modalities to diagnose lung trauma? What are the optimal methods to control pain and prevent respiratory compromise following these injuries? Is there an ideal maneuver for initial control of pulmonary hemorrhage? What are the optimal modalities by which to resolve persistent air leaks or wean mechanical ventilation following thoracic trauma? How should retained hemothorax be managed? These questions continue to warrant debate and investigation.

WHAT ARE THE MOST RELIABLE IMAGING MODALITIES FOR THE DIAGNOSIS OF LUNG INJURY?

The overall mortality rate attributable to chest trauma has been estimated at approximately 15%, increasing to over 70%

in the presence of shock or certain associated injuries (6). The effective treatment of thoracic injuries requires expedient diagnosis of injuries occurring due to both blunt and penetrating mechanisms, including pneumothorax, hemothorax, pulmonary contusion, lung laceration, and tracheobronchial injuries. The appropriate utilization of imaging adjuncts is paramount in this effort.

One of the most frequent sequelae of thoracic injury is pneumothorax; estimated to occur in 20% of trauma patients (7). In most instances, pneumothorax can safely and effectively be managed through conservative management or chest tube placement, and it typically resolves over a short time period. The optimal management of occult pneumothoraces detected following trauma, however, remains a matter of debate. The incidence of occult pneumothorax, or a small pneumothorax noted on computed tomography (CT) but not initial chest x-ray, has been reported as 2–8% following blunt trauma (8–10). Although most of these can safely be managed conservatively, the ideal management for patients requiring positive pressure ventilation has been argued. Two small, prospective randomized trials examining this very question reported conflicting results regarding the role of tube thoracostomy in these situations. At

present, there are not enough conclusive data to determine the optimal approach in this situation, although most occult pneumothoraces likely do not warrant the potential risk associated with a tube thoracostomy.

Pulmonary contusion and pulmonary laceration are also common concerns following thoracic injury (6). Reported mortality rates associated with these pathologies range from 13% to 40%, but greater risk appears to be associated with advanced age, higher injury severity score (ISS), advanced transfusion requirements, and more severe contusion patterns (11–13). In the absence of data comparing CT to other imaging alternatives, this modality remains the standard of care for the identification and classification of pulmonary contusion and pulmonary laceration.

Tracheobronchial injury (TBI) is a rare entity following thoracic trauma, but the presence of these injuries after blunt mechanisms suggests that significant mechanical forces were involved in injury. The effective identification and classification of these injuries is important, as several retrospective studies have concluded that surgical repair is usually necessary for best outcome (14,15). The most useful imaging modality in these cases has, however, not been well defined. In one small retrospective study, Cassada et al. (16) identified 20 patients with TBI and found that no patient with intrathoracic TBI had a normal chest x-ray. All of the patients with TBI in this study presented with pneumothorax and/or pneumomediastinum on initial plain radiography. The investigators found that independent of mechanism or anatomic location of injury, delay in diagnosis was significantly associated with adverse outcome. Although the specificity of chest x-ray in the conclusive diagnosis of TBI is probably low, suspicion based on mechanism should warrant expedient attempts at identifying or excluding TBI following thoracic injury. The optimal route to diagnosis, either via endoscopy, CT, or other advanced imaging, has not been subjected to well-constructed investigations.

Regardless of the pulmonary pathology following trauma, the use of chest x-ray, as outlined in the Advanced Trauma Life Support guidelines, remains the standard of care for initial imaging evaluation. Despite potential sensitivity and specificity limitations, this approach is rapid and does not require the delay or transportation associated with obtaining CT or other advanced imaging. The use of ultrasound is also gaining significant attention, but it requires appropriately trained personnel for exams and interpretation (17). For most pulmonary pathologies, therefore, CT remains the gold standard for the diagnosis of intrathoracic injury after trauma. In 2001, Omert and colleagues (18) prospectively evaluated the use of CT for patients with and without clinical or chest x-ray findings after trauma due to severe mechanisms. These investigators found that CT identified a significant number of injuries not identified by both physical exam and chest x-ray. Even among the group with a positive chest x-ray, 20% of patients underwent a change in management based on the improved classification of injury using CT. In those patients with normal chest x-ray, 5% underwent a subsequent change in management based on CT findings. Several additional small studies have supported the use of CT for more conclusive diagnosis of thoracic injury, noting that approximately 50% of patient with normal chest x-ray will have additional finding on CT, and 20% of these patients will need a subsequent alteration in management

based on these findings (10,18–22). At present, however, no Level I examinations specifically validating the superiority of CT in the diagnosis of lung injury have been conducted.

The role of ultrasound in thoracic imaging following trauma has recently received increasing attention. In a prospective examination, Rozycki and colleagues have previously demonstrated the utility of this modality in identifying the need for precordial intervention following injury (23). Three prospective studies specifically examining the sensitivity and specificity of ultrasound in the diagnosis of the occult pneumothorax have also been reported. In 2002, Rowan et al. (24) prospectively compared chest x-ray to ultrasound and found sensitivity and specificity of ultrasound comparable to CT scan in the identification of occult pneumothorax. In another prospective examination conducted by Zhang and colleagues (25), the investigators found that emergency room clinicians could perform the ultrasound to identify and characterize pneumothorax with a sensitivity and specificity comparable to that of trained radiologists. A subsequent study, reported in 2008 by Soldati et al. (17), concluded that ultrasound is capable of accurately detecting the presence and progression of occult pneumothorax with an accuracy on par with CT scan. With its portability, reproducibility, and rapidity, ultrasound represents a promising tool for the detection of pneumothorax. This modality is, however, operator-dependent and requires appropriate training for consistent use.

Magnetic resonance imaging (MRI) has also been used selectively following thoracic injury, primarily for the diagnosis of diaphragm, myocardial, or pericardial injuries and persistent pain due to sternal fractures (26–30). Even for these indications, however, only data from case reports and small case series are available.

Answer: At present, there are no large Level I studies examining the role of imaging following thoracic trauma. The majority of existing literature supports the use of CT as the most sensitive and specific subsequent imaging modality, over a range of commonly encountered pathologies. Emerging evidence supporting the use of ultrasound for pulmonary pathology appears promising, but the widespread use of ultrasound as an alternative to chest x-ray or CT has not been well validated. Grade of recommendation: C.

WHAT ARE THE OPTIMAL METHODS, INCLUDING MEDICATIONS, FOR PAIN CONTROL AND PREVENTION OF IMPENDING RESPIRATORY COMPROMISE IN PATIENTS WITH CHEST WALL TRAUMA?

The effective treatment of chest wall trauma requires the restoration of effective thoracic excursion and pulmonary mechanics. The significant discomfort that is commonly associated with these injuries, however, remains one of the greatest impediments to achieving this goal. Older methods used to decrease pain and subsequently improve voluntary respiratory effort included the use of restrictive dressings and splints to stabilize the chest wall. These adjuncts, however, were noted to further impede effective chest wall motion and normal pulmonary physiology. Subsequently, investigators in the modern era have focused their emphasis on the important role of pain as an

impediment to normal thoracic function. Several pain control modalities have demonstrated promise in assisting in this effort.

Traditionally, effective narcotic utilization proved the standard of care in ameliorating the pain associated with chest wall injury. Even in the modern era, effective morphine use remains the cornerstone of initial treatment, and it is the standard to which newer approaches are most commonly compared. The use of morphine, however, raises several concerns in this setting, including ileus, urinary retention, and the hemodynamic instability and respiratory suppression associated with excessive use. Additionally, although advances in patient-controlled analgesic (PCA) delivery systems may have improved the safety of use, the optimal delivery route of morphine remains a matter of investigation. In a recent, prospective, randomized trial conducted by Fulda and colleagues (31), the investigators examined the use of nebulized morphine for the management of acute thoracic pain. They found that in this setting, nebulized morphine could be safely and effectively used to control post-traumatic thoracic pain with less sedative effects than PCA and without compromising pulmonary function.

Regardless of the delivery system, the concerns regarding morphine use have incited discussion regarding other pharmacologic adjuncts to decrease the requirements for opioids. In an examination of nonsteroidal anti-inflammatory drug (NSAID) analgesia following cardiothoracic surgery, Bainbridge et al. (32) reviewed the results of 20 randomized trials investigating the role of this morphine adjunct following operation. In their analysis they noted that in patients less than 70 years old undergoing cardiothoracic surgery, the adjunctive use of NSAIDs with narcotic analgesia reduced 24-hour pain scores and narcotic requirements. Although similar data in the trauma setting are wanting, these findings suggest that the use of NSAIDs may warrant further investigation.

The use of the epidural pain control following thoracic surgery and chest wall injury has emerged as a promising development in this field. In several well-designed studies in cardiothoracic surgery and trauma, epidural use has been associated with better analgesia (33,34) and post-operative pulmonary function (35–37) compared to narcotic use alone. In the largest meta-analysis of randomized control trials examining the effects of preemptive epidural analgesia on post-thoracotomy pain, Bong and colleagues (34) found that preemptive use of a thoracic epidural significantly reduced the severity of acute pain following surgery. Several investigators have reported similar findings for patients with thoracic pain due to trauma. In a prospective, randomized comparison of epidural versus parenteral opioid analgesia following thoracic trauma, Moon et al. (38) found that epidural use was associated with a significant improvement in both pain control and tests of voluntary pulmonary function. A subsequent prospective, randomized trial conducted by Bulger and colleagues (39) found that epidural use for patients with multiple rib fractures resulted in significantly fewer ventilator days and pneumonia. Although these investigations have demonstrated the utility of epidural pain control, the enthusiasm for this modality must be balanced against the potential complications of epidural placement, including infection and epidural hematoma.

The use of controlled-release local anesthetics has also been proposed for use following thoracic injury. The use of these approaches has the potential to decrease both the risk for potential adverse effects associated with opioid use and the procedural risks of epidural placement. The use of these systems to deliver both intrapleural and extrapleural local anesthetics after elective thoracic surgery has been previously examined (40–47). Unfortunately, however, the utility of these devices following trauma has not been validated, although small experiences have been reported (48–50). In one small, prospective randomized trial conducted by Short and colleagues (51), the use of intrapleural analgesia did not result in decreased narcotic requirements or improved pulmonary function over a narcotic-based pain control regimen.

External bandaging and splinting for chest wall stabilization has been abandoned, and several recent investigators have examined operative alternatives for chest wall stabilization. (52–59). To date, however, only one small prospective, randomized trial has examined the use of operative fixation. In this study, Tanaka et al. (60) found that the use of operative fixation for patients with severe flail chest decreased ventilatory support requirements, intensive care unit (ICU) length of stay, medical costs, and the rate of pneumonia. The optimal timing and type of procedure that should be utilized in this setting, however, has not been well defined. This topic warrants further investigation and validation.

Answer: Thoracic epidural use should be strongly considered for victims of thoracic wall trauma who do not achieve adequate pain control using narcotic-based regimens. The use of operative fixation for patients with severe flail chest warrants further investigation. Grade of recommendation: B.

WHAT IS THE OPTIMAL INITIAL METHOD FOR CONTROL OF PULMONARY PARENCHYMAL HEMORRHAGE WHICH ALLOWS FOR REPAIR AND/OR DEFINITIVE CONTROL OF BLEEDING?

In the majority of thoracic trauma with pulmonary hemorrhage, the low-pressure system within the pulmonary parenchyma will facilitate coagulation and subsequent cessation of bleeding. When surgical bleeding is encountered, however, the rapid control of the bleeding source can prove challenging. Several initial maneuvers to achieve temporary control have been proposed, including cross-clamping or twisting the lung hilum (61). The use of these maneuvers may not be tolerated well by critically injured patients, but as a matter of last resort they are important to know. The use of packing and other principles of damage control principles in extreme cases has also been proposed (62–64). It is unlikely, given the expediency with which the maneuvers must be employed, that prospective randomized studies will ever examine their use.

If hemorrhage can initially be controlled with compression, weighing the subsequent surgical options should not be considered lightly. As has been demonstrated by several investigators (2,65,66), the degree of subsequent resection required directly correlates strongly with outcome following pulmonary injury. The use of a lung-sparing

tractotomy, described by several authors for use in penetrating trauma (67–73), represents an abbreviated technique that may facilitate rapid but selective ligation of bleeding sources. Despite the absence of randomized data, the use of this approach should be considered in appropriate situations.

Answer: Surgical hemorrhage of the pulmonary parenchyma can represent a significant challenge. Although no prospective, randomized data to guide decision making is available, surgeons should be familiar with a variety of hemorrhage control techniques and the situations in which they are likely to be of use. Grade of recommendation: D.

WHAT ARE THE MOST EFFICIENT VENTILATORY WEANING MODALITIES IN PATIENTS WITH ACUTE LUNG INJURY?

Liberation from mechanical ventilation requires both the appropriate identification of candidates for weaning and the safe withdrawal of support. Although a variety of weaning predictors have been for use to identify patients ready for extubation, none has proven consistently powerful. One of the most frequently studied has been the rapid shallow breathing index, although the pooled likelihood ratio for a positive test ranges widely in large reviews (74), and the use of this modality remains controversial (75). Until more definitive data are learned, the identification of patients for weaning will continue to rely on clinician judgment and experience.

Irrespective of the ventilation approach used to facilitate weaning, concomitant sedation weaning appears to be an important adjunct (76,77). A recent randomized, controlled trial of a paired sedation and ventilator weaning protocol conducted by Girard and colleagues (76) found that the use of such a protocol resulted in earlier extubation compared to controls, as well as shorter ICU and hospital length of stay. The use of a daily sedation holiday and a protocol for sedation weaning may therefore prove a critical component of any attempt at liberation from mechanical ventilation.

The optimal design and implementation of ventilation approaches to facilitate weaning have been examined by several investigators. Several well-designed prospective studies have suggested that a protocolized approach to weaning, even using computer-based decision tools (78), appears to be beneficial in reducing ventilation requirements and improving outcomes (78–80). The specific weaning modality that should be used in the protocols, however, continues to be investigated.

Based on a growing body of literature, the use of synchronized intermittent mandatory ventilation as a weaning modality has largely been replaced by the use of spontaneous breathing trials (SBTs). Several randomized controlled trials have demonstrated that the duration of mechanical ventilation is significantly reduced in patients undergoing daily assessment with a SBTs (81–85). The precise manner in which an SBT should be performed, however, remains a matter of debate. Specifically, the use of pressure support versus T-tube has been examined in prospective, randomized trials (74,86–88). In one of these examinations, Estaban and colleagues of the Spanish Lung

Failure Collaborative Group (86) found no difference between a group of patients utilizing T-tube or pressure-supported SBT. In a subsequent study by Matic et al. (88), researchers found that pressure support for patients with weaning difficulties resulted in a higher rate of successful weaning than T-tube. In another randomized study by Ezingard and colleagues (89), the investigators found that for patients failing T-tube trial, pressure supported SBT salvaged 18% of weaning failures.

Although a number of randomized trials examining the use of SBT exist, pooling and analysis of these trials are made difficult by the significant variation of definitions and protocols utilized (84). Whereas SBT is emerging as a standard of care, the use of T-tube or pressure supported SBT trials warrants further investigation. Several other questions regarding SBT use also remain, including the number of daily trials and the duration of trials that should be used (74,79).

Finally, the use of noninvasive positive pressure ventilation (NPPV) as a weaning strategy has also been examined (90). This modality has been effectively used for a select group of chronic obstructive pulmonary disease patients to avoid potential intubation. There may be substantial benefits to early extubation with back-up institutional of NPPV, although this remains an experimental approach (91). At present, NPPV has not been shown to effect weaning failure rates or the duration of mechanical ventilation support related to weaning (90).

Answer: Protocolized approaches to liberation from mechanical ventilation, including concomitant sedation weaning, appear superior in discontinuation of prolonged requirements. Daily pressure supported or T-tube SBTs have been shown to be superior to synchronized intermittent mandatory ventilation weaning. Grade of recommendation: A.

WHAT ARE THE OPTIMAL METHODS OF RESOLVING PERSISTENT AIR LEAKS INCLUDING BRONCHOPLEURAL FISTULAS AFTER PULMONARY TRAUMA?

Persistent air leaks are uncommon but concerning sequelae of traumatic injury. They may occur for several reasons, including extensive parenchymal damage, bronchial injuries, retained hemothorax, ongoing mechanical ventilation, or empyema. Typically, leaks resolve with thoracostomy tube management, although lengthy periods of conservative management may be required. Several investigators have examined the role of video-assisted thoracoscopic surgery (VATS) techniques in repairing the inciting injury and decreasing the subsequent time to resolution of leak. In one such study, conducted by Carrillo et al. (92), 11 stable patients were taken for VATS after failure of resolution of the pneumothorax with chest tube treatment after 72 hours. After double lumen tube endotracheal intubation, the parenchymal sites of leak were directly identified by releasing the occluded side of the tube. These sites were, subsequently, resected using an endostapler and a 28 French chest tube placed. Postoperatively, patients stayed an average of 10 days prior to their VATS procedure and 3 days after, significantly decreasing costs according to the investigators' hypothesis. Their lungs were also found to be

completely reexpanded with resolution of their air leak by postoperative day 1. Schermer et al. (93) have also reported decreased requirement for prolonged thoracostomy tube use and decreased hospital stay using a similar approach. In this study, the investigators selected those patients that were otherwise ready for discharge except for the presence of a persistent air leak. They also offered VATS only to patients with the presence of a persistent air leak beyond three days. The investigators found that the subsequent mean chest tube days required was 8 for those electing to undergo VATS, compared to 11 for those not undergoing operation. Various other VATS techniques of closure of leaks have been reported, including the recently described use of surgical sealant in 13 patients by Carrillo et al. (94). Using this technique, these investigators were able to achieve complete resolution of all air leaks within 72 hours of procedure.

Bronchopleural fistula, a rare sequela of trauma, remains one of the most problematic sources of persistent air leak. The majority of these patients require repair by an open thoracotomy. The majority of literature regarding bronchopleural fistula management has originated from examinations of patients with this complication due to thoracic malignancy. In this population, several approaches at less invasive techniques have been described in case reports or small case series, including stenting, single lung ventilation, bronchial blockers, the use of biological agents to block the affected bronchus by bronchoscopy, collagen screws, and one-way valves (95–102). Other less invasive approaches to fistula due to trauma have been described in case reports describing the use of independent lung ventilation (103,104), fibrin glue deployment via bronchoscopy (105), or fibrin glue pleurodesis (106). At present, however, the standard for definitive treatment of persistent bronchopleural fistula remains operative repair via thoracotomy. Repairing of bronchopleural fistula follows general surgery principles in primary repair with little tension and buttressing the repair with a vascularized pedicle, such as pericardial, pleural, or omental flaps (107). Due to the fortunate rarity of this complication, no large studies examining optimal techniques or management have been reported.

Answer: The majority of persistent leaks following trauma resolve with conservative management using tube thoracostomy. Although a number of approaches designed to decrease the time to closure have been described, particularly VATS-based techniques, none of these have been validated in well-designed trials. The standard of management for bronchopleural fistula, a very rare complication of trauma, remains operative repair via thoracotomy. Grade of recommendation: D.

WHAT IS THE OPTIMAL MANAGEMENT OF RETAINED HEMOTHORAX?

The diagnosis and optimal management of retained post-traumatic hemothorax remains a problematic issue. It is generally accepted that persistent blood within the thoracic cavity represents a concerning finding, primarily due to concern for the subsequent development of fibrothorax (“trapped lung”) and empyema. Although a link between uncomplicated retained hemothorax and trapped lung has

been less well established, (108) the presence of retained blood within the chest has more clearly been identified as a risk factor for the development of empyema (109–112). Although empyema remains an infrequent complication of thoracic trauma (110–112), diagnosis and management of this infectious process remains controversial (113–116), and the occurrence of empyema may be associated with significant morbidity and mortality (117). For this reason, the establishment of the ideal modality for the effective evacuation of retained hemothorax has remained an area of active investigation.

The identification of individuals at greatest risk for subsequent complications due to retained hemothorax is, however, problematic. Although liquefied hemothorax can frequently be drained effectively with the placement of an initial or secondary thoracostomy tube, clotted and loculated collections may be more likely to require more aggressive management for evacuation. The natural history of retained hemothoraces, particularly smaller collections, has also not been well defined (118,119). Although largely dependent on the screening modality, even the incidence of this entity has not been well defined, although small studies have reported rates as high as 10% (120). Additionally, although computed tomography appears a more sensitive and specific modality by which to characterize and quantify retained hemothorax (121), the effective use of radiographic assessment to stratify risk and guide therapeutic decisions has remained elusive (114, 118, 119).

Despite these controversies, several evacuation strategies for retained hemothorax have been effectively used, including open thoracotomy, thoracostomy, VATS, and the use of intrapleural fibrinolytics. Thoracotomy remains the gold standard to which newer approaches are compared, but this surgical approach can be associated with significant morbidity. Less invasive modalities are more commonly employed in the modern era. VATS has emerged as an increasingly utilized modality in recent years, although the use of intrapleural fibrinolytics has garnered some interest.

Increasing experience with thoracoscopy has increased the enthusiasm for the use of this modality to evacuate retained hemothoraces (122–132). Although early VATS appears to be beneficial, the definition of “early” has varied among available retrospective series, and there is a paucity of prospective studies available in the literature (122,123,127,129–132). In one prospective, randomized report of VATS use within 72 hours of initial thoracostomy tube placement, however, Meyer et al. (122) found that VATS at this interval was associated with shorter hospital stays and lower hospital costs compared to individuals randomized to additional thoracostomy tube placement.

The use of intrapleural fibrinolytics for the degradation and subsequent drainage of retained hemothorax has also been investigated. The safe utilization of this approach for the treatment of organized hemothorax and infectious collections of the pleural space has already been reported by several groups (114,120,133–150). In a review of studies from the Cochrane Database of Systematic Reviews reported in 2008, Cameron and Davies (114) identified seven randomized control trials examining the use of fibrinolytics for empyema and parapneumonic effusions. These investigators found that fibrinolytics used in these settings safely resulted in a significant decrease in the risk of

requiring subsequent surgical drainage. Although these findings appear to demonstrate the utility of intrapleural fibrinolytic use, none of these studies included post-traumatic retained hemothorax in their examinations.

At present, no Level I evidence exists supporting the use of fibrinolytics for the treatment of post-traumatic retained hemothorax. In one small, prospective observational study reported by Kimbrell and colleagues, however, the use of fibrinolytics resulted in successful resolution of residual hemothorax in 92% of patients (144). Another limited retrospective examination conducted by Oguzkaya et al. (120) compared the use of VATS to intrapleural streptokinase for management of post-traumatic retained hemothorax, finding that the use of VATS resulted in shorter hospital stays and a decreased need for subsequent

thoracotomy. Given the documented success of these adjuncts in the treatment of pleural space infections, the utility of fibrinolytics for the treatment of retained hemothorax warrants further examination.

Answer: Reflective of the complexities in diagnosis and risk stratification for patients with the finding of retained hemothorax, no single therapeutic approach has emerged as a superior modality. At present, VATS appears to hold the most promise, having been shown to decrease hospital stay and cost in one small, randomized trial comparing the use of this approach to additional tube thoracostomy placement. To date, however, no prospective examination of less invasive techniques has shown any treatment modality to prove superior in decreasing the need for subsequent thoracotomy. Grade of recommendation: B.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Imaging modalities for lung trauma	2001–2008	17, 18–22	IIIb	C	In the absence of Level I evidence, initial screening chest x-ray remains standard of care. CT has the highest demonstrated overall sensitivity and specificity among available series.
Pain control in chest wall trauma	1999, 2004	38, 39	Ib	B	Thoracic epidural use should be strongly considered in patients with thoracic pain refractory to narcotic-based regimens.
Retained hemothorax management	1997	122	Ib	B	Early VATS may decrease hospital stay and cost.

Abbreviations: CT, computed tomography; VATS, video-assisted thoracoscopic surgery.

REFERENCES

- Flagel BT, Luchette FA, Reed RL, et al. Half-a-dozen ribs: the breakpoint for mortality. *Surgery* 2005; 138: 717–23; discussion 723–5.
- Karmy-Jones R, Jurkovich GJ, Shatz DV, et al. Management of traumatic lung injury: a western trauma association multicenter review. *J Trauma* 2001; 51: 1049–53.
- Pettiford BL, Luketich JD, Landreneau RJ. The management of flail chest. *Thorac Surg Clin* 2007; 17: 25–33.
- Testerman GM. Adverse outcomes in younger rib fracture patients. *South Med J* 2006; 99: 335–9.
- Zargar M, Khaji A, Karbakhsh Davari M. Thoracic injury: a review of 276 cases. *Chin J Traumatol* 2007; 10: 259–62.
- Gavelli G, Canini R, Bertaccini P, et al. Traumatic injuries: Imaging of thoracic injuries. *Eur Radiol* 2002; 12: 1273–94.
- Di Bartolomeo S, Sanson G, Nardi G, et al. A population-based study on pneumothorax in severely traumatized patients. *J Trauma* 2001; 51: 677–82.
- Anderson BL, Abdalla R, Frame SB, et al. Tube thoracostomy for occult pneumothorax: a prospective randomized study of its use. *J Trauma* 1993; 35: 726–9; discussion 729–30.
- Brasel KJ, Stafford RE, Weigelt JA, et al. Treatment of occult pneumothoraces from blunt trauma. *J Trauma* 1999; 46: 987–90; discussion 990–1.
- Plurad D, Green D, Demetriades D, et al. The increasing use of chest computed tomography for trauma: is it being overutilized? *J Trauma* 2007; 62: 631–5.
- Balci AE, Balci TA, Eren S, et al. Unilateral post-traumatic pulmonary contusion: findings of a review. *Surg Today* 2005; 35: 205–10.
- Tyburski JG, Collinge JD, Wilson RF, et al. Pulmonary contusions: quantifying the lesions on chest x-ray films and the factors affecting prognosis. *J Trauma* 1999; 46: 833–8.
- Cohn SM. Pulmonary contusion: review of the clinical entity. *J Trauma* 1997; 42: 973–9.
- Kiser AC, O'Brien SM, Detterbeck FC. Blunt tracheobronchial injuries: treatment and outcomes. *Ann Thorac Surg* 2001; 71: 2059–65.
- Rossbach MM, Johnson SB, Gomez MA, et al. Management of major tracheobronchial injuries: a 28-year experience. *Ann Thorac Surg* 1998; 65: 182–6.
- Cassada DC, Munyikwa MP, Moniz MP, et al. Acute injuries of the trachea and major bronchi: importance of early diagnosis. *Ann Thorac Surg* 2000; 69: 1563–7.
- Soldati G, Testa A, Sher S, et al. Occult traumatic pneumothorax: diagnostic accuracy of lung ultrasonography in the emergency department. *Chest* 2008; 133: 204–11.
- Omert LA, Salyer D, Dunham CM, et al. Implications of the “contrast blush” finding on computed tomographic scan of the spleen in trauma. *J Trauma* 2001; 51: 272–7; discussion 277–8.
- Exadaktylos AK, Sclabas G, Schmid SW, et al. Do we really need routine computed tomographic scanning in the primary evaluation of blunt chest trauma in patients with “normal” chest radiograph? *J Trauma* 2001; 51: 1173–6.

20. Renton J, Kincaid S, Ehrlich PF. Should helical CT scanning of the thoracic cavity replace the conventional chest x-ray as a primary assessment tool in pediatric trauma? An efficacy and cost analysis. *J Pediatr Surg* 2003; 38: 793–7.
21. Traub M, Stevenson M, McEvoy S, et al. The use of chest computed tomography versus chest x-ray in patients with major blunt trauma. *Injury* 2007; 38: 43–7.
22. Salim A, Sangthong B, Martin M, et al. Whole body imaging in blunt multisystem trauma patients without obvious signs of injury: results of a prospective study. *Arch Surg* 2006; 141: 468–73; discussion 473–5.
23. Rozycki GS, Ballard RB, Feliciano DV, et al. Surgeon-performed ultrasound for the assessment of truncal injuries: lessons learned from 1540 patients. *Ann Surg* 1998; 228: 557–67.
24. Rowan KR, Kirkpatrick AW, Liu D, et al. Traumatic pneumothorax detection with thoracic US: correlation with chest radiography and CT—initial experience. *Radiology* 2002; 225: 210–14.
25. Zhang M, Liu ZH, Yang JX, et al. Rapid detection of pneumothorax by ultrasonography in patients with multiple trauma. *Crit Care* 2006; 10: R112.
26. Barbiera F, Nicastro N, Finazzo M, et al. The role of MRI in traumatic rupture of the diaphragm. Our experience in three cases and review of the literature. *Radiol Med (Torino)* 2003; 105: 188–94.
27. Tepe SM, Glockner JF, Julsrud P. MRI demonstration of acute myocardial infarction due to posttraumatic coronary artery dissection. *Int J Cardiovasc Imaging* 2006; 22: 97–100.
28. Descat E, Montaudon M, Latrabe V, et al. MRI imaging of myocardial haematoma after blunt chest injury. *Eur Radiol* 2002; 12 Suppl 3: S174–S176.
29. Sohn JH, Song JW, Seo JB, et al. Case report: pericardial rupture and cardiac herniation after blunt trauma: a case diagnosed using cardiac MRI. *Br J Radiol* 2005; 78: 447–9.
30. Grosse A, Grosse C, Steinbach L, et al. MRI findings of prolonged post-traumatic sternal pain. *Skeletal Radiol* 2007; 36: 423–9.
31. Fulda GJ, Giberson F, Fagraeus L. A prospective randomized trial of nebulized morphine compared with patient-controlled analgesia morphine in the management of acute thoracic pain. *J Trauma* 2005; 59: 383–8; discussion 389–90.
32. Bainbridge D, Martin JE, Cheng DC. Patient-controlled versus nurse-controlled analgesia after cardiac surgery—a meta-analysis. *Can J Anaesth* 2006; 53: 492–9.
33. Behera BK, Puri GD, Ghai B. Patient-controlled epidural analgesia with fentanyl and bupivacaine provides better analgesia than intravenous morphine patient-controlled analgesia for early thoracotomy pain. *J Postgrad Med* 2008; 54: 86–90.
34. Bong CL, Samuel M, Ng JM, Ip-Yam C. Effects of preemptive epidural analgesia on post-thoracotomy pain. *J Cardiothorac Vasc Anesth* 2005; 19: 786–93.
35. Bauer C, Hentz JG, Ducrocq X, et al. Lung function after lobectomy: a randomized, double-blinded trial comparing thoracic epidural ropivacaine/sufentanil and intravenous morphine for patient-controlled analgesia. *Anesth Analg* 2007; 105: 238–44.
36. Gruber EM, Tschernko EM, Kritzing M, et al. The effects of thoracic epidural analgesia with bupivacaine 0.25% on ventilatory mechanics in patients with severe chronic obstructive pulmonary disease. *Anesth Analg* 2001; 92: 1015–19.
37. Wisner DH. A stepwise logistic regression analysis of factors affecting morbidity and mortality after thoracic trauma: effect of epidural analgesia. *J Trauma* 1990; 30: 799–804; discussion 804–5.
38. Moon MR, Luchette FA, Gibson SW, et al. Prospective, randomized comparison of epidural versus parenteral opioid analgesia in thoracic trauma. *Ann Surg* 1999; 229: 684–91; discussion 691–2.
39. Bulger EM, Edwards T, Klotz P, et al. Epidural analgesia improves outcome after multiple rib fractures. *Surgery* 2004; 136: 426–30.
40. Chan VW, Chung F, Cheng DC, et al. Analgesic and pulmonary effects of continuous intercostal nerve block following thoracotomy. *Can J Anaesth* 1991; 38: 733–9.
41. Barron DJ, Tolan MJ, Lea RE. A randomized controlled trial of continuous extra-pleural analgesia post-thoracotomy: efficacy and choice of local anaesthetic. *Eur J Anaesthesiol* 1999; 16: 236–45.
42. Liu M, Rock P, Grass JA, et al. Double-blind randomized evaluation of intercostal nerve blocks as an adjuvant to subarachnoid administered morphine for post-thoracotomy analgesia. *Reg Anesth* 1995; 20: 418–25.
43. Eng J, Sabanathan S. Continuous paravertebral block for postthoracotomy analgesia in children. *J Pediatr Surg* 1992; 27: 556–7.
44. Drager C, Benziger D, Gao F, et al. Prolonged intercostal nerve blockade in sheep using controlled-release of bupivacaine and dexamethasone from polymer microspheres. *Anesthesiology* 1998; 89: 969–79.
45. Exadaktylos AK, Trampitsch E, Mares P, et al. Pre-operative intercostal nerve blockade for minimally invasive coronary bypass surgery: a standardised anaesthetic regimen for rapid emergence and early extubation. *Cardiovasc J S Afr* 2004; 15: 178–81.
46. Kristek J, Kvolik S, Sakic K, et al. Intercostal catheter analgesia is more efficient vs. intercostal nerve blockade for post-thoracotomy pain relief. *Coll Antropol* 2007; 31: 561–6.
47. Detterbeck FC. Efficacy of methods of intercostal nerve blockade for pain relief after thoracotomy. *Ann Thorac Surg* 2005; 80: 1550–9.
48. Luchette FA, Radafshar SM, Kaiser R, et al. Prospective evaluation of epidural versus intrapleural catheters for analgesia in chest wall trauma. *J Trauma* 1994; 36: 865–9; discussion 869–70.
49. Appelboam A, McLauchlan CA, Murdoch J, et al. Delivery of local anaesthetic via a sternal catheter to reduce the pain caused by sternal fractures: first case series using the new technique. *Emerg Med J* 2006; 23: 791–3.
50. Duncan MA, McNicholas W, O'Keeffe D, et al. Periosteal infusion of bupivacaine/morphine post sternal fracture: a new analgesic technique. *Reg Anesth Pain Med* 2002; 27: 316–18.
51. Short K, Scheeres D, Mlakar J, et al. Evaluation of intrapleural analgesia in the management of blunt traumatic chest wall pain: a clinical trial. *Am Surg* 1996; 62: 488–93.
52. Richardson JD, Franklin GA, Heffley S, et al. Operative fixation of chest wall fractures: an underused procedure? *Am Surg* 2007; 73: 591–6; discussion 596–7.
53. Engel C, Krieg JC, Madey SM, et al. Operative chest wall fixation with osteosynthesis plates. *J Trauma* 2005; 58: 181–6.
54. Mayberry JC, Terhes JT, Ellis TJ, et al. Absorbable plates for rib fracture repair: preliminary experience. *J Trauma* 2003; 55: 835–9.
55. Mouton W, Lardinois D, Furrer M, et al. Long-term follow-up of patients with operative stabilisation of a flail chest. *Thorac Cardiovasc Surg* 1997; 45: 242–4.
56. Ahmed Z, Mohyuddin Z. Management of flail chest injury: internal fixation versus endotracheal intubation and ventilation. *J Thorac Cardiovasc Surg* 1995; 110: 1676–80.
57. Balci AE, Eren S, Cakir O, et al. Open fixation in flail chest: review of 64 patients. *Asian Cardiovasc Thorac Ann* 2004; 12: 11–1215.
58. Lardinois D, Krueger T, Dusmet M, et al. Pulmonary function testing after operative stabilisation of the chest wall for flail chest. *Eur J Cardiothorac Surg* 2001; 20: 496–501.

59. Voggenreiter G, Neudeck F, Aufmkolk M, et al. Operative chest wall stabilization in flail chest—outcomes of patients with or without pulmonary contusion. *J Am Coll Surg* 1998; 187: 130–8.
60. Tanaka H, Yukioka T, Yamaguti Y, et al. Surgical stabilization of internal pneumatic stabilization? A prospective randomized study of management of severe flail chest patients. *J Trauma* 2002; 52: 727–32; discussion 732.
61. Wilson A, Wall MJ Jr, Maxson R, et al. The pulmonary hilum twist as a thoracic damage control procedure. *Am J Surg* 2003; 186: 49–52.
62. Caceres M, Buechter KJ, Tillou A, et al. Thoracic packing for uncontrolled bleeding in penetrating thoracic injuries. *South Med J* 2004; 97: 637–41.
63. Phelan HA, Patterson SG, Hassan MO, et al. Thoracic damage-control operation: principles, techniques, and definitive repair. *J Am Coll Surg* 2006; 203: 933–41.
64. Xian-kai H, Yu-jun Z, Lian-yang Z. Damage control surgery for severe thoracic and abdominal injuries. *Chin J Traumatol* 2007; 10: 279–83.
65. Martin MJ, McDonald JM, Mullenix PS, et al. Operative management and outcomes of traumatic lung resection. *J Am Coll Surg* 2006; 203: 336–44.
66. Huh J, Wall MJ Jr, Estrera AL, et al. Surgical management of traumatic pulmonary injury. *Am J Surg* 2003; 186: 620–4.
67. Kamiyoshihara M, Ibe T, Takeyoshi I. A middle lobe tractotomy of the lung for a stab injury: report of a survival case. *Gen Thorac Cardiovasc Surg* 2007; 55: 193–6.
68. Muraoka M, Akamine S, Tagawa T, et al. Pulmonary tractotomy for a patient with traumatic penetrating lung injury: report of a case. *Surg Today* 2005; 35: 972–5.
69. Cothren C, Moore EE, Biffl WL, et al. Lung-sparing techniques are associated with improved outcome compared with anatomic resection for severe lung injuries. *J Trauma* 2002; 53: 483–7.
70. Gasparri M, Karmy-Jones R, Kralovich KA, et al. Pulmonary tractotomy versus lung resection: viable options in penetrating lung injury. *J Trauma* 2001; 51: 1092–5; discussion 1096–7.
71. Velmahos GC, Baker C, Demetriades D, et al. Lung-sparing surgery after penetrating trauma using tractotomy, partial lobectomy, and pneumonorrhaphy. *Arch Surg* 1999; 134: 186–9.
72. Wall MJ Jr, Hirshberg A, Mattox KL. Pulmonary tractotomy with selective vascular ligation for penetrating injuries to the lung. *Am J Surg* 1994; 168: 665–9.
73. Wall MJ Jr, Villavicencio RT, Miller CC III, et al. Pulmonary tractotomy as an abbreviated thoracotomy technique. *J Trauma* 1998; 45: 1015–23.
74. Agency for Healthcare Research and Quality, ed. Criteria for Weaning from Mechanical Ventilation. ARHQ publication 00-E028. Agency for Healthcare Research and Quality, 2000.
75. Tanios MA, Nevins ML, Hendra KP, et al. A randomized, controlled trial of the role of weaning predictors in clinical decision making. *Crit Care Med* 2006; 34: 2530–5.
76. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. *Lancet* 2008; 371: 126–34.
77. Arroliga AC, Thompson BT, Ancukiewicz M, et al. Use of sedatives, opioids, and neuromuscular blocking agents in patients with acute lung injury and acute respiratory distress syndrome. *Crit Care Med* 2008; 36: 1083–8.
78. Lellouche F, Mancebo J, Joliet P, et al. A multicenter randomized trial of computer-driven protocolized weaning from mechanical ventilation. *Am J Respir Crit Care Med* 2006; 174: 894–900.
79. Perren A, Domenighetti G, Mauri S, et al. Protocol-directed weaning from mechanical ventilation: clinical outcome in patients randomized for a 30-min or 120-min trial with pressure support ventilation. *Intensive Care Med* 2002; 28: 1058–63.
80. Krishnan JA, Moore D, Robeson C, et al. A prospective, controlled trial of a protocol-based strategy to discontinue mechanical ventilation. *Am J Respir Crit Care Med* 2004; 169: 673–8.
81. Esteban A, Alia I, Tobin MJ, et al. Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Spanish Lung Failure Collaborative group. *Am J Respir Crit Care Med* 1999; 159: 512–18.
82. Esteban A, Frutos F, Tobin MJ, et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. *N Engl J Med* 1995; 332: 345–50.
83. Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 1996; 335: 1864–9.
84. Meade M, Guyatt G, Sinuff T, et al. Trials comparing alternative weaning modes and discontinuation assessments. *Chest* 2001; 120: 425S–437S.
85. Putensen C, Muders T, Varelmann D, et al. The impact of spontaneous breathing during mechanical ventilation. *Curr Opin Crit Care* 2006; 12: 13–18.
86. Esteban A, Alia I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med* 1997; 156: 459–65.
87. Haberthur C, Mols G, Elsasser S, et al. Extubation after breathing trials with automatic tube compensation, T-tube, or pressure support ventilation. *Acta Anaesthesiol Scand* 2002; 46: 973–9.
88. Matic I, Majeric-Kogler V. Comparison of pressure support and T-tube weaning from mechanical ventilation: randomized prospective study. *Croat Med J* 2004; 45: 162–6.
89. Ezingard E, Diconne E, Guyomarc'h S, et al. Weaning from mechanical ventilation with pressure support in patients failing a T-tube trial of spontaneous breathing. *Intensive Care Med* 2006; 32: 165–9.
90. Burns KE, Adhikari NK, Meade MO. Noninvasive positive pressure ventilation as a weaning strategy for intubated adults with respiratory failure. *Cochrane Database Syst Rev* 2003; 4: CD004127.
91. Meade MO, Guyatt GH, Cook DJ. Weaning from mechanical ventilation: the evidence from clinical research. *Respir Care* 2001; 46: 1408–15; discussion 1415–17.
92. Carrillo EH, Schmacht DC, Gable DR, et al. Thoracoscopy in the management of posttraumatic persistent pneumothorax. *J Am Coll Surg* 1998; 186: 636–9; discussion 639–40.
93. Schermer CR, Matteson BD, Demarest GB III, et al. A prospective evaluation of video-assisted thoracic surgery for persistent air leak due to trauma. *Am J Surg* 1999; 177: 480–4.
94. Carrillo EH, Kozloff M, Saridakis A, et al. Thoracoscopic application of a topical sealant for the management of persistent posttraumatic pneumothorax. *J Trauma* 2006; 60: 111–14.
95. Chang CC, Hsu HH, Kuo SW, et al. Bronchoscopic gluing for post-lung-transplant bronchopleural fistula. *Eur J Cardiothorac Surg* 2007; 31: 328–30.
96. Ferguson JS, Sprenger K, Van Natta T. Closure of a bronchopleural fistula using bronchoscopic placement of an endobronchial valve designed for the treatment of emphysema. *Chest* 2006; 129: 479–81.

97. Jones NC, Kirk AJ, Edwards RD. Bronchopleural fistula treated with a covered wallstent. *Ann Thorac Surg* 2006; 81: 364–6.
98. Sivrikoz CM, Kaya T, Tulay CM, et al. Effective approach for the treatment of bronchopleural fistula: application of endovascular metallic ring-shaped coil in combination with fibrin glue. *Ann Thorac Surg* 2007; 83: 2199–201.
99. Tao H, Araki M, Sato T, et al. Bronchoscopic treatment of postpneumectomy bronchopleural fistula with a collagen screw plug. *J Thorac Cardiovasc Surg* 2006; 132: 99–104.
100. Madden BP, Sheth A, Ho TB, et al. A novel approach to the management of persistent postpneumectomy bronchopleural fistula. *Ann Thorac Surg* 2005; 79: 2128–30.
101. Shah AM, Singhal P, Chhajed PN, et al. Bronchoscopic closure of bronchopleural fistula using gelfoam. *J Assoc Physicians India* 2004; 52: 508–9.
102. Carvalho P, Thompson WH, Riggs R, et al. Management of bronchopleural fistula with a variable-resistance valve and a single ventilator. *Chest* 1997; 111: 1452–4.
103. Cheatham ML, Promes JT. Independent lung ventilation in the management of traumatic bronchopleural fistula. *Am Surg* 2006; 72: 530–3.
104. Byhahn C, Habler OP, Bingold TM, et al. The wire-guided endobronchial blocker: applications in trauma patients beyond mere single-lung ventilation. *J Trauma* 2006; 61: 755–9.
105. Regel G, Sturm JA, Neumann C, et al. Occlusion of bronchopleural fistula after lung injury—a new treatment by bronchoscopy. *J Trauma* 1989; 29: 223–6.
106. Nicholas JM, Dulchavsky SA. Successful use of autologous fibrin gel in traumatic bronchopleural fistula: case report. *J Trauma* 1992; 32: 87–8.
107. Puskas JD, Mathisen DJ, Grillo HC, et al. Treatment strategies for bronchopleural fistula. *J Thorac Cardiovasc Surg* 1995; 109: 989–95; discussion 995–6.
108. Doelken P, Sahn SA. Trapped lung. *Semin Respir Crit Care Med* 2001; 22: 631–6.
109. Aguilar MM, Battistella FD, Owings JT, et al. Posttraumatic empyema. Risk factor analysis. *Arch Surg* 1997; 132: 647–50; discussion 650–1.
110. Eren S, Esme H, Sehitogullari A, et al. The risk factors and management of posttraumatic empyema in trauma patients. *Injury* 2008; 39: 44–9.
111. Sriussadaporn S, Poomsuwan P. Post-traumatic empyema thoracis in blunt chest trauma. *J Med Assoc Thai* 1995; 78: 393–8.
112. Mandal AK, Thadepalli H, Mandal AK, et al. Posttraumatic empyema thoracis: a 24-year experience at a major trauma center. *J Trauma* 1997; 43: 764–71.
113. Wong KS, Lin TY, Huang YC, et al. Scoring system for empyema thoracis and help in management. *Indian J Pediatr* 2005; 72: 1025–8.
114. Cameron R, Davies HR. Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema. *Cochrane Database Syst Rev* 2008; 2: CD002312.
115. Bilgin M, Akcali Y, Oguzkaya F. Benefits of early aggressive management of empyema thoracis. *ANZ J Surg* 2006; 76: 120–2.
116. Molnar TF. Current surgical treatment of thoracic empyema in adults. *Eur J Cardiothorac Surg* 2007; 32: 422–30.
117. Wehr CJ, Adkins RB Jr. Empyema thoracis: a ten-year experience. *South Med J* 1986; 79: 171–6.
118. Stafford RE, Linn J, Washington L. Incidence and management of occult hemothoraces. *Am J Surg* 2006; 192: 722–6.
119. Meyer DM. Hemothorax related to trauma. *Thorac Surg Clin* 2007; 17: 47–55.
120. Oguzkaya F, Akcali Y, Bilgin M. Videothoracoscopy versus intrapleural streptokinase for management of post traumatic retained haemothorax: a retrospective study of 65 cases. *Injury* 2005; 36: 526–9.
121. Velmahos GC, Demetriades D, Chan L, et al. Predicting the need for thoracoscopic evacuation of residual traumatic hemothorax: chest radiograph is insufficient. *J Trauma* 1999; 46: 65–70.
122. Meyer DM, Jessen ME, Wait MA, et al. Early evacuation of traumatic retained hemothoraces using thoracoscopy: a prospective, randomized trial. *Ann Thorac Surg* 1997; 64: 1396–400; discussion 1400–1.
123. Morales Uribe CH, Villegas Lanau MI, Petro Sanchez RD. Best timing for thoracoscopic evacuation of retained post-traumatic hemothorax. *Surg Endosc* 2008; 22: 91–5.
124. Cetindag IB, Neideen T, Hazelrigg SR. Video-assisted thoracic surgical applications in thoracic trauma. *Thorac Surg Clin* 2007; 17: 73–9.
125. Casas SR, Richardson JD. Role of thoracoscopy in acute management of chest injury. *Curr Opin Crit Care* 2006; 12: 584–9.
126. Carrillo EH, Richardson JD. Thoracoscopy in the management of hemothorax and retained blood after trauma. *Curr Opin Pulm Med* 1998; 4: 243–6.
127. Navsaria PH, Vogel RJ, Nicol AJ. Thoracoscopic evacuation of retained posttraumatic hemothorax. *Ann Thorac Surg* 2004; 78: 282–5; discussion 285–6.
128. Tomaselli F, Maier A, Renner H, et al. Thoracoscopic water jet lavage in coagulated hemothorax. *Eur J Cardiothorac Surg* 2003; 23: 424–5.
129. Velmahos GC, Demetriades D. Early thoracoscopy for the evacuation of undrained haemothorax. *Eur J Surg* 1999; 165: 924–9.
130. Vassiliu P, Velmahos GC, Toutouzas KG. Timing, safety, and efficacy of thoracoscopic evacuation of undrained post-traumatic hemothorax. *Am Surg* 2001; 67: 1165–9.
131. Heniford BT, Carrillo EH, Spain DA, et al. The role of thoracoscopy in the management of retained thoracic collections after trauma. *Ann Thorac Surg* 1997; 63: 940–3.
132. Brutsche MH, Tassi GF, Gyorik S, et al. Treatment of sonographically stratified multiloculated thoracic empyema by medical thoracoscopy. *Chest* 2005; 128: 3303–9.
133. Khalil BA, Corbett PA, Jones MO, et al. Less is best? The impact of urokinase as the first line management of empyema thoracis. *Pediatr Surg Int* 2007; 23: 129–33.
134. Agarwal R, Aggarwal AN, Gupta D. Intrapleural fibrinolysis in clotted haemothorax. *Singapore Med J* 2006; 47: 984–6.
135. Aye RW, Froese DP, Hill LD. Use of purified streptokinase in empyema and hemothorax. *Am J Surg* 1991; 161: 560–2.
136. Mithos P, Sepsas E, Konstantinou M, et al. Early use of intrapleural fibrinolytics in the management of postpneumonic empyema. A prospective study. *Eur J Cardiothorac Surg* 2005; 28: 599–603.
137. Basile A, Boulosa-Seoane E, Dominguez Viguera L, et al. Intrapleural fibrinolysis in the management of empyemas and haemothoraces. our experience. *Radiol Med (Torino)* 2003; 105: 12–16.
138. Lim TK, Chin NK. Empirical treatment with fibrinolysis and early surgery reduces the duration of hospitalization in pleural sepsis. *Eur Respir J* 1999; 13: 514–18.
139. Sahn SA. Use of fibrinolytic agents in the management of complicated parapneumonic effusions and empyemas. *Thorax* 1998; 53(Suppl 2): S65–S72.
140. De Gregorio MA, Ruiz C, Alfonso ER, et al. Transcatheter intracavitary fibrinolysis of loculated pleural effusions: experience in 102 patients. *Cardiovasc Intervent Radiol* 1999; 22: 114–18.
141. Davies RJ, Traill ZC, Gleeson FV. Randomised controlled trial of intrapleural streptokinase in community acquired pleural infection. *Thorax* 1997; 52: 416–21.
142. Davies CW, Lok S, Davies RJ. The systemic fibrinolytic activity of intrapleural streptokinase. *Am J Respir Crit Care Med* 1998; 157: 328–30.

143. Jerjes-Sanchez C, Ramirez-Rivera A, Elizalde JJ, et al. Intrapleural fibrinolysis with streptokinase as an adjunctive treatment in hemothorax and empyema: a multicenter trial. *Chest* 1996; 109: 1514–19.
144. Kimbrell BJ, Yamzon J, Petrone P, et al. Intrapleural thrombolysis for the management of undrained traumatic hemothorax: a prospective observational study. *J Trauma* 2007; 62: 1175–8; discussion 1178–9.
145. Bouros D, Schiza S, Patsourakis G, et al. Intrapleural streptokinase versus urokinase in the treatment of complicated parapneumonic effusions: a prospective, double-blind study. *Am J Respir Crit Care Med* 1997; 155: 291–5.
146. Bouros D, Schiza S, Siafakas N. Fibrinolytics in the treatment of parapneumonic effusions. *Monaldi Arch Chest Dis* 1999; 54: 258–63.
147. Bouros D, Schiza S, Tzanakis N, et al. Intrapleural urokinase in the treatment of complicated parapneumonic pleural effusions and empyema. *Eur Respir J* 1996; 9: 1656–9.
148. Diacon AH, Theron J, Schuurmans MM, et al. Intrapleural streptokinase for empyema and complicated parapneumonic effusions. *Am J Respir Crit Care Med* 2004; 170: 49–53.
149. Maskell NA, Davies CW, Nunn AJ, et al. U.K. controlled trial of intrapleural streptokinase for pleural infection. *N Engl J Med* 2005; 352: 865–74.
150. Tuncoguzur B, Ustunsoy H, Sivrikoz MC, et al. Intrapleural urokinase in the management of parapneumonic empyema: a randomised controlled trial. *Int J Clin Pract* 2001; 55: 658–60.

Evidence-Based Surgery: Injury to the Thoracic Great Vessels

Mark Cockburn

Clinical Questions		
Question	Answer	Grade of recommendation
What is the ultimate imaging modality for diagnosing blunt thoracic aortic injury?	Angiography is the ultimate modality for making the diagnosis of blunt thoracic aortic injury.	B
What modality should be used to follow minimal aortic injuries from blunt trauma?	TEE appears to be a good modality in following minimal aortic injuries.	B
What medications should we use in the medical management of MAIs and how long should patients be required to take these medications?	Beta-blockade and intravenous vasodilator therapy should be used for the medical management of MAIs. There is no study answering the question as to how long these medications should be used.	B
When is nonoperative management to be considered?	MAIs can be managed nonoperatively with specific medical treatment protocols to control heart rate and blood pressure. Similarly, patients who are poor operative candidates can have their injuries managed nonoperatively with treatment protocols (beta-blockade and intravenous vasodilator). Patients who are initially managed nonoperatively because of concerns of concomitant injuries and whose follow-up studies reveal resolution of the aortic injury can continued to be managed nonoperatively on beta-blockade and intravenous vasodilator.	B
What is the target blood pressure to maintain when nonoperative management or delayed surgical therapy is considered?	Controlling the heart rate and blood pressure (systolic between 100 and 120 mmHg) using beta-blockade and intravenous vasodilator is effective in preventing rupture of blunt thoracic aortic injury.	B
Which operative technique should be used for repair of descending thoracic aortic injuries? Is any technique superior?	Some form of distal perfusion should be used because neurologic complications seem to correlate with ischemia time.	B
Are endovascular stent procedures superior to open vascular procedures?	Endovascular stent grafts are associated with lower mortality, fewer postoperative neurologic complications including paraplegia, and fewer systemic complications than open procedures.	B
Abbreviations: MAI, minimal aortic injury; TEE, transesophageal echocardiography.		

INTRODUCTION

Chest injury from blunt trauma is a significant cause of morbidity and mortality. Most of the literature published on injury to the thoracic great vessels has focused on the aorta and blunt thoracic aortic injury, which is a devastating injury that requires early recognition to minimize morbidity and mortality. It has been estimated that there are about 8,000 cases of blunt aortic injury (BAI) each year in the United States (1). Approximately 80% to 85% die at the scene or in transport (2). This injury most commonly results from motor vehicle collisions (3) but we have seen an increase in fatality from this injury among pedestrians hit by cars (4). The remaining mechanisms for this injury include falls from heights and crushing chest injuries. In 2000 the Eastern Association for the Surgery of Trauma (EAST)

Practice Management Groups published their guidelines for the diagnosis and management of blunt aortic injury (3). This group reviewed 137 articles from a MEDLINE search of English language citations published between 1966 and 1997. They analyzed these papers and produced recommendations based on Level I, Level II, and Level III data. Since 2000, a number of other studies have been published looking at the diagnosis and management of BAI.

DIAGNOSIS OF BAI

What Is the Ultimate Imaging Modality for Diagnosing BAI?

The EAST guidelines stated that Level II data supported chest x-ray as a good screening tool and angiography as

the standard by which most other diagnostic tests are compared. The Level II data also supported that helical or spiral computed tomographic scanners have an extremely high negative predictive value and may be used to rule out BAI (3). Since the EAST guidelines, other studies have been done looking at the ability of the newer generation computed tomography (CT) scanners to diagnose BAI. In 2004 Chen et al. published their data looking at the use of helical computed tomography to detect acute thoracic aortic and branch vessel injury after blunt thoracic trauma. This was a retrospective study of 85 patients who had BAI diagnosed by chest CT, aortography, or both. Isolated aortic, branch vessel, or combined injuries were found in 71 (84%), 11 (13%), and 3 (4%) patients, respectively. All patients with branch vessel injuries were diagnosed by aortography. Ninety-eight percent of patients with aortography were true positives, and 20% with chest CT had indirect signs of aortic injury. They concluded that patients with indirect signs on chest CT require further evaluation and that angiography remains the optimal diagnostic modality for evaluating aortic branch vessel injuries (5). Melton et al. also looked at the evolution of chest CT for the definitive diagnosis of BAI. Their study was also retrospective, and they performed 113 aortograms, which confirmed 28 BAI cases. Twenty-seven of these were congruently diagnosed by CT. Only one CT scan diagnostic for BAI had a negative aortogram. Seventeen BAIs were diagnosed with CT alone. Ten BAIs were confirmed operatively, and seven were treated nonoperatively because of age, comorbid conditions, severity of injury, or presence of small intimal defects. They concluded that CT has evolved to allow for the definitive diagnosis and treatment of BAI (6).

Answer: Angiography is the ultimate modality for making the diagnosis of blunt thoracic aortic injury. Level of evidence IIb. Helical CT as an imaging modality for diagnosing blunt thoracic aortic injury. Level of evidence IIb. Grade recommendation: B.

MINIMAL AORTIC INJURIES

What Modality Should Be Used to Follow Minimal Aortic Injuries from Blunt Trauma? What Medications Should We Use in the Medical Management of These Injuries, and How Long Should Patients Be Required to Take These Medications?

As a direct result of the improvement in the diagnostic techniques, minimal aortic injuries (MAIs) are being recognized more frequently. The management of such injuries have created some anxiety among surgeons and has left some questions unanswered. What modalities should be used to follow these injuries? How often should follow-up studies be obtained? What medications should be used in the medical management of these injuries, and how long should patients be required to take these medications? What should the target blood pressure be?

Malhotra and colleagues published a paper in 2001 describing their experience with MAIs. They conducted a retrospective review of all patients suspected of BAI seen on screening helical computed tomography (HCT) over the study period July 1994 to June 2000. For their discussion,

MAI was defined as a small (<1cm) intimal flap with minimal to no periaortic hematoma. These patients underwent confirmatory aortography with or without intravascular ultrasound. All patients were admitted to the trauma intensive care unit, and all received short acting beta-blockade infusion (esmolol or labetalol) to control heart rate (<90 beats/minute) and blood pressure (systolic blood pressure <120mmHg). Sodium nitroprusside was added to the regimen when beta-blockade alone did not adequately control blood pressure. Patients were changed to oral antihypertensive therapy over the following five to seven days. BAI was suspected in 198 (1.3%) of the 15,000 patients evaluated with screening HCT and confirmed in 87 (0.6%) of these. Nine of these 87 patients met the criteria for MAI as just defined, and the remaining 78 patients had significant aortic injuries. Aortography was performed in 189 patients who had suspicious HCT. The initial aortogram was positive in 77 patients and, of these, 71 were true positives. Of the 112 negative aortograms, 105 were true negatives, and 7 were false negatives. Of the seven patients with false negative initial aortogram, five had MAI and two had significant aortic injuries. The correct diagnosis in patients with false negative aortograms was established by further tests including intravascular ultrasound (five patients), repeat aortography (one patient), video angiography (one patient). Although the overall sensitivity and specificity of the initial aortogram were 91% and 94.6%, respectively, the actual sensitivity of the initial aortogram for MAI was 37.5% and for significant aortic injury was 97.1%. Eight of the nine patients with MAI were managed nonoperatively. One patient refused nonoperative management and was operated on five days after injury. Aortotomy at the time of surgery revealed an intimal defect that was repaired by incorporating it into the aortotomy closure using three pledgeted prolene sutures (7).

The foregoing study demonstrated the low sensitivity of aortograms in making the diagnosis of MAI. Kepros and colleagues reviewed their experience with MAIs (8). In their report five blunt trauma patients treated for an aortic injury demonstrated by transesophageal echocardiography (TEE) to be limited to the intima with or without thrombus were reviewed. All were managed nonoperatively on the basis of the limited and superficial nature of their aortic injury. They used a management strategy that included serial TEE studies to visualize and monitor the progression or resolution of injury, hypotension (systolic blood pressure between 80 and 90mmHg) and prevention of tachycardia (heart rate between 60 and 80beats/min) using beta-blockade, close invasive monitoring in the intensive care unit, and standard intravenous fluid resuscitation using serum lactate levels and base deficit as endpoints of adequate tissue perfusion. They noted that TEE was more sensitive in diagnosing aortic intimal injuries compared with aortic arch angiography or HCT of the chest because the latter two studies failed to identify any of the intimal injuries. Nonoperative management was successfully completed in all cases. Complete resolution of all intimal tears was documented by TEE within 3–19 days (mean, 9.4 ± 6.6 days). In one patient the intimal tear extended during the first 48 hours. This patient was still managed nonoperatively because there was no sonographic evidence of transmural involvement and/or dissection. There was complete

resolution of injury by 11 days. There were no complications related to the aortic injuries in any of the patients during a mean follow-up of 16.8 months. Thus, TEE appears to be a good modality in diagnosing and following these MAIs.

Answer: TEE appears to be a good modality in following minimal aortic injuries. Level of evidence IIb. Grade recommendation: B. beta-blockade and intravenous vasodilator therapy should be used for the medical management of minimal aortic injuries. There is no study answering the question as to how long these medications should be used. Controlling the heart rate and blood pressure (systolic between 100 and 120 mmHg) using beta-blockade and intravenous vasodilator is effective in treating patients with minimal aortic injuries. Level of evidence IIb. Grade recommendation: B.

NONOPERATIVE MANAGEMENT OF BLUNT TRAUMATIC AORTIC INJURIES

When Is Nonoperative Management to Be Considered? What Is the Target Blood Pressure to Maintain When Nonoperative Management or Delayed Surgical Therapy Is Considered?

The nonoperative management of BAIs stemmed out of studies reporting the use of medical management of these injuries in patients who were poor operative candidates due advanced age or comorbidities that prohibit emergency thoracic surgery (9,10). Another subset of patients that are treated medically and in whom immediate repair is not possible are those patients unstable from intra-abdominal injuries who require laparotomy or patients with severe closed head injuries who require craniotomies (11–13). The use of pharmacologic treatment to decrease wall stress in acute aortic dissection and thereby reduce the risk of rupture was originally introduced by Wheat et al. in 1965 (14). Nonoperative management of BAI was first described by Akins in 1981 when five patients were managed with antihypertensive therapy and all survived (15). Most of these nonoperative cases had surgery purposefully delayed or indefinitely postponed because of severe comorbidities.

The concerns with the nonoperative management of BAIs are risk of subsequent rupture of the aorta and the risk of development of chronic thoracic aneurysms. Reports estimate that the risk of aortic rupture is less than 4% in patients presenting to the emergency room with stable hemodynamics during the initial work-up; however, once rupture occurred, survival was rare (16,17). A recent literature search by Hirose et al. (18) showed that only 1.5% of patients died of aortic rupture if they survived the initial few hours. Pate's study showed that only 7% of patients with a history of acute aortic injury developed chronic thoracic aneurysm over 7–48 years (16). Interestingly, some patients have regression of the aortic injury with antihypertensive management.

The use of antihypertensives for BAI was based on the successful management of type B dissection (15,16). In 1995, Pate and colleagues described two cases of aortic rupture during nonoperative management when blood pressure was not adequately managed (16). They

later published follow-up results in 1997 and 1999 showing that there was no aortic rupture using a blood pressure control strategy during a waiting period for delayed surgery or among medically managed patients (9,19). In the study, Pate et al. used the beta-blockade when the cardiac rate was >90 bpm and the systolic blood pressure was >100 mmHg. When the systolic blood pressure persisted at levels of >100 mmHg after beta-blockade, an intravenous vasodilator (usually nitroprusside) was used to control the pressure.

Answer: MAIs can be managed nonoperatively with specific medical treatment protocols to control heart rate and blood pressure. Similarly, patients who are poor operative candidates can have their injuries managed nonoperatively with the same treatment protocols (beta-blockade and intravenous vasodilator). Patients who are initially managed nonoperatively because of concerns of concomitant injuries and whose follow-up studies reveal resolution of the aortic injury can continued to be managed nonoperatively on beta-blockade and intravenous vasodilator.

There are no Level I data that have answered this question specifically. Pate et al.'s study provides Level IIb data. References to a target systolic blood pressure quote between 100 mmHg and 110 mmHg (Pate), 110 mmHg (Hirose), systolic blood pressure of less than a 120 mmHg (Malhotra), and between 80 and 90 mmHg (Kepros). Controlling the heart rate and blood pressure (systolic between 100 mmHg and 120 mmHg) using beta-blockade and intravenous vasodilator is effective in preventing rupture of blunt thoracic aortic injury. Level of evidence IIb. Grade recommendation: B.

OPERATIVE TECHNIQUE FOR REPAIR OF BLUNT TRAUMATIC THORACIC AORTIC INJURIES

Which Operative Technique Should Be Used for Repair of Descending Thoracic Aortic Injuries? Is any Technique Superior?

The optimal intraoperative technique for the repair of BAIs remains controversial. The EAST management guidelines stated that there were Level III data to support that the repair of aortic injury is best accomplished with some form of distal perfusion, either bypass or shunt (3).

Cardarelli et al. looked at the University of Maryland 30-year experience with traumatic aortic rupture (20). There were 219 patients with a diagnosis of traumatic aortic rupture between 1971 and 2001. Patients were divided according to surgical technique. There were 82 patients in the clamp-and-sew technique group (group A), 64 in the passive shunt group (group B), and 73 in the heparin-less partial cardiopulmonary bypass (group C). Mortality was 18 patients for group A (21.9%), 23 patients for group B (35.9%), and 13 patients for group C (17.8%) ($p = 0.03$). Paraplegia occurred in 15 of the 64 survivors in group A (23.4%), 7 of the 41 survivors in group B (17%), and 0 of the 60 survivors in group C ($p = 0.0005$). Aortic occlusion without lower body perfusion for longer than 30 minutes ($p = 0.004$) and surgical technique without lower body bypass support ($p = 0.0005$)

were associated with paraplegia. They concluded that the use of heparin-less distal cardiopulmonary bypass in the authors' hands is safe and is associated with a reduced incidence of paraplegia.

Whitson et al. describe their experience with the repair of this injury (21). They did a retrospective review (1991–2004) of patients with traumatic thoracic aortic injuries to evaluate whether an individualized approach to operative management provides acceptable neurologic outcomes. Ninety-one percent of the 67 patients who met the study criteria had concomitant injuries. Distal aortic perfusion was used in 81% of cases (75% left heart bypass, 6% cardiopulmonary bypass), and 19% underwent clamp-and-sew technique without heparinization. There were no spinal cord deficits or adverse cerebral events related to repair. If definitive repair was completed, the mortality was 16%. They concluded that judicious use of clamp-and-sew techniques can achieve excellent neurologic outcomes, equivalent to distal aortic perfusion.

Answer: Distal perfusion has been shown to decrease the incidence of paraplegia compared to clamp-and-sew technique when the aortic cross-clamp time exceeds 30 minutes. Some form of distal perfusion should be used because neurologic complications seem to correlate with ischemia time. Level of evidence IIa. Grade recommendation: B.

ENDOVASCULAR TREATMENT OF BLUNT TRAUMATIC THORACIC AORTIC INJURIES

Are Endovascular Stent Procedures Superior to Open Vascular Procedures?

Patients with BAIs frequently have significant associated injuries that can preclude them from immediate surgical repair. Some of these associated injuries were described earlier in this chapter. Endovascular grafts have been used since 1991 for the repair of abdominal aortic aneurysms, and this approach was first described as an alternative to open repair by Parodi et al. (22). Since then there has been improvement in the stent graft technology, which has led to the use of stent grafts for the treatment of traumatic BAIs. Most of the studies published on the use of this technology for the treatment of BAIs have been retrospective. In 2001, Fujikawa et al. published the first prospective case study on the use of endovascular stent grafting for the treatment of traumatic BAIs (23). They treated six patients who had sustained blunt thoracic aortic injuries confirmed by digital subtraction angiogram with stent grafts. All patients had injury of the aortic isthmus. All patients except one had an event-free clinical course. One patient died because of rupture of the ascending aorta. They concluded that an endovascular stent graft is a valid therapeutic option with minimal surgical invasion for patients with acute-phase aortic injury.

In 2004, Ott et al. published their review of 18 patients who underwent repair of a blunt thoracic aortic injury over an 11-year period, comparing the outcomes of patients treated with endovascular repair and open repair. Six of these patients had an endovascular repair and 12 an open repair. There were no significant differences in demographics, injury, or crash statistics between the two groups. The open

group had a 17% early mortality rate, a paraplegia rate of 16%, and an 8.3% incidence of recurrent laryngeal nerve injury compared to a 0% rate of mortality, paraplegia, and recurrent laryngeal nerve injury in the endovascular group. A definite trend toward decreased morbidity, mortality, intensive care unit length of stay, and number of ventilator days was seen with endovascular repair. They concluded that there was a clear trend toward improved outcomes after endovascular repair of thoracic aortic injuries compared with the standard open repair in the setting of trauma (24). In 2004, Dunham et al. also published their retrospective review of 28 patients treated with endovascular stent grafts for blunt thoracic aortic injuries. Twelve patients were excluded because injuries occurred more than 30 days before grafting or under a different protocol or the procedure was performed in a different center, leaving 16 patients for review. Technical success was achieved in all patients, no graft-related complications were detected during follow-up, and no patient developed postoperative paraplegia. There was one postoperative mortality secondary to comorbid injury. There was one patient with a preoperative traumatic carotid dissection who demonstrated a postoperative stroke and another patient who required thoracentesis for a pleural effusion. They concluded that endovascular stent-graft repair of blunt thoracic aortic injuries can be performed safely (25).

In 2006, Andrassy et al. published a retrospective review of all patients treated for acute and chronic traumatic injury of the thoracic aorta and compared the outcome of the endovascular approach versus surgery (26). In the study period of 14 years, 46 patients were treated. The overall 30-day mortality was 16% in patients treated for acute or contained rupture ($n = 31$) and not significantly different after endovascular versus open repair (13.3% versus 18.8%). There was no mortality in the patients undergoing elective stent grafting or open surgery for chronic post-traumatic aortic aneurysms ($n = 15$). Conversion and/or operative revision following stent graft implantation occurred in three patients (12.5%). Neurologic complications were absent in the stent graft group (0 of 24), whereas paraplegia ($n = 2$) or minor neurologic deficits ($n = 3$) developed following open surgery (5 of 22; 22.7%; $p = 0.013$). Length of intensive care and overall hospital stay were significantly shorter for patients after elective stent graft treatment compared to open surgery ($p = 0.045$). They concluded that minimally invasive endovascular repair for patients with acute and chronic post-traumatic aneurysms is an equally effective treatment option compared with open surgery, with advantages regarding perioperative neurologic complications and duration of hospital stay under elective circumstances.

Demetriades et al. published the results of a prospective, multicenter study assessing the early efficacy and safety of endovascular stent grafts in traumatic thoracic aortic injuries and comparing outcomes with standard operative repair (27). The decision for open or endovascular repair was surgeon's preference. One hundred twenty-five patients (64.9%) were selected for stent grafts and 68 (35.2%) for operative repair. Stent grafts were selected in 71.6% of the 74 patients with major extrathoracic injuries and in 60% of the 115 patients with no extrathoracic injuries. Twenty-five patients in the stent graft group (20%) developed 32 device-related complications. There were 18

endoleaks (14.4%), of which 6 needed open repair. Procedure related paraplegia developed in 2.9% in the open repair group and 0.8% in the stent graft group ($p = 0.28$). Multivariate analysis adjusting for severe extrathoracic injuries, hypotension, Glasgow Coma Score, and age revealed that the stent graft group had a significantly lower mortality [adjusted odds ratio: 8.42; 95% confidence interval (CI): 2.76–25.69; adjusted p value < 0.001], and fewer blood transfusions (adjusted mean difference: 4.98; 95% CI: 0.14–9.82; adjusted p value = 0.046) than the open repair group. Among the 115 patients without major extrathoracic injuries, higher mortality and higher transfusion requirements were also found in the open repair group (adjusted odds ratio for mortality: 13.08; 95% CI: 2.53–67.53; adjusted p value = 0.002; adjusted mean difference in the transfusion units: 4.45; 95% CI: 1.39–7.51; adjusted p value = 0.004). Among the 74 patients with major extrathoracic injuries, significantly higher mortality and pneumonia rates were found in the open repair group (adjusted p values 0.04 and 0.03, respectively). Multivariate analysis also showed that centers with high volume of endovascular procedures had significantly fewer systemic complications (adjusted p value = 0.001), fewer local complications (adjusted p value = 0.033), and shorter hospital length of stay (adjusted p value = 0.005) than low-volume centers. They concluded that most surgeons at the centers in the study select stent grafts for traumatic thoracic aortic ruptures, irrespective of associated injuries, injury severity, and age. Stent graft repair is associated with significantly lower mortality and fewer blood transfusions, but there is a considerable risk of serious device-related complications.

Answer: Endovascular stent grafts are associated with lower mortality, fewer postoperative neurologic complications including paraplegia, and fewer systemic complications than open procedures. Endovascular stent grafts can be safely used in the treatment of acute and chronic post-traumatic thoracic aortic aneurysms as an alternative to open repair. Level of evidence IIa. Grade recommendation: B.

PENETRATING INJURIES OF THE AORTA

There are fewer numbers of studies published on penetrating injury to the aorta compared to BAI. Penetrating injury to the thoracic aorta accounts for approximately 1% of traumatically injured aortas (28). Mortality from such injuries has not changed in the past decade, and open surgical repair remains the gold standard in emergent situations. Endovascular stent grafts have been used successfully for the management of BAIs, and there are case reports in the literature describing the use of endovascular stent grafts in penetrating injuries to the aorta (29).

Demetriades et al. conducted a retrospective analysis of all patients with penetrating aortic injuries admitted over a five-year period (30). The abdominal aorta was injured in 72% of 93 patients and the thoracic aorta in 28%. Eighty-two percent of the patients were admitted in shock and 41% with unrecordable blood pressures. Victims with thoracic aortic injuries were more likely to have an unrecordable blood pressure on admission than patients with abdominal aortic injuries (73% versus 28.4%) and more likely to require an emergency room thoracotomy (76.9% versus 20.9%). There were no survivors among the 36 patients who required an emergency thoracotomy. The overall mortality was 80.6% (87.5% for gunshot wounds and 64.7% for knife wounds). Patients with abdominal aortic injuries were three times more likely to survive than those with thoracic aortic injuries (23.9% versus 7.7%).

Injury to the thoracic aorta, gunshot wounds, unrecordable blood pressure on admission, and the need for emergency room thoracotomy, are important predictors of mortality. Level of evidence IIb.

INJURY TO THE THORACIC VENA CAVA

Injury to the thoracic vena cava is extremely rare and usually fatal. Most of the literature published on these injuries are case studies and describe experience in the management of these injuries. Management involves surgical repair, and there are not enough papers to render any Level I, II, or III data.

Levels of Evidence

Question	Answer	Grade of recommendation	Level of evidence	Ref.
What is the ultimate imaging modality for diagnosing blunt thoracic aortic injury?	Angiography is the ultimate modality for making the diagnosis of blunt thoracic aortic injury.	B	IIB	5, 6
What modality should be used to follow minimal aortic injuries from blunt trauma?	TEE appears to be a good modality in following minimal aortic injuries.	B	IIB	8
What medications should we use in the medical management of MAIs and for how long should patients be required to take these medications?	beta-blockade and intravenous vasodilator therapy should be used for the medical management of MAIs. There is no study answering the question as to how long these medications should be used.	B	IIB	8
When is nonoperative management to be considered?	MAIs can be managed nonoperatively with specific medical treatment protocols to control heart rate and blood pressure. Similarly, patients who are poor operative candidates can have their injuries managed nonoperatively with treatment protocols (beta-blockade and intravenous vasodilator). Patients who are initially managed nonoperatively because of concerns of concomitant injuries and whose follow-up studies reveal resolution of the aortic injury can continued to be managed nonoperatively on beta-blockade and intravenous vasodilator.	B	IIB	9–3

(Continued)

Levels of Evidence (Continued)

Question	Answer	Grade of recommendation	Level of evidence	Ref.
What is the target blood pressure to maintain when nonoperative management or delayed surgical therapy is considered?	Controlling the heart rate and blood pressure (systolic between 100 and 120 mmHg) using beta-blockade and intravenous vasodilator is effective in preventing rupture of blunt thoracic aortic injury.	B	IIB	8, 18, 19
Which operative technique should be used for repair of descending thoracic aortic injuries? Is any technique superior?	Some form of distal perfusion should be used because neurologic complications seem to correlate with ischemia time.	B	IIB	3
Are endovascular stent procedures superior to open vascular procedures?	Endovascular stent grafts are associated with lower mortality, fewer postoperative neurologic complications including paraplegia, and fewer systemic complications than open procedures.	B		26,27

Abbreviations: MAI, minimal aortic injury; TEE, transesophageal echocardiography.

REFERENCES

- Jackson DH. Of TRAs and ROCs. *Chest* 1984; 85: 585–687.
- Smith RS, Chang FC. Traumatic rupture of the aorta: still a lethal injury. *Am J Surg* 1986; 152: 660–3.
- Nagy K, Fabian T, Rodman G, et al. Guidelines for the diagnosis and management of blunt aortic injury: an EAST practice management guidelines work group. *J Trauma* 2000; 48: 1128–43.
- Burkhart HM, Gomez GA, et al. Fatal blunt aortic injuries: a review of 242 cases. *J Trauma* 2001; 50: 113–15.
- Chen MY, Miller PR, McLaughlin CA, et al. The trend of using computed tomography in the detection of acute thoracic aortic and branch vessel injury after blunt thoracic trauma: single-center experience over 13 years. *J Trauma* 2004; 56: 783–5.
- Melton SM, Kerby JD, McGiffin D, et al. The evolution of chest computed tomography for the definitive diagnosis of blunt aortic injury: a single-center experience. *J Trauma* 2004; 56: 243–50.
- Malhotra AK, Fabian TC, et al. Minimal aortic injury: a lesion associated with advancing diagnostic techniques. *J Trauma* 2001; 51: 1042–8.
- Kepros J, Angood P, et al. Aortic intimal injuries from blunt trauma: resolution profile in nonoperative management. *J Trauma* 2002; 52: 475–8.
- Camp PC, Shackford SR. Outcome after blunt traumatic aortic laceration: identification of a high risk cohort. *J Trauma* 1997; 43: 413–22.
- Camp PC, Rogers RB, Shackford SR, et al. Blunt traumatic thoracic aortic lacerations in the elderly: an analysis of outcome. *J Trauma* 1994; 37: 418–23.
- Borman KR, Aurbakken CM, Weigelt JA. Treatment priorities in combined blunt abdominal and aortic trauma. *Am J Surg* 1982; 144: 728–32.
- Hudson HM, Woodson J, Hirsch E. The management of traumatic aortic tear in the multiply-injured patient. *Ann Vasc Surg* 1991; 5: 445–8.
- Maggisano R, Nathens A, Alexandrova NA, et al. Traumatic rupture of the thoracic aorta: should one always operate immediately? *Ann Vasc Surg* 1995; 9: 44–52.
- Wheat MW, Palmer FF, et al. Treatment of dissecting aneurysms of the aorta without surgery. *J Thorac Cardiovasc Surg* 1965; 50: 364–73.
- Akins CW, Buckley MJ, Daggett W, et al. Acute traumatic disruption of the thoracic aorta: a ten year experience. *Ann Thorac Surg* 1981; 31: 305–9.
- Pate JW, Fabian TC, Walker W. Traumatic rupture of the aortic isthmus: an emergency? *World J Surg* 1995; 19: 119–26.
- Fabian TC, Richardson JD, Croce MA, et al. Prospective study of blunt aortic injury: multicenter trial of the American Association for the Surgery of Trauma. *J Trauma* 1997; 42: 374–83.
- Hirose H, Gill IS, Malangoni MA. Nonoperative management of traumatic aortic injury. *J Trauma* 2006; 60: 597–601.
- Pate JW, Gavant ML, Weiman DS, et al. Traumatic rupture of the aortic isthmus: program of selective management. *World J Surg* 1999; 23: 59–63.
- Cardarelli MG, McLaughlin JS, Downing SW, et al. Management of traumatic aortic rupture: a 30-year experience. *Ann Surg* 2002; 236: 465–9.
- Whitson BA, Nath DS, Knudtson JR, et al. Is distal aortic perfusion in traumatic thoracic aortic injuries necessary to avoid paraplegic postoperative outcomes? *J Trauma* 2008; 64: 115–20.
- Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg* 1991; 5: 491–9.
- Fujikawa T, Yukioka T, Ishimaru S, et al. Endovascular stent grafting for the treatment of blunt thoracic aortic injury. *J Trauma* 2001; 50: 223–9.
- Ott MC, Stewart TC, Lawlor DK et al. Management of blunt thoracic injuries: endovascular stents versus open repair. *J Trauma* 2004; 56: 565–70.
- Dunham MB, Zygun D, Petrask P, et al. Endovascular stent grafts for acute blunt aortic injury. *J Trauma* 2004; 56: 1173–8.
- Andrassy J, Weidenhagen R, Meimarakas G, et al. Stent versus open surgery for acute and chronic traumatic injury of the thoracic aorta: a single-center experience. *J Trauma* 2006; 60: 765–72.
- Demetriades D, Velhamos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the surgery of trauma multicenter study. *J Trauma* 2008; 64: 561–71.
- Cornwell EE III, Kennedy F, Berne TV, et al. Gunshot wounds to the thoracic aorta in the '90s: only prevention will make a difference. *Am Surg* 1995; 61: 721–2.
- Fang TD, Peterson DA, Kirilcuk NN, et al. Endovascular management of a gunshot wound to the thoracic aorta. *J Trauma* 2006; 60: 204–8.
- Demetriades D, Theodorou D, Murray J, et al. Mortality and prognostic factors in penetrating injuries of the aorta. *J Trauma* 1996; 40: 761–3.

Evidence-Based Surgery: Cardiac Trauma

Dror Soffer and Edan Sarid

Cardiac Trauma Question Summary		
Question	Answer	Grade
How do you rule out a significant blunt cardiac injury?	The combination of repeated normal cTnI levels with a normal ECG	C+
Who should and should not get a continuous ECG monitoring, and for how long?	Young (<40–50 years) asymptomatic stable patients with a normal ECG do not need further monitoring	C+
Which patients with suspected blunt cardiac injury should undergo echocardiography?	Unstable patients and patients with high suspicion of complications should be subjected to echocardiography dependent on the questionable need for urgent surgery	C
Is there a role for pericardiocentesis in penetrating cardiac trauma?	There is not enough data to support the usage of pericardiocentesis in patients with penetrating cardiac injury	C
How do you manage a foreign body in the heart?	The management of foreign bodies in the heart should be conservative unless the patient has signs of complications	C
Must one use pledgets when suturing the heart?	There is not enough data to show that pledgets must be used in every cardiac trauma surgery	C
Abbreviations: cTnI, cardiac troponin I; ECG, electrocardiogram.		

HOW DO YOU RULE OUT A SIGNIFICANT BLUNT CARDIAC INJURY?

Blunt cardiac injury (BCI) in a stable patient seems an elusive diagnosis. Many clinical observations, laboratory tests, and imaging modalities are suggested as an aid in diagnosing that pathology. The main suggested, “investigated,” and most commonly used parameters are electrocardiogram (ECG), cardiac enzymes (CPK-MB, troponin I), echocardiography, isotopic scans, and computed tomography (CT). A MEDLINE search from January 1996 through February 2008 was performed. All English-language citations during this time period with the subject words “blunt cardiac injury troponin” were retrieved. This yielded 35 papers, of which 7 were primarily well-conducted studies with Level I evidence.

Adams et al. examined the importance of troponin levels in 44 consecutive patients. They concluded that measurement of cardiac troponin I (cTnI) levels, accurately detects cardiac injury in patients with blunt chest trauma and should facilitate the diagnosis and management of such patients (1). Rajan et al. evaluated prospectively 187 patients with blunt cardiac trauma in Switzerland. They found that cTnI levels below 1.05 mcg/L in asymptomatic patients at admission and within the first six hours after admission rule out myocardial injury, whereas positive cTnI above 1.05 mcg/L mandate further cardiologic workup for the detection and management of myocardial injury.

Furthermore, the dynamics and peak levels of pathological cTnI levels allow estimation of arrhythmia risk and left ventricular dysfunction in trauma patients with BCI (2). Another study from the University of Southern California and the Los Angeles County and University of Southern California Medical Center examined the combination of ECG and cTnI as a screening tool. Three hundred thirty-three consecutive patients with significant blunt thoracic trauma were followed prospectively. The authors’ conclusions were that the combination of normal ECG and cTnI at admission and eight hours later rules out the diagnosis of significant BCI. In the absence of other reasons for hospitalization, such patients can be safely discharged (3). That observation was already demonstrated by Salim et al., who prospectively followed 115 patients with evidence of significant blunt thoracic trauma (4) and by Fulda et al. (5). Collins and colleagues demonstrated with 72 consecutive patients that in the hemodynamically stable patient, a normal cTnI level, four to six hours after injury excludes clinically significant BCI. This holds true whether the admission ECG is normal or not. An elevated cTnI does not definitively diagnose a clinically significant contusion. Patients suspicious for cardiac contusions who have normal troponins and no other serious injuries may be safely discharged from the emergency department (6). The need for repeated cTnI level testing in the range of six to eight hours after admission was also shown to be of importance in repeated studies (3,7).

Recommendations: There are sufficient Level I data to suggest that cTnI levels are important in the diagnosis and evaluation of BCI. The combination of repeated normal cTnI levels with a normal ECG can preclude a severe BCI. Level of evidence: I. Grade of recommendation: C+.

WHO SHOULD AND SHOULD NOT GET A CONTINUOUS ECG MONITORING, AND FOR HOW LONG?

Cardiac arrhythmias are considered to be one of the most common manifestations of BCI. Therefore, continuous ECG monitoring was advocated in these patients.

Cachecho et al. conducted a prospective study on 336 patients and found that none of the stable young patients (under 40 years old) had any cardiac complications—with and without a normal ECG. They concluded that young patients with minor blunt thoracic trauma and a normal or minimally abnormal ECG do not benefit from cardiac monitoring (8). McLean and colleagues conducted a prospective study in which 312 BCI patients were followed for cardiac arrhythmias. They concluded that all arrhythmias were present already on admission and the majority were of atrial fibrillation type. They also could not recommend on the length of a desirable continuous ECG monitoring (9). Christensen et al. analyzed 18 studies regarding that issue. Their review suggests that clinically significant myocardial contusions as a result of blunt trauma are rare and may be detected simply and inexpensively using ECG and careful physical examination (10). Fildes and colleagues prospectively studied the safety of limiting the cardiac evaluation to patients who were hemodynamically stable, had no history of cardiac disease, had a normal baseline ECG, did not require surgery or neurological observation for associated injuries, and were less than 55 years of age. These patients were simply admitted for 24 hours of continuous cardiac monitoring. No patient developed any complications of myocardial contusion requiring therapy. They concluded that it is safe to limit the cardiac evaluation in this group of patients (11).

Recommendations: There is enough Level I–II evidence to support the estimation that young (under 40 years) asymptomatic stable patients with a normal ECG do not need further monitoring. Patients who do not enter this category might benefit from continuous ECG monitoring, but there are not enough data to support its clinical benefit and the length of that monitoring. Level of evidence: I. Grade of recommendation: C+.

WHICH PATIENTS WITH SUSPECTED BCI SHOULD UNDERGO ECHOCARDIOGRAPHY?

Injury to the cardiac tissue is a common cause of fatality in patients with BCI. Many studies have been done to assess the usefulness of echocardiography (echo), as a quick, non-invasive method of diagnosing significant pathology, such as cardiac tamponade, myocardial contusion, valvular injury, or any type of wall rupture. A PubMed search of “blunt trauma echocardiography” from the past 12 years revealed several studies. Many case reports published specific experiences of the diagnostic value of echo as a rapid and effective imaging technique. The majority of formal research

performed was prospective observational studies that followed patients with cardiac pathology evaluated by echo and then verified by surgical thoracotomy.

In 2001, a three-year study by Vignon et al. followed 100 consecutive severe blunt chest trauma patients who prospectively underwent transesophageal echocardiography (TEE) and chest CT as part of their initial evaluation. They discovered that CT and TEE had equal value in diagnosis of aortic injury, whereas TEE demonstrated superiority in diagnosis of cardiac injury (12).

In 2002, Lindstaedt et al. documented a prospective study of 118 patients with BCI that elucidated the limited role of transthoracic echocardiography (TTE). They concluded that “prognosis in patients with myocardial contusion is favorable and, thus, routine cardiac workup is not indicated,” and that diagnostic measures should be limited to cases with complications (13).

In 2004, Schultz and colleagues conducted a systematic review of 25 prospective and 16 retrospective studies on blunt chest trauma. They discovered that as far as diagnosis is concerned, no statistical correlation existed between an abnormal TTE and the risk of a BCI-related complication that required treatment. They concluded that TEE was less limited as a diagnostic tool and preferential as such, but either TTE or TEE should always be performed when any BCI-related cardiac complication is suspected (14).

In 2006, a Level I systematic review was reported by Van Dantzic in which he described the use of TEE in BCI traumas. He referenced a study in which 32 consecutive trauma patients were prospectively evaluated by TEE. Injury observed by echo was then compared to their gold standard of an aortogram study. A diagnostic sensitivity of 91% and a specificity of 100% were observed (15).

Recommendations: There is an overall lack of evidence to guide criteria for when to use echo in blunt cardiac trauma. With support from numerous observational studies and reviews of literature, it is generally agreed that echo plays a significant but limited role in the diagnosis of cardiac complications to injury. Yet it remains unclear which trauma patients are to be tested. In this regard, the approach to BCI patients can be divided into three basic categories: a single approach to (1) all suspected BCI patients, (2) the unstable patients, and (3) the stable patients with a high level of suspicion of complication. There is no level of evidence to suggest that all victims of suspected BCI should receive an echo examination. There is, however, some Level III evidence suggesting that all unstable patients be subjected to echo dependent on the questionable need for urgent surgery. Finally, there is Level III evidence to support that all patients with high suspicion of cardiac complication should be evaluated by echo. Level of evidence: III. Grade of recommendation: C.

IS THERE A ROLE FOR PERICARDIOCENTESIS IN PENETRATING CARDIAC TRAUMA?

The role of pericardiocentesis in the management of penetrating cardiac injury (PCI) is disputed among physicians. The historical notion that a possible pericardial hemorrhage or effusion must be quickly assessed and treated by pericardiocentesis has been challenged by many studies in recent decades, mainly retrospective studies and case reports.

In 2004, Gao et al. retrospectively reviewed 82 cases of penetrating PCI over 16 years. All 82 were treated operatively, and 3 received preoperative pericardiocentesis. The authors report that “early establishment of diagnosis and prompt thoracotomy against time are the fundamental factors affecting the outcome of penetrating cardiac injuries.” They recommend against the use of pericardiocentesis before surgery (16).

In 1999, two extensive retrospective chart reviews were conducted on penetrating PCI patients. Tanaka and colleagues considered the cases of 19 consecutive PCI patients over 18 years admitted to their institution due to hemopericardium. They concluded that surgeons should not perform pericardiocentesis for relief of tamponade. Surgical fenestration, they recommend, should be “the first choice for relief of acute hemopericardium due to trauma” (17). Thourani et al., in a similar retrospective study, concluded that pericardiocentesis had no effect on mortality rates of admitted cardiac tamponade patients (18). Another retrospective analysis was performed by Symbas et al. in 1976. They reviewed 102 patients over 10 years who were treated for PCI and analyzed the therapeutic results of pericardiocentesis as compared to immediate surgical intervention. Based on their findings, they recommended that all patients should undergo operative intervention as quickly as possible, and pericardiocentesis should only be used to “provide time for a safe operation” (19).

Breaux et al. in 1979 followed 197 patients over 20 years who underwent surgery for their injuries. Sixty-eight percent were treated with pericardiocentesis preoperatively. The authors found that mortality was reduced in these patients, and thus concluded that prompt pericardial decompression is essential, whether operatively or through aspiration (20). Several published case reports varied in their recommendations, though most described pericardiocentesis as an effective and useful treatment of cardiac tamponade (21–24).

Recommendations: Current Level III evidence consistently suggests that pericardiocentesis should not be considered as a preoperative treatment in PCI patients. Alternatively, there is some Level V evidence to support pericardiocentesis as an important therapy to relieve tamponade, with scarce and dated Level 3 studies also supporting this idea.

Recommendations: There is only weak evidence to support the use of pericardiocentesis in patients with PCI. Level of evidence: IV. Grade of recommendation: C.

HOW DO YOU MANAGE A FOREIGN BODY IN THE HEART?

There is a lack of data yielding evidence in the management of foreign bodies in the heart. Very few experimental studies were found establishing criteria or suggesting recommendations in the proper management of such cases. However, numerous case reports have been published with case-related analysis.

In 1989, one study was published by Symbas et al. that retrospectively analyzed 24 gunshot patients with bullets retained in the heart. Fourteen were managed without surgical intervention. Their results suggest that the management of bullets in the heart should be “individualized

according to the patient’s clinical course” and that “bullets left in the heart are tolerated well” (25). A 1990 summarizing review of the literature by Symbas et al. resulted in similar recommendations, this time stating that “the management of missiles in the heart should be individualized according to the patient’s clinical course, the site, shape and size of the missile, and that in selected patients missiles in the heart are tolerated well” (26). These recommendations are quoted in multiple case studies of foreign bodies in the heart.

In one such case report in 1998, LeMaire et al. published the occurrence of a needle that broke off during an intravenous injection and subsequently embolized to the right heart, causing perforation. In their report, the authors suggest that “if a foreign body is small and smooth, if the risk of contamination is minimal and if the symptoms are absent, there is no indication to remove it” (27).

As a response to this case in 1999, Actis Dato et al. reported their own retrospective observational study of 12 patients over 35 years with foreign bodies in their hearts. Eight of these were treated operatively, and the other four were managed conservatively. The authors report that there is no need for surgery if the patients are asymptomatic (28).

Similar recommendations were made in 2006, by Zhang et al. in the case report of a rusted metallic foreign body retained in the posterior papillary muscles of the left ventricle in a 40-year-old man. In their report, the patient was successfully treated with surgery, yet the authors maintain that their case is rare, and surgical removal of a foreign body should be used only in such rare instances (29).

Recommendations: The management of foreign bodies in the heart should be conservative unless the patient has signs of complications. There is some Level III evidence and much Level V evidence to support the removal of foreign bodies in cases where complications are likely. Level of evidence: III. Grade of recommendation: C.

MUST ONE USE PLEDGETS WHEN SUTURING THE HEART?

The role of pledgets in cardiac surgery is a widely debated but hardly researched topic. A search over the past several decades yielded few published studies on cardiac suturing techniques. In 1981, Katz et al. conducted an observational experiment regarding the dehiscence of sutured atrioventricular valves. They found, through in vivo and in vitro studies, that in such cases, pledget-supported sutures showed advantageous higher line strength and that non-pledgetted stitches should only be used when necessary (30). In 1984, Newton and colleagues discussed the role of pledgets in mitral valve replacements. They conducted a prospective cohort study in which the yield force of initial disruption of pledget sutures was compared to that of non-pledget sutures. They found that the technique of pledget suturing was more stable and thus recommended in mitral valve replacement surgery (31).

In 1996, Bowman et al. published a relevant prospective, randomized study on cardiac suturing, comparing the use of pledget sutures to the use of a skin stapling device. After performing left thoracotomy, pericardiotomy, cardiac exposure, and repair on 20 canines, the authors compared

resulting parameters such as gross blood loss, hemodynamic instability, and integrity of repair. They concluded that “stapling is faster to perform, has similar repair integrity, and has less risk of accidental contaminated needle injury than does traditional suture/pledget repair” (32).

In other somewhat dated reviews, the potential complications of pledget suturing were discussed. In 1987, Lifschult et al. reported two accidental deaths as a result of embolization of cotton pledgets following heart valve implant operations (33). In addition, Weingarten et al. published in 1977 a case report with evidence that pledgets were a cause of Teflon embolization to the pulmonary arteries (34).

Recommendations: The sparse Level II evidence available suggests that pledget usage in suturing can in fact be useful in cardiac surgery. However, there is also limited Level IV evidence to suggest that the use of pledgets can be life-threatening. Though the technique has been used for many years, there are insufficient data to justify any evidence-based recommendations on the use of pledgets in cardiac trauma surgery. Level of evidence: IV. Strength of recommendation: C.

REFERENCES

- Adams JE III, Davila-Roman VG, Bessey PQ, et al. Improved detection of cardiac contusion with cardiac troponin I. *Am Heart J* 1996; 131: 308–12.
- Rajan GP, Zellweger R. Cardiac troponin I as a predictor of arrhythmia and ventricular dysfunction in trauma patients with myocardial contusion. *J Trauma* 2004; 57: 801–8; discussion 808.
- Velmahos GC, Karauskakis M, Salim A, et al. Normal electrocardiography and serum troponin I levels preclude the presence of clinically significant blunt cardiac injury. *J Trauma* 2003; 54: 45–50; discussion 50–51.
- Salim A, Velmahos GC, Jindal A, et al. Clinically significant blunt cardiac trauma: role of serum troponin levels combined with electrocardiographic findings. *J Trauma* 2001; 50: 237–43.
- Fulda GJ, Giberson F, Hailstone D, et al. An evaluation of serum troponin T and signal-averaged electrocardiography in predicting electrocardiographic abnormalities after blunt chest trauma. *J Trauma* 1997; 43: 304–10; discussion 310–12.
- Collins JN, Cole FJ, Weireter LJ, et al. The usefulness of serum troponin levels in evaluating cardiac injury. *Am Surg* 2001; 67: 821–5; discussion 825–6.
- Swaanenburgh JC, Klaase JM, DeJongste MJ, et al. Troponin I, troponin T, CKMB-activity and CKMB-mass as markers for the detection of myocardial contusion in patients who experienced blunt trauma. *Clin Chim Acta* 1998; 272: 171–81.
- Cachecho R, Grindlinger GA, Lee VW. The clinical significance of myocardial contusion. *J Trauma* 1992; 33: 68–71; discussion 72–3.
- McLean RF, Devitt JH, Dubbin J, et al. Incidence of abnormal RNA studies and dysrhythmias in patients with blunt chest trauma. *J Trauma* 1991; 31: 968–70.
- Christensen MA, Sutton KR. Myocardial contusion: new concepts in diagnosis and management. *Am J Crit Care* 1993; 2: 28–34.
- Fildes JJ, Betlej TM, Mangano R, et al. Limiting cardiac evaluation in patients with suspected myocardial contusion. *Am Surg* 1995; 61: 832–5.
- Vignon P, Boncoeur MP, Francois B, et al. Comparison of multiplane transesophageal echocardiography and contrast-enhanced helical CT in the diagnosis of blunt traumatic cardiovascular injuries. *Anesthesiology* 2001; 94: 615–22; discussion 5A.
- Lindstaedt M, Gerding A, Lawo T, et al. Acute and long-term clinical significance of myocardial contusion following blunt thoracic trauma: results of a prospective study. *J Trauma* 2002; 52: 479–85.
- Schultz JM, Trunkey DD. Blunt cardiac injury. *Crit Care Clin* 2004; 20: 57–70.
- Van Dantzig JM. Echocardiography in the emergency department. *Semin Cardiothorac Vasc Anesth* 2006; 10: 79–81.
- Gao JM, Gao YH, Wei GB, et al. Penetrating cardiac wounds: principles for surgical management. *World J Surg* 2004; 28: 1025–9.
- Tanaka H, Fujita T, Endoh Y, et al. Pericardial tamponade type injury: a 17-year study in an urban trauma center in Japan. *Surg Today* 1999; 29: 1017–23.
- Thourani VH, Feliciano DV, Cooper WA, et al. Penetrating cardiac trauma at an urban trauma center: a 22-year perspective. *Am Surg* 1999; 65: 811–16; discussion 817–18.
- Symbas PN, Harlaftis N, Waldo WJ. Penetrating cardiac wounds: a comparison of different therapeutic methods. *Ann Surg* 1976; 183: 377–81.
- Breaux EP, Dupont JB Jr, Albert HM, et al. Cardiac tamponade following penetrating mediastinal injuries: improved survival with early pericardiocentesis. *J Trauma* 1979; 19: 461–6.
- Forauer AR, Dasika NL, Gemmette JJ, et al. Pericardial tamponade complicating central venous interventions. *J Vasc Interv Radiol* 2003; 14: 255–9.
- Mullens W, Dupont M, De Raedt H. Pneumopericardium after pericardiocentesis. *Int J Cardiol* 2007; 118: e57.
- Park JH, Shin HJ, Choo SJ, et al. Successful removal of migrated acupuncture needles in a patient with cardiac tamponade by means of intraoperative transesophageal echocardiographic assistance. *J Thorac Cardiovasc Surg* 2005; 130: 210–12.
- Sughiura T, Nishida H, Ishitoya H, et al. Chronic expanding intrapericardial hematoma after pericardial paracentesis. *J Card Surg* 2006; 21: 491–3.
- Symbas PN, Vlasits-Hale SE, Picone AL, et al. Missiles in the heart. *Ann Thorac Surg* 1989; 48: 192–4.
- Symbas PN, Picone AL, Hatcher CR, et al. Cardiac missiles. A review of the literature and personal experience. *Ann Surg* 1990; 211: 639–47; discussion 47–8.
- LeMaire SA, Wall MJ Jr, Mattox KL. Needle embolus causing cardiac puncture and chronic constrictive pericarditis. *Ann Thorac Surg* 1998; 65: 1786–7.
- Actis Dato GM, Aidala E, Zattera GF. Foreign bodies in the heart: surgical or medical therapy? *Ann Thorac Surg* 1999; 68: 291–2.
- Zhang C, Hu J, Ni Y, et al. Successful salvage of post-traumatic metallic foreign body partially retained in the posterior papillary muscle of the left ventricle. *Interact Cardiovasc Thorac Surg* 2006; 5: 507–8.
- Katz NM, Blackstone EH, Kirklin JW, et al. Suture techniques for atrioventricular valves: experimental study. *J Thorac Cardiovasc Surg* 1981; 81: 528–36.
- Newton JR Jr, Glower DD, Davis JW, et al. Evaluation of suture techniques for mitral valve replacement. *J Thorac Cardiovasc Surg* 1984; 88: 248–52.
- Bowman MR, King RM. Comparison of staples and sutures for cardiorrhaphy in traumatic puncture wounds of the heart. *J Emerg Med* 1996; 14: 615–18.
- Lifschultz BD, Donoghue ER, Leestma JE, et al. Embolization of cotton pledgets following insertion of porcine cardiac valve bioprostheses. *J Forensic Sci* 1987; 32: 1796–800.
- Weingarten J, Kauffman SL. Teflon embolization to pulmonary arteries. *Ann Thorac Surg* 1977; 23: 371–3.

Injury to the Esophagus, Trachea, and Bronchus

Deborah L. Mueller

Clinical Question Summary		
Question	Answer	Grade of recommendation
What are the most common symptoms and signs of tracheobronchial injury?	Respiratory distress and subcutaneous emphysema/crepitus	B
What is the best diagnostic test for tracheobronchial injury?	Bronchoscopy	C
Is there a role for nonoperative management of traumatic tracheobronchial injuries?	Yes in patients with small <2 cm tears and a benign clinical presentation	C
What are the most common symptoms and signs of esophageal injury?	Pain (neck, chest, or on swallowing) and crepitus on physical exam	B
What is the best initial diagnostic test for esophageal injury?	Esophagography or esophagoscopy	C
Is there a role for nonoperative management of traumatic esophageal injury?	Not enough evidence to recommend for traumatic injuries at this time	D

David Hume, a Scottish philosopher, remarked that a wise man proportions his belief to the evidence. In the case of traumatic injuries to the esophagus and tracheobronchial tree, the evidence consists mostly of case reports, retrospective analyses, and opinions. The rarity of these injuries is perhaps the major culprit preventing the accumulation of significant prospective data in the literature. Even in a retrospective multicenter study involving 34 U.S. urban trauma centers focusing on outcomes of penetrating esophageal injuries, 357 years of data yielded slightly over one patient per year per center (1). This brief synopsis covers incidence, mechanism of injury, and current practices in the diagnosis and management of these rare injuries. It may not strengthen the wise physician's beliefs, but it accurately reflects the current evidence.

TRACHEA AND BRONCHUS

What Is the Incidence of Blunt and Penetrating Tracheobronchial Injuries?

Dated autopsy studies of blunt trauma patients reveal an incidence of tracheobronchial injury in 1–2.8% of fatalities (2,3). In a more recent review spanning nine years, only 16 of 12,789 trauma patients arriving at a Level I trauma center were identified with tracheobronchial injury for an overall incidence of 0.13% (4). This report included blunt and penetrating mechanisms of injury. When focusing exclusively on penetrating tracheobronchial injuries, it is helpful to distinguish between cervical and thoracic wounds.

Cervical tracheal injury occurred in 8% of patients in a contemporary study of penetrating neck injuries (5). In contrast, tracheobronchial injury is uncommon, with penetrating thoracic injuries occurring in less than 1% (6).

What Is the Mechanism for Penetrating and Blunt Tracheobronchial Injuries?

Although most penetrating injuries from knives and bullets require no explanation, the clothesline injury pattern is more unique. An obvious penetrating or subtle closed injury to the trachea can occur when a patient strikes an unseen wire while on a moving vehicle. All-terrain vehicles are the most recent addition to the list of vehicles in which a clothesline injury mechanism has been reported (7). Blunt cervical tracheal injury can occur from hyperextension or flexion and contact of the neck with the dashboard or steering wheel in a motor vehicle crash. It has also been described after a blow to the neck from a table corner, a knee, and bicycle handlebars in children (8). Blunt thoracic tracheobronchial injury has been reported more commonly after forceful anterior–posterior compression of the thoracic cage with presumed lateral traction, causing injury at the carina or by shearing forces exerted at the fixed carina (9). Additional reports suggest a closed glottis with high airway pressures may also lead to injury (10). In an analysis of 88 cases with the site of blunt tracheobronchial injury recorded, 76% occurred within 2 cm of the carina, lending credibility to the postulated mechanisms (11).

What Are the Most Reliable Initial Symptoms and Signs of Traumatic Tracheobronchial Injury?

Series that include data on symptomatology and physical findings report the most common symptom as respiratory distress in as many as 59% of patients and the most common physical finding as subcutaneous emphysema in as many as 81% of patients (8,12–14,29). The initial chest x-ray (CXR) findings of patients in one of these series demonstrated subcutaneous emphysema in 81%, pneumothorax in 56% and pneumomediastinum in 37% (14). In most case series in the literature, there are occasional patients with a delay in diagnosis due to minimal symptoms and findings or due to findings that are attributed to other etiologies (9).

What Is the Best Diagnostic Test for Traumatic Tracheobronchial Injury?

Certain patients with airway injury will have obvious findings on physical exam, such as air bubbling from a penetrating neck wound. An additional subset of patients will require operative intervention immediately for injury to adjacent vascular structures leading to discovery of airway injury. Patients with a blunt mechanism of injury can be more difficult to diagnose.

Though an initial CXR may demonstrate an abnormality, it can be normal in 12% of patients on presentation (14). In addition, the findings on abnormal CXRs such as subcutaneous emphysema, pneumothorax and pneumomediastinum are not specific for tracheobronchial injury. In a recent review of 51 blunt thoracic trauma patients who had a CXR followed by chest computed tomography (CT) demonstrating pneumomediastinum, only 10% had tracheobronchial injury (15). More often pneumomediastinum was ascribed to the Macklin effect, originally described in 1939 when blunt alveolar rupture leads to air dissection along bronchovascular sheaths and into the mediastinum.

In this era of high-quality, immediately available, rapid imaging with CT, many stable patients will undergo chest CT as part of their trauma evaluation. In a retrospective review of 18 patients with either blunt or penetrating tracheobronchial injury who underwent both chest CT and bronchoscopy, Scaglione et al. described radiologic findings that showed the site of injury was detectable by CT in 94% of cases (16). Findings included over distension of the endotracheal cuff (>4cm), endotracheal cuff herniation through a tracheal wall defect, displacement of the endotracheal tube, tracheal/bronchial wall discontinuity, enlargement of the bronchus, and the “fallen lung” sign. There was no comparison group in this retrospective review of patients without tracheobronchial injuries, and these scans were read by experienced radiologists with extensive reformatting of some of the images. In a prospective trial of multislice CT angiography (CTA) for penetrating cervical wounds, although CTA was sensitive for aerodigestive injury, it lacked specificity because the most common finding was nonspecific subcutaneous air (5). Four of five false-positive CTAs were suspicious for aerodigestive injury that was subsequently ruled out by operative exploration or other diagnostic modalities.

Bronchoscopy with direct visualization of the airway remains the best diagnostic tool for tracheobronchial injury. Though most injuries are obvious, a few can be more

subtle to the eye. Peribronchial tissue can make the airway tree seem intact with only slight distraction of the cartilaginous rings (9,17). Kiser et al. found reports of 46 patients with repair of chronic tracheobronchial obstruction from 3 months to 34 years after injury (11). Repeat bronchoscopy may be necessary if suspicion for the injury is high but the initial bronchoscopy appeared normal.

What Are the Surgical Management Options for Tracheobronchial Injuries?

The principles of surgical repair are for the most part consistent throughout the literature (4,12–14). The cervical trachea is approached through a collar or anterior sternocleidomastoid incision, whereas the mediastinal trachea and right mainstem bronchus are best approached through a right posterolateral thoracotomy at the level of the fifth rib to avoid the aorta. The left mainstem bronchus is best approached through a left posterolateral thoracotomy. The high mediastinal tracheal injury with associated vascular injury may also be approached through a sternotomy incision (14). Debridement of devitalized tissue is recommended with the use of absorbable sutures with knots secured exterior to the airway to prevent granulation tissue formation in the airway. Minimal dissection of the lateral aspects of the trachea is recommended to prevent ischemia to the repair. The use of a tracheostomy, though touted by some authors, is discouraged by others who suggest extubation without a tracheostomy or endotracheal tube avoiding positive pressure ventilation in the postoperative period would be best for healing of the injury (12).

In the setting of larger destructive wounds, several centimeters of trachea can be resected and primary anastomosis performed. More length can be obtained if spine fracture has been eliminated and the neck can be flexed. There are additional maneuvers to gain length for a tracheal repair that are beyond the scope of this chapter. Most authors recommend buttressing of complex repairs with flaps of pericardium or intercostal muscle in the chest or strap muscles or the sternocleidomastoid in the neck (4,12–14). Alternatively, the use of a silicone T-tube placed in the trachea to extend from below the vocal cords to the carina with an airway maintained by cannulating the horizontal exteriorized limb with an endotracheal tube has been described in at least 16 traumatic tracheal injuries (18). This maneuver can allow damage control in an unstable patient with repair of the airway in a more elective manner or the T-tube can serve as a stent while healing by secondary intention occurs.

What Is the Role of Nonoperative Management for Tracheobronchial Injuries?

Nonoperative management of small, iatrogenic injuries of the trachea sustained during endotracheal intubation has been described by multiple authors (19–21). The largest of these types of injuries managed nonoperatively was 4cm (20). Duval et al. described five children with noniatrogenic traumatic tracheobronchial injuries that were successfully managed nonoperatively with intubation and antibiotics (8). A retrospective review at one institution over a 10-year period in adults described a nonoperative approach for both iatrogenic and traumatic tracheobronchial injuries (12). Though 89% of iatrogenic intubation

injuries in these adults were managed nonoperatively, only 27% of traumatic injuries met their criteria to be managed nonoperatively. Surgical management was performed if patients had concomitant esophageal injury, progressive subcutaneous or mediastinal emphysema, severe dyspnea requiring intubation, difficulty with mechanical ventilation, pneumothorax with a persistent air leak, presence of an open tracheal injury, or mediastinitis. The traumatic injuries managed nonoperatively were all blunt mechanism small (<2cm) injuries. Interestingly, they followed patients for up to two years with repeat bronchoscopy and the incidence of scarring, granuloma formation, and stenosis did not appear significantly different between the nonoperative and operative management groups.

It may be reasonable to allow some tracheobronchial injuries to heal by secondary intention if the patient has no associated injuries requiring surgical repair, no significant respiratory difficulty, no persistent air leak, and well-opposed edges at the site of injury. Antibiotic utilization to prevent mediastinitis is described in all of these nonoperative approaches. It is important to remember that the numbers of patients in all of these reports whether operative or nonoperative is incredibly small and therefore the only evidence we have is past experience.

ESOPHAGUS

What Is the Incidence of Blunt and Penetrating Esophageal Injuries?

Autopsies from all fatal traffic accidents occurring in one metropolitan area demonstrated blunt esophageal injury is rarer than tracheobronchial injury, even in the worst motor vehicle collisions occurring in only 1 of 585 victims or 0.2% (3). In blunt trauma patients arriving at a hospital, Beal et al. found three esophageal injuries in 2,560 patients for an incidence of 0.001% (22). Not surprisingly, in studies of penetrating trauma, the incidence of esophageal injury, both cervical and thoracic, is nearly identical to the incidence of penetrating tracheobronchial injury. Cervical esophageal injuries occurred in 8.5% of penetrating neck wounds, and thoracic esophageal injuries occurred in 1.2% of penetrating thoracic wounds (23,24).

What Is the Mechanism for Penetrating and Blunt Esophageal Injuries?

The most common mechanism for penetrating esophageal injury is iatrogenic endoscopic perforation, with rates of perforation escalating significantly when therapeutic interventions are undertaken, such as dilation for achalasia (25). Although many articles in the literature lump iatrogenic and noniatrogenic injuries together to achieve a better number of injuries to analyze, the average trauma patient has significant other associated injuries that may affect the presentation, management, and outcome of esophageal injuries. The focus of this chapter remains strictly penetrations from knives and bullets, which require no explanation but do allow a more narrow focus on the true presentation, diagnosis, and management of these specific types of injuries.

Blunt cervical esophageal injury is thought to occur from a sudden blow to a hyperextended neck and either the steering wheel or dashboard, similar to cervical tracheal

injury with the esophagus stretched against the cervical spine (26). In the most extensive review published of 63 patients with blunt esophageal injury, Beal et al. demonstrated that 82% of the injuries occurred in the cervicothoracic esophagus, defined as the esophagus from origination to the tracheal carina (22). Interestingly, in this same series 56% had concomitant tracheal injuries. When both the trachea and esophagus are injured at the level of the carina, Martel et al. reviewing 20 cases of blunt tracheoesophageal injury suggest that this traumatic disruption is best described as “acute tracheoesophageal burst injury” and is the result of an acute increase in tracheal intraluminal pressure after rapid compression of the thoracic cavity with a closed glottis, which leads to rupture of the membranous trachea and the adjacent esophagus (27). This mechanism was delineated most clearly in a case report by Martin de Nicolas et al. when a 14-year-old boy was struck abruptly in the chest while lying flat and sustained a tracheoesophageal injury (10). The majority of these combined tracheoesophageal injuries occur in young patients without accompanying rib fractures, which Martel and colleagues suggest demonstrates that the rapid compressive force to an elastic chest cavity causes a pneumatic blast in the distal trachea as the pulmonary alveoli empty rupturing the trachea and then the esophagus (27).

What Are the Most Reliable Initial Symptoms and Signs of Traumatic Esophageal Injury?

In a large retrospective series of 405 penetrating esophageal injuries, Asensio et al. state that most patients had no symptoms or signs on initial presentation (1). However, if one looks closely at the hospital course of these patients, the early mortality defined as death in the emergency room or operating room was 14.6%. These patients may have had symptoms or signs of esophageal injury, but the urgency of their other injuries probably superseded any detailed examination or documentation. Another 175 patients went directly to the operating room, and careful evaluation for symptoms or signs may also have been appropriately abbreviated. Delving into single-center studies of penetrating cervical trauma, several authors report symptoms or signs were present in 70–100% of patients with esophageal injury (28–30,37). The symptoms mentioned in these studies include dysphagia, odynophagia, dysphonia, hoarseness, and hematemesis. Beal et al. demonstrated that 66% of patients with blunt esophageal injury had symptoms including neck pain, chest pain, dyspnea, dysphagia, and/or hoarseness (22).

The most reliable physical exam finding was subcutaneous emphysema in both blunt and penetrating esophageal injuries. This sign was found in 33% of patients sustaining blunt esophageal injury and 45% of patients sustaining penetrating esophageal injury (22,31). The most likely etiology for crepitus on palpation is a concomitant tracheal injury, as the incidence of this finding drops to 13% in blunt trauma patients and 28% in penetrating trauma patients when only the esophagus is injured (22,32). The presence of subcutaneous cervical emphysema or pneumomediastinum was also the most common finding on initial x-rays occurring in 30–40% of patients with both mechanisms of injury (22,31). It is important to note that based on these more detailed studies in regards to signs and symptoms, 25% of patients may still be completely

asymptomatic, with minimal physical findings and normal initial x-rays.

What Is the Best Diagnostic Test for Traumatic Esophageal Injury?

The overall mortality rates in the largest series of blunt and penetrating esophageal injuries in the literature were high at 17% and 19%, respectively (1,22). The majority of the deaths in the penetrating group occur early from associated injuries, and most of these patients go directly to the operating room with no diagnostic work-up. In patients stable enough to undergo diagnostic studies, though, it does appear that infectious morbidity is increased secondary to the delay in operative repair that occurs with a lengthy diagnostic work-up, which took a mean of 13 hours in the largest retrospective review of penetrating injuries (1). Although this large study didn't demonstrate a difference in mortality secondary to delays in diagnosis, several single-center reviews of esophageal perforation have (32,37,40,41). This section will focus on the diagnosis of esophageal injury in the stable trauma patient.

The rapid, readily available, noninvasive CT scan is emerging as a screening test for esophageal injury in both blunt and penetrating trauma. In blunt trauma patients, there are often indications to CT scan the neck and chest for other types of injuries. In stable gunshot wound penetrating injury patients the CT scan can usually demonstrate the trajectory of a bullet. If the tract is clearly remote from the vascular and aerodigestive structures, the CT may eliminate a substantial number of additional studies, such as angiography and esophagography (33,34). In stable knife penetrating injury patients, the trajectory can be much more difficult to appreciate. Castelguidone and colleagues have described retrospectively the CT findings in six patients with traumatic esophageal injuries (35). The most common findings were periesophageal air and fluid in 83% and esophageal wall thickening in 66%. Other, more non-specific findings included pneumothorax, pleural effusion, and subcutaneous emphysema. It is important to note that in a prospective study of CT angiography for stable asymptomatic patients with zone II penetrating neck wounds in which every patient had CTA followed by subsequent operative exploration, two esophageal injuries were missed (36). Both injuries were from knives and described as less than 5 mm in size. These two patients had also undergone barium esophagography preoperatively, which also missed these small injuries. Endoscopy was not utilized in this study. A multiyear multi-institutional study would be necessary to truly define the most sensitive and specific CT findings of esophageal injury. CT will probably remain most useful as a tool to exclude penetrating injury if a bullet trajectory can clearly be defined completely away from the esophagus without retained fragments causing artifact.

The most methodologically sound study of diagnostic techniques for esophageal injuries remains a prospective study in 118 stable patients with penetrating Zone II and III injuries performed in the early 1980s (28). After consent, patients underwent angiography and barium esophagography, followed by a trip to the operating room for exploration. Prior to surgical exploration, fiber optic and rigid endoscopy were both performed by an endoscopist unaware of the barium esophagography results. Sensitivity and specificity were calculated for each diagnostic technique.

Barium esophagography had a sensitivity of 89% and a specificity of 100%, flexible esophagoscopy had a sensitivity of 37% and a specificity of 99%, and rigid esophagoscopy had a sensitivity of 89% and specificity of 95%. Weigelt et al. therefore summarized that patients should undergo barium esophagography first. If an injury is seen, the patient should proceed to neck exploration, but if the study is equivocal, a rigid esophagoscopy should be performed.

Subsequently, several small retrospective studies evaluating the role of flexible endoscopy in the diagnosis of esophageal trauma have been published. The sensitivity of flexible endoscopy reported in these trials ranged from 67% to 100% with specificities also of 67–100% (37–39). Perhaps the improvement in sensitivity in these studies was secondary to technological advances in the equipment with substantial improvement in resolution and magnification over time, or perhaps it is just a sequela of weaker study design. There are clearly some advantages to flexible endoscopy, one of which is the ability to perform it in any location. Flowers et al. performed 65% of their endoscopies in the emergency room with an average time between presentation and procedure of 2.6 hours (38). Though rigid esophagoscopy can probably be performed as expediently, it requires endotracheal intubation and general anesthesia. In addition, in blunt trauma patients with unclear cervical spine status, the procedure cannot be performed.

The choice of initial diagnostic test should probably be the one that can be performed most expediently at any individual institution and is most appropriate for the clinical scenario of the patient. Flexible esophagoscopy can be done in the emergency room, and more recent studies show improved sensitivity, so it may be a reasonable test to start with. If the study is positive, the patient can go to the operating room for exploration. There will be false-positive exams, predominantly from blood clot seen in the esophagus, but a limited number of negative explorations seems warranted given the gravity of a missed injury (38,39). Likewise, esophagography is a reasonable first test as well, if readily available, given the reported sensitivity and specificity. In either case, if one test is equivocal, the second study should be undertaken to try to ensure minimization of missed injuries. The role of rigid esophagoscopy cannot be dismissed given the lack of a prospective contemporary trial to demonstrate that flexible esophagoscopy is equivalent for diagnosis. Unfortunately as the pendulum has swung away from mandatory exploration for penetrating neck trauma, it is unlikely that any further strict prospective data will emerge. Because rigid esophagoscopy requires general anesthesia and intubation, it doesn't seem logical as an initial diagnostic tool. It is important to remember that if an injury is suspected in the proximal esophagus, rigid esophagoscopy is probably a better endoscopic choice because the flexible scope is often routinely passed blindly in this area, and hence there appears to be a higher incidence of false negatives with the flexible technique in this location (37).

What Are the Surgical Management Options for Esophageal Injuries?

The surgical options described in the literature range from primary repair to multiple variations on diversion with drainage (31,37,40–42). Primary repair has been described

with both single-layer and two-layer closures of the esophagus after debridement of devitalized tissue (31,41,42). Drainage as an adjunct to primary repair was used in the majority of patients in the largest studies of noniatrogenic penetrating esophageal injuries (1,42). Buttressing of repairs with flaps of muscle, pleura, pericardium, omentum, and stomach have all been described, and their use seems predicated on the amount of local tissue destruction, injuries to adjacent structures such as the trachea, and the location of the primary injury (1,23,27,31,40–42). After primary repair, the most common procedure performed in the largest studies of both penetrating and blunt esophageal injury was drainage alone (1,22). More complex esophageal resection, exclusion, or diversion only occurred in 7% of penetrating esophageal injuries and 9% of blunt esophageal injuries. Instead of resection, Richardson and colleagues suggest that patients with large defects not amenable to primary repair are candidates for primary muscle flap closure (41). In his review of factors that affected mortality, surgical management with esophageal exclusion and diversion was statistically significant for an increase in mortality. These patients in all likelihood had more severe injuries, but that is difficult to elucidate from the article.

Past experience would therefore suggest that primary repair with drainage is appropriate in most patients. Primary repair without drainage for simple stab wounds with minimal tissue destruction is also reasonable. Drainage alone if the injury is difficult to identify or the patient's condition warrants abbreviated surgery is a reasonable choice as well. Finally, more extensive esophageal surgery such as diversion, resection with or without anastomosis, or exclusion may be necessary but portends a poor prognosis similar to delays in diagnosis.

Is There Any Role for Nonoperative Management in Traumatic Esophageal Injury?

In some reviews of esophageal perforation there seems to be a category of conservative or nonoperative management (25,37,40). Looking closely at these reviews, most articles have a mix of etiologies for the perforation including iatrogenic, external trauma, emetogenic, and foreign body ingestion. On further inspection, almost none of the external trauma patients were managed nonoperatively except in a few studies from South Africa (42,43).

Smakman et al. reported on two patients managed nonoperatively (42). One had arrived in a delayed fashion with nonoperative management instituted at another facility and appeared to be doing well, so it was continued. The second patient had what appeared to be a sealed-off small thoracic perforation at endoscopy. It is impossible to discern whether this was a false-positive endoscopy or a true injury. These patients were hospitalized an average of 22 days for unclear reasons. Mandiba et al. reported on 17 patients with esophageal injury managed nonoperatively after penetrating cervical trauma, which represented 61% of patients identified with this injury in a five-year retrospective review (43). Criteria for nonoperative management included a contained extravasation on esophagography with no other indication for operative intervention. These patients were managed with enteral tube feeds and antibiotics. The median hospital stay was 18 days for all patients but any difference between the operative and nonoperative groups in regard to length of stay was not discussed. One patient (6%) of those managed conservatively subsequently developed local sepsis requiring operative intervention. Although this approach was relatively effective for this subset of esophageal injuries, it may not be very efficient.

Levels of Evidence

Author	Ref.	Year	Design	Level of evidence
Asensio	1	2001	Retrospective multicenter outcomes study	SX IIb
Beal	22	1988	Retrospective very limited population	SX IIIa
Cassada	13	2000	Retrospective single-center case series	SX IIIb
				DX IV
Castelguidone	35	2006	Prospective single-center case series	DX V
Conti	20	2006	Retrospective single-center case series	TH IV
Demetriades	29	1997	Prospective single-center study	SX Ib
Duval	8	2007	Restrospective two-center case series	TH IV
				SX IIIb
				DX IV
Flowers	38	1996	Retrospective single-center case series	DX IV
Gomez-Caro	12	2006	Retrospective single-center case series	TH IV
				SX IIIb
				DX IV
Gonzalez	36	2003	Prospective single-center study	DX IIb
Inaba	5	2006	Prospective single-center study	DX IIb
Jougon	21	2000	Retrospective single-center case series	TH IV
Mandiba	43	2003	Retrospective single-center case series	TH IV
Rossbach	14	1998	Retrospective single-center case series	SX IIIb
				DX IV
Scaglione	16	2006	Retrospective single-center case series	DX IV
Smakman	42	2004	Retrospective single-center case series	TH IV
Srinivasan	39	2000	Retrospective single-center case series	DX IV
Vassiliu	30	2001	Retrospective single-center case series	SX IIb
Weigelt	28	1987	Prospective single-center study	SX Ib
				DX IIb
White	37	1992	Retrospective single-center case series	DX IV

Note: Using the Oxford Centre for Evidence-based Medicine Levels of Evidence, studies may be classified differently according to the topic addressed. Studies used in more than one category are given a level based on each category as follows.

Abbreviations: DX, diagnosis; PR, prognosis; SX, differential diagnosis/symptom prevalence; TH, therapy, prevention, etiology, harm.

REFERENCES

- Asensio JA, Chahwan S, Forno W, et al. Penetrating esophageal injuries: multicenter study of the American Association for the Surgery of Trauma. *J Trauma* 2001; 50: 289–96.
- Bertelsen S, Howitz P. Injuries of the trachea and bronchi. *Thorax* 1972; 27: 188–94.
- Kemmerer WT, Eckert WG, Gathright JB, et al. Patterns of thoracic injuries in fatal traffic accidents. *J Trauma* 1961; 1: 595–9.
- Huh J, Milliken JC, Chen JC. Management of tracheobronchial injuries following blunt and penetrating trauma. *Am Surg* 1997; 63: 896–9.
- Inaba K, Munera F, McKenney M, et al. Prospective evaluation of screening multislice helical computed tomographic angiography in the initial evaluation of penetrating neck injuries. *J Trauma* 2006; 61: 144–9.
- Inci I, Ozelik C, Tacyildiz I, et al. Penetrating chest injuries: unusually high incidence of high-velocity gunshot wounds in civilian practice. *World J Surg* 1998; 22: 438–42.
- Graham J, Dick R, Parnell D, et al. Clothesline injury mechanism associated with all-terrain vehicle use by children. *Pediatric Emergency Care* 2006; 22: 45–7.
- Duval EL, Geraerts SD. Management of blunt tracheal trauma in children: a case series and review of the literature. *Eur J Pediatr* 2007; 166: 559–63.
- Kirsh MM, Orringer MB, Behrendt DM, et al. Management of tracheobronchial disruption secondary to nonpenetrating trauma. *Ann Thorac Surg* 1976; 22: 93–101.
- Martin de Nicolas JL, Gamez AP, Cruz F, et al. Long tracheobronchial and esophageal rupture after blunt chest trauma: injury by airway bursting. *Ann Thorac Surg* 1996; 62: 269–72.
- Kiser AC, O'Brien SM, Detterbeck FC. Blunt tracheobronchial injuries: treatment and outcomes. *Ann Thorac Surg* 2001; 71: 2059–65.
- Gomez-Caro A, Ausin P, Moradiellos FJ, et al. Role of conservative medical management of tracheobronchial injuries. *J Trauma* 2006; 61: 1426–35.
- Cassada DC, Munyikwa MP, Moniz MP, et al. Acute injuries of the trachea and major bronchi: importance of early diagnosis. *Ann Thorac Surg* 2000; 69: 1563–7.
- Roszbach MM, Johnson SB, Gomez MA, et al. Management of major tracheobronchial injuries: a 28-year experience. *Ann Thorac Surg* 1998; 65: 182–6.
- Wintermark M, Schnyder P. The Macklin effect: a frequent etiology for pneumomediastinum in severe blunt chest trauma. *Chest* 2001; 120: 543–7.
- Scagilone M, Romano S, Pinto A, et al. Acute tracheobronchial injuries: impact of imaging on diagnosis and management implications. *European Journal of Radiology* 2006; 59: 336–43.
- Allan PF, Kelley TC, Taylor TL, et al. Bronchial transection: diagnosis and management. *Clin Pulm Med* 2006; 13: 203–8.
- Miller BS, Shafi S, Thal ER. Damage control in complex penetrating tracheal injury and silicone T-tube. *J Trauma* 2008; 64: E18–E20.
- Ross HM, Grant FJ, Wilson RS, et al. Nonoperative management of tracheal laceration during endotracheal intubation. *Ann Thorac Surg* 1997; 63: 240–2.
- Conti M, Pougeoise M, Wurtz A, et al. Management of postintubation tracheobronchial ruptures. *Chest* 2006; 130: 412–18.
- Jougon J, Ballester M, Choukroun E, et al. Conservative treatment for postintubation tracheobronchial rupture. *Ann Thorac Surg* 2000; 69: 216–20.
- Beal SL, Pottmeyer EW, Spisso JM. Esophageal perforation following external blunt trauma. *J Trauma* 1988; 28: 1425–32.
- Winter RP, Weigelt JA. Cervical esophageal trauma incidence and cause of esophageal fistulas. *Arch Surg* 1990; 125: 849–51.
- Cornwell EE, Kennedy F, Ayad IA, et al. Transmediastinal gunshot wounds a reconsideration of the role of aortography. *Arch Surg* 1996; 131: 949–53.
- Plott E, Jones D, McDermott D, et al. A state-of-the-art review of esophageal trauma: where do we stand? *Dis Esoph* 2007; 20: 279–89.
- Stringer WL, Kelly DL Jr, Johnston FR, et al. Hyperextension injury of the cervical spine with esophageal perforation. Case report. *J Neurosurg.* 1980; 53: 541–3.
- Martel G, Al-Sabti H, Mulder D, et al. Acute tracheoesophageal burst injury after blunt chest trauma: case report and review of the literature. *J Trauma* 2007; 62: 236–42.
- Weigelt JA, Thal ER, Snyder WH, et al. Diagnosis of penetrating cervical esophageal injuries. *Am J Surg* 1987; 154: 619–22.
- Demetriades D, Theodorou D, Cornwell E, et al. Evaluation of penetrating injuries of the neck: prospective study of 223 patients. *World J Surg* 1997; 21: 41–48.
- Vassiliu P, Baker J, Henderson S, et al. Aerodigestive injuries of the neck. *Am Surg* 2001; 67: 75–79.
- Glatterer MS, Toon RS, Ellestad C, et al. Management of blunt and penetrating external esophageal trauma. *J Trauma* 1985; 25: 784–92.
- Sheely CH, Mattox KL, Beall AC, et al. Penetrating wounds of the cervical esophagus. *Am J Surg* 1975; 130: 707–10.
- Woo K, Magner D, Wilson M, et al. CT angiography in penetrating neck trauma reduces the need for operative neck exploration. *Am Surg* 2005; 71: 754–8.
- Hanpeter DE, Demetriades D, Asensio JA, et al. Helical computed tomographic scan in the evaluation of mediastinal gunshot wounds. *J Trauma* 2000; 49: 689–95.
- Castelguidone E, Merola S, Pinto A, et al. Esophageal injuries: spectrum of multidetector row CT findings. *Eur J Rad* 2006; 59: 344–8.
- Gonzalez RP, Faliminski M, Holevar MR. Penetrating zone II neck injury: does dynamic computed tomographic scan contribute to diagnostic sensitivity of physical examination for surgically significant injury? A prospective blinded study. *J Trauma* 2003; 54: 61–5.
- White RK, Morris DM. Diagnosis and management of esophageal perforations. *Am Surg* 1992; 58: 112–19.
- Flowers JL, Graham SM, Ugarte MA, et al. Flexible endoscopy for the diagnosis of esophageal trauma. *J Trauma* 1996; 40: 261–6.
- Srinivasan R, Haywood T, Horwitz B, et al. Role of flexible endoscopy in the evaluation of possible esophageal trauma after penetrating injuries. *Am J Gastroenterol* 2000; 95: 1725–9.
- Goldstein LA, Thompson WR. Esophageal perforations: a 15 year experience. *Am J Surg* 1982; 143: 495–503.
- Richardson JD, Martin LF, Borzotta AP, et al. Unifying concepts in treatment of esophageal leaks. *Am J Surg* 1985; 149: 157–62.
- Smakman N, Nicol AJ, Walther G, et al. Factors affecting outcome in penetrating oesophageal trauma. *Br J Surg* 2004; 91: 1513–19.
- Madiba TE, Muckart DJJ. Penetrating injuries to the cervical oesophagus: is routine exploration mandatory? *Ann R Coll Surg Engl* 2003; 85: 162–6.

An Evidence-Based Approach to Spleen Trauma: Management and Outcomes

Anne Saladyga and Robert Benjamin

Clinical Questions			
Questions	Answers	Level of evidence	Grade of recommendation
What is the role of nonoperative management in penetrating spleen injury?	Very little. Has 93% failure rate.		No recommendation
Which patients are candidates for nonoperative management of blunt spleen injury, and who is likely to fail?	- Hemodynamically stable patient with reliable abdominal examination is standard.	IIA	B
	- SAE can augment nonoperative management.	IIA	B
	- Age should not exclude a patient from nonoperative management. Older patients' increased mortality is a function of their decreased overall reserve.	IIC	No recommendation
	- >2 units PRBCs greatly increase chance of nonoperative management failure.	IIA	B
	- Evidence of contrast extravasation or other vascular injury increases chance of failure.		B
Which patients are angiography candidates, and who fail embolization?	- SAE can improve nonoperative management in stable patients with CT scans showing	IIA	B
	1. Grade III–V injury 2. Contrast extravasation 3. Concern for pseudo-aneurysm or arteriovenous fistula - There are conflicting data concerning factors indicative of embolization failure.	IIA	No recommendation
What radiologic studies should be obtained in patients with splenic injuries?	- Patients should undergo FAST exam in trauma room.	IIA	B
	- Stable patients with blunt mechanism should undergo abdomen/pelvis CT scan.	IIA	B
	- Imaging has highest yield when clinical symptoms of failure are present.	IIA	B
	- There is conflicting evidence about inpatient imaging studies.		No recommendation
	- Outpatient imaging is of little use in asymptomatic patients.		B
What are the steps to prevent OPSS?	- Intact, functional spleen is best defense against OPSS,	IIA	B
	- Up-to-date immunization recommendations can be found on the CDC Web site,	IIA	B
	- Pneumococcus, meningococcus, and Hib vaccine should be given >14 days postsplenectomy, may not be feasible in trauma population,	IIA	B
When is it safe to resume activities after splenic injuries?	- Refer to APSA's 2000 recommendations	IC	B
	- Graduated return based on injury severity, both inpatient and outpatient		
	- Reimaging as outpatient unnecessary without clinical indicators		
How are patients with special circumstances managed nonoperatively?	- Pediatric patients should be managed according to AAPSA 2000 guidelines for splenic injuries.	IIA	B
	- Cirrhotics do much worse. Carries 50% overall mortality.		No recommendation
	- Anticoagulation administration has few data.		No recommendation

Abbreviations: APSA, American Pediatric Surgical Association; CDC, Centers for Disease Control and Prevention; CT, computed tomography; FAST, focused abdominal sonography for trauma; Hib, Haemophilus influenza B; OPSS, overwhelming postsplenectomy sepsis; PRBCs, packed red blood cells; SAE, splenic artery aneurysm.

INTRODUCTION

The spleen is a solid organ that sits in the left upper quadrant of the abdominal cavity. It is frequently injured in both blunt and penetrating traumatic events. According to the National Trauma Data Bank during the years from 2002 to 2006 there were 35,414 traumatic spleen injuries. These injuries resulted in 3,796 deaths for a mortality rate of 10.7% (1). The incidence of injury has been increasing since the mid-twentieth century and the proportion of penetrating injuries has increased as well. Penetrating mechanisms currently account for 15% of spleen injuries (1,2). Recent technological improvements in diagnostic and interventional techniques have invalidated the old surgical dogma of mandatory exploration of splenic injuries. One of the driving forces behind splenic salvage has been overwhelming postsplenectomy sepsis (OPSS), which was first described in children after splenectomy (2,3). OPSS, as its name describes, is a systemic infectious condition most frequently due to encapsulated organisms in asplenic patients. The movement toward splenic preservation was a response to the significant morbidity and mortality of OPSS. The era of nonoperative management has been augmented with the addition of routine diagnostic imaging and therapeutic angiography, but new questions have arisen. This chapter attempts to answer some of the current management controversies involving traumatic spleen injury by evaluating relevant Class I–III data and developing evidence-based recommendations.

WHAT IS THE ROLE OF NONOPERATIVE MANAGEMENT IN PENETRATING SPLEEN INJURY?

Many Class II and III articles with prospective observation and retrospective analysis have been written purporting the safety of selective nonoperative management in penetrating abdominal wounds. These articles stress that the ideal candidate for nonoperative management of penetrating wounds to the abdomen is hemodynamically stable, without peritonitis, and have a reliable clinical exam (4–6). In-house surgical staff are required to perform serial clinical exams and detect a change in condition without delay. These studies also validate computed tomography (CT) scan as a comprehensive means for diagnosis and follow-up (6).

However, when the spleen is involved in a penetrating injury, the outcome for salvage is not promising. Demetriades published a prospective observational study on selective nonoperative management of patients with penetrating abdominal solid organ injury. This protocol-driven study included immediate laparotomy for patients with hemodynamic instability, peritonitis, unreliable abdominal exam, or CT scan indicative of hollow organ injury. Only 1 of the 28 patients with penetrating splenic injuries had successful nonoperative management (7).

Recommendations

Management of penetrating abdominal trauma with splenic injury remains exploratory laparotomy. The literature does not support nonoperative management. The best Class II study had a small population, and only 3.5% of those with the spleen involved had successful nonoperative management. A lack of Level I evidence precludes grade A

treatment recommendations to diverge from the current standards.

WHICH PATIENTS ARE CANDIDATES FOR NONOPERATIVE MANAGEMENT OF BLUNT SPLEEN INJURY AND WHO IS LIKELY TO FAIL?

In the past 15 years, selective nonoperative management of blunt abdominal solid organ trauma has become the standard of care (8). The impetus for splenic salvage included the risks of negative laparotomy and OPSS (2,9). Patients that qualify for nonoperative management are hemodynamically stable, without peritonitis, and have a reliable and a reproducible physical exam (9). Data from Shaftan showed that physical examination of the abdomen reliably predicts the need for laparotomy in trauma patients (10). Nonoperative management failure is defined as patients who require surgical exploration in an attempt to correct ongoing hemorrhage. Strict adherence to a protocol based on these criteria has been shown to increase salvage rates from 56% to 88% and decrease mortality rate from 11.7% to 5.5% (11).

The gold standard for blunt trauma abdominal evaluation in the stable patient is the abdominal CT scan (12,13). CT scan findings of contrast extravasation, pseudoaneurysm, or arteriovenous malformation increase the risk of failing nonoperative management 40–67% (14,15). Other CT scan findings indicative of failure include Grade III or higher injury and large hemoperitoneum, which increase the risk 12–13% (14). Peitzman stratified the risk of failure according to injury grade: Grade III 19%, Grade IV 33%, and Grade V 75%. He also noted that increasing injury grade is directly proportional to the amount of hemoperitoneum, and this combination is the most predictive of failure (9). Large hemoperitoneum is defined as abdominal free fluid extending from the splenic recess to the pelvis, whereas small and moderate hemoperitoneum is free fluid contained in the splenic recess and free fluid extending into the pericolic gutters (14,16). The therapeutic options for these findings are institutionally dependent and are discussed in the next sections concerning angiography and surveillance.

Associated injuries revealed by CT scan or physical exam were present in 52% of nonoperative failures, compared to 20% of successes (17). Management of associated injuries sometimes require interventions that preclude a reliable abdominal exam (18,19). There is no recent Class II or III article that studies this scenario in depth. Thus, it is up to the individual surgeon to keep the entire patient and injuries in mind when deciding how to manage a splenic injury.

The management of older patients with splenic injuries has been the subject of debate in recent literature. Patients older than 55 have a 20–30% chance of failing nonoperative management (20,21). Bee et al. found that 22% of those patients over 55 failed nonoperative management compared to 6% of those younger than 55 (14). The mortality rate of those older patients who have successful nonoperative management is 8%, whereas younger patients have a mortality rate of 4%. For those patients over 55 who fail nonoperative management, the mortality rate was 29% compared to 12% of those younger than 55 (22). In multiple studies, the cause of death in the elderly was due to associated injuries, such as closed head injuries, multisystem organ failure, and acute respiratory distress syndrome

(21,23,24). Elderly trauma patients as a population have higher mortality rate compare to those younger than 55. This was true whether they underwent nonoperative management or had immediate operative therapy. In fact, elderly patients who failed nonoperative management had a lower mortality rate than those elderly patients who had immediate laparotomy (20,24). Nix et al. found that the elderly had a 40% mortality with immediate laparotomy, 13% mortality with failed nonoperative management, and 14% mortality with successful nonoperative management (24). This factor is attributed to their limited pulmonary and metabolic reserve as well as their many comorbidities, which prevent healing of multiple injuries (25).

Another indicator of failure for nonoperative management of blunt splenic injury is blood transfusions within the first 24 hours of presentation. Most nonoperative management protocols have a first 24-hour transfusion limit that alerts physicians to ongoing bleeding (14,26). This was derived from the literature, which shows that patients who were successfully managed nonoperatively received a mean of 1.2–1.9 units of blood within the first 24 hours of presentation. Those who received more than 6 units had a statistically significant higher mortality rate, incidence of splenectomy, and infectious complications (9,18,22). Velmahos and colleagues confirmed this finding in a prospective observation study evaluating the risk factor indicative of failing nonoperative management. He found that patients who failed nonoperative management received a mean of 1.7 units of blood in the first six hours of management compared to the successful management who received 0.4 units in the first six hours (27).

Recommendations

The data are based on prospective Class II and multiple large retrospective Class III studies. Recommendations are IIA and IIC.

1. (Level IIA) Algorithm-driven protocols for selective nonoperative management of splenic trauma have shown to be successful with increased splenic salvage, decreased cost, and decreased mortality. They should be used as the standard for selective management of blunt splenic injury for hemodynamically stable patients without peritonitis and with a reliable clinical exam. There are two well-done Class II prospective studies by Brasel and Meguid. Although these studies reviewed a small number of patients, they are supported by large retrospective reviews which support their findings.
2. (Level IIA) Patients who have CT scan findings consistent with ongoing bleeding or large hemoperitoneum should be evaluated by adjunctive measures or surgical management because these findings are associated with a high nonoperative management failure rate.
3. There are no available data to change the standard of care for patients going to the operating room for associated injury. The decision to observe or to perform laparotomy is based on the surgeon's judgment of the patient's status.
4. (Level IIC) Large retrospective studies and some with comparative controls to younger patients. Age should not be an exclusion criterion for selective nonoperative management of blunt splenic injury because 70–80% of these patients will have successful splenic salvage.
5. (Level IIA) Data from large prospective study and large retrospective studies. Blood transfusion trigger of 2 units of packed red blood cells is a reasonable guideline for the first 24 hours, but the surgeon should take in account the patient's hemodynamics, age (physiologic reserve), grade of injury, and associated or missed injury to ensure that the guideline fits the clinical situation.

Grade of recommendation: B.

WHICH PATIENTS ARE ANGIOGRAPHY CANDIDATES, AND WHICH ARE AT RISK TO FAIL EMBOLIZATION?

Splenic artery embolization was first introduced in 1981 by Sclafani (28). Splenic artery embolization has become an important adjunct in patients at highest risk for nonoperative management failure. Although patient selection varies between institutions, generally a patient with CT-documented Grade III–V splenic injury, contrast extravasation, and/or pseudo-aneurysm qualify for a diagnostic angiogram. If on angiography a contrast blush or pseudo-aneurysm is confirmed, the physician will deploy a coil or gelfoam to occlude the proximal splenic artery, selective distal arteries, or a combination thereof (29–31). Though many institutions have instituted splenic angiogram protocols, controversy remains concerning who benefits from this technique. Currently Class III data exist, but many of the articles have large populations and are well done.

Early Class III data reported that Grade IV and V splenic injuries had a failure rate of 100% (19). Bee and colleagues found that embolization decreased failure rates of Grade IV and V injuries to 12–13% for patients with moderate/large hemoperitoneum (14). These data are supported by a large retrospective study done on 645 patients, of whom 368 were managed nonoperatively. The study was protocol driven; patients with Grade III, IV, or V injuries and a blush on CT scan qualified for angiography and embolization. The overall nonoperative success rate was 94%. One hundred thirty-two patients underwent embolization with a salvage rate of 90%. However, patients with a Grade IV or V injury had a success rate of 80%. The failure rate for arteriovenous fistulas was 40%. Patients with moderate/large hemoperitoneum or pseudo-aneurysm had a failure rate of 10% and 12%, respectively. Individual Grade III, IV, V salvage rate were 92%, 83%, and 83%, which was significantly higher than the Eastern Association for the Surgery of Trauma salvage rate of 80%, 66%, and 25% for these level of injuries, respectively (15). This article documents 167 negative angiographies, however, there is no identification of grade or size of hemoperitoneum to which negative findings correlate. In previous studies, this group had negative angiography rates of 70% in Grade III injuries and 41% in Grade IV injuries with embolization performed in 30% and 59%, respectively (32). This negative angiography-to-embolization ratio infers that more angiography may be performed than needed.

Other published data comparing non-protocol-driven and protocol-driven management further supports protocol-driven management. Gaarder et al. supported a prospective evaluation of patients in a protocol-driven nonoperative management and compared this group to historical controls. The historical control group had 69 patients compared to

64 in the protocol group. The data showed that the protocol group had more attempts at nonoperative management, better success rate, lower laparotomy rates, and lower splenectomy rates. Patients who were stable and had splenic injury without other indications for laparotomy were managed nonoperatively. Their criteria for angiography and embolization was similar to the Haan group, and their overall nonoperative success rate was 96% (33).

Both groups use distal, proximal, and combined embolization with no clear benefit in any technique. Combined embolization has led to a higher incidence of significant splenic parenchyma necrosis (defined as necrosis of greater than 50% of the spleen parenchyma). This increased splenic parenchyma necrosis was clinically followed and did not impact management (15,33). In addition, in a small retrospective review, Haan et al. noted that 12 out of 96 patients developed splenic air postembolization. Six were asymptomatic and were successfully observed. The other six had fever, pain, and leukocytosis. Two had percutaneous drainage and the fluid was sterile, possibly from preprocedure antibiotics. The other four patients underwent splenectomy, and two spleens were infected with alpha-hemolytic *Streptococcus* and *Clostridia perfringens* (29).

Finally, there is controversy concerning factors predicting failure of embolization. Another group performed a large retrospective study that revealed patients with arteriovenous fistulas failed embolization 40% of the time. They also found that pseudo-aneurysm and high-grade injuries were not associated with a significant failure rate (15). Other institutions published conflicting data. These institutions' embolization failure rates were 43% for high-grade injuries, 56% for large hemoperitoneum, and 59% for extravasation (31,33). This discrepancy may be accounted for by the frequency and familiarity that each institution has concerning embolization. In addition, different embolization protocols may produce different outcomes.

Recommendations

(Level IIA) Class II data and Class III data (large retrospective studies).

1. Protocol driven non-operative management with splenic artery embolization is a safe adjunct which has increased success rates, decrease mortality rates, and lower splenectomy rates.
2. Patients who are hemodynamically stable with evidence of ongoing bleeding or at high risk to failing non-operative management benefit the most from embolization. The major studies perform angiography on patients who have contrast blush on CT scan and who have a grade 3, 4, or 5 injury. This is a reasonable approach, however grade 3 injuries have a failure rate of 19%, and the negative angiography rate is as high as 70%. None of the recent studies have updated this rate. This fact calls into question the practice of having all grade 3 injuries undergo angiography.
3. There is conflicting data concerning factors indicative of embolization failure. No recommendations can be made and further large population studies are needed.

Grade of recommendation: B.

WHAT IMAGING STUDIES SHOULD BE OBTAINED IN PATIENTS WITH SPLENIC INJURIES?

The standard imaging work-up in a patient with blunt abdominal trauma has become a focused abdominal sonography for trauma scan in the trauma room, followed by contrast-enhanced abdominal CT scan if the patient is hemodynamically stable. Prior evidence-based practice management guidelines have deemed CT scan (when compared to DPL, laparoscopy, and ultrasound) "the most accurate, specific, and sensitive in delineating the extent and severity of injury" (34). There is little new evidence to refute that statement, and CT scan remains the screening study of choice in blunt abdominal trauma.

Some studies have sought to expand the use of ultrasound to diagnose and characterize the extent of solid organ injuries. Rozycki et al. attempted to describe the severity of solid organ injuries with conventional ultrasound, but found only 46% of solid organ injuries and 81% of injury-related complications (35). The authors cite inability to obtain images of the entire organ as limitations leading to only a modest detection rate.

More promising studies use contrast-enhanced ultrasound (CEU) in the detection and grading of solid organ injuries. McGahan et al. studied the sensitivity of both CEU and noncontrast ultrasound to detect solid organ injury and found that CEU revealed 91% of injuries, whereas non-contrast ultrasound found only 50% (36). Catalano et al. performed a prospective trial using CEU in 153 emergency room patients who had suspected trauma or internal bleeding (37). The study used microbubble contrast injected into a 20-gauge venous catheter and was performed by an attending radiologist. CEU correctly diagnosed all 20 patients with active extravasation of contrast and correctly excluded extravasation in 133 patients. This and other studies have found CEU sensitivity from 91% to 100% (36–38). Potential drawbacks include concerns about contrast administration, personnel issues, and time frame to perform the exam. This technique can be used in subsets of the population in which repeat radiation exposure is undesired (pregnancy) or patient characteristics limit CT scan quality (implanted hardware).

With CT scan already established as the gold standard for determining the extent of splenic injury, recent literature has sought to answer questions pertaining to follow-up scans and their indications. When Haan and colleagues looked at inpatients with Grade I or II blunt splenic injuries, they found repeat CT scan 24–48 hours postinjury showed progression of injury in only 2 of 140 patients (39). Both patients had clinical symptoms of worsening injury. Uecker et al. had published similar findings; the three patients who had radiologic evidence of injury progression also had clinical symptoms. The 10 asymptomatic patients had no radiologic evidence of injury progression (40). Weinburg et al. disagreed somewhat with the previous two papers, as he found 11 of 330 late pseudo-aneurysms in his study population (41). Although the spectrum of both early and late pseudo-aneurysms was present in all injury grades, the authors did not mention clinical symptoms of those who had injury progression. Though it seems unlikely that there would be injury progression in patients with low-grade injuries without clinical symptoms, there is conflicting evidence to make recommendations for or against

inpatient imaging follow-up. Repeat splenic imaging has the highest yield in the symptomatic patient, that is, patients with hemodynamic instability, abdominal pain, decrease hemoglobin, or fevers.

Several studies have followed patients with splenic injuries after discharge and noted that patients who had injury progression usually also had clinical symptoms (42,43). There is no evidence to recommend repeat radiologic imaging of outpatients due to the low incidence of delayed complications and complications without clinical symptoms.

Recommendations

Based on Class II data (multiple prospective studies) and Class III data (retrospective studies), the level of recommendations are IIA.

1. CT scan is the diagnostic tool of choice for diagnosing splenic injury in stable trauma patients.
2. There is no evidence to support using noncontrast ultrasound for anything other than initial screening tool in the trauma room.
3. There is evidence that CEU is a useful adjunct to conventional imaging techniques in the trauma resuscitation area and during the inpatient hospitalization. No recommendations can be made due to the concerns about the contrast media and time frame to obtain the study.
4. There is conflicting evidence regarding repeat imaging in the inpatient splenic injury population, and we can make no recommendations.
5. There is no evidence to support repeat imaging after hospital discharge in absence of clinical symptoms.

Grade of recommendation: B.

WHAT STEPS CAN BE TAKEN TO PREVENT OVERWHELMING POSTSPLENECTOMY SEPSIS?

OPSS is rare (<2%) but carries a high mortality rate (>50%) (44). OPSS was first recognized in 1952 in asplenic infants, and causative organisms were later identified as encapsulated bacteria, in particular *S. pneumoniae* (3). Vaccinations against the encapsulated bacteria were initially used to prevent OPSS. Now splenic salvage is preferred to prevent the life-threatening disease.

It has been difficult to study the true benefit of vaccination and splenic salvage in reducing the rates of OPSS. Trauma patients have a high rate of loss to follow-up, and there is long time frame needed for observation before the disease develops. Recent studies have focused on immunologic surrogates for splenic function such as immunoglobulin G, immunoglobulin A, red blood cell pit test, and splenic macrophage radio nucleotide uptake. Nearly all studies have shown that immunologic markers in patients with spleens, either noninjured controls or nonoperatively managed splenic injuries, are markedly higher than those without spleens (45–47). Resende found Howell-Jolly bodies in all patients who underwent splenectomy for trauma, but none in noninjured controls or patients with subtotal splenectomy (46). Another study showed that the immunologic profile of nonoperatively managed Grade IV

or V injuries more closely resembled patients with spleens than without (45).

Current recommendations from the Centers for Disease Control and Prevention (CDC) recommend immunization for *S. pneumoniae* (pneumococcus), *N. meningitidis* (meningococcus), and *Haemophilus influenza B* (Hib; in those not already vaccinated for *H. influenza*) as soon as the patient's condition stabilizes (48). However, several studies show improved functional antibody titers when the vaccine is given at 14 days versus less than 14 days, and no difference when comparing 14 days with 28 days (44,49). The CDC recommends a booster pneumococcus vaccination five years after the initial vaccine, and physicians may consider a booster meningococcus at three to five years after the initial vaccine. Despite these clear guidelines, a recent survey showed a wide variance among trauma surgeons with respect to vaccination schedules after splenectomy: 99.2% vaccinate against pneumococcus, 62.8% meningococcus, 72.4% Hib, and there was significant disparity with respect to timing (50).

Recommendations

Level of evidence consist of multiple Class II data, and recommendations are Level IIA.

1. There is evidence to support that spleens preserve their immunologic function after trauma, even with the more severe injuries. We recommend nonoperative management as the single most effective step in preventing OPSI.
2. We recommend following the current CDC guidelines for the most up-to-date information regarding immunizations for asplenic patients.
3. There is literature to support administering immunizations at least 14 days after injury. We recommend that pneumococcus, meningococcus, and Hib vaccine be given at least 14 days postsplenectomy, but patients who are high risk for loss to follow-up should be immunized prior to discharge.

Grade of recommendation: B.

WHEN IS IT SAFE TO RESUME ACTIVITIES AFTER SPLENIC INJURIES?

Evidence-based in-hospital resumption of diet and activity recommendations were previously based on retrospective studies in which individual institutions and surgeons determined appropriate time frames. This lack of prospective data persists. In the adult population a few studies provided prospective data on their protocol-based management of splenic injuries. Haan et al. allowed patients with stable Grade I injuries out of bed and taking oral liquids by the morning after their injury and at 36 hours for all stable patients. When compared with a historical control, this group had a decrease length of stay from 6.8 to 3.3 days, while maintaining a 95% splenic salvage rate (29). This data is similar to a validation study of the American Pediatric Surgical Association (APSA) Trauma Committee's guidelines for the management of splenic trauma, which validated the evidence-based recommendations published in 2000 (51). The APSA's recommendations include a graduated

length of hospitalization and return to activity based on splenic injury grade (52).

Recommendations

Level of recommendation is IC, based on a large Class II prospective study.

1. We recommend compliance with the APSA guidelines for splenic injury management in children. They provide guidelines for return to both inpatient and full-contact activities.
2. We recommend similar APSA practices adapted and employed for adult patients, with minimal activity restriction for low-grade injuries and longer restriction for those with more severe injuries. There is no evidence that imaging is required for activity resumption in the asymptomatic patient, and we do not recommend regular imaging.

Grade of recommendation: B.

HOW ARE PATIENTS WITH SPECIAL CIRCUMSTANCES MANAGED NONOPERATIVELY?

As stated in the previous question, the APSA published guidelines in 2000 regarding the management of splenic injuries in the pediatric patients (52). These recommendations were validated by a 2006 study from 316 patients in 16 trauma centers. While achieving a 1.3% splenectomy rate, there was a statistically significant reduction in intensive care unit stay, hospital stay, follow-up imaging, and interval of activity restructure when compared to historical controls (51). Many studies have looked at splenectomy rates at various hospitals and found that children have a lower splenectomy rate when they are treated at pediatric specialty centers compared to adult trauma centers or rural hospitals (53–55). Other risks for splenectomy in the pediatric patient include Glasgow Coma Score ≤ 8 , Grade III–V injury, older age, and associated injuries (53, 55–57).

Fang et al. performed a prospective, protocol-driven study of 487 patients with traumatic splenic injuries, paying particular attention to 12 cirrhotic patients. All 12 patients had attempted nonoperative management, 11 of 12 failed, and 6 of 12 died (58). When compared to noncirrhotics who failed nonoperative management, cirrhotics had lower Injury Severity Score (ISS), lower splenic injury grade, and higher amounts of blood transfusions. Risk factors for mortality in cirrhotics included higher ISS, higher transfusions, higher prothrombin times, and lower serum albumins. The study did not have a matched group of cirrhotic patients who were managed with initial operation.

Anticoagulation in the blunt splenic injury patient has only been addressed in one publication. Alejandro et al. reviewed the timing of low-molecular-weight heparin, and separated the administration into early (<48 hours) and late (>48 hours) groups. In similar groups, that study found no difference in nonoperative management failures and mortality (59).

Recommendations

1. There is validation of APSA 2000 guidelines for management of pediatric blunt splenic injuries. Previously stated Level IIA recommendation.

2. There is evidence that cirrhotics do worse with blunt splenic injuries than noncirrhotics. We cannot make recommendations for management strategies with one prospective study with small population of cirrhotics. There is a small study showing equivalence of outcomes regarding timing of anticoagulation administration. There are no studies comparing deep vein thrombosis prophylaxis versus a control without prophylaxis in patients with blunt splenic injuries. We cannot make recommendations on this topic.

REFERENCES

1. Clark DE. Annual report of the National Trauma Data Bank 2007.
2. Richardson JD. Changes in the management of injuries to the liver and spleen. *J Am Coll Surg* 2005; 200: 648–69.
3. King H, Shumacker HB Jr. Splenic studies. I. Susceptibility to infection after splenectomy performed in infancy. *Ann Surg* 1952; 136: 239–42.
4. Chmielewski GW, Nicholas JM, Dulchavsky SA, et al. Non-operative management of gunshot wounds of the abdomen. *Am Surg* 1995; 61: 665–8.
5. Renz BM, Feliciano DV. Gunshot wounds to the right thoracoabdomen: a prospective study of nonoperative management. *J Trauma* 1994; 37: 737–44.
6. Velmahos GC, Demetriades D, Toutouzas KG, et al. Selective nonoperative management in 1,856 patients with abdominal gunshot wounds: should routine laparotomy still be the standard of care? *Ann Surg* 2001; 234: 395–403.
7. Demetriades D, Hadjizacharia P, Constantinou C, et al. Selective nonoperative management of penetrating abdominal solid organ injuries. *Ann Surg* 2006; 244: 620–8.
8. Konstantakos AK, Barnoski AL, Plaisier BR, et al. Optimizing the management of blunt splenic injury in adults and children. *Surgery* 1999; 126: 805–13.
9. Peitzman AB, Heil B, Rivera L, et al. Blunt splenic injury in adults: multi-institutional study of the Eastern Association for the surgery of trauma. *J Trauma* 2000; 49: 177–89.
10. Shaftan GW. Indications for operation in abdominal trauma. *Am J Surg* 1960; 99: 657–64.
11. Rajani RR, Claridge JA, Yowler CJ, et al. Improved outcome of adult blunt splenic injury: a cohort analysis. *Surgery* 2006; 140: 625–31; discussion 31–2.
12. Federle MP, Goldberg HI, Kaiser JA, et al. Evaluation of abdominal trauma by computed tomography. *Radiology* 1981; 138: 637–44.
13. Meredith JW, Trunkey DD. CT scanning in acute abdominal injuries. *Surg Clin North Am* 1988; 68: 255–68.
14. Bee TK, Croce MA, Miller PR, et al. Failures of splenic non-operative management: is the glass half empty or half full? *J Trauma* 2001; 50: 230–6.
15. Haan JM, Bochicchio GV, Kramer N, et al. Nonoperative management of blunt splenic injury: a 5-year experience. *J Trauma* 2005; 58: 492–8.
16. Peitzman AB, Harbrecht BG, Rivera L, et al. Failure of observation of blunt splenic injury in adults: variability in practice and adverse consequences. *J Am Coll Surg* 2005; 201: 179–87.
17. Meguid AA, Bair HA, Howells GA, et al. Prospective evaluation of criteria for the nonoperative management of blunt splenic trauma. *Am Surg* 2003; 69: 238–43.
18. Carlin AM, Tyburski JG, Wilson RF, et al. Factors affecting the outcome of patients with splenic trauma. *Am Surg* 2002; 68: 232–9.
19. Cogbill TH, Moore EE, Jurkovich GJ, et al. Nonoperative management of blunt splenic trauma: a multicenter experience. *J Trauma* 1989; 29: 1312–17.

20. Albrecht RM, Schermer CR, Morris A. Nonoperative management of blunt splenic injuries: factors influencing success in age >55 years. *Am Surg* 2002; 68: 227–31.
21. Cocanour CS, Moore FA, Ware DN, et al. Age should not be a consideration for nonoperative management of blunt splenic injury. *J Trauma* 2000; 48: 606–12.
22. Harbrecht BG, Peitzman AB, Rivera L, et al. Contribution of age and gender to outcome of blunt splenic injury in adults: multicenter study of the eastern association for the surgery of trauma. *J Trauma* 2001; 51: 887–95.
23. Abu-Hatoum O, Bashenko Y, Hirsh M, et al. Continuous fluid resuscitation and splenectomy for treatment of uncontrolled hemorrhagic shock after massive splenic injury. *J Trauma* 2002; 52: 253–8.
24. Nix JA, Costanza M, Daley BJ, et al. Outcome of the current management of splenic injuries. *J Trauma* 2001; 50: 835–42.
25. Siriratsivawong K, Zenati M, Watson GA, et al. Nonoperative management of blunt splenic trauma in the elderly: does age play a role? *Am Surg* 2007; 73: 585–90.
26. Brasel KJ, Weigelt JA, Christians KK, et al. The value of process measures in evaluating an evidence-based guideline. *Surgery* 2003; 134: 605–12.
27. Velmahos GC, Toutouzas KG, Radin R, et al. Nonoperative treatment of blunt injury to solid abdominal organs: a prospective study. *Arch Surg* 2003; 138: 844–51.
28. Sclafani SJ. The role of angiographic hemostasis in salvage of the injured spleen. *Radiology* 1981; 141: 645–50.
29. Haan J, Ilahi ON, Kramer M, et al. Protocol-driven nonoperative management in patients with blunt splenic trauma and minimal associated injury decreases length of stay. *J Trauma* 2003; 55: 317–22.
30. Sclafani SJ, Shaftan GW, Scalea TM, et al. Nonoperative salvage of computed tomography-diagnosed splenic injuries: utilization of angiography for triage and embolization for hemostasis. *J Trauma* 1995; 39: 818–27.
31. Smith HE, Biffl WL, Majercik SD, et al. Splenic artery embolization: have we gone too far? *J Trauma* 2006; 61: 541–6.
32. Haan J, Scott J, Boyd-Kranis RL, et al. Admission angiography for blunt splenic injury: advantages and pitfalls. *J Trauma* 2001; 51: 1161–5.
33. Gaarder C, Dormagen JB, Eken T, et al. Nonoperative management of splenic injuries: improved results with angioembolization. *J Trauma* 2006; 61: 192–8.
34. EPMGW Group. Non-Operative Management of Blunt Injury to the Liver and Spleen. 2003.
35. Rozycki GS, Knudson MM, Shackford SR, et al. Surgeon-performed bedside organ assessment with sonography after trauma (BOAST): a pilot study from the WTA multicenter group. *J Trauma* 2005; 59: 1356–64.
36. McGahan JP, Horton S, Gerscovich EO, et al. Appearance of solid organ injury with contrast-enhanced sonography in blunt abdominal trauma: Preliminary experience. *Am J Roentgenol* 2006; 187: 658–66.
37. Catalano O, Sandomenico F, Raso MM, et al. Real-time, contrast-enhanced sonography: a new tool for detecting active bleeding. *J Trauma* 2005; 59: 933–9.
38. Valentino M, Serra C, Zironi G, et al. Blunt abdominal trauma: emergency contrast-enhanced sonography for detection of solid organ injuries. *Am J Roentgenol* 2006; 186: 1361–7.
39. Haan JM, Boswell S, Stein D, et al. Follow-up abdominal CT is not necessary in low-grade splenic injury. *Am Surg* 2007; 73: 13–18.
40. Uecker J, Pickett C, Dunn E. The role of follow-up radiographic studies in nonoperative management of spleen trauma. *Am Surg* 2001; 67: 22–5.
41. Weinberg JA, Magnotti LJ, Croce MA, et al. The utility of serial computed tomography imaging of blunt splenic injury: still worth a second look? *J Trauma* 2007; 62: 1143–8.
42. Minarik L, Slim M, Rachlin S, et al. Diagnostic imaging in the follow-up of nonoperative management of splenic trauma in children. *Pediatr Surg Int* 2002; 18: 429–31.
43. Thompson SR, Holland AJ. Current management of blunt splenic trauma in children. *ANZ J Surg* 2006; 76: 48–52.
44. Shatz DV, Romero-Steiner S, Elie CM, et al. Antibody responses in postsplenectomy trauma patients receiving the 23-valent pneumococcal polysaccharide vaccine at 14 versus 28 days postoperatively. *J Trauma* 2002; 53: 1037–42.
45. Falimirski M, Syed A, Prybilla D. Immunocompetence of the severely injured spleen verified by differential interference contrast microscopy: the red blood cell pit test. *J Trauma* 2007; 63: 1087–92.
46. Resende V, Petroianu A. Functions of the splenic remnant after subtotal splenectomy for treatment of severe splenic injuries. *Am J Surg* 2003; 185: 311–15.
47. Theodorou GL, Mouzaki A, Tsiftsis D, et al. Effect of non-operative management (NOM) of splenic rupture versus splenectomy on the distribution of peripheral blood lymphocyte populations and cytokine production by T cells. *Clin Exp Immunol* 2007; 150: 429–36.
48. Kroger AT, Atkinson WL, Marcuse EK, et al. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006; 55(RR-15): 1–48.
49. Shatz DV, Schinsky MF, Pais LB, et al. Immune responses of splenectomized trauma patients to the 23-valent pneumococcal polysaccharide vaccine at 1 versus 7 versus 14 days after splenectomy. *J Trauma* 1998; 44: 760–6.
50. Shatz DV. Vaccination practices among North American trauma surgeons in splenectomy for trauma. *J Trauma* 2002; 53: 950–6.
51. Stylianos S. Compliance with evidence-based guidelines in children with isolated spleen or liver injury: a prospective study. *J Pediatr Surg* 2002; 37: 453–6.
52. Stylianos S. Evidence-based guidelines for resource utilization in children with isolated spleen or liver injury. *The APSA Trauma Committee. J Pediatr Surg* 2000; 35: 164–9.
53. Bowman SM, Zimmerman FJ, Christakis DA, et al. Hospital characteristics associated with the management of pediatric splenic injuries. *JAMA* 2005; 294: 2611–17.
54. Mooney DP, Rothstein DH, Forbes PW. Variation in the management of pediatric splenic injuries in the United States. *J Trauma* 2006; 61: 330–3.
55. Stylianos S, Egorova N, Guice KS, et al. Variation in treatment of pediatric spleen injury at trauma centers versus nontrauma centers: a call for dissemination of American Pediatric Surgical Association benchmarks and guidelines. *J Am Coll Surg* 2006; 202: 247–51.
56. Holmes JH, Wiebe DJ, Tataria M, et al. The failure of non-operative management in pediatric solid organ injury: a multi-institutional experience. *J Trauma* 2005; 59: 1309–13.
57. Potoka DA, Schall LC, Ford HR. Risk factors for splenectomy in children with blunt splenic trauma. *J Pediatr Surg* 2002; 37: 294–9.
58. Fang JF, Chen RJ, Lin BC, et al. Liver cirrhosis: an unfavorable factor for nonoperative management of blunt splenic injury. *J Trauma* 2003; 54: 1131–6.
59. Alejandro KV, Acosta JA, Rodriguez PA. Bleeding manifestations after early use of low-molecular-weight heparins in blunt splenic injuries. *Am Surg* 2003; 69: 1006–9.

Injury to the Liver

Alberto Garcia, Maria Fernanda Jimenez and Juan Carlos Puyana

Clinical Questions		
Question	Answer	Grade of recommendation
What criteria best defined the optimal candidate for non operative management of hepatic trauma?	Hemodynamic stability regardless of CT findings or amount of hemoperitoneum.	B
Are serial CTs useful for follow-up?	No. Routine CT studies are not indicated.	C
When are drains indicated in hepatic trauma, and what kind should be used?	The systematic use of drainage of the biliary tract does not benefit hepatic trauma patients and T-tube choledocostomy increases the risk of intra-abdominal infection and mechanical complications. The use of open drainages is not warranted as they may increase the risk of intra-abdominal infection after surgical treatment of liver trauma.	B
Is CT useful in the assessment of GSW to the liver?	CT with IV contrast and in some cases with oral and rectal contrast discriminates stable GSW patients who do not need to be operated. NOM based on clinical evaluation and evolution, complemented with early IV contrast CT, can be implemented safely for abdominal solid organ injury secondary to GSW.	C
Is hepatic angio-embolization effective in controlling hemorrhage in liver trauma?	With a multidisciplinary approach, arterial embolization is safe and effective in the management of severe hepatic trauma and can be safely performed as an adjunct to the principles of damage control.	C
Abbreviations: CT, computed tomography; GSW, gunshot wound; NOM, nonoperative management.		

The liver is the organ most commonly injured in patients with abdominal trauma (1). The treatment and outcome of liver injuries have evolved in the past three decades due to multiple new modes of diagnoses and therapeutic approaches as well as improvement of hemorrhage control (2). Although the incidence of severe liver injuries (Grade IV and V) has not changed, the treatment modalities have changed dramatically. In 1970 the main treatment was surgical homeostasis with liver packing, which registered a death rate of 40–80%. Currently less than 20% of the blunt injury patients undergo surgery. Nonoperative management (NOM) as the treatment of choice for hepatic blunt trauma represents a shift in a paradigm and has become the standard of practice (3,4). In penetrating trauma, the liver may be severely damaged, and the operative management of hepatic injuries remains one of the greatest technical challenges in trauma surgery, yet new tendencies in NOM for penetrating trauma have been reported as well. Patients with hepatic trauma may also suffer a number of severe associated injuries. They may require damage control techniques and may be at risk for serious complications in the intensive care unit (ICU). Despite that advances in imaging techniques and critical care medicine over the past 40 years resulting in improved mortality,

many questions regarding best practices in patients with liver injuries remained unanswered.

WHAT ARE THE CRITERIA FOR SELECTING BLUNT TRAUMA PATIENT FOR NOM?

Since the publication of the Eastern Association for the Surgery of Trauma (EAST) guidelines on NOM of hepatic injuries in 2003, there have been 33 new publications on this subject. There are no controlled randomized trials comparing efficacy of operative versus NOM, and there is only one new prospective cohort trials published in 2003 (2) similar to those published in 1994 and 1995 by Sherman et al. (5) and Croce et al. (6), respectively. Although the recommendations for NOM are based mostly on Class III references, it would appear that the decision to operate on the injured liver based solely on the hemodynamic status of the patient have withstood the test of time (7,8). There is no new evidence contradicting the statement that appearance of the injury on computed tomography (CT) scan or amount of hemoperitoneum should not be by themselves indications for explorations in hemodynamically stable patients, unless there is other significant abdominal injury

that required a surgical exploration (9). Based on these criteria, close to 80% of blunt trauma patients are candidates for NOM. This trend has evolved over the past decade even in areas with low populations characterized as rural trauma centers (10). Less than 20% of patients with blunt liver injury will require emergent celiotomies either because of the liver or associated intra-abdominal injuries. Most recently, publications from all continents have described series with NOM of liver trauma. Although these series have different proportions of mild to severe hepatic trauma, the rate of NOM ranges from 40% to 70% (7,11–14).

Special circumstances such as concomitant or combined lesions have been also studied. The failure rate doubled to approximately 12% in patients with both spleen and liver injuries (15).

Answers: Patients with blunt liver trauma who are hemodynamically stable are best candidates for NOM. Level of evidence Class III, Recommendation grade B. Patients with combination of injuries are more likely to fail NOM.

HOW USEFUL IS THE USE OF SERIAL ABDOMINAL CT SCANS FOR FOLLOW-UP ASSESSMENT IN PATIENTS WITH LIVER INJURIES?

The use of routine or serial abdominal CT scans without clinical indications has not been shown to influence either the outcome or the management of the patient with hepatic trauma. The most recent publication addressing this issue reported on 530 patients who underwent a follow-up CT within one week of admission (16). Follow-up scans showed that most injuries were either unchanged (51%) or improved (34.7%). Only three patients underwent intervention based on their follow-up scans: two had arteriography (one with therapeutic embolization) and one had percutaneous drainage. Each of those patients had clinical signs or symptoms that were indicative of ongoing hepatic abnormality. A recommendation class C could be made at this point indicating that regardless of injury grade, routine in-hospital follow-up scans are not indicated as part of the NOM of blunt liver injuries. Follow-up scans are indicated for patients who develop signs or symptoms suggestive of hepatic abnormality. A study by Cuff et al. in 2000 hypothesized that follow-up abdominal CT scans were not routinely necessary in patients with blunt liver injury treated nonoperatively. This was an eight-year retrospective review of hospital chart and outpatient clinic records. There were 42 adults and 12 children. Two patients died during the first 24 hours, both from associated injuries. NOM was successful in 51 (98%) of the remaining 52 patients. No follow-up abdominal CT scans were performed on 21 (40%) patients; none developed hepatic complications. An initial follow-up CT scan was obtained in 31 (60%) patients. Information from these scans directly affected management in three (9%) patients; in each case, the scans were prompted by a change in clinical status. Additional late follow-up CT scans were obtained in 13 patients; no clinically useful information was evident on any of these examinations. This study concluded that follow-up abdominal CT scans are not routinely necessary in patients with liver injuries treated nonoperatively (17).

Answer: Routine in-hospital follow-up scans are not indicated as part of the NOM of blunt liver injuries. Follow-up scans are indicated for patients who develop signs or symptoms suggestive of hepatic abnormality. Recommendation grade C.

DOES DRAINAGE PREVENT COMPLICATIONS IN SURGICALLY TREATED HEPATIC INJURIES?

The use of systematic drainage of the biliary tract in patients operated on for hepatic trauma, was addressed by Lucas and Walt (18). The authors randomized 189 patients to three groups: Group 1 was drained with a perihepatic drain; group 2 had a perihepatic drain and a cholecystostomy tube; and group 3 underwent perihepatic drain and T-tube choledochostomy. The groups were similar in terms of demographics, severity of the hepatic lesion, or treatment. T-tube choledochostomy + abdominal drains were associated with increased morbidity, mainly due to intra-abdominal infections and technical complications of the tube. Cholecystostomy + abdominal drains did not show any benefit compared with the abdominal drainage alone. The association of drainage and infection risk was analyzed retrospectively by several authors: Fisher and co-workers studied 254 surgically treated hepatic trauma patients surviving more than one day (19). Perihepatic drains were used in six patients. Peritoneal drains were used in 21 patients. Intra-abdominal abscess occurred in 7.4% of the drained patients compared to 4.8% in the group with no drains. Drainage did not affect the risk of infection. Bender et al. (20) investigated the role of perihepatic open drainage as risk factor of infection in 295 surgically treated hepatic trauma patients surviving more than 72 hours. All the infections occurred in drained patients. Remarkably, the group of patients with liver trauma grades I, II, and III had an incidence of infection of 6% compared to none in the group of patients with no drains. Noyes and associates performed an analysis of the risk of intra-abdominal infection in 164 patients with liver trauma. They also assessed the morbidity associated with the type of drains used (21). One intra-abdominal abscess developed in 57 patients who receive no drains compare to no abscesses in 29 who were drained with a closed suction drainage system. Eleven of 78 patients who underwent open/suction drainage cases developed an intra-abdominal abscess.

The potential effect of abdominal drainage on morbidity was studied in two randomized controlled trials (RCTs). Mullins et al. (22) randomized 161 liver trauma patients who were surgically treated. They compared the use of a Penrose drain versus no drain. Subphrenic abscesses occurred in 5 of the 78 drained patients and in 4 of the 83 not drained. Biliary fistula occurred in two of the drained and in one of the not drained. Gillmore et al. treated 24 patients with drain and 32 with no drain. Intra-abdominal abscess occurred in one patient in each group (23).

The effect of drainage on patients submitted to elective liver resection has been investigated in five RCTs. A meta-analysis on the subject was published (24). The authors did not find differences between the two groups regarding mortality, intra-abdominal collections, infected

intra-abdominal collections, wound infection, ascites, or hospital stay.

Answer: The systematic use of drainage of the biliary tract does not benefit hepatic trauma patients and the T-tube choledochostomy increases the risk of intra-abdominal infection and mechanical complications (Grade of recommendation: B). The current evidence does not support the routine use of drainage after surgical treatment of liver injuries (Grade of recommendation: B). The use of open drains is not warranted because they may increase the risk of intra-abdominal infection after surgical treatment of liver trauma (Grade of recommendation: C).

CAN GUNSHOT WOUNDS TO THE LIVER OF STABLE PATIENTS BE MANAGED NONOPERATIVELY, BASED ON CT SCAN?

The policy of mandatory laparotomy in patients with gunshot wounds of the abdomen has been challenged in the last years and selective NOM of stable gunshot wound (GSW) patients has been performed safely in some trauma centers (25–27). The strategy was based formerly on serial physical examinations, which have been replaced by CT, with or without oral and rectal contrast.

The ability to identify penetration to the peritoneal cavity or visceral lesions as a means of selecting the optimal candidate for NOM in penetrating trauma has been studied. In 1998 two retrospective studies addressing the potential role of abdominal CT in the management of patients with GSWs of the abdomen were published. Ginzburg et al. retrospectively studied 83 patients with abdominal GSW in which triple-contrast CT was used as screening tool. Surgical exploration was avoided in 53 cases, and the liver was the most frequent viscera involved in nonoperated patients. There was a case of a missed colon injury (28). Grossman and co-workers reported a retrospective series of GSW to the torso in stable patients who underwent CT for trajectory determination. In 37 patients the CT was performed for the study of abdominal or pelvic wounds. It showed extracavitary trajectories in 20 cases. The patients were not operated on. In the 17 remaining cases, the study identified transabdominal trajectories or visceral lesions. Nine patients were submitted to laparotomy. In four cases the CT was read as exclusive injury to liver and these patients were managed nonoperatively without complications (29). The operative characteristics of helical CT as a tool to identify “need for laparotomy” in stable patients were reported in three studies. Múnera et al. compared prospectively the result of the triple contrast CT with laparotomy findings or the result of the clinical observation in 47 patients with abdominal GSW. The sensitivity was 96%; the specificity, 95%; and the accuracy, 96% (13). Velmahos et al. compared, in a prospective study involving 100 patients with nontangential abdominal GSW, the result of helical CT with IV contrast versus surgical findings or the clinical observation. They found a sensitivity of 91%, a specificity of 96%, and an accuracy of 93% (30). Beekley et al. reported the selective management of 145 stable patients with abdominal injury for fragmentation in combat casualties. A protocol based on CT with other diagnostic aids was used in selected cases. Surgery was performed after positive

CT findings in 60 cases. Eighty-five patients were managed nonoperatively, based in negative CT (75 patients) or findings of penetration without a clear necessity of surgical exploration. They found sensitivity 98%; specificity, 85%; and area under the receiver operating characteristic (ROC) curve 0.929. The liver was the solid abdominal organ most commonly involved (31).

Ginzburg et al. also studied the value of CT to rule out peritoneal penetration in a retrospective study. They reported a sensitivity of 100%, a specificity of 54%, and an accuracy of 71% (28). Shanmuganathan et al. found prospectively in 200 patients 97% sensitivity (66 of 68 findings), 98% specificity (130 of 132 findings), and 98% accuracy (196 of 200 findings). Two patients with negative CT findings failed to improve with observation and underwent therapeutic laparotomy. CT had 97% sensitivity (66 of 68 findings), 98% specificity (130 of 132 findings), and 98% accuracy (196 of 200 findings) for peritoneal violation. CT aided diagnosis of 28 hepatic, 34 bowel or mesenteric, 7 splenic, and 6 renal injuries. Laparotomy based on CT findings in 38 patients was considered therapeutic in 87% (33 of 38) and nontherapeutic in 8% (3 of 38) and had negative results in 5% (2 of 38) (32). The NOM of patients with abdominal GSW with penetration and lesion of solid organs was proposed in 1994 by Renz et al. They collected a prospective series of 13 patients with GSW in the right thoracoabdomen, hemodynamically stable, and without peritonitis. CT was performed in 12, and liver wounds were found in 7. The patients were included in a NOM protocol, which was successful in all patients. There were no complications attributable to NOM (33). In 1995, Chmielewski et al. published a similar prospective series of 12 hemodynamically stable patients with GSW in the right upper quadrant of the abdomen, without signs of peritonitis. These patients were included in a protocol of NOM. CT was performed in eight, diagnostic peritoneal lavage (DPL) or ultrasound were performed in four. One patient required laparotomy, which was nontherapeutic. Liver trauma was documented in all the patients imaged. There were not complications attributable to NOM (34). Subsequently NOM of patients with abdominal GSW and solid organ trauma, based on clinical stability and CT, has been reported by several authors. Demetriades et al. reported 16 cases collected retrospectively, with success in 10 (63%) and a missed diaphragmatic tear secondary to the NOM (35). Munera and co-workers had a success rate of 93% (13 of 14), with a missed cecal hematoma, found in a delayed laparotomy (13). Shanmuganathan et al. reported a success rate of 91% (21 of 23) without adverse effects (32). Demetriades and colleagues subsequently published a prospective series of 43 patients with NOM in solid organ injury secondary to penetrating trauma (70% GSW, 30% stab wounds). The liver was compromised in 36 cases; NOM was successful in 31 (86%), without any complication attributable to liver trauma (36). DuBose et al. reported a 90% success rate (9 of 10) without complications (37).

The severity of the liver trauma was reported only in two studies. Five of the cases published by DuBose and co-workers were Grade I or II and five Grade III or IV of the American Association for the Surgery of Trauma AAST classification (37). In the Demetriades report, 21 of 36 (58%) cases with NOM were Grade I or II, and 15 (42%)

Grades III–V. In this study the probability of being definitively treated nonoperatively was slightly higher for lesions Grade I or II (19 of 58, 33%) than for lesions Grades III–V (12 of 51, 24%) (36).

Answers: CT with IV contrast and in some cases with oral and rectal contrast discriminates the stable GSW patients who do not need to be operated. Grade of recommendation: C. NOM based on clinical evaluation and evolution, complemented with early IV contrast CT, can be implemented safely for abdominal solid organ injury secondary to GSW. Grade of recommendation: C. Further investigation is required to determine risk factors of NOM failure, the optimal length of clinical observation, and the need of control CT.

IS ARTERIAL EMBOLIZATION EFFECTIVE IN THE MANAGEMENT OF PENETRATING AND BLUNT HEPATIC INJURIES?

The advent of nonsurgical therapy, expeditious technologies for the diagnosis of solid organ injuries, and better critical care monitoring have allowed minimally invasive approaches. The use of angiography and arterial hepatic embolization has increased from 1% to 9% according to Richardson et al. over three decades (38). The efficacy of arterial embolization (AE) for severe hepatic injuries has been evaluated by many authors in case control studies with a success rate ranging from 89% to 100% (39–41). However, the outcomes for adjunctive modalities, such as AE, are not well characterized. Immediate laparotomy is decided on the basis of resuscitation failure more than the severity of the injury. All experts agree that unresponsive shock and/or presence of findings suggestive of associated injuries are absolute indications for exploratory laparotomy and damage control. Hemodynamically stable patients with CT findings of active extravasation or pooling of blood within the liver parenchyma are candidates for AE. In a recent European study (39) comparing outcomes of patients with or without use of angiography and AE for the treatment of severe liver injuries, the implementation of angiography protocol in hemodynamic stable patients with abbreviated injury score (AIS) >3 resulted in a reduction of the number of laparotomies. The number of nonoperative rate increased from 51% to 76% ($p > 0.05$) without increasing failure rate, mortality, transfusion, or liver-related complications.

Hagiwara et al., in a case-control study (40), suggested that a combination of a CT scan Grade IV and V lesion and fluid requirements of >2,000 ml/h to maintain normotension are indications for laparotomy. However,

Monnin et al. (41), using a multidisciplinary approach (surgeon, interventional radiologist, and anesthetist) were less restricted to perform AE in unstable patients requiring large volume of transfusion and fluids and high-grade injuries with similar results and a successful rate of 100% with only two angiographic-related complications. Thus, they recommend this AE aggressive approach to avoid immediate surgery and consider embolization to be more effective to stop arterial bleeding than surgery without a concomitant increase in failure rate or mortality. The rationale to include mandatory angiography after a damage control laparotomy for liver injuries is based on the concept that an ongoing arterial bleeding is difficult to rule out at the end of damage control surgery, especially if there is some degree of coagulopathy. The role of interventional radiology following damage control laparotomy to control hemorrhage in inaccessible hepatic deep parenchyma regions was studied by Johnson and colleagues (42). This approach was demonstrated to be a safe adjunct procedure to perihepatic packing with a therapeutic success for angiographic embolization of 75% in this retrospective study. Nonoperative strategy associated to AE has been associated with high complication rate. Angiography-related complications have been reported: hepatic necrosis, bile leak, gallbladder infarction, and hepatic abscesses. However, the total number of complications per patient decreased significantly with the nonoperative approach, probably due to a lower rate of laparotomies (39). AE is not efficient to control bleeding from juxtahepatic venous injuries. Many patients have good results with NOM even when the low-density area on CT scan involves a juxtahepatic vein. Nonsurgical treatment has contributed to the decline of death even in presence of major venous injuries. Avoidance of manipulation of low-pressure system venous injuries may actually benefit these patients.

In summary, arterial embolization should be the treatment of choice for managing hemodynamic stable patients in whom CT scan shows extravasation of contrast medium when the injury is severe (Grade IV or greater according AAST classification) (Grade C recommendation). New reports suggest aggressive AE in patients with hemodynamic instability that are responsive to fluid therapy. Hepatic angiography and embolization have a high therapeutic success (75%) and provide a safe adjunct to the principles of damage control regardless of whether bleeding appears to be controlled with perihepatic packing (Grade C recommendation).

Answer: With a multidisciplinary approach, arterial embolization is safe and effective in the management of severe hepatic trauma and can be safely performed as an adjunct to the principles of damage control. Grade of recommendation: C.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Grade of recommendation	Findings
Efficiency of NOM	1994 1995 2003	1–7	IIb–III	B	NOM is the standard of care for hemodynamically stable patients.
Routine CTs for follow-up	2000 2005	16, 17	III	C	Follow-up CT scans were obtained in 13 patients; no clinically useful information was evident on any of these examinations. These studies concluded that follow-up abdominal CT scans are not routinely necessary in patients with liver injuries treated nonoperatively.
Drainage techniques	1978 1988 1989 1987 2007	18, 19, 20–23	IIb	B–C	Current evidence does not support the routine use of drainage after surgical treatment of liver injuries. The use of open drainages is not warranted as they may increase the risk of intra-abdominal infection after surgical treatment of liver trauma.
NOM in patients with GSW to the liver	1994 1998 2005 2008 2004	27–35	IIb	B	The operative characteristics for the need of surgical treatment were sensitivity 96%; specificity, 95%; positive predictive value, 96%; negative predictive value, 95%; and accuracy, 96% Operative characteristics for peritoneal violation were sensitivity 100%, specificity 54%, positive predictive value 56%, negative predictive value 100%, and accuracy 71%.
Angio-embolization as adjuvant therapy	2002 2007	38–41	III	C	Hepatic angiography and embolization has a high therapeutic success (75–100%) and is a safe adjunct to the principles of damage control regardless of whether bleeding appears to be controlled with peri-hepatic packing. New reports suggest aggressive AE in patients with hemodynamic instability that are responsive to fluid therapy.

Abbreviations: AE, arterial embolization; CT, computed tomography; GSW, gunshot wound; NOM, nonoperative management.

REFERENCES

- Trunkey DD. Hepatic trauma: contemporary management. *Surg Clin North Am* 2004; 84: 437–50.
- Velmahos GC, Toutouzas K, Radin R, et al. High success with nonoperative management of blunt hepatic trauma: the liver is a sturdy organ. *Arch Surg* 2003; 138: 475–80; discussion 480–81.
- EAST Trauma Guidelines. www.east.org/tpg/livspleen.pdf 2003.
- Hurtuk M, Reed RL II, Esposito TJ, et al. Trauma surgeons practice what they preach: the NTDB story on solid organ injury management. *J Trauma* 2006; 61: 243–54; discussion 254–5.
- Sherman HF, Savage BA, Jones LM, et al. Nonoperative management of blunt hepatic injuries: safe at any grade? *J Trauma* 1994; 37: 616–21.
- Croce MA, Fabian TC, Menke PG, et al. Nonoperative management of blunt hepatic trauma is the treatment of choice for hemodynamically stable patients. Results of a prospective trial. *Ann Surg* 1995; 221: 744–53; discussion 753–5.
- Fang JF, Wong YC, Lin BC, et al. The CT risk factors for the need of operative treatment in initially hemodynamically stable patients after blunt hepatic trauma. *J Trauma* 2006; 61: 547–53; discussion 553–4.
- Asensio JA, Roldan G, Petrone P, et al. Operative management and outcomes in 103 AAST-OIS grades IV and V complex hepatic injuries: trauma surgeons still need to operate, but angioembolization helps. *J Trauma* 2003; 54: 647–53; discussion 653–4.
- Galvan DA, Peitzman AB. Failure of nonoperative management of abdominal solid organ injuries. *Curr Opin Crit Care* 2006; 12: 590–4.
- Somasundar PS, Mucha P, McFadden DW. The evolving management of blunt hepatic trauma in a rural setting. *Am Surg* 2004; 70: 45–8.
- Gourgiotis S, Vougas V, Germanos S, et al. Operative and nonoperative management of blunt hepatic trauma in adults: a single-center report. *J Hepatobil Pancreat Surg* 2007; 14: 387–91.
- Markogiannakis H, Sanidas E, Messaris E, et al. Management of blunt hepatic and splenic trauma in a Greek level I trauma centre. *Acta Chir Belg* 2006; 106: 566–71.
- Munera F, Morales C, Soto JA, et al. Gunshot wounds of abdomen: evaluation of stable patients with triple-contrast helical CT. *Radiology* 2004; 231: 399–405.
- Al-Mulhim AS, Mohammad HA. Non-operative management of blunt hepatic injury in multiply injured adult patients. *Surgeon* 2003; 1: 81–5.
- Malhotra AK, Fabian TC, Croce MA, et al. Blunt hepatic injury: a paradigm shift from operative to nonoperative management in the 1990s. *Ann Surg* 2000; 231: 804–13.
- Cox JC, Fabian TC, Maish GO III, et al. Routine follow-up imaging is unnecessary in the management of blunt hepatic injury. *J Trauma* 2005; 59: 1175–8; discussion 1178–80.
- Cuff RF, Cogbill TH, Lambert PJ. Nonoperative management of blunt liver trauma: the value of follow-up abdominal computed tomography scans. *Am Surg* 2000; 66: 332–6.

18. Lucas CE, Walt AJ. Analysis of randomized biliary drainage for liver trauma in 189 patients. *J Trauma* 1972; 12: 925–30.
19. Fischer RP OFK, Perry JF. The value of peritoneal drains in the treatment of liver injuries. *J Trauma* 1978; 18: 393–8.
20. Bender JS GE, Wilson RF. Intra-abdominal sepsis following liver trauma. *J Trauma* 1989; 29: 1140–4.
21. Noyes LD DD, McSwain NE Jr. Septic complications associated with the use of peritoneal drains in liver trauma. *J Trauma* 1988; 28: 337–46.
22. Mullins RJ, Stone HH, Dunlop WE, et al. Hepatic trauma: evaluation of routine drainage. *South Med J* 1985; 78: 259–61.
23. Gillmore D MNJ, Browder IW. Hepatic trauma: to drain or not to drain? *J Trauma* 1987; 27: 898–902.
24. Gurusamy KS SK, Davidson BR. Routine abdominal drainage for uncomplicated liver resection. *Cochrane Database Syst Rev* 2007.
25. Shaftan GW. Indications for operation in abdominal trauma. *Am J Surg* 1960; 99: 657–64.
26. Shaftan GW. Selective conservatism in penetrating abdominal trauma. *J Trauma* 1969; 9: 1026–8.
27. Nance FC, Wennar MH, Johnson LW, et al. Surgical judgment in the management of penetrating wounds of the abdomen: experience with 2212 patients. *Ann Surg* 1974; 179: 639–46.
28. Ginzburg E, Carrillo EH, Kopelman T, et al. The role of computed tomography in selective management of gunshot wounds to the abdomen and flank. *J Trauma* 1998; 45: 1005–9.
29. Grossman MD, May AK, Schwab CW, et al. Determining anatomic injury with computed tomography in selected torso gunshot wounds. *J Trauma* 1998; 45: 446–56.
30. Velmahos GC, Constantinou C, Tillou A, et al. Abdominal computed tomographic scan for patients with gunshot wounds to the abdomen selected for nonoperative management. *J Trauma* 2005; 59: 1155–60; discussion 1160–1.
31. Beekley AC, Blackburne LH, Sebesta JA, et al. Selective nonoperative management of penetrating torso injury from combat fragmentation wounds. *J Trauma* 2008; 64(2 Suppl): S108–S116; discussion S116–S117.
32. Shanmuganathan K, Mirvis SE, Chiu WC, et al. Penetrating torso trauma: triple-contrast helical CT in peritoneal violation and organ injury—a prospective study in 200 patients. *Radiology* 2004; 231: 775–84.
33. Renz BM, Feliciano DV. Gunshot wounds to the right thoracoabdomen: a prospective study of nonoperative management. *J Trauma* 1994; 37: 737–44.
34. Chmielewski GW, Nicholas JM, Dulchavsky SA, et al. Non-operative management of gunshot wounds of the abdomen. *Am Surg* 1995; 61: 665–8.
35. Demetriades D, Gomez H, Chahwan S, et al. Gunshot injuries to the liver: the role of selective nonoperative management. *J Am Coll Surg* 1999; 188: 343–8.
36. Demetriades D, Hadjizacharia P, Constantinou C, et al. Selective nonoperative management of penetrating abdominal solid organ injuries. *Ann Surg* 2006; 244: 620–8.
37. DuBose J, Inaba K, Teixeira PG, et al. Selective non-operative management of solid organ injury following abdominal gunshot wounds. *Injury* 2007; 38: 1084–90.
38. Richardson J, Franklin GA, Lukan JK, et al. Evolution in the management of hepatic trauma: a 25-year perspective. *Ann Surg* 2000; 232: 324–30.
39. Gaarder C, Naess PA, Eken T, et al. Liver injuries—improved results with a formal protocol including angiography. *Injury* 2007; 38: 1075–83.
40. Hagiwara A, Murata A, Matsuda T, et al. The efficacy and limitations of transarterial embolization for severe hepatic injury. *J Trauma* 2002; 52: 1091–6.
41. Monnin V, Sengel C, Thony F, et al. Place of arterial embolization in severe blunt hepatic trauma: a multi-disciplinary approach. *Cardiovasc Intervent Radiol* 2008; 31: 875–82.
42. Johnson JW, Gracias VH, Gupta R, et al. Hepatic angiography in patients undergoing damage control laparotomy. *J Trauma* 2002; 52: 1102–6.

Small Bowel and Colon Injuries

Daniel L. Dent

Levels of Evidence			
Question	Answer	Level of evidence	Grade of recommendation
Anastomosis or ostomy after colon resection for trauma?	Anastomosis, except in selected patients	2A	B
Is it safe to perform colon anastomosis after damage control laparotomy?	Yes, in selected patients	4	C
Stapled or hand-sewn anastomosis after hollow viscus injury for trauma?	Either, although handsewn may be better in patients with edematous bowel	4	D
Should the skin be closed after laparotomy for colon trauma?	No	1B	B
How long should antibiotics be continued after repair of hollow viscus injury?	No more than 24 hours	1A	A
Should presacral drains be used in the management of rectal trauma?	No, except in selected cases	2A	D

Injuries to the small intestine and colon are found in less than 5% of victims of blunt abdominal trauma but are the most common injuries sustained after penetrating abdominal trauma. Despite a large experience with these injuries in both military and civilian environments, management of hollow viscus injuries remains controversial.

Important questions to consider in the care of a patient with a hollow viscus injury include need for ostomy in colon trauma, management of resected bowel after damage control surgery, consideration for stapled versus hand-sewn anastomosis, abdominal skin management, duration of antibiotics, and presacral drainage of rectal injuries.

WHEN IS AN OSTOMY PREFERRED OVER AN ANASTOMOSIS IN COLON TRAUMA?

Multiple prospective randomized trials have been performed to answer the question of repair versus anastomosis in colon trauma. For partial circumference colon injuries that do not require resection and full anastomosis, primary repair is clearly preferred. It is also clear that the majority of penetrating civilian colon injuries do not require resection. For this reason, the trials that have been done have not accrued enough patients with destructive colon wounds to definitively answer the question of what to do after resection for colon trauma (1–4). It is also unclear if blunt, destructive colon injuries should be managed in the same manner as penetrating injuries. One prospective and two retrospective studies have evaluated relatively large numbers of patients with destructive colon wounds requiring

resection (5–7). In all series, management was left to surgeon discretion. Risk factors that may be related to anastomotic leak—and therefore may lead one to manage a patient with a colostomy—include underlying medical condition, transfusion requirement of 4 or more units of packed red blood cells, hypotension on presentation, or Abdominal Trauma Index >25. It is also generally not recommended that anastomosis be performed in the case of severe bowel wall edema or poor perfusion to the segments of colon in question. It is clear from the literature on colon trauma that regardless of how a colon injury is managed, the risk of abdominal septic complications exceeds 20% in this patient population.

Answer: Nondestructive or partial circumference wounds that don't require resection should be closed primarily. Destructive wounds that require resection may usually be managed with anastomosis, although the following factors may lead to increased risk of anastomotic leak: hypotension on presentation, transfusion requirement of 4 or more units of packed red blood cells, underlying medical condition, Abdominal Trauma Index >25. Colostomy may be considered if one or more of these risk factors is present or if the edges of the resected colon do not appear optimal for anastomosis (Grade B recommendation).

IS IT SAFE TO DO A COLON ANASTOMOSIS AFTER DAMAGE CONTROL LAPAROTOMY?

To date, only one publication has addressed this issue. Miller et al. (8) performed colon anastomosis at a relaparotomy

after an initial damage control procedure in 11 of 17 patients. The other six patients were managed with a colostomy. None of the 11 patients managed with delayed anastomosis developed anastomotic leak. Abdominal septic complications were not increased in either group when compared to patients who had definitive management of their colon injury at their initial exploration. Reasons cited for not creating an anastomosis at the relaparotomy include bowel edema, medical comorbidity, recent shock, and prolonged interval from injury to operation.

Answer: It appears to be safe to perform colon anastomosis at relaparotomy in selected patients. Factors that may influence the decision to manage the patient with a colostomy include bowel edema, medical comorbidity, recent shock, and prolonged interval between injury and definitive operation (Grade C recommendation).

WHEN IS HAND-SEWN ANASTOMOSIS PREFERABLE TO STAPLED ANASTOMOSIS, IF EVER?

This question has been debated since the invention of intestinal stapling devices. In the setting of elective surgical procedures, the literature can best be summarized by stating that no outcome difference between stapled and hand-sewn anastomoses has been identified (9). However, when this question has been raised in trauma patient populations, there has been a slight but sometimes statistically significant increase in anastomotic leak in trauma patients who received stapled anastomoses (10–13). The postulated mechanism for an increased leak rate in patients with stapled anastomoses is bowel edema. A stapler does not alter its depth based on bowel wall thickness, although in a hand-sewn anastomosis the surgeon can do so.

Answer: There is no consensus on the issue of stapled versus hand-sewn anastomosis after small bowel or colon resection for trauma. Some data suggest that hand-sewn anastomosis is associated with a lower rate of anastomotic leak in trauma patients. Hand-sewn anastomosis may be preferable in situations where the portion of intestine under consideration for anastomosis is edematous or is at risk for becoming edematous, such as a patient requiring a large-volume resuscitation (Grade D recommendation due to nonconsensus of the literature).

SHOULD THE SKIN BE CLOSED AFTER LAPAROTOMY FOR COLON INJURY?

Injury to the small intestine has not been shown to result in a high rate of infectious complications, and skin closure after small bowel trauma is generally recommended (14). However, surgical site infection rates have been shown to range from 2.7% to over 50% after colonic trauma (15–18). This has led some authors to recommend closing only abdominal fascia and leaving the skin open. The best study on this topic is a prospective, randomized trial published by Velmahos et al. (19). In this trial, the infection rate for open wounds was noted to be 36% and the infection rate in closed wounds was seen to be 65%. Wound infection was predictive of risk for wound dehiscence and

necrotizing soft tissue infection. Subjecting 29% of patients to this increased risk in an effort to avoid the need to care for an open wound does not seem prudent.

Answer: Skin should be left open after laparotomy for colon trauma (Grade B recommendation).

WHAT IS THE APPROPRIATE DURATION OF ANTIBIOTICS AFTER COLON INJURY?

Three double-blind, prospective, randomized trials have compared 24 hours versus longer antibiotic coverage in patients with abdominal trauma. All studies found no significant difference in infectious complications between patients randomized to one day versus five days of perioperative antibiotics (20–22). Specifically, in 1992 Fabian and colleagues published a double-blind, prospective randomized trial in 515 patients. After sustaining penetrating abdominal trauma, the patients were randomized to receive either five days of a broad-spectrum antibiotic postoperatively or one day of the same antibiotic plus four days of saline placebo. The patients who received five days of antibiotics had a slightly but statistically insignificant higher rate of abdominal infections and were more likely to develop infection from multidrug-resistant organisms. In 1999, Cornwell et al. published the results a study in which they randomized 63 patients to five days versus one day of antibiotics after penetrating abdominal trauma. They also found a higher infection rate (38% versus 19%) in the patients who received a longer duration of antibiotics, although statistical significance was not reached, possibly due to the small sample size. In a trial of similar design involving 317 patients, published in 2000, Kirton et al. found similar results although the infection rate was slightly higher in the patients who received antibiotics for one day as opposed to five days. This difference was not statistically significant.

From the data in these well-designed and executed trials, it is safe to conclude that in patients with penetrating abdominal trauma, duration of postoperative antibiotics should be limited to a maximum of 24 hours.

Answer: Antibiotic prophylaxis should be limited to no more than 24 hours after laparotomy for intestinal injury (Grade A recommendation).

SHOULD PRESACRAL DRAINS BE USED IN THE MANAGEMENT OF RECTAL INJURIES?

Placement of presacral drains has been thought to be a useful adjunct to colonic diversion to prevent development of pelvic sepsis in the management of rectal injuries. Although the concept seems sound, at the time of placement it is difficult to ensure that the drains are placed in a position that drains the space directly adjacent to the injury. This is especially true for anterior injuries. Gonzalez et al. (23) reported their results from a prospective randomized trial and found that presacral drainage did not reduce the incidence of pelvic sepsis. Because this is the only prospective randomized trial on this topic in the literature and as only 48 patients were included, it is difficult to consider this question as having a definitive answer. Two reports have suggested that pelvic sepsis is relatively rare in patients with penetrating rectal trauma, even in the absence of presacral drains

Trial (Ref.)	Year	Randomized (Y/N)?	Total Patients	# Resection/Anastomosis	Selective (Y/N)?	Leaks	Major endpoint	Interpretations/Comments
1	1979	Y	139	0	Y			
2	1991	Y	56	11	N			

suggesting that they are of little utility (24,25). Other authors, such as Weinberg et al. (26), have argued that having a pelvic infection that is decompressed by a presacral drain is preferable to having undrained pelvic sepsis. Based on this review of the literature, it appears that presacral drainage is not routinely necessary for rectal injuries. These data are derived almost exclusively from low-velocity, penetrating trauma patients. This may not apply to patients with blunt injury or significant perirectal soft tissue damage. The author's personal practice is to selectively place a presacral drain(s) in patients who have obvious extraperitoneal tissue destruction with perirectal hematoma and/or soilage that is accessible via presacral drainage.

Answer: In general, presacral drains should do not appear to be necessary in the management of civilian penetrating rectal injuries. In the case of a destructive wound with significant hematoma and tissue destruction that is in direct communication with a rectal injury, presacral drainage may be considered (Grade D recommendation).

REFERENCES

- Stone HH, Fabian TC. Management of perforating colon trauma: randomization between primary closure and exteriorization. *Ann Surg* 1979; 190: 430–6.
- Chappuis CW, Frey DJ, Dietzen CD, et al. Management of penetrating colon injuries. A prospective randomized trial. *Ann Surg* 1991; 213: 492–7.
- Sasaki LS, Allaben RD, Golwala R, et al. Primary repair of colon injuries: a prospective randomized study. *J Trauma* 1995; 39: 895–901.
- Gonzalez RP, Falimirsky ME, Holevar MR. Further evaluation of colostomy in penetrating colon injury. *Am Surg* 2000; 66: 342–7.
- Murray JA, Demetriades D, Colson M, et al. Colonic resection in trauma: colostomy versus anastomosis. *J Trauma* 1999; 46: 250–4.
- Stewart RM, Fabian TC, Croce MA, et al. Is resection with primary anastomosis following destructive colon wound always safe? *Am J Surg* 1994; 168: 316–19.
- Demetriades D, Murray JA, Chan L, et al. Penetrating colon injuries requiring resection: diversion or primary anastomosis? An AAST prospective multicenter study. *J Trauma* 2001; 50: 765–75.
- Miller PR, Chang MC, Hoth JJ, et al. Colonic resection in the setting of damage control laparotomy: is delayed anastomosis safe? *Am Surg* 2007; 73: 606–9; discussion 609–10.
- Lustosa SA, Matos D, Atallah AN, et al. Stapled versus hand-sewn methods for colorectal anastomosis surgery. *Cochrane Database Syst Rev* 2001; CD003144.
- Brundage SI, Jurkovich GJ, Grossman DC, et al. Stapled versus sutured gastrointestinal anastomoses in the trauma patient. *J Trauma* 1999; 47: 500–7.
- Brundage SI, Jurkovich GJ, Hoyt DB, et al. Stapled versus sutured gastrointestinal anastomoses in the trauma patient: a multicenter trial. *J Trauma* 2001; 51: 1054–61.
- Demetriades D, Murray JA, Chan LS, et al. Handsewn versus stapled anastomosis in penetrating colon injuries requiring resection: a multicenter study. *J Trauma* 2002; 52: 117.
- Behrman SW, Bertken KA, Stefanacci HA, et al. Breakdown of intestinal repair after laparotomy for trauma: incidence, risk factors, and strategies for prevention. *J Trauma* 1998; 45: 227–31; discussion 231–3.
- Borlase BC, Moore EE, Moore FA. The Abdominal Trauma Index: a critical reassessment and validation. *J Trauma* 1990; 30: 1340–4.
- Adkins RB, Zirkle PK, Waterhouse G. Penetrating colon trauma. *J Trauma* 1984; 24: 491.
- Voyles CR, Flint LM Jr. Wound management after trauma to the colon. *South Med J* 1977; 70: 1067.
- Demetriades D, Charalambides D, Pantanowitz D. Gunshot wounds of the colon: role of primary repair. *Ann R Coll Surg Engl* 1992; 74: 381.
- Velmahos GC, Souter I, Degiannis E, et al. Primary repair for colonic gunshot wounds. *Aust N Z J Surg* 1996; 66: 344.
- Velmahos GC, Vassiliu P, Demetriades D, et al. Wound management after colon injury: open or closed? A prospective randomized study. *Am Surg* 2002; 68: 795.
- Fabian TC, Croce MA, Payne LW, et al. Duration of antibiotic therapy for penetrating abdominal trauma: a prospective trial. *Surgery* 1992; 112: 788.
- Cornwell EE III, Dougherty WR, Berne TV, et al. Duration of antibiotic prophylaxis in high-risk patients with penetrating abdominal trauma: a prospective randomized trial. *J Gastroint Surg* 1999; 3: 648.
- Kirton OC, O'Neill PA, Kestner M, et al. Perioperative antibiotic use in high-risk penetrating hollow viscus injury: a prospective randomized, double-blind, placebo-control trial of 24 hours versus 5 days. *J Trauma* 2000; 49: 822–32.
- Gonzalez RP, Falimirski ME, Holevar MR. The role of presacral drainage in the management of penetrating rectal injuries. *J Trauma* 45: 656, 1998.
- Navsaria PH, Edu S, Nicol AJ. World civilian extraperitoneal rectal gunshot sounds: surgical management made simpler. *J Surg* 2007; 31: 1345–51.
- Navsaria PH, Shaw JM, Zellweger R, et al. Diagnostic laparoscopy and diverting sigmoid loop colostomy in the management of civilian extraperitoneal rectal gunshot injuries. *Br J Surg* 2004; 91: 460–4.
- Weinberg JA, Fabian TC, Magnotti LJ, et al. Penetrating rectal trauma: management by anatomic distinction improves outcome. *J Trauma* 2006; 60: 508–14.

Diaphragmatic Injuries

Fahim Habib

Question Summary		
Question	Answer	Grade of recommendation
What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in blunt trauma?	There is no single diagnostic modality of choice. The optimal approach is to use the cited studies in a sequential manner until the diagnosis has either been suspected to a degree where operative intervention is warranted or excluded beyond reasonable doubt.	C
What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in penetrating trauma?	In unstable patients, diagnosis is established at operation. In stable patients, obtain a chest x-ray and CT scan. If equivocal, proceed with laparoscopy or thoracoscopy.	C
What is a clinically useful classification system that guides operative management?	Diaphragmatic injuries are best classified as contusions requiring no intervention, lacerations that can be primarily repaired, avulsions that can be reattached, or associated with significant tissue loss where prosthetics have to be used for adequate repair.	D
What is the optimal approach to the operative management of diaphragmatic injuries?	In the acute phase, approach the injury abdominally. In the latent phase, use a thoracic approach. In the obstructive phase, use an abdominal approach for the left side; a combined approach for the right side is preferred.	C
What is the ideal suture material/prosthesis for repair of diaphragmatic injuries?	Nonabsorbable material applied as simple interrupted, continuous, or horizontal mattress sutures is appropriate. Prosthetics, possibly biologics, should be used when the defect cannot be closed primarily.	C
What are the differences in the approach to left versus right-sided injuries?	On the left side, repair all injuries irrespective of the mechanism. On the right, repair those due to blunt trauma and due to penetrating trauma only if large.	C
What are the consequences of missed injuries?	A wide spectrum of often dramatic consequences may result. These make early diagnosis and repair desirable.	C
Abbreviation: CT, computed tomography.		

The optimal approach to the evaluation and management of diaphragmatic injuries (DIs) remains poorly defined. Several factors contribute to the dilemma. First, the diaphragm is a thin musculoaponeurotic layer at the junction of the thoracic and peritoneal cavities. As a result, it may be involved in traumatic injuries involving either of these cavities. Second, associated injuries are frequent. These may dominate the clinical pictures and dictate the course of management, making the issue of diaphragm injury secondary. Third, when isolated, these injuries usually have no pathognomonic features, and hence require a high index of suspicion if the diagnosis is to be made in a timely manner. This is becoming increasingly important as non-operative strategies are being more commonly employed in select cases of thoracoabdominal trauma. Also, key differences exist in injuries due to blunt and penetrating trauma and in injuries to the left and right sides of the diaphragm. This effectively precludes a universal algorithm for the management of all diaphragmatic injuries.

Finally, although some of these missed injuries may never manifest, the potential for an adverse outcome with its attendant increase in morbidity and mortality makes prompt diagnosis desirable.

At the same time, there remains a paucity of scientific evidence to guide clinical decision making. The overwhelming majority of descriptions involve case reports and case series. These usually describe the unusual and often dramatic presentation of isolated cases. Few retrospective reviews are available that summarize individual practices. Prospective studies are even fewer and are mostly directed toward establishing the diagnosis. The relative infrequency of these injuries makes it unlikely that a single center will be able to address the key issues in a timely manner. A multicenter study is more likely to be able to generate the required evidence to answer some of the key questions.

These questions include (1) What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in blunt trauma? (2) What is the optimal diagnostic

modality for the diagnosis of diaphragmatic injury in penetrating trauma? (3) What is a clinically useful classification system that guides operative management? (4) What is the optimal approach to the operative management of diaphragmatic injuries? (5) What is the ideal suture material/prosthesis for repair of diaphragmatic injuries? (6) What are the differences in the approach to left versus right-sided injuries? (7) What are the consequences of missed injuries?

As the available evidence is limited, much of what is presented here represents a summary of the current state of the knowledge and that of expert opinion.

WHAT IS THE OPTIMAL DIAGNOSTIC MODALITY FOR THE DIAGNOSIS OF DI IN BLUNT TRAUMA?

No single diagnostic test emerges as the clear modality of choice. This is compounded by the fact that the true incidence of DI remains unknown. A more prudent approach, therefore, is to use each of these methods in a sequential manner until the diagnosis has either been suspected to a degree where operative intervention is warranted or excluded beyond reasonable doubt.

Maintaining a high index of suspicion is key. Mechanisms of blunt trauma most commonly associated with DI are motor vehicle collisions, falls, and crush injury to the thoracoabdominal region (1).

Physical examination is notoriously unreliable. Signs and symptoms depend on the stage of presentation, which may be divided into the acute, latent, and obstructive phases (2). In the acute phase, variable degrees of respiratory distress occur. This is accompanied by chest and/or abdominal tenderness, reduced breath sounds in the chest, and possibly bowel sounds in the chest (3,4). The latent phase is usually asymptomatic, with the diagnosis being made incidentally when bowel sounds are heard in the chest or the patient undergoes imaging for unrelated reasons. In the obstructive phase, intra-abdominal contents herniate into the thoracic cavity. This may result in obstruction of the gastrointestinal tract, ischemia of the herniated organ, or compression of thoracic structures with possible mediastinal shift. The patient may therefore present with bowel obstruction, an acute abdomen, or even features suggestive of a tension pneumothorax (4,5), a condition to which the term *tension gastrothorax* is applied.

The chest x-ray is usually the initial diagnostic modality employed. When present, location of the nasogastric tube in the left chest, elevated hemidiaphragm, a visceral fluid level in the pleural space, and obscuring of the diaphragmatic shadow are highly suggestive (6,7). Increase in the elevation of the hemidiaphragm on the right on a repeat x-ray is another reported finding. Having the film reviewed by a radiologist increases accuracy. In a retrospective review, the accuracy of diagnosis on chest x-ray increased from 23% when read by the trauma team leader in the trauma bay to 44% when interpreted by a radiologist (1). Limitations of the technique include the fact that the film is almost always obtained in the supine position, the machine is portable and hence often of suboptimal quality, patient is usually limited, and cooperation may be influenced by associated injuries and use of positive pressure ventilation (8).

Ultrasonography is most useful for right-sided injuries where the lung sliding sign, visualization of the hepatic veins in the chest, and loss of the hepatorenal interface have been reported (9). Other findings include movement of the free edge of the diaphragm in pleural fluid, splenic herniation into the thorax, inability to visualize the diaphragm, and identification of bowel loops in the chest. Using m-mode imaging, a failure to identify rise of the diaphragm tracing with respiratory movements is considered diagnostic (10). It must be remembered however, that even a ruptured diaphragm will move in mechanically ventilated patients, limiting the use of this technique to spontaneously breathing patients alone.

Computed tomography (CT) with oral and intravenous contrast, reformatted in the coronal and sagittal planes is a useful diagnostic modality in the hemodynamically stable patient. When available, multidetector row CT is preferable because it also allows reformatting in the axial plane. Suggestive findings include diaphragmatic discontinuity, segmental nonrecognition of the diaphragm, abnormally elevated abdominal organs, herniation of intra-abdominal organs, thickening of the diaphragm to more than 10 mm, and hemothorax associated with hemoperitoneum (11). Other signs that have been described are dependent viscera sign, where on axial images the liver is seen in contact with the posterior thoracic wall, and the hump sign, where a collar of diaphragm is seen surrounding the liver (7). In a retrospective case control study using a single-detector helical CT with coronal and sagittal reconstruction, the sensitivity and specificity of the technique were 82% and 75%, respectively (12). The dependant viscera sign was most sensitive, and the collar sign and active extravasation of contrast were the most specific (13). Presence of pleural effusions and perisplenic hematomas were the most common reasons for false negative examination (13). In right-sided injuries, the presence of an associated hemothorax may limit the ability to make a diagnosis. Here, the high position of the liver may suggest the diagnosis (14).

Nuclear medicine scan techniques have been described where 2.1 mCi of technetium-99m sulfur colloid in 500 ml sterile saline are injected into the peritoneal cavity. Imaging is performed immediately and at two and four-hour intervals. The appearance of a large amount of radioactivity in the chest confirms the presence of a diaphragmatic defect (15).

Intraoperative evaluation of the diaphragm remains the gold standard against which all other modalities have been compared.

Answer: There is no single diagnostic modality of choice. The optimal approach is to use the above studies in a sequential manner until the diagnosis has either been suspected to a degree where operative intervention is warranted or excluded beyond reasonable doubt. (Recommendation grade: D).

WHAT IS THE OPTIMAL DIAGNOSTIC MODALITY FOR THE DIAGNOSIS OF DI IN PENETRATING TRAUMA?

DIs due to penetrating trauma result most often from stab wounds and gunshot wounds to the thoracoabdominal region. For purposes of definition, this region extends from the nipples cranially to the costal margin caudally.

The initial approach is determined by the hemodynamic stability of the patient. In unstable patients, urgent operative intervention is indicated. Evaluation of the diaphragm is then performed intraoperatively. In the stable patient, work-up progresses from simple noninvasive modalities to more invasive methods until the injury has been ruled out or ruled in.

The chest x-ray is once again the initial imaging modality of choice. Radio-opaque markers must be used to mark the site of the external injury. Determination of the resultant trajectory allows estimation of the likelihood of diaphragmatic involvement. However, findings may be subtle or masked by associated injuries, making diagnosis difficult. As was seen in a prospective study, 21% of patients with DIs had a normal chest x-ray (16). In another retrospective series, the chest x-ray was normal in 68% and showed only a nonspecific hemopneumothorax in the remaining 32% of patients with DI confirmed at laparoscopy.

CT, especially with multidetector row scanners and appropriate reformatting, has over 90% accuracy in detecting the presence of DI when the wound tract is seen extending to the diaphragm. In a retrospective series of 803 patients with penetrating torso injury over a four-year period, CT had a sensitivity, specificity, and accuracy of 76%, 98%, and 91%, respectively, to detect injury and 92%, 89%, and 90%, respectively, to exclude injury (12). Equivocal findings necessitate use of additional diagnostic techniques.

Laparoscopy is a useful diagnostic modality, especially in injuries involving the left side. Improved image quality and routine availability of angled scopes has allowed almost all areas of the diaphragm to be visualized. Identification of injuries of the posterior right diaphragm may still prove challenging, however. Utility of this technique was prospectively studied for penetrating trauma involving the left thoracoabdominal region. Of 110 patients studied, diaphragmatic injuries were identified in 26 (24%). Similar incidences were detected for anterior, lateral, and posterior wounds (22%, 27%, and 22%, respectively) (16). A similar incidence, 22 of 108 (20%) was reported in another retrospective series (17).

Thoracoscopy is an alternative approach to the identification of DI. The patient must be hemodynamically stable, able to tolerate single lung ventilation, and able to be placed in a lateral decubitus position. There must also be the absence of any indication for emergent laparotomy or thoracotomy. In a prospective study of 28 patients who met these criteria, DI were found in 9 cases (32%) (18). All injuries were confirmed and repaired at laparotomy. Associated intra-abdominal injuries were present in 89%.

Magnetic resonance imaging allows superior delineation of the anatomy but is challenging to employ in the acute setting. It may not always be readily available, requires transport of a quasi-stable patient to a remote location, and places the patient in a situation where adequate monitoring and access to the patient for ongoing resuscitation may not be optimal. Its use is mostly restricted to cases that are identified in the latent or obstructive phases.

Intraoperative evaluation of the diaphragm during laparotomy or thoracotomy remains the gold standard.

Answer: In unstable patients, diagnosis is established at operation. In stable patients, obtain a chest x-ray and CT scan. If equivocal, proceed with laparoscopy or thoracoscopy. Recommendation grade: D.

WHAT IS A CLINICALLY USEFUL CLASSIFICATION SYSTEM THAT GUIDES OPERATIVE MANAGEMENT?

The most popular current classification system for diaphragmatic injuries is that of the American Association for the Surgery of Trauma (AAST). Here a contusion is classified as Grade I, lacerations <2 cm as Grade II, laceration 2–10 cm as Grade III, laceration ≥10 cm with tissue loss <25 cm² as Grade IV, and lacerations with tissue loss >25 cm² as Grade V. The clinical significance of this classification system remains unclear (19).

In reviewing the operative techniques described in a number of case reports and case series (6,7,14,16,20–23), a common theme emerges. Using this, the author proposes the following classification system.

- Grade I: Contusion: No acute intervention is required, maintain high index of suspicion for progression.
- Grade II: Linear tears with viable tissue on either side of the defect that can be primarily approximated without significant tension.
- Grade III: Avulsion of the diaphragm off the chest wall, reattachment is possible, however.
- Grade IV: Significant tissue loss that precludes primary repair, necessitating the use of a prosthesis for repair.

Answer: Diaphragmatic injuries are best classified as contusions requiring no intervention, lacerations that can be primarily repaired, avulsions that can be reattached, or associated with significant tissue loss where prosthetics have to be used for adequate repair. Recommendation grade: D.

WHAT IS THE OPTIMAL APPROACH TO THE OPERATIVE MANAGEMENT OF Dis?

Because the diaphragm borders the thoracic and abdominal cavities, it can be adequately approached from either side. The optimal approach is determined by the timing of injury identification, presence of associated injuries, and the side of the injury.

For injuries identified in the acute phase, the incidence of associated intra-abdominal injuries, most commonly to the liver and spleen, requiring operative intervention is as high as 89% (18). Here, the injury is best approached via a laparotomy.

If the injury presents in the latent phase, a thoracic approach is preferred. Here, compromise of intra-abdominal contents is much less likely, and the need for formal abdominal exploration is minimal. An abdominal component may become necessary if the herniated contents cannot be adequately reduced through the chest alone.

For injuries presenting in the obstructive phase, the initial approach can be made through the chest. If the herniated organs are viable and can easily be reduced into the abdominal cavity the repair can be completed through the chest. If however, there is the need to resect nonviable or marginally viable intra-abdominal organs or adhesions preclude effective reduction, a combined thoracic and subcostal approach may be employed.

Left-sided injuries can be visualized well from the abdominal cavity and can be approached as such. The liver may preclude adequate visualization on the right, especially

in posteriorly located injuries. A thoracic approach is then more appropriate in this circumstance (6,7).

In experienced hands, laparoscopy can be employed as both a diagnostic and therapeutic modality (14, 16,22,23).

Answer: In the acute phase, approach the injury abdominally. In the latent phase, use a thoracic approach. In the obstructive phase, use an abdominal approach for the left side; a combined approach for the right side is preferred. Recommendation grade: D.

WHAT IS THE IDEAL SUTURE MATERIAL/PROSTHESIS FOR REPAIR OF DIs?

In 13 of 105 patients available for long-term follow-up (1), two recurrences were noted. In both cases, absorbable suture was used for repair. In all other reported cases, nonabsorbable suture has been used. As the diaphragm is a thin muscle in constant motion, healing of injuries is likely slow. The use of nonabsorbable material therefore appears justified. Polypropylene, nylon, or polyester applied as simple interrupted, continuous, or figure-of-eight sutures have all been reported. It is the author's preference to use polypropylene in the presence of contamination from associated intra-abdominal injuries and braided polyester when such contamination is absent. The sutures are placed in a horizontal mattress manner. For all defects requiring more than one or two sutures, the resultant ridge of approximated tissue is oversewn with a running simple continuous stitch. In cases where the edges of the diaphragm could not be brought together primarily, the use of expanded polytetrafluoroethylene has been described (6,14). More recently, biologic prostheses are being used increasingly for the repair of large abdominal wall defects. Their use has also been reported in the repair of paraesophageal hernia. Although the use of biologics in repair of DI has not yet been reported, this offers an attractive option, especially in cases with associated contamination from intra-abdominal injuries.

Answer: Nonabsorbable material applied as simple interrupted, continuous, or horizontal mattress sutures is appropriate. Prosthetics, possibly biologics, should be used when the defect cannot be closed primarily. Recommendation grade: D.

WHAT ARE THE DIFFERENCES IN THE APPROACH TO LEFT- VERSUS RIGHT-SIDED INJURIES?

Injuries to the left side are three times more frequent than those on the right. This is believed to be a result of the left

side being congenitally weaker and lacking the protective effect of the liver. These factors make it less resistant to pressure. The incidence of right-sided injuries, however, is increasing due to increasing number of automobile accidents and improvements in CT technology.

All injuries on the left, those due to both blunt and penetrating trauma, must be sought and repaired early. Even small defects will likely progress over time because the diaphragm is a thin muscle in constant motion that is subject to differential pressure gradients between the peritoneal and pleural cavities. This pressure gradient eventually causes intra-abdominal contents to herniate through placing them at risk for obstruction or strangulation.

For right-sided injuries, the mechanism must be taken into account. In penetrating injuries, especially stab wounds, the defect is often small, is sealed by the liver, and prevents the herniation of bowel. In blunt injuries, on the other hand, there is a significant transfer of force, causing a larger defect with progressive herniation of the liver (6,14). This may occur years after the initial injury (24,25).

Answer: On the left side, repair all injuries irrespective of the mechanism. On the right, repair those due to blunt trauma and due to penetrating trauma only if large. Recommendation grade: D.

WHAT ARE THE CONSEQUENCES OF MISSED INJURIES?

A large number of case reports describe patients with delayed presentation of DI that were missed at initial presentation. Latent periods of up to 28 years have been reported. The presentation depends on the herniation organ. Right-sided injuries are associated with progressive herniation of the liver, which compresses the lung causing progressive respiratory embarrassment. On the left, gastrothorax, gastrointestinal bleeding from splenic vein thrombosis due to herniation of the spleen, tension fecopneumothorax from acute rupture of a herniated colon, and symptoms of bowel obstruction have all been reported. Yet the true number of patients with unidentified diaphragmatic injuries that remain asymptomatic remains unknown. It is unlikely that this number will ever be known. The consequence of missed injuries will therefore remain anecdotal. It does seem prudent, however, to aggressively seek out these injuries with early repair.

Answer: A wide spectrum of often dramatic consequences may result. These make early diagnosis and repair desirable. Recommendation grade: D.

Diaphragmatic Injuries: Levels of Evidence and Grades of Recommendation

Question	Answer	Levels of evidence	Grade of recommendation
What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in blunt trauma?	There is no single diagnostic modality of choice. The optimal approach is to use the cited studies in a sequential manner until the diagnosis has either been suspected to a degree where operative intervention is warranted or excluded beyond reasonable doubt.	III	D
What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in penetrating trauma?	In unstable patients, diagnosis is established at operation. In stable patients, obtain a chest x-ray and CT scan. If equivocal, proceed with laparoscopy or thoracoscopy.	III	D
What is a clinically useful classification system that guides operative management?	Diaphragmatic injuries are best classified as contusions requiring no intervention, lacerations that can be primarily repaired, avulsions that can be reattached, or associated with significant tissue loss where prosthetics have to be used for adequate repair.	IV	D
What is the optimal approach to the operative management of diaphragmatic injuries?	In the acute phase, approach the injury abdominally. In the latent phase, use a thoracic approach. In the obstructive phase, use an abdominal approach for the left side; a combined approach for the right side is preferred.	III	D
What is the ideal suture material/prosthesis for repair of diaphragmatic injuries?	Nonabsorbable material applied as simple interrupted, continuous, or horizontal mattress sutures is appropriate. Prosthetics, possibly biologics, should be used when the defect cannot be closed primarily.	III	D
What are the differences in the approach to left versus right-sided injuries?	On the left side, repair all injuries irrespective of the mechanism. On the right, repair those due to blunt trauma and due to penetrating trauma only if large.	III	D
What are the consequences of missed injuries?	A wide spectrum of often dramatic consequences may result. These make early diagnosis and repair desirable.	IV	D

Abbreviation: CT, computed tomography.

REFERENCES

- Hanna WC, Ferri LE, Fata P, et al. The current status of traumatic diaphragmatic injury: lessons learned from 105 patients over 13 years. *Ann Thorac Surg* 2008; 85: 1044–8.
- Grimes OF. Traumatic injuries of the diaphragm. *RN* 1975; 38: OR8, OR10, OR12.
- Howard R, Alijani A, Munshi IA. Right-side diaphragm injury resulting from blunt trauma. *J Emerg Med* 2008; 34: 85–7.
- Matsevych OY. Blunt diaphragmatic rupture: Four year's experience. *Hernia* 2008; 12: 73–8.
- Nishijima D, Zehbtachi S, Austin RB. Acute posttraumatic tension gastrothorax mimicking acute tension pneumothorax. *Am J Emerg Med* 2007; 25: 734.e5–6.
- Igai H, Yokomise H, Kumagai K, et al. Delayed hepatothorax due to right-sided traumatic diaphragmatic rupture. *Gen Thorac Cardiovasc Surg* 2007; 55: 434–6.
- Dineen S, Schumacher P, Thal E, et al. CT reconstructions of right-sided blunt diaphragm rupture. *J Trauma* 2008; 64: 1412.
- Iochum S, Ludig T, Walter F, et al. Imaging of diaphragmatic injury: A diagnostic challenge? *Radiographics* 2002; 22: S103–116; discussion S116–118.
- Kirkpatrick AW, Ball CG, Nicolaou S, et al. Ultrasound detection of right-sided diaphragmatic injury; the "liver sliding" sign. *Am J Emerg Med* 2006; 24: 251–2.
- Blaivas M, Brannam L, Hawkins M, et al. Bedside emergency ultrasonographic diagnosis of diaphragmatic rupture in blunt abdominal trauma. *Am J Emerg Med* 2004; 22: 601–4.
- Nchimi A, Szapiro D, Ghaye B, et al. Helical CT of blunt diaphragmatic rupture. *Am J Roentgenol* 2005; 184: 24–30.
- Stein DM, York GB, Boswell S, et al. Accuracy of computed tomography (CT) scan in the detection of penetrating diaphragm injury. *J Trauma* 2007; 63: 538–43.
- Larici AR, Gotway MB, Litt HI, et al. Helical CT with sagittal and coronal reconstructions: accuracy for detection of diaphragmatic injury. *Am J Roentgenol* 2002; 179: 451–7.
- Mintz Y, Easter DW, Izhar U, et al. Minimally invasive procedures for diagnosis of traumatic right diaphragmatic tears: a method for correct diagnosis in selected patients. *Am Surg* 2007; 73: 388–92.
- May AK, Moore MM. Diagnosis of blunt rupture of the right hemidiaphragm by technetium scan. *Am Surg* 1999; 65: 761–5.
- Murray JA, Demetriades D, Asensio JA, et al. Occult injuries to the diaphragm: Prospective evaluation of laparoscopy in penetrating injuries to the left lower chest. *J Am Coll Surg* 1998; 187: 626–30.
- Powell BS, Magnotti LJ, Schroepfel TJ, et al. Diagnostic laparoscopy for the evaluation of occult diaphragmatic injury following penetrating thoracoabdominal trauma. *Injury* 2008; 39: 530–4.
- Paci M, Ferrari G, Annessi V, et al. The role of diagnostic VATS in penetrating thoracic injuries. *World J Emerg Surg* 2006; 1: 30.
- Asensio JA, Demetriades D, Rodriguez A. Injury to the diaphragm. In: Feliciano DV, Moore EE, Mattox KL, eds., *Trauma*, 3rd edition. Stamford, CT: Appleton and Lange, 1996, 461–85.

20. Konstantinos S, Georgios I, Christos C, et al. Traumatic avulsion of kidney and spleen into the chest through a ruptured diaphragm in a young worker: a case report. *J Med Case Reports* 2007; 1: 178.
21. Hacıbrahimoglu G, Solak O, Olcmen A, et al. Management of traumatic diaphragmatic rupture. *Surg Today* 2004; 34: 111–14.
22. Baldassarre E, Valenti G, Gambino M, et al. The role of laparoscopy in the diagnosis and the treatment of missed diaphragmatic hernia after penetrating trauma. *J Laparoendosc Adv Surg Tech A* 2007; 17: 302–6.
23. Matz A, Landau O, Alis M, et al. The role of laparoscopy in the diagnosis and treatment of missed diaphragmatic rupture. *Surg Endosc* 2000; 14: 537–9.
24. Christie DB III, Chapman J, Wynne JL, et al. Delayed right-sided diaphragmatic rupture and chronic herniation of unusual abdominal contents. *J Am Coll Surg* 2007; 204: 176.
25. Peker Y, Tatar F, Kahya MC, et al. Dislocation of three segments of the liver due to hernia of the right diaphragm: Report of a case and review of the literature. *Hernia* 2007; 11: 63–5.

Pancreatic and Duodenal Trauma

Adrian W. Ong and Elan Jeremitsky

Questions		
Question	Recommendation	Grade
1. Is serum amylase a reliable indicator of pancreatic injury?	No. Although the majority of patients with pancreatic injury will present with an elevated serum amylase, its specificity is unknown, and therefore it should not be used to diagnose pancreatic injury.	B
2. Is CT reliable in detecting pancreatic injuries? When should pancreatography be used?	CT is accurate in detecting abnormalities suggesting pancreatic injury. There is conflicting evidence as to its reliability in predicting ductal injury. There is insufficient evidence to recommend either routine or selective use of ERCP.	C
3. Is MRCP reliable for the evaluation of pancreatic injuries?	There is insufficient evidence to assess the reliability of MRCP in the evaluation of pancreatic injury.	N/A
4. Is NOM of adult blunt pancreatic injuries feasible?	NOM of hemodynamically stable adult patients with blunt pancreatic injuries lacking other associated injuries requiring laparotomy may succeed if there is no pancreatic duct injury. Endoscopic stenting of patients with known ductal injuries may avert surgical therapy in selected cases.	C
5. Is NOM of pediatric blunt pancreatic injuries feasible?	NOM of hemodynamically stable pediatric patients with blunt pancreatic injuries lacking other associated injuries requiring laparotomy is feasible, and is more likely to succeed if the pancreatic ductal status is normal. Selected patients with known ductal injuries may be managed nonoperatively.	B
6. Does octreotide lower the likelihood of developing a pancreatic fistula after surgery for pancreatic trauma?	There is insufficient evidence for or against the prophylactic use of octreotide to reduce postoperative pancreatic-related complications.	N/A
7. Is drainage alone a sufficient operative treatment for pancreatic ductal injuries?	Pancreatic ductal injuries except for those in the pancreatic head should be managed with resection rather than drainage.	C
8. Is CT reliable to diagnose duodenal perforation after blunt trauma? Is oral contrast necessary? Is fluoroscopic duodenography useful?	In patients with duodenal perforation, CT will reliably show a constellation of abnormalities. There is insufficient evidence to recommend the use of oral contrast or duodenography.	C
9. Does pyloric exclusion decrease the likelihood of a duodenal leak after primary repair of a duodenal perforation?	Pyloric exclusion does not decrease the likelihood of duodenal leak after primary repair of a duodenal perforation.	C
Abbreviations: CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; NOM, nonoperative management.		

INTRODUCTION

Managing pancreatic and duodenal traumatic injuries remains extremely challenging to the surgeon for several reasons. These injuries are uncommon, and accurate diagnosis requires a high index of suspicion. In addition, the retroperitoneal location of these organs often makes physical examination unreliable in the detection of these injuries. Consequently, delay in diagnosis and treatment is not uncommon, which may affect outcome. Operative management may also be complex depending on the severity of injury, which could also influence outcome.

METHODS

An online search of PubMed was performed for all articles from January 1990 to March 2008 using the terms "pancreatic trauma," "duodenal trauma," "octreotide," "magnetic resonance cholangiopancreatography," "endoscopic retrograde cholangiopancreatography (ERCP)," "magnetic resonance cholangiopancreatography (MRCP)," "amylase," and "pyloric exclusion." Abstracts were reviewed and selected for suitability with regard to the questions being examined, and relevant articles were obtained for further review. The search was limited to English-language articles on human

subjects only. We also performed an online search of the Cochrane Library, U.K. National Library of Health, and the U.S. National Guidelines Clearinghouse using similar key terms.

Review articles that were not systematic reviews, expert opinion without explicit critical appraisal, and case series including fewer than five subjects were excluded.

Suitable articles were graded according to the levels of evidence developed by the Oxford Centre for Evidence Based Medicine, and grades of recommendations were formulated based on the same system. Articles with Level V evidence based on this system were excluded.

QUESTIONS TO BE ADDRESSED

Diagnosis of Pancreatic Injury

1. Is serum amylase a reliable indicator of pancreatic injury?
2. Is computed tomography (CT) reliable in detecting pancreatic injuries? When should ERCP be used?
3. Is MRCP reliable for the evaluation of pancreatic injuries?

Treatment of Pancreatic Injuries

4. Is nonoperative management (NOM) of adult blunt pancreatic injuries (BPIs) feasible?
5. Is NOM of pediatric BPI feasible?
6. Does octreotide lower the likelihood of developing a pancreatic fistula following trauma?
7. Is drainage alone sufficient operative treatment for pancreatic ductal injuries?

Diagnosis of Duodenal Injuries

8. Is CT reliable to diagnose duodenal perforation after blunt trauma? Is oral contrast necessary? Is an upper gastrointestinal fluoroscopic series reliable?

Treatment of Duodenal Injuries

9. Does pyloric exclusion decrease the likelihood of a duodenal leak after primary repair of a duodenal perforation?

IS SERUM AMYLASE A RELIABLE INDICATOR OF PANCREATIC INJURY?

The incidence of pancreatic injuries among all admissions for trauma is less than 0.5% (1). Almost all of the available studies focused on evaluation of the sensitivity of serum amylase in predicting pancreatic injuries. In 73 patients with pancreatic injury, Takishima et al. (2) using CT, operative findings, and ERCP as reference standards for pancreatic injury, found that if the measurement was made less than three hours from the time of injury, 76% of patients had an elevated amylase, whereas if the time of injury was more than three hours, all (23/23) had an elevated amylase. The authors therefore advocated measurement of a serum amylase three hours after admission if the initial value was normal. In a multi-institutional study, Bradley et al. (3) found that of 101 proven pancreatic injuries by laparotomy, autopsy, or CT, the amylase was elevated in 73.4%, and

sensitivity improved to 89.1% with serial determinations. On the other hand, an elevation of amylase did not necessarily indicate the presence of a pancreatic injury. Ryan et al. (4) studied patients with persistent elevations of amylase three days after admission. Of 17 patients with persistently elevated amylase, none had pancreatic injury by CT or laparotomy. Five of the 17 had "clinical pancreatitis," which resolved without intervention. The authors concluded that elevation of amylase was a poor predictor of pancreatic injury or injury requiring surgical intervention.

Summary: An elevated amylase is not a reliable indicator of pancreatic injury. Although the majority of patients with pancreatic injury will present with an elevated serum amylase, its specificity is unknown, and therefore it should not be used to make a diagnosis of pancreatic injury. Strength of recommendation: B.

IS CT RELIABLE IN DETECTING PANCREATIC INJURIES? WHEN SHOULD ERCP BE USED?

Studies of CT in pancreatic injury show varying conclusions with respect to the ability of CT to detect pancreatic injury and define the degree of injury. One possible variable that would be outside the scope of this discussion is the rapid advancement in CT technology over this study period. Whether ERCP should be used routinely or selectively is also unclear. Takishima et al. (5) retrospectively analyzed patients who underwent pancreatography to attempt to classify pancreatic ductal injuries due to blunt trauma. Of 64 patients, 37 had pancreatography within three days. A classification system for ductal injuries was devised based on location of injury [main pancreatic duct (MPD) versus branch pancreatic duct] and whether contrast had extravasated outside of the pancreas in branch duct injuries. These findings were correlated to outcome. The authors concluded that the use of ERCP early in the course of injury could prevent unnecessary laparotomy, prevent major complications due to nonoperative treatment, and determine appropriate surgical procedures. In a prospective study of 23 patients with blunt pancreatic injuries, Kim et al. (6) found that CT predicted only 55% (6/11) patients with MPD injuries and concluded that early ERCP was indicated routinely because CT could underestimate the severity of injury. On the other hand, several authors advocate a selective approach to the use of ERCP primarily based on CT findings. Houben et al. (7) retrospectively studied 15 pediatric patients, where both CT and ERCP were done in 11. CT predicted 10/11 (91%) with ductal injuries. The authors concluded that CT should dictate the need for ERCP. Teh et al. (1) and Wong et al. (8) evaluated the accuracy of CT retrospectively. Wong and colleagues compared blinded radiologists' evaluation with operative findings. They concluded that CT could accurately predict the likelihood of ductal injury based on the depth of laceration (superficial, <50% parenchyma, versus deep, >50% parenchyma). Similarly, Teh and colleagues studied 50 patients with BPI where 33 had both preoperative CT and laparotomy and found that CT was 91% sensitive and 91% specific for identifying pancreatic ductal injury.

Summary: CT is accurate in detecting abnormalities suggesting pancreatic injury. There is conflicting evidence

as to its reliability in predicting ductal injury. There is insufficient evidence to recommend either routine or selective use of ERCP. Strength of recommendation: C.

IS MRCP RELIABLE FOR THE EVALUATION OF PANCREATIC INJURIES?

There was only one suitable study. Fulcher et al. (9) studied 10 hemodynamically stable patient with pancreatic trauma who underwent MRCP: 6 showed no injury, and were managed nonoperatively without complications. Pancreatic duct injuries were detected in four patients; pseudo-cysts were detected in three of these four patients. The authors concluded that MRCP could detect pancreatic ductal injuries that may be used to guide management decisions.

Summary: There is insufficient evidence to assess the reliability of MRCP in the evaluation of pancreatic injury. Strength of recommendation: not applicable.

IS NOM OF ADULT BPI FEASIBLE?

Only a few studies in the adult literature address this question. Bradley et al. (3) studied 99 blunt injuries where 42 were observed initially and 22 (52%) were successfully managed without surgery. Of the 42, 13 had ductal injuries, and 12 required delayed operative management. When there was no ductal injury, NOM was successful in 21 of 29 (72%) patients. They concluded that the integrity of the pancreatic duct was important to predict failure. Takishima et al. (5) found that if there were no ductal injuries by ERCP ($n = 13$), in the 8 patients out of the 13 that were treated nonoperatively, only 1 developed a pseudo-cyst. Kim et al. (6) also found that when the MPD was injured in 11 patients, the 3 that had contrast extravasation confined to the pancreatic parenchyma were treated successfully with transpapillary stenting. Three other patients with branch duct injuries recovered after nonoperative treatment. Lin et al. (10) studied 15 patients with ductal injury (out of 102 patients with BPI) who underwent ERCP. Six of the 15 underwent stenting; 3 underwent laparotomy with postoperative stenting after duct injury was initially missed, and 3 underwent ERP and stenting as primary therapy early in their course. One patient died of sepsis, four of the six developed ductal stricture, and one had stent migration. The authors concluded that although stent placement is a viable alternative to acute surgery in ductal injuries, more data are needed to determine its efficacy and safety in the long term.

Summary: NOM of hemodynamically stable adult patients with BPIs lacking other associated injuries requiring laparotomy may succeed if there is no pancreatic duct injury. Endoscopic stenting of patients with known ductal injuries may avert surgical therapy in selected cases. Grade of recommendation: C.

IS NOM OF PEDIATRIC BPIS FEASIBLE?

Shilyansky et al. (11) studied 28 children who were enrolled in a prospective protocol for NOM after excluding patients who had hollow viscus injury and/or hemodynamic instability. In group 1 with pancreatic contusions, 2 of 14

developed pseudo-cysts versus 5 of 11 in group 2 with transections ($p < 0.05$). None of the pseudo-cysts in group 1 required intervention, whereas four out of the five pseudo-cysts in group 2 required percutaneous drainage. There were no deaths, all pseudo-cysts were managed with drainage, and two required surgery for duodenal perforation and duodenal stricture, giving an overall success rate of 26/28 for NOM. Keller et al. (12) retrospectively studied data obtained from two hospitals and the National Pediatric Trauma Registry. Of the blunt Grade I and II injuries (without ductal involvement), 23 out of 120 required pancreas-specific operative intervention (19%). The patients were well matched for age, Injury Severity Score (ISS), PTS, and % requiring transfusions. For the Grade III–V blunt injuries with ductal involvement, only 10 of 17 patients required pancreas-specific intervention (59%). Mortality rates were equal for Grades I–II blunt injuries managed nonoperatively versus operatively. For Grades III–V blunt injuries, mortality was 13% for NOM versus 6% for operative intervention. Authors concluded that NOM is possible for Grade I–II blunt injuries “with careful observation” and in the absence of ductal injury.

Mattix et al. (13) retrospectively analyzed 173 patients with BPIs: Failure of NOM occurred in 26%. There was no difference in age, gender, ISS, Glasgow Coma Score mechanism, intensive care unit length of stay, and overall length of stay between the failure group versus the NOM group. When ductal injuries were analyzed, the NOM failure rate was 23/53 (43%) with the NOM failure group showing a significantly higher ISS (29 versus 16). There were no significant differences in the incidence of pseudo-cyst, fistula, and length of stay when patients with Grade III–V injuries were compared with respect to method of treatment. The authors concluded that higher grade injuries (III–V, i.e., with ductal involvement) and ISS were predictors of NOM failure.

Summary: NOM of hemodynamically stable pediatric patients with BPIs lacking other associated injuries requiring laparotomy is feasible and is more likely to succeed if the pancreatic ductal status is normal. Selected patients with known ductal injuries may be managed nonoperatively initially. Grade of recommendation: C.

DOES OCTREOTIDE LOWER THE LIKELIHOOD OF DEVELOPING A PANCREATIC FISTULA AFTER SURGERY FOR PANCREATIC TRAUMA?

Only two suitable papers addressing this question were found. Nwariaku et al. (14) retrospectively analyzed patients who received octreotide postoperatively ($n = 21$) versus no octreotide ($n = 96$). The octreotide group had higher injury grades and longer hospital stay, with age, mechanism, and ISS matched. Pancreatic fistula rates were no different between the two groups (48% versus 40%). Grade of injury did not appear to influence fistula formation. The authors concluded that octreotide to reduce pancreatic complications was not beneficial, but they acknowledged that there might have been problems with patient selection. On the other hand, Amirata et al. (15) studied retrospectively 28 patients, of which 7 received octreotide postoperatively. There were 0/7 pancreatic complications versus 6/21 (29%). The cases

were “well matched” for age, mechanism of injury, and ISS. The authors concluded that octreotide use was associated with fewer pancreatic-related complications postoperatively.

Summary: There is insufficient evidence for or against the prophylactic use of octreotide to reduce postoperative pancreatic-related complications. Grade of recommendation: Not applicable.

IS DRAINAGE ALONE SUFFICIENT OPERATIVE TREATMENT FOR PANCREATIC DUCTAL INJURIES?

Although a significant correlation between injury to the MPD and pancreatic-related complications has been reported (1), only a few publications have addressed the type of surgical therapy (drainage alone versus resection) required when a ductal injury is encountered. Wind et al. (16) retrospectively analyzed outcomes following distal pancreatic trauma (89% blunt). Of 38 patients, 23 patients were identified as having a distal MPD injury based on ERCP or laparotomy. Of these, 19 patients with duct injury treated without resection developed either fistulas ($n = 14$) or pseudo-cysts ($n = 5$). Half the patients with fistulas required distal pancreatectomy for failure to close. All five patients with pseudo-cysts underwent some sort of drainage procedure. Twelve patients without ductal injury were treated without resection. Ultimately, 9 of the 12 subsequently underwent drainage procedures mainly for pseudo-cysts. The authors concluded that although the majority of all patients required surgical procedures, those with ductal injury required resection, whereas those without ductal injury required only drainage procedures.

Lewis et al. (17) studied 13 patients (11 had penetrating injury) with pancreatic head injury. Patients with intact ductal system were treated with simple drainage and had no complications. Six patients with ductal injury treated with simple drainage all had either fistula or pseudo-cyst formation. The authors concluded that pancreatic head ductal injuries require more than drainage alone. On the other hand, DeGiannis and colleagues (18) analyzed the outcome of external drainage and debridement for penetrating injuries to the head of the pancreas and found that although the fistula rate was 100% in 14 patients, 11 closed spontaneously and 3 died from sepsis. He concluded that for ductal injuries without massive disruption (Grade III) to the pancreatic head, drainage was a safe alternative to pancreaticoduodenectomy.

Patton et al. (19) retrospectively studied 124 patients using a simplified management algorithm. Eighty-one percent were due to penetrating trauma. For distal injuries, those with ductal injury and those with “indeterminate” ductal status but high probability for injury were treated with resection, and those with no ductal injury and those with indeterminate status but low probability were treated with drainage alone. When the group with indeterminate ductal status was examined separately, those treated with resection had an equivalent complication rate to those treated with drainage (27–33%). Multivariate analysis revealed that only “definitive ductal injury” and colonic injury were independent predictors of outcome. Distal resection itself did not appear to play a significant role. The authors suggested that “indeterminate” ductal status could be managed with either operative strategy with equivalent outcomes and that

intraoperative pancreatograms to assess ductal status were not essential.

Summary: Pancreatic ductal injuries except for those in the pancreatic head should be managed with resection. Grade of recommendation: C.

IS CT RELIABLE TO DIAGNOSE DUODENAL PERFORATION AFTER BLUNT TRAUMA? IS ORAL CONTRAST NECESSARY? IS FLUOROSCOPIC DUODENOGRAPHY USEFUL?

Shilyansky et al. (20) retrospectively studied 27 pediatric patients with blunt duodenal injury (BDI). CT was performed on a total of 19 patients (9 with perforation, 10 with hematoma). All patients with duodenal perforation had either retroperitoneal air (8/9) and/or retroperitoneal contrast (4/9). Free air only occurred in two of nine (22%) patients. In 10 patients with duodenal hematoma, 0% had retroperitoneal contrast or air. Retroperitoneal fluid did not reliably distinguish the two conditions. The authors concluded that CT will show some sort of abnormality in 100% of the patients with duodenal perforation, but only retroperitoneal air or contrast could reliably distinguish perforation from duodenal hematoma. Oral contrast may increase sensitivity in this setting.

Ballard et al. (21) studied 30 cases of blunt duodenal rupture from the Pennsylvania Trauma Outcome Study database. Eighteen patients had CT done as the primary diagnostic study with 15 done within four hours of admission. CT was normal in four (27%), retroperitoneal air seen in only two (13%), and contrast extravasation in two (13%). Most of the patients had intraperitoneal fluid ($n = 11$), duodenal hematoma ($n = 6$), or pneumoperitoneum ($n = 5$). The authors concluded that CT for the diagnosis of blunt duodenal perforation was often inaccurate, as the classic findings were often absent when the CT was performed within four hours after admission. It was unclear how many patients received oral contrast. Desai et al. (22) studied BDI in children retrospectively at a Level I pediatric trauma center. Of the five patients with duodenal perforation, three had either intraperitoneal air or retroperitoneal air (3/5, 60%). The remaining two were diagnosed at laparotomy with abnormal findings on CT. All five were given oral contrast, but none had oral contrast extravasation. Due to the small number of patients with perforation, it is difficult to draw valid conclusions about the sensitivity of CT in this study. The role of duodenography was not evaluated in these patients with perforations.

In the only study to specifically evaluate duodenography, Timaran and colleagues (23) assessed patients with BDI. In their analysis of four patients with perforation, duodenography showed extravasation in three, with two already having CT findings of retroperitoneal air. Their conclusion was that duodenography was of minimal utility in diagnosing duodenal perforations. This study again had very few patients with duodenal perforations to draw valid conclusions.

Summary: In patients with duodenal perforation, CT will reliably show a constellation of abnormalities. However, there is insufficient evidence to recommend the use of oral contrast or duodenography. Grade of recommendation: C.

DOES PYLORIC EXCLUSION DECREASE THE LIKELIHOOD OF A DUODENAL LEAK AFTER PRIMARY REPAIR OF A DUODENAL PERFORATION?

Velmahos et al. (24) reported in a series with 84% penetrating injuries to the duodenum the outcomes of primary repair versus repair with pyloric exclusion (PE). Primary repair was performed in 34 (68%) and PE in 16 (32%) of patients. The two groups were similar for age, injury severity, abdominal Abbreviated Injury Score, and time to operation. However, the PE group had more pancreatic injuries (63% versus 24%). The duodenal leak rate was not significantly different (18% with primary repair versus 24% with PE). Seamon et al. (25) also retrospectively analyzed the outcome of PE versus primary repair after penetrating injuries, with > Grade II duodenal injuries. Both groups were well matched for age, sex, % of gunshot wounds, duodenal injury grade, shock, pancreatic injuries, vascular injuries, and injury severity score. Of the 29 patients, 0 of 15 (0%) with no exclusion versus 0 of 14 (0%) with exclusion developed duodenal fistula, with similar length of stay and mortality.

On the other hand, DeGiannis et al. (26) studied 58 patients where 31 had American Association for the Surgery of Trauma Grade III injuries. Leak rates were 43% for the primary repair versus 11% with the addition of PE. The authors concluded that PE should be used for high-grade injuries. However, no statistical analysis was used. Jansen et al. (27) studied primary repair in 18 patients versus

PE in 11 patients. No analysis of injury severity between the two groups was available for comparison. No duodenal leaks were seen. The authors concluded that PE should be used liberally to minimize duodenal-related morbidity.

Summary: PE does not decrease the likelihood of duodenal leak after primary repair of a duodenal perforation. Grade of recommendation: C.

FINAL WORD

In regard to the acute care surgeon who is faced with a possible pancreatic/duodenal traumatic injury, will this evidence-based medicine approach change current practices, given the relative paucity of Level I and II data available for pancreatic/duodenal injuries?

Our current practice is that if CT shows a transected pancreas, and presumably a transected main duct, then operative intervention is required. What is unclear is the management of nonspecific pancreatic findings. This evidence-based review has not produced strong recommendations. What the literature suggests is that a multi-modality approach using CT, ERCP, and possibly MRCP may be required in equivocal cases. Whether a persistently normal amylase can effectively rule out pancreatic injury is also unclear. The management of duodenal injuries is equally complex, given the wide surgical armamentarium available that is described well in the literature. Further prospective studies are clearly needed in this realm.

Evidentiary Table for Questions to be Addressed

Subject	Ref.	Level of evidence	Grade	Summary
Reliability of serum amylase	2	IIb	B	Serum amylase is not reliable to make the diagnosis of pancreatic injury.
	4	IIIb		
	3	IIIb		
	28	IIIb		
	29	IV		
	30	IV		
	31	IV		
Reliability of CT to diagnose pancreatic injury; Routine versus selective use of ERCP	5	IV	C	CT is reliable in diagnosing pancreatic abnormalities suggesting pancreatic injuries. Insufficient evidence to recommend either routine versus selective use of ERCP.
	6	IIb		
	32	IV		
	16	IV		
	7	IIIb		
	3	IIIb		
	1	IIIb		
	8	IIb		
	33	IIIb		
	34	IIIb		
	35	IIIb		
	36	IV		
	37	IV		
	38	IV		
	9	IV		
Reliability of MRCP to diagnose pancreatic injuries	9	IV	N/A	Insufficient evidence.
Feasibility of NOM of adult blunt pancreatic injuries	3	IV	C	NOM may be feasible if there is no pancreatic duct injury. In selected cases, ERCP with stenting may avert surgical therapy.
	5	IV		
	6	IV		
	10	IV		

(Continued)

Evidentiary Table for Questions to be Addressed (Continued)

Subject	Ref.	Level of evidence	Grade	Summary
Feasibility of NOM of pediatric blunt pancreatic injuries	11	IIb	C	NOM is feasible, and is more likely to succeed if the pancreatic ductal status is normal. Selected patients with known ductal injuries may be managed nonoperatively initially.
	12	IIIb		
	13	IIIb		
	39	IV		
	28	IV		
	40	IV		
	41	IV		
	42	IV		
	7	IV		
	43	IV		
Prophylactic use of octreotide	14	IV	N/A	Insufficient evidence.
	15	IV		
Operative management of ductal injuries	16	IV	C	Resection preferable to drainage except for injuries to the pancreatic head.
	17	IV		
	18	IV		
	44	IV		
	19	IV		
Reliability of CT to diagnose blunt duodenal perforation; role of oral contrast and duodenography	21	IV	C	CT is reliable in showing abnormalities in cases of duodenal perforation. Insufficient evidence to support the use of oral contrast in CT or fluoroscopic duodenography.
	20	IIIb		
	22	IV		
	23	IV		
Pyloric exclusion in primary repair of duodenal perforations	24	IIIb	C	Pyloric exclusion does not decrease the likelihood of duodenal leak after primary repair.
	25	IIIb		
	26	IV		
	27	IV		

Abbreviations: CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; NOM, nonoperative management.

REFERENCES

1. Teh S, Shepperd BC, Mullins RJ, et al. Diagnosis and management of blunt pancreatic injury in the era of high-resolution computed axial tomography. *Am J Surg* 2007; 97: 641–3.
2. Takishima T, Sugimoto K, Hirata M, et al. Serum amylase level on admission in the diagnosis of blunt injury to the pancreas. *Ann Surg* 1997; 226: 70–6.
3. Bradley EL, Young PR, Chang MC, et al. Diagnosis and initial management of blunt pancreatic trauma. *Ann Surg* 1998; 227: 861–9.
4. Ryan S, Sandler A, Trenhaile S, et al. Pancreatic enzyme elevations after blunt trauma. *Surgery* 1994; 116: 622–7.
5. Takashima T, Hirata M, Kataoka Y, et al. Pancreatographic classification of pancreatic ductal injuries caused by blunt injury to the pancreas. *J Trauma* 2000; 48: 745–52.
6. Kim HS, Lee DK, Kim IW, et al. The role of endoscopic retrograde pancreatography in the treatment of traumatic pancreatic duct injury. *Gastrointest Endosc* 2001; 54: 49–55.
7. Houben CH, Ade-Ajayi N, Patel S, et al. Traumatic pancreatic duct injury in children: minimally invasive approach to management. *J Pediatr Surg* 2007; 42: 629–35.
8. Wong YC, Wang LJ, Lin BC, et al. CT grading of blunt pancreatic injuries: prediction of ductal disruption and surgical correlation. *J Comput Assist Tomogr* 1997; 21: 246–50.
9. Fulcher AS, Turner MA, Yelon JA, et al. Magnetic resonance cholangiopancreatography (MRCP) in the assessment of pancreatic duct trauma and its sequelae: preliminary findings. *J Trauma* 2000; 48: 1001–7.
10. Lin BC, Liu NJ, Fang JF, et al. Long-term results of endoscopic stent in the management of blunt major pancreatic duct injury. *Surg Endosc* 2006; 20: 1551–5.
11. Shilyansky J, Sena LM, Kreller M, et al. Nonoperative management of pancreatic injuries in children. *J Pediatr Surg* 1998; 33: 343–9.
12. Keller MS, Stafford PW, Vane DW. Conservative management of pancreatic trauma in children. *J Trauma* 1997; 42: 1097–100.
13. Mattix KD, Tataria M, Holmes J, et al. Pediatric pancreatic trauma: predictors of nonoperative management failure and associated outcomes. *J Pediatr Surg* 2007; 42: 340–4.
14. Nwariaku FE, Terracina A, Mileski WJ, et al. Is octreotide beneficial following pancreatic injury? *Am J Surg* 1995; 170: 582–5.
15. Amirata E, Livingston DH, Elcavage J. Octreotide decreases pancreatic complications after pancreatic trauma. *Am J Surg* 1994; 168: 345–7.
16. Wind P, Turet E, Cunningham C, et al. Contribution of endoscopic retrograde pancreatography in management of complications following distal pancreatic trauma. *Am Surg* 1999; 65: 777–83.
17. Lewis G, Knottenbelt JD, Krige JEJ. Conservative surgery for trauma to the pancreas: is it safe? *Injury* 1991; 22: 372–4.
18. DeGiannis E, Levy RD, Velmahos GC, et al. Gunshot injuries of the head of the pancreas: conservative approach. *World J Surg* 1996; 20: 68–72.
19. Patton JH, Lyden SP, Croce MA, et al. Pancreatic trauma: a simplified management guideline. *J Trauma* 1997; 43: 234–41.

20. Shilyansky J, Pearl RH, Kreller M, et al. Diagnosis and management of duodenal injuries in children. *J Pediatr Surg* 1997; 32: 880–6.
21. Ballard RB, Badellino MM, Eynon CA, et al. Blunt duodenal rupture: a 6-year statewide experience. *J Trauma* 1997; 43: 229–33.
22. Desai KM, Dorward IG, Minkes RK, et al. Blunt duodenal injuries in children. *J Trauma* 2000; 54: 640–8.
23. Timaran CH, Daley BJ, Enderson BL. Role of duodenography in the diagnosis of blunt duodenal injuries. *J Trauma* 2001; 51: 648–51.
24. Velmahos GC, Constantinou C, Kasotakis G. Safety of repair for severe duodenal injuries. *World J Surg* 2008; 32: 7–12.
25. Seamon MJ, Pieri PG, Fisher CA, et al. A ten-year retrospective review: does pyloric exclusion improve clinical outcome after penetrating duodenal and combined pancreaticoduodenal injuries? *J Trauma* 2007; 62: 829–33.
26. Degiannis E, Krawczykowski D, Velmahos GC, et al. Pyloric exclusion in severe penetrating injuries of the duodenum. *World J Surg* 1993; 17: 751–4.
27. Jansen M, DuToit DE, Warren BL. Duodenal injuries: surgical management adapted to circumstances. *Injury* 2002; 33: 611–15.
28. Jobst MA, Canty TG, Lynch FP. Management of pancreatic injury in pediatric blunt abdominal trauma. *J Pediatr Surg* 1999; 34: 818–24.
29. Wisner DH, Wold RL, Frey CF. Diagnosis and treatment of pancreatic injuries. *Arch Surg* 1990; 125: 1109–13.
30. Craig MH, Talton DS, Hauser CJ, et al. Pancreatic injuries form blunt trauma. *Am Surg* 1994; 61: 125–8.
31. Adamson WT, Hebra A, Thomas PB, et al. Serum amylase and lipase alone are not cost-effective screening methods for pediatric pancreatic trauma. *J Pediatr Surg* 2003; 38: 354–7.
32. Wolf A, Bernhardt J, Patrzyk M, et al. The value of endoscopic diagnosis and the treatment of pancreas injuries following blunt abdominal trauma. *Surg Endosc* 2005; 19: 665–9.
33. Ilahi O, Bochicchio GV, Scalea TM. Efficacy of computed tomography in the diagnosis of pancreatic injury in adult blunt trauma patients: a single-institutional study. *Am Surg* 2002; 68: 704–8.
34. Bigattini D, Boverie JH, Dondelinger RF. CT of blunt trauma of the pancreas in adults. *Eur Radiol* 1999; 9: 244–9.
35. Lane MJ, Mindelzun RE, Sandhu JS, et al. CT diagnosis of blunt pancreatic trauma: Importance of detecting fluid between the pancreas and splenic vein. *Am J Roentgenol* 1994; 163: 833–5.
36. Akhrass R, Kim K, Brandt C. Computed tomography: an unreliable indicator of pancreatic trauma. *Am Surg* 1996; 62: 647–51.
37. El-Boghdady S, Al-yousef Z, Al-Bedah K. Pancreatic injury: an audit and a practical approach. *Ann R Coll Surg Engl* 2000; 82: 258–62.
38. Canty TG, Weinman D. Management of major pancreatic duct injuries in children. *J Trauma* 2001; 50: 1001–7.
39. Kouchi K, Tanabe M, Yoshida H, et al. Nonoperative management of blunt pancreatic injury in childhood. *J Pediatr Surg* 1999; 34: 1736–9.
40. Wales PW, Shuckett B, Kim PCW. Long-term outcome after nonoperative management of complete pancreatic transaction in children. *J Pediatr Surg* 2001; 36: 823–7.
41. Fabbro MA, D'Agostino S, Romanini MV, et al. Management of severe blunt pancreatic trauma in children. Personal experience. *Ped Med Chir* 2001; 23: 179–82.
42. Graham CA, O'Toole SJ, Watson AJM, et al. Pancreatic trauma in Scottish children. *J R Coll Surg Edinb* 2000; 45: 223–6.
43. Nadler EP, Gardner M, Schall LC, et al. Management of blunt pancreatic injury in children. *J Trauma* 1999; 47: 1098–103.
44. Young PR, Meredith JW, Baker CC, et al. Pancreatic injuries resulting from penetrating trauma: a multi-institution review. *Am Surg* 1998; 64: 838–44.

Abdominal Vascular Trauma

Joseph E. Glaser and Alexandra A. MacLean

Clinical Questions		
Question	Answer	Grade
Is color duplex doppler a good diagnostic tool for abdominal vascular trauma?	Not enough evidence	Not enough evidence
Is CTA a good diagnostic tool for abdominal vascular trauma?	Yes	B
Is MRA a good diagnostic tool for abdominal vascular trauma?	Not enough evidence	Not enough evidence
Is there a role for thoracotomy to control the aorta in abdominal vascular exsanguinations?	No for EDT; possible yes for prelaparotomy thoracotomy	C
Under what circumstances are interventional and endovascular techniques superior to open vascular repair?	Angioembolization for hemodynamically stable active bleed; stent indication not detailed in abdominal vascular trauma literature	C
Regarding optimal control of aorta, is there a role for intraoperative placement of an endovascular balloon?	Not enough evidence	Not applicable
Should SMV injuries be ligated or repaired?	Ligate hemodynamically unstable patients; repair hemodynamically stable patients	C
In difficult vascular repairs, should anticoagulation be used postoperatively? If so, for how long?	Not enough evidence	Not applicable
How should vascular repairs of large vessels be followed: ultrasonography or CT scan?	Extrapolate from vascular surgery literature	Not enough evidence
What are the outcomes of abdominal vascular surgery?	Mortality rate ranging from 39–54%	C
Abbreviations: CT, computed tomography; CTA, computed tomography angiography; EDT, emergency department thoracotomy; MRA, magnetic resonance angiography; SMV, superior mesenteric vein.		

INTRODUCTION

The management of vascular trauma, in particular injury to abdominal vessels, has changed dramatically in the United States over the past 10 years. The advances in interventional and endovascular techniques have contributed new algorithms to the therapeutic approach. In addition, advances in imaging techniques have increased the complexity of the decision tree that addresses questions of how to image, diagnose, treat, and follow such patients.

This chapter raises more questions than answers and highlights the need to continue to conduct high-quality studies so we can practice with confidence from evidence. It is challenging to answer each question without relying on dogma that is easily found in other textbooks and from surgical colleagues. With this in mind, we pose questions and provide the best evidence currently available to

answer them. Finally, we also delineate other questions without any evidenced answers to provide themes for further research.

INITIAL EVALUATION AND DIAGNOSIS

Often when abdominal vasculature is injured, the patient will present with obvious signs and symptoms that point directly to the correct diagnosis and therapy. But the clinical indications for operative intervention on abdominal vessels are not always clear. The patient may be hemodynamically stable without obvious blood loss, and there may be a high index of suspicion of injury due to a minor decrease in femoral pulse examination or questionable findings on the initial trauma CT exam that require further imaging. The armamentarium for examining abdominal vessels now includes duplex examination, computed

tomography angiography (CTA), and magnetic resonance angiography (MRA). Which modality is most sensitive and specific for this vasculature?

Is Color Duplex Doppler a Good Diagnostic Tool for Abdominal Vascular Trauma?

Color duplex doppler is a noninvasive, inexpensive way to assess the integrity of vessels. The value of this technique in imaging peripheral vessels is understood, however, its role in diagnosing defects in abdominal vessels is not well demonstrated in the literature, especially with respect to trauma. There are some case reports that detail experience in using duplex examination to diagnose postinjury pseudo-aneurysms, arteriovenous fistulas, and dissections (1). In a study of 68 patients, the three doppler modalities [color duplex doppler (CDD), power doppler (PD) and B mode (BM)] were compared to assess injury to the iliac arteries and aorta among others. CDD had the lowest sensitivity versus PD and BM—67%, 75%, and 98%, respectively, for iliac arteries and 85%, 85%, and 98% for the aorta (2). Among the different doppler modalities, BM was the best for the detection of intima flaps, fissures of membranes, and residual flow within the true and false lumen compared with CDD and PD. In addition laparoscopic color duplex ultrasound (LDCU) has been used to diagnose hepatic artery injury following laparoscopic injury in animals (3). In this study, all injuries were correctly identified by LDCU. The applicability of this modality for humans is not well known.

Answer: There is a paucity of literature about the utility of duplex examination in diagnosing traumatic injury to abdominal vessels. This is not the imaging study of choice given that other modalities are easier to perform and the results are therefore less user dependent. Grade of recommendation: There is not sufficient evidence to form a recommendation.

Is CTA a Good Diagnostic Tool for Abdominal Vascular Trauma?

Despite the widespread use of CTA, there are few studies examining the utility of this diagnostic tool for abdominal vascular trauma. A study by Maturen et al. examined contrast-enhanced CT (CECT) and compared this with angiographic findings for the detection of torso hemorrhage in a retrospective study of 48 patients (4). Of note, CECT was not specialized CTA. CECT findings were statistically associated with angiographic findings (active hemorrhage and need for intervention) ($p < 0.0001$). The sensitivity of CECT was 94.1% and the negative predictive value (NPV) was 97.6% for active hemorrhage detection. The sensitivity and NPV for need for intervention were 92.6% and 91.2%, respectively.

There is also a study that examined 50 consecutive patients where both CTA and multidetector computed tomography (MDCT) were used to image all major arteries, veins, and parenchymatous organs (5). Apart from the infrarenal vena cava, both modalities achieved high imaging quality.

Answer: CTA is a good diagnostic tool. There is a paucity of literature about the utility of CTA for the diagnosis of abdominal vascular trauma, but it has great potential when compared with MDCT and angiography. Grade of recommendation: B.

Is MRA a Good Diagnostic Tool for Abdominal Vascular Trauma?

There is no literature pertaining to the use of MRA in vascular trauma. Its utility is in the diagnosis of late complications, including dissections, pseudo-aneurysms, and arteriovenous fistulas. It is used most commonly for preoperative mapping for intervention with angioplasty and stents and open procedures in patients with renal failure or other contraindications to intravenous contrast.

Answer: There is a paucity of literature about the utility of MRA for the diagnosis of abdominal vascular trauma. Grade of recommendation: There is not sufficient evidence to form a recommendation.

MANAGEMENT

Is There a Role for Thoracotomy to Control of the Aorta in Abdominal Vascular Exsanguinations?

Laparotomy plays an important role in abdominal trauma, especially vascular. When is a thoracotomy the correct maneuver to gain control of the aorta? The purpose of cross-clamping the thoracic aorta is to obtain proximal control of exsanguinating abdominal hemorrhage and redistribute intravascular volume to the heart and brain. This maneuver is also used when the infradiaphragmatic aorta is in a hostile environment or itself injured.

A retrospective review from 2001 examined variables for death versus survival in the operating room (OR) in abdominal vascular injury. It showed that *not* undergoing emergency department thoracotomy (EDT) or OR thoracotomy was an independent risk factor favoring survival in the OR, in addition to Injury Severity Score (ISS) ≤ 20 , spontaneous ventilation in the emergency department, packed red blood cell replacement $< 4,000$ ml, or absence of abdominal vascular injury ($p < 0.001$, max R(2) 0.55, concordance 89%) (6).

In 2003, a retrospective review of 185 iliac vessel injuries revealed significant predictors of outcome: EDT, associated aortic injury, inferior vena cava injuries, iliac artery and vein injury, intraoperative arrhythmia, and intraoperative coagulopathy. Logistic regression showed independent risk factors for survival: absence of thoracotomy in the emergency department, surgical management, and arrhythmia (7).

In a retrospective review of 470 patients with abdominal vascular injury, the mortality rate was 45%, and in patients where the aorta was injured proximal to the renal arteries, the mortality rate was 91%. Twenty-nine patients in this series had a good response to a prelaparotomy thoracotomy with aortic cross-clamping, and this resulted in systolic blood pressure (SBP) > 90 mmHg within five minutes and 38% of patients (11/29) survived (8).

Answer: No for EDT and possibly yes for prelaparotomy thoracotomy. Grade of recommendation: C.

INTRAOPERATIVE MANAGEMENT

Under What Circumstances Are Interventional Endovascular Techniques Superior to Open Vascular Repair?

Interventional techniques remain valuable in the treatment of bleeding vessels and solid organs. The main techniques

involve angiographic embolization (AE) and stent placement. The role of AE in the arrest of bleeding in penetrating wounds to the abdomen was evaluated by Velmahos et al. in a retrospective study of 40 patients (9). Embolization of both intraperitoneal and retroperitoneal vessels was performed for the following indications: angiographic findings in 6 patients (nonoperative), postsurgery with failure to control bleeding in 23 patients, and to treat late vascular complications in 11 patients. In 32 patients there was active bleeding, and 29 underwent successful AE. In this retrospective series, AE proved to be a helpful technique to arrest bleeding from abdominal vessels.

The other important interventional technique with widespread elective vascular use is the placement of stents (covered or uncovered). In the trauma literature, there is an increasing number of case reports that detail different experiences with stents. In 2006, results from a retrospective subgroup analysis of traumatic vascular injuries treated with a covered stent (data from a prospectively collected registry) was published in the *Journal of Trauma* (10). The injuries included 33 iliac arteries, 18 subclavian arteries, and 11 femoral arteries, and indications were distributed among perforation/rupture, pseudo-aneurysm, arteriovenous fistula, and dissection. Imaging was performed postprocedure and at 12 months. In 93.5% of cases, exclusion was successful by the placement of the Wallgraft endoprosthesis. At one-year follow-up, the exclusion rates were 91.3% and 90% for iliac and subclavian arteries, respectively, but only 62.3% for femoral arteries. Complications were a 4.8% stenosis rate, and 6.5% early and 1.6% late occlusion rates. The complication rates are less than open surgical repair at these follow-up points.

Answer: Whether one technique is superior to the other has not been specifically studied in abdominal vascular trauma. AE is a good method to arrest bleeding in hemodynamically stable patients with an active bleed. The indications for stent placement can be extrapolated from the vascular surgery literature, especially in studies that examine the treatment of complications like pseudo-aneurysms, fistulas, and dissections. Grade of recommendation: C.

Regarding Optimal Control of the Aorta, Is There a Role for Intraoperative Placement of Endovascular Aortic Occlusion Balloon?

The guiding principle of vascular surgery is to obtain proximal and distal control of a vessel prior to repair or incision. This is typically performed with vessel loops, clamps, or Fogarty balloons. We now have an additional technique available: endovascular intra-aortic balloon. This can be inserted via the femoral or brachial artery and placed in the aorta to occlude the vessel from further blood flow. The literature detailing this experience is mainly in the clinical context of ruptured abdominal aortic aneurysms (11).

A case series from 2003 describes a novel technique of using CT-guided balloon occlusion in polytrauma patients. The trauma CT scan showed active abdominal or pelvic bleeding, and patients subsequently became hypotensive with SBP <80. A 9 French sheath was introduced and a 20 × 40mm balloon placed under CT guidance and subsequently evaluated with additional CT scans and CT

fluoroscopy (12). This innovative technique could be very useful in the case of bleeding seen immediately on CT scan, as it could be followed immediately by placement of an occlusion balloon in the CT scanner without moving the patient to an angiography suite or operating room.

Answer: Further studies are needed to elucidate the utility of this technology. Areas to address include developing and refining the techniques for use by trauma and endovascular personnel in these settings and to establish standard, rapid algorithms for their use. The technique needs to be adequately compared to open aortic control and ultimately evaluated for incorporation into trauma algorithms and trauma training. It is a promising area but needs more experience before its use can become standard. Grade of recommendation: There is not enough evidence to form a recommendation.

Should SMV Injuries Be Ligated or Repaired?

A retrospective study of all patients admitted at a Level I trauma center with superior mesenteric vein (SMV) injuries was published in 2007. In 59% of cases the vessels were ligated, 31% were primarily repaired, and 10% exsanguinated prior to repair. The overall survival rate was 24/50 (47%). The study concluded that SMV injuries are highly lethal. Survival for patients apart from those with more than three or four associated injuries was 65%. Combined superior mesenteric artery (SMA) and SMV mortality was 55%, whereas SMV and portal vein was 40%. Multiple associated vessel injuries increase mortality further. Patients undergoing primary repair have higher survival rates (63%) and lower numbers of associated vascular and nonvascular injuries, whereas those undergoing ligation have a smaller survival rate (40%) and greater numbers of associated vascular and nonvascular injuries. Repair, if possible, should be performed, but hemodynamics, acid-base status, and temperature should dictate approach. Ligation appears to be safe and should be selected for hemodynamically unstable patients with a large number of associated injuries (13).

Answer: The best available evidence suggests that both ligation and primary repair are reasonable, but ligation is best done in unstable patients with multiple injuries, whereas primary repair can be done in stable patients once standard proximal and distal control has been achieved. Various options are given for repair: lateral suture, end-to-end anastomosis, and autologous venous reconstructions. We did not find any references to using artificial grafts, although that could be an option. More studies and larger reviews are needed to shed more light on the subject. Grade of recommendation: C.

In Difficult Vascular Repairs, Should Anticoagulation Be Used Postoperatively? If so, for How Long?

There is no Level I, II, or III evidence on this subject. The recommendation at this stage without appropriate abdominal vascular trauma literature would be extrapolate evidence from the general vascular literature. This literature is evaluated in other chapters, but some general principles can be stated. If there is concern regarding the quality of the conduit or patch, if there may be locations of nonrepaired intimal damage, or if the patient has undergone extensive vascular operations prior to the

trauma and likely has poor runoff, then consideration of prescribing an antiplatelet agent and possibly heparin in the immediate postoperative period is reasonable.

Answer: For now we should follow the recommendations from vascular surgery evidence literature. Grade of recommendation: There is not sufficient evidence to form a recommendation.

FOLLOW-UP

There are guidelines that help the surgeon determine frequency of follow-up for patients with vascular disease with or without having undergone an intervention. With widespread use of devices, especially endografts, the follow-up regimen is very important because we know that late complications occur and these can be detected by imaging studies. How should we follow trauma patients who underwent vascular repair? These patients are a different cohort not only because of disease causality but also because they are usually healthy to start with especially compared with the typical vascular patient.

Question: How Should Vascular Repairs of Large Vessels be Followed: Ultrasonography or CT?

There is very little trauma-related literature to help us answer this question. Therefore, we must derive a response from the vascular surgery literature. There are two main situations to consider: (1) patients who underwent angiography with the placement of a stent or endograft, (2) patients who had open surgery with primary repair, patch angioplasty, or graft (vein or prosthetic) placement.

To determine the appropriate follow-up of patients in the first scenario, we look to literature from interventional radiology and endovascular surgery. Whether an ultrasound or CT scan is appropriate is likely determined by the experience of the ultrasonographer and the location of the repair. If an aortic endograft has been placed, it is reasonable to perform a postoperative one-month CT scan and, if this is normal, do another CT scan at one year. However, if the initial CT is abnormal, then a six-month CT scan should be performed and followed with a one-year CT scan (14).

In the situation of renal artery reconstruction, Eidt et al. performed a retrospective study to examine results of duplex exams in patients who also underwent arteriography (15). The duplex exam resulted in a diagnostic accuracy of 86%, sensitivity of 80%, and specificity of 87%. A normal duplex exam obviated the need for arteriography, but an abnormal exam mandated arteriography. A duplex exam seems to be a reasonable first step for the follow-up of renal artery reconstruction. There are no data to support this sequence of follow-up in other visceral artery reconstructions, and this should be studied.

The appropriate follow-up of patients who underwent open surgical repair, especially following trauma, is not clear from the literature. This group of patients is often without significant comorbidities and risk factors for the future development of vascular disease like aneurysms, unlike the elective/emergent atherosclerotic aneurysmal vascular surgery group of patients. This is an important area to study because it is difficult to gather data from the literature to help answer this question.

Answer: For now we should follow the recommendations from vascular surgery evidence literature. Grade of recommendation: There is not sufficient evidence to form a recommendation.

What Are the Outcomes of Abdominal Vascular Injury?

A retrospective study by Asensio and colleagues examined one urban trauma center's experience with abdominal vascular injury with the primary endpoint being survival (16). Three hundred two patients were included. Mechanism of injury was predominantly penetrating, and 504 vessels were injured: 47% arteries and 53% veins. Mortality was 54% and increased as the number of vessels injured also increased: one vessel had a mortality rate of 45%, two vessels 60%, three vessels 73%, four or more vessels 100%. Of the named arteries, aortic injury isolated and combined with another vessel had the highest mortality rate compared with SMA, iliac, and renal. Likewise, inferior vena cava injury (IVC) isolated or combined had the highest mortality rate compared with SMV, or inferior mesenteric vein (IMV). Aortic and IVC injury together had a mortality rate of 93%.

Tyburski et al. retrospectively reviewed data on 470 patients to try to determine factors that affect mortality rates in patients with abdominal vascular injury (8). Like Asensio and colleagues' study, the overall mortality rate was high at 45%. The following risk factors were found to be significantly associated with death: trauma score ≤ 9 , initial OR SBP < 90 mmHg, final OR core temperature $< 34^{\circ}\text{C}$, 10 or more blood transfusions in the first 24 hours, and an initial emergency department SBP < 70 mmHg.

Asensio et al. also retrospectively examined a multi-institutional experience with SMA injuries (17). Two hundred fifty patients were examined from a 10-year period in 34 trauma centers. Mortality was 39%, with greatest rate associated with injury in Fullen zone I (76.5%). Transfusion of greater than 10 units of packed red blood cells, intraoperative acidosis, dysrhythmias, multiple system organ failure (MSOF), and injury to Fullen zones I or II were independent risk factors for mortality. Lead by the same investigator, injury to 185 iliac vessels was examined retrospectively at a single center (7). The vessels included in analysis were aorta, IVC, iliac artery, iliac vein. IVC injury had the highest relative risk of mortality (1.86%) and when three vessels were injured, as occurred in three patients, there were no survivors. Independent risk factors associated with survival were the lack of need for an EDT and the ability to manage the injury surgically; the presence of an intraoperative arrhythmia was associated with a decrease in survival.

Answer: Thirty-nine percent to 54% mortality rate of patients with abdominal vascular trauma. Grade of recommendation: C.

QUESTIONS FOR FUTURE WORK

What is the role of pericardial patches or homografts in vascular injury repairs?

Is it okay to leave the abdomen open after vascular repair with foreign material?

In isolated abdominal vascular injuries, should anti-coagulation be used with vessel occlusion?

How long should antibiotics be used in cases of vascular repair with prosthetic material and bowel injury?

What is the appropriate imaging study for follow-up of nonoperative management of vascular injury? For how long and how frequently should these patients be followed?

Levels of Evidence

Trial (Ref no.)	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Major endpoint	Interpretations/Comments
1	2007	V	N/A	Case report	N/A	None
2	2005	IIb	N/A	Exploratory cohort study	Sensitivity of test	Compared 3 doppler methods
3	2000	N/A	N/A	Animal study	N/A	Evaluated new technique
4	2007	IIb	N/A	Retrospective cohort study	Sensitivity of test	Compared CECT with angiography
5	2008	Ib	N/A	Prospective cohort study	Evaluated test	Compared CTA with MDCT
6	2001	IV	N/A	Case series	Mortality	Determined outcome variables
7	2003	IV	N/A	Case series	Mortality	Determined outcome variables
8	2001	IV	N/A	Case series	Mortality	Determined outcome variables
9	1999	IV	N/A	Case series	Arrest of bleeding	Evaluated angioembolization
10	2006	IV	N/A	Case series	Fistula, PSA, dissection exclusion from blood flow	Examined stent placement
11	2006	IV	N/A	Case series	N/A	Endo aortic balloon in ruptured AAAs
12	2003	IV	N/A	Case series	N/A	CT-guided endo aortic balloon
13	2007	IV	N/A	Case series	N/A	SMV injuries
14	2008	IV	N/A	Case series	Development of a complication	CT scan to follow endo repair
15	1988	IV	N/A	Case series	Sensitivity of test	Evaluate duplex for follow-up
16	2000	IV	N/A	Case series	Outcomes	None
17	2001	IV	N/A	Multi-institutional case series	Outcomes	SMA injuries

Abbreviations: AAA, abdominal aortic aneurysm; CECT, contrast enhanced computed tomography; CT, computed tomography; CTA, computed tomography angiography; MDCT, multidetector computed tomography; N/A, not applicable; PSA, pseudo-aneurysm; SMA, superior mesenteric artery; SMV, superior mesenteric vein.

REFERENCES

- Al-Khayat H, Haider HH, Al-Haddad A, et al. Endovascular repair of traumatic superior mesenteric artery to splenic vein fistula. *Vasc Endovasc Surg* 2007; 41: 59–63.
- Clevert DA, Rupp N, Reiser M, et al. Improved diagnosis of vascular dissection by ultrasound B-flow: a comparison with color-coded Doppler and power Doppler sonography. *Eur Radiol* 2005; 15: 342–7.
- Birch M, Lossin P, Brugmans F, et al. Vascular injuries within the hepatoduodenal ligament: recognition by laparoscopic color Doppler ultrasound. *Surg Endosc* 2000; 14: 246–9.
- Maturen KE, Adusumilli S, Blane CE, et al. Contrast-enhanced CT accurately detects hemorrhage in torso trauma: direct comparison with angiography. *J Trauma* 2007; 62: 740–5.
- Loupatatzis C, Schindera S, Gralla J, et al. Whole-body computed tomography for multiple traumas using a triphasic injection protocol. *Eur Radiol* 2008; 18: 1206–14.
- Asensio JA, McDuffie L, Petrone P, et al. Reliable variables in the exsanguinated patient which indicate damage control and predict outcome. *Am J Surg* 2001; 182: 743–51.
- Asensio JA, Petrone P, Roldan G, et al. Analysis of 185 iliac vessel injuries: risk factors and predictors of outcome. *Arch Surg* 2003; 138: 1187–93.
- Tyburski JG, Wilson RF, Dente C, et al. Factors affecting mortality rates in patients with abdominal vascular injuries. *J Trauma Inj Infect Crit Care* 2001; 50: 1020–6.
- Velmahos GC, Demetriades D, Chahwan S, et al. Angiographic embolization for arrest of bleeding after penetrating trauma to the abdomen. *Am J Surg* 1999; 178: 367–73.
- White R, Krajcer Z, Johnson M, et al. Results of a multicenter trial for the treatment of traumatic vascular injury with a covered stent. *J Trauma* 2006; 60: 1189–95.
- Arthurs Z, Starnes B, See C, et al. Clamp before you cut: proximal control of ruptured abdominal aortic aneurysms using endovascular balloon occlusion—case reports. *Vasc Endovasc Surg* 2006; 40: 149–55.
- Linsenmaier U, Kanz KG, Rieger J, et al. CT-guided aortic balloon occlusion in traumatic abdominal and pelvic bleeding. *Rofo: fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* 2003; 175: 1259–63.
- Asensio JA, Petrone P, Garcia-Nunez L, et al. Superior mesenteric venous injuries: to ligate or to repair remains the question. *J Trauma Inj Infect Crit Care* 2007; 62: 668–75.
- Go MR, Barbato JE, Rhee RY, et al. What is the clinical utility of a 6-month computed tomography in the follow-up of endovascular aneurysm repair patients? *J Vasc Surg* 2008; 47: 1181–7.
- Eidt JF, Fry RE, Clagett GP, et al. Postoperative follow-up of renal artery reconstruction with duplex ultrasound. *J Vasc Surg* 1988; 8: 667–73.
- Asensio JA, Chahwan S, Hanpeter D, et al. Operative management and outcome of 302 abdominal vascular injuries. *Am J Surg* 2000; 180: 528–33.
- Asensio JA, Britt LD, Borzotta A, et al. Multiinstitutional experience with the management of superior mesenteric artery injuries. *J Am Coll Surg* 2001; 193: 354–65.

An Evidence-Based Approach to Pregnant Trauma Patients

Igor Jeroukhimov

Question Summary		
Question	Answer	Grade
What is appropriate time for fetal monitoring after trauma?	All pregnant trauma patients >20 weeks of gestation should have fetal monitoring for at least 6 hours.	C
Should KB test be performed in pregnant trauma patient?	KB test should be performed in all pregnant patients >12 weeks of gestation.	B
Should FAST be performed in every pregnant patient with suspected abdominal trauma?	FAST should be performed in every pregnant trauma patient with suspected intrabdominal injury.	C
Should diagnostic radiologic studies be withheld in pregnant trauma patient?	Radiologic studies necessary for maternal evaluation should not be withheld on the basis of its potential danger to the fetus. Unnecessary duplication of studies should be avoided, and appropriate mandatory shielding should be used whenever possible.	C
What is the role of CS section and when it should be performed?	Perimortem CS should be considered in moribund pregnant patient after 24 weeks of gestation. Delivery must occur in 20 minutes of maternal death, but should ideally begin within 4 minutes of maternal arrest.	C
Abbreviations: CS, cesarean section; FAST, focused abdominal sonography for trauma; KB, kleihauer-betke.		

INTRODUCTION

Trauma is a leading cause of nonobstetric morbidity and mortality in pregnancy and complicates 6–7% of all pregnancies (1). Significant trauma occurs in 1 of 12 pregnant women. About two-thirds of these injuries are the result of motor vehicle crashes, and fall and physical abuse account for 10–31% of injuries (2). Maternal death from trauma ranges from 10% to 20% (3,4). Fetal mortality of 9% has been reported (5) and increases to about two-thirds if maternal shock is present (6).

ANATOMIC AND PHYSIOLOGIC CHANGES UNIQUE TO PREGNANCY

The specific anatomic and physiologic changes that occur during pregnancy may alter the response to injury and, hence, necessitate a modified approach to management.

Cardiovascular System

Plasma volume begins to expand at 10 weeks of gestation and increases to 45% of pregravid levels by full term. Tubular resorption of sodium and water is significantly increased (7). This hypervolemic state is protective for the mother because fewer red blood cells are lost during hemorrhage and, hence, the oxygen-carrying capacity of the blood is less affected (8). Thus, volume expansion may

cause a false sense of security for the resuscitating physician because as much as 35% of maternal blood may be lost before first signs of hemodynamic instability appear. Increases in plasma volume by 30–40% are accompanied by a 15% increase in red blood cells cell mass resulting in the physiological anemia of pregnancy.

A hypercoagulable state is common during the pregnancy. Factors VII, VIII, IX, X, XII, and fibrinogen are increased, and fibrinolytic activity is reduced, putting the patient at increased risk for thromboembolic events.

Maternal heart rate increases by about 10–15 beats/min. As the diaphragm becomes progressively more elevated secondary to the enlarging uterus, the heart is displaced to the left and upward, resulting in a lateral displacement of the cardiac apex. Moreover, each pregnant woman has some degree of benign pericardial effusion. Both of these changes result in an enlarged cardiac silhouette and increased pulmonary vasculature on the chest radiograph (9).

Cardiac output increases to 25% above normal. In the healthy gravida, this increased workload on the heart is well tolerated (7). However, in supine position gravid uterus partially obstructs the inferior vena cava decreasing preload to the heart, resulting in a lower cardiac output, causing the supine hypotensive syndrome. This syndrome is marked by dizziness, pallor, tachycardia, sweating, nausea, and hypotension. Turning the mother onto her left side restores the cardiac output.

Respiratory System

Secondary to uterus enlargement, the diaphragm rises about 4 cm and the diameter of the chest enlarges by 2 cm, increasing the substernal angle by 50% (7). Care should be taken to consider these anatomic changes when thoracic procedures, such as tube thoracostomies or thoracenteses are being performed.

The most prominent changes in respiratory physiology include progressive increase in tidal volume and minute ventilation. Functional residual capacity decreases because of a decline in expiratory reserve and residual volumes. Relative to these changes, the injured pregnant patient poorly tolerates hypoxia, hence, supplemental oxygen is always indicated.

Progesterone stimulates the medullary respiratory center, resulting in hyperventilation and respiratory alkalosis. PCO_2 decreases to level of 27–32 mmHg in pregnant woman. Therefore, pregnancy is a state of partially compensated respiratory alkalosis.

Gastrointestinal System

Increased levels of progesterone and estrogen inhibit gastrointestinal motility, intestinal secretion, and nutrient absorption. Additionally, the angle of the gastroesophageal junction is altered such that the lower esophageal sphincter is displaced into the thorax. This alteration decreases the competency of the lower gastroesophageal sphincter, which increases the potential for aspiration as early as 8–12 weeks (10). It is therefore prudent to insert a nasogastric tube to decompress the stomach and prevent aspiration. Furthermore, as the uterus enlarges, it displaces the intestines upward and laterally, making physical examination unreliable.

Renal System

Renal blood flow increases by 30% during pregnancy. As pregnancy progresses, the ureters and bladder are compressed by the uterus, resulting in hydronephrosis and hydroureter; consequently, a dilated collecting system visualized on imaging studies is normal.

Increases in blood volume and cardiac output cause a rise in glomerular filtration rate and renal plasma flow. Therefore, more plasma is filtered, reducing the serum protein concentration and hence the plasma oncotic pressure (12). This change also results in an increase in the renal clearance of many substances during pregnancy, and a review of the metabolism of pharmaceutical agents prior to their administration to pregnant patient is recommended (13).

Endocrine System

The placenta produces human chorionic gonadotropin and human placental lactogen (hPL), as well as progesterone, estrogen, thyroid-stimulating hormone, and adrenocorticotropic hormone (14).

Maternal utilization of glucose is decreased, and maternal lipolysis is enhanced, making nutrients available to the fetus. hPL is the physiologic antagonist of insulin and contributes to the diabetogenic effect of pregnancy by causing increased peripheral resistance to insulin. The pituitary gland enlarges during pregnancy by approximately 135%, and demands increased blood flow (14). Shock may

cause necrosis of the anterior pituitary gland, resulting in pituitary insufficiency or Sheehan syndrome.

Reproductive System

By the end of full-term gestation, the weight of the uterus has increased to 20 times its prepregnancy weight. Intrapelvic location protects uterine from injury, but after the twelfth week of pregnancy, it extends out of the pelvis and ascends into the abdominal cavity to displace the intestines laterally and superiorly. This makes the uterine more vulnerable for injury but protects intra-abdominal organs.

With progressive uterine enlargement, uterine blood flow increases, constituting up to 20% of the cardiac output at term. Uterine veins may dilate up to 60 times, increasing the risk of massive blood loss with pelvic injury.

Musculoskeletal System

The softening and relaxation of the interosseous ligaments during pregnancy cause increased mobility of the sacroiliac and sacrococcygeal joints and widening of the symphysis pubis. These changes, coupled with an enlarged uterus, disrupt the maternal center of gravity and gait stability, putting the gravida at increased risk for trauma, especially from falls.

ASSESSMENT OF PREGNANT TRAUMA PATIENTS

A key management principle of an injured pregnant patient is to treat the mother first because most medical measures that aid in the resuscitation of the mother will be helpful to the fetus. The pregnant patient is best cared for using a team approach. The trauma surgeon and obstetrician should be involved early. All necessary tests and procedures should be performed if indicated. Because the most common cause of fetal death is maternal death, efforts to assess fetal well-being are secondary to resuscitation of the pregnant woman. However, fetal well-being may represent the most valuable measurement of maternal health. Fetal distress appears early and represents maternal hemorrhage even if the mother is hemodynamically stable. Waiting for maternal signs of instability will worsen the fetal compromise.

Assessment and establishment of the maternal airway is critical, and all pregnant patients should receive supplemental oxygen at a minimum. Late in gestation the oropharynx is swollen from tissue edema and endotracheal intubation of the gravid patient can be difficult; therefore, use of a smaller than normal diameter endotracheal tube, such as a 6.5 mm or less, may be necessary (15). During the pregnancy the risk of aspiration increased and monitoring of oxygenation is necessary. Precaution must be taken when chest tube thoracostomy is required.

After the primary survey and stabilization of the patient, diagnostic modalities are used to determine extent of injuries to the mother and fetus. Laboratories pertinent to the trauma setting are obtained, and all female patients of childbearing age should have a β -human chorionic gonadotropin test performed (16) (Grade B recommendation). A rapid secondary survey must include evaluation of pregnancy. This consists of determination of fetal heart rate and movement, assessment of uterine size and tone, and examination of vaginal bleeding or leakage of amniotic

fluid. Fetal monitoring is initiated. Fetal heart tones are discernable by Doppler by the tenth week of gestation, allowing a simple and noninvasive method of monitoring. After the twentieth week of pregnancy, standard continuous fetal heart rate monitoring should be employed under the obstetrician guidance (2). If fetal heart tones are absent, resuscitation of the fetus should not be attempted. There were no fetal survivors in a series of 441 pregnant trauma patients with initially absent fetal heart tones (17) (Grade B recommendation).

What Is Appropriate Time for Fetal Monitoring After Trauma?

Controversies exist concerning the duration of fetal monitoring following trauma. Early studies indicating that placenta abruption can occur up to 48 hours post-trauma recommend continuous fetal monitoring during this period (18).

A widely used protocol is based on a prospective study of 60 patients at more than 20 weeks of gestation (19). This protocol has a sensitivity of 100% for predicting adverse outcomes within four hours. In the prospective study, 70% of patients required more than 4 hours of fetal monitoring because of continued contractions (four or more per hour), abnormal laboratory values, or vaginal bleeding, but all of the patients discharged at the end of 4 or 24 hours had similar outcomes compared with noninjured control patients. If fetal tachycardia is present or a nonstress test is nonreactive, monitoring usually is continued for 24 hours, but no studies exist to support this practice. Some experts recommend prolonged electronic fetal monitoring in patients with high-risk mechanisms of injury. These mechanisms include automobile versus pedestrian and high-speed motor vehicle crashes (20). No evidence supports the use of routine electronic fetal monitoring for more than 24 hours after noncatastrophic trauma (21).

Answer: All pregnant trauma patients >20 weeks of gestation should have fetal monitoring for at least of six hours (Grade C recommendations).

Five conditions are associated with signaling an acute status of the pregnancy. These include vaginal bleeding, rupture of amniotic sac, presence of contractions, bulging perineum, and abnormal fetal heart rate and rhythm.

Vaginal bleeding before the onset of full-term labor is abnormal. It is potentially indicative of preterm labor, placental abruption, or placenta previa. Rupture of the amniotic sac can allow prolapse of the umbilical cord, resulting in compression of the cord and potential compromise of the fetal circulation. Suspected amniotic fluid can be tested using nitrazine paper, which will turn deep blue if the test is positive. Rupture of the amniotic sac is an obstetrical emergency because of the risk of infection and umbilical cord prolapse. Bulging of the perineum represents pressure from a presenting part of the fetus and delivery or spontaneous abortion may be in progress. The presence of strong contractions is associated with true labor.

Should Kleihauer-Betke Test Be Performed in Pregnant Trauma Patient?

Traumatic injury to the uterus can result in transplacental or fetomaternal hemorrhage. The Kleihauer-Betke (KB) test

is used to detect the presence of fetal cells in the maternal circulation. Because of its high sensitivity, the KB test by itself does not necessarily indicate pathologic fetal-maternal hemorrhage (22). The KB test is recommended for injured Rh-negative patients in the second or third trimester to detect impending fetal hemorrhage and determine risk of Rh isosensitization.

As little as 0.001 L of fetal blood can cause sensitization of Rh-negative mother. Therefore, all Rh-negative pregnant trauma patients should receive immunoglobulin to suppress potential immune response (17). Recent evidence suggests that the KB test accurately predicts the risk of preterm labor, and in a patient with a negative KB test, fetal monitoring duration can be terminated (23). When used as a predictor of preterm labor, the KB test has benefit to all maternal trauma patients, regardless of Rh status.

Answer: KB test should be performed in all pregnant patients >12 weeks of gestation (Grade B recommendation).

DIAGNOSTIC CONSIDERATIONS

After maternal assessment, there is a need for rapid and accurate imaging. A pregnant patient with blunt abdominal injury or unconsciousness poses the greatest dilemma for imaging. Evaluation of the abdomen for hemoperitoneum can be performed by ultrasonography (US), diagnostic peritoneal lavage (DPL), or computed tomography (CT) scan.

DPL can be performed safely in the pregnant patient and carries the same sensitivity as in the nonpregnant state (18). In these cases, DPL is performed using an open technique in a supraumbilical location. DPL is rarely used with advent of focused abdominal sonography for trauma (FAST). It may be indicated where FAST is either unavailable or equivocal, particularly when the patient is hemodynamically unstable. The disadvantages of DPL include the relative invasiveness of the procedure and that, although hemoperitoneum is easily detected, the source of bleeding is not.

Table 27.1 Fetal Radiation Exposure to Commonly used Radiographic Studies

Imaging study	Fetal radiation exposure (rads)
Plain film	
Cervical spine	0
Chest AP	0.0001
Pelvis AP	0.103
Thoracic spine	0.0001
Lumbar spine	0.090
Computed tomography	
Head	<0.05
Chest + abdomen	1.6
Abdomen + pelvis	1.6
Chest/abdomen/pelvis (angio)*	4.5

*CT angiography protocol.

Should FAST Be Performed in Every Pregnant Patient with Suspected Abdominal Trauma?

FAST is an important tool performed for diagnosis of free intrabdominal fluid. Sensitivity of this method ranges from 42% to 100% (24–26). FAST is less sensitive in pregnant than in nonpregnant trauma patients, but this examination remains highly specific (24). Some studies report false-negative US results and recommend further imaging or clinical follow-up (24,27). However, a recent study showed that in patients with negative FAST results, 96% did not need additional testing that used ionizing radiation, and US was therefore recommended as an accurate screening tool (27). In that study, the patients who had false-negative findings were diagnosed within 24 hours of the injury.

Answer: FAST should be performed in every pregnant trauma patient with suspected intra-abdominal injury (Grade C recommendation).

Should Diagnostic Radiologic Studies Be Withheld in Pregnant Trauma Patient?

During the period of major organogenesis (2–15 weeks), ionizing radiation has the highest potential for teratogenesis and neonatal neoplastic effect (2,28,29). In the remainder of pregnancy radiation may produce growth retardation, microcephaly, and mental retardation (30). The American College of Obstetricians and Gynecologists stated that a 5rad exposure to the fetus is not associated with increased risk of fetal loss or birth defects (31). Radiation dosage by study commonly used in trauma imaging listed in Table 27.1. If multiple diagnostic studies are performed, particularly when radiation exposure approaches 5–10rad, then consultation with radiologist or radiation specialist should be considered (31).

Answer: Radiologic studies necessary for maternal evaluation should not be withheld on the basis of its potential danger to the fetus. Unnecessary duplication of studies should be avoided and appropriate mandatory shielding should be used whenever possible. (Grade and C recommendation).

EMERGENT CESAREAN SECTION FOR TRAUMA

What Is the Role of Perimortem Cesarean Section and When it Should Be Performed?

Performance of an emergency cesarean section (CS) at more than 25 weeks' gestation for appropriate indications following trauma is associated with 45% fetal survival and 72% maternal survival (17). The absence of fetal heart tones ordinarily predicts mortality from an emergent CS.

Perimortem CS should be performed in traumatic maternal arrest with potential fetal viability, when resuscitative measures have failed. The best outcomes occur if the infant is delivered within five minutes of maternal cardiac arrest. This means the surgery should begun by four minutes into the arrest (17,32). The latest reported survival was of an infant delivered 22 minutes after documented maternal cardiac arrest (33,34). Several factors must be considered when deciding whether to undertake perimortem CS (32,34). These include estimated gestational age of the fetus and the resources of the hospital. Before 23 weeks' gestational age, delivery of the fetus may not improve maternal venous return. Therefore aggressive maternal resuscitation is the only indicated intervention (1).

Answer: Perimortem CS should be considered in moribund pregnant patient after 24 weeks of gestation. Delivery must occur in 20 minutes of maternal death, but should ideally begin within 4 minutes of maternal arrest (Grade C recommendations).

SUMMARY

Trauma is a leading cause of nonobstetrical maternal mortality. Most studies on trauma during pregnancy are retrospective studies performed in single institution based on small amount of patients to make definitive conclusions. Multi-institutional retrospective data collection following prospective phone follow-up may shed more light on the existing controversies.

Level of Evidence

Ref.	Year	Level of evidence	Randomization groups	Design	Minor end-point	Major end-point	Comments
4	2003	II	2	Large retro-spective cohort study	Pregnant women using seatbelts were not significantly more at risk for adverse fetal outcomes than pregnant women not in crashes.	Unbelted pregnant women 2.8 times more likely to experience a fetal death than belted pregnant women in crashes.	Grade B recommendations based on large population
5	1999	II	1	Multi-institutional retrospective study	Increased use of cardiographic monitoring may decrease the mortality caused by placental abruption.	Fetal death was more likely with greater severity of injury.	Grade B recommendations
6	1992	III	1	Retrospective case-control study	ISS and admission serum bicarbonate level have the most significant correlation with fetal outcome.	Performance of DPL doesn't have a significant association with fetal loss.	Grade B recommendations based on small population
11	1980	II	2	Prospective observational study (small group)	Gallbladder function isn't affected by contraceptive steroids.	Pregnancy increases the risk of cholesterol gallstones.	Grade B recommendations based on small population
12	1981	II	2	Prospective observational study with control group	GFR increased by 50% above the nonpregnant level throughout pregnancy.	Filtration fraction significantly reduced during early pregnancy but rose to nonpregnant level during the third trimester.	Physiological data. No recommendations drawn.
16	2001	II	1	Retrospective cohort study	Trauma patients with incidental pregnancy are routinely exposed to exceeding doses of radiation.	Rapid pregnancy test should be considered in all female trauma victims.	Grade B recommendations based on large cohort
17	1996	II	1	Multi-institutional, retrospective cohort study	Infant survival is independent of maternal distress or ISS.	In viable infants, survival after emergency CS is acceptable (75%).	Grade B recommendations based on large population
18	1989	III	1	Individual case-control study	Pregnant patients with minor injuries and blunt abdominal trauma may be safely observed.	DPL proved to be safe and accurate in pregnant trauma patients.	Grade B recommendations based on small population
19	1990	II	2	Prospective observational study	Routine screening for fetomaternal transfusion should occur in all pregnant trauma patients beyond 11 weeks' gestation.	4 hours of cardiographic monitoring used as a screening tool found to be an extremely sensitive.	Grade B recommendations based on small population
20	2000	III	1	Retrospective case-control study	Pregnant patients with risk factors for contractions, preterm labor, or fetal loss should be monitored for at least 24 hours.	Patients without risk factors can safely be monitored for 6 hours after trauma before discharge.	Grade B recommendations based on small population
22	2004	II	2	Prospective control study	Incidence of a positive KB test in low-risk pregnancies does not differ from maternal trauma patients.	Positive KB test alone does not necessarily indicate fetal-maternal hemorrhage.	Grade B recommendations based on small population
23	2004	III	1	Retrospective study	Fetal monitoring may be limited in presence of negative KB test.	KB testing accurately predicts the risk of preterm labor.	Grade B recommendations
24	2001	III	2	Retrospective study	Negative initial examination should not be used as conclusive evidence that intra-abdominal injury is not present.	The sensitivity and specificity of FAST in pregnant trauma patients is similar to that seen in nonpregnant.	Grade B recommendations based on small population

(Continued)

Level of Evidence (Continued)

Ref.	Year	Level of evidence	Randomization groups	Design	Minor end-point	Major end-point	Comments
25	2004	II	2	Retrospective cohort study	The sensitivity of US was highest in pregnant patients during the first trimester.	US is less sensitive in pregnant patients than in nonpregnant patients, but highly specific.	Grade B recommendations based on large population
26	2005	III	1	Retrospective cohort study		Sonography is an effective screening examination.	Grade B recommendations
28	2007	II	2	Retrospective follow-up cohort study with untreated control group	Primitive neuroectodermal tumors had the highest estimated risk.	No increased risk of brain tumor after abdominal x-ray exposure.	Grade B recommendations based on large population
29	1985	III	1	Retrospective case-controlled study	Child birth was lower in children who underwent irradiation.	Low-dose prenatal irradiation may increase the risk of childhood cancer.	Grade B recommendation
30	1998	III	1	Retrospective cohort study	Microcephalia and mental retardation may occur as a result of ionizing radiation.	Threshold of ionizing radiation may exist, but it is not supported statistically.	Grade B recommendations based on large population
32	1986	III	1	Retrospective case-controlled study		Perimortem CS initiated within 4 minutes of maternal cardiac arrest results the highest rates of maternal survival.	Grade B recommendations based on small population
34	2008	III	1	"Outcomes" research study	CS does not cause deterioration of maternal condition.	State that early perimortem CS improves maternal and fetal outcomes is far from to be proved.	Grade C recommendation

Abbreviations: CS, cesarean section; DPL, diagnostic peritoneal lavage; FAST, focused abdominal sonography for trauma; GFR, glomerular filtration rate; ISS, injury severity score; KB, kielhauer-betke; US, ultrasonography.

REFERENCES

- Muench MV, Canterio JC. Trauma in pregnancy. *Obstet Gynecol Clin N Am* 2007; 34: 555–83.
- Tsuei BJ. Assessment of pregnant trauma patient. *Injury* 2006; 37: 367–73.
- Warner MW, Salfinger SG, Rao S, et al. Management of trauma during pregnancy. *ANZ J Surg* 2004; 74: 125–8.
- Hyde LK, Cook LJ, Olson LM, et al. Effect of motor vehicle crashes on adverse fetal outcomes. *Obstet Gynecol* 2003; 102: 279–86.
- Rogers F, Rozycki G, Tuner O, et al. A multi-institutional study of factors associated with fetal death in injured pregnant patients. *Arch Surg* 1999; 134: 1274–7.
- Scorpio RJ, Esposito TJ, Smith LG. Blunt trauma during pregnancy: factors affecting fetal outcome. *J Trauma* 1992; 32: 213–16.
- Knudson MM, Rozycki GS, Paquin MM. Reproductive system trauma. In: Feliciano DV, Mattox KL, Moor EE, eds. *Trauma*, 5th edition. New York: McGraw-Hill, 2004, 609–43.
- Smith CV, Phalen JP. Trauma in pregnancy. In: Clark SL, Cotton DB, Hankins GDV, Phalen JP, eds., *Critical Care Obstetrics*, 2nd edition. Boston: Blackwell, 1991, 498.
- Lee W, Cotton DB. Cardiorespiratory changes during pregnancy. In: Clark SL, Cotton DB, Hankins GDV, Phalen JP, eds., *Critical Care Obstetrics*, 2nd edition. Boston: Blackwell, 1991, 2.
- Bynum TE. Hepatic and gastrointestinal disorders in pregnancy. *Med Clin North Am* 1977; 61: 129.
- Braverman DZ, Johnson ML, Kern F Jr. Effects of pregnancy and contraceptive steroids on gallbladder function. *N Engl J Med* 1980; 302: 362.
- Dunlop W. Serial changes in renal hemodynamics during normal human pregnancy. *Br J Obstet Gynaecol* 1981; 88: 1.
- Briggs GC, Freeman RK, Yaffe SJ. *A Reference Guide to Fetal and Neonatal Risk: drugs in Pregnancy and Lactation*, 3rd edition. Baltimore: Williams & Wilkins, 1990.
- Gonzalez JG, Elizondo G, Saldiver D, et al. Pituitary gland growth during normal pregnancy: an in vivo study using magnetic resonance imaging. *Am J Med* 1988; 85: 217.
- Munnur U, de Boisblanc B, Suresh MS. Airway problems in pregnancy. *Crit Care Med* 2005; 33: S259–S268.
- Bochicchio GV, Napolitano LM, Haan J, et al. Incidental pregnancy in trauma patients. *J Am Coll Surg* 2001; 192: 566–9.
- Morris JA Jr, Rosenbower TJ, Jurkovich GJ, et al. Infant survival after cesarean section for trauma. *Ann Surg* 1996; 223: 481–91.
- Esposito TJ. Evaluation of blunt abdominal trauma occurring during pregnancy. *J Trauma* 1989; 29: 1621–32.
- Pearlman MD, Tintinalli JE, Lorenz RP. A prospective controlled study of outcome after trauma during pregnancy. *Am J Obstet Gynecol* 1990; 162: 1502–10.
- Curet MJ, Schermer CR, Demarest GB, et al. Predictors of outcome in trauma during pregnancy: identification of patients who can be monitored for less than 6 hours. *J Trauma* 2000; 49: 18–25.
- Grossman NB. Blunt trauma in pregnancy. *Am Fam Physician* 2004; 70: 1303–10, 1313.
- Dhanraj D, Lambers D. The incidences of positive Kleihauer-Betke test in low-risk pregnancies and maternal trauma patients. *Am J Obstet Gynecol* 2004; 190: 1461–3.
- Muench MV, Baschat AA, Reddy UM, et al. Kleihauer-Betke testing is important in all cases of maternal trauma. *J Trauma* 2004; 57: 1094–8.
- Goodwin H, Holmes JF, Wisner DH. Abdominal ultrasound examination in pregnant blunt trauma patients. *J Trauma* 2001; 50: 689–93.
- Richards JR, Ormsby EL, Romo MV, et al. Blunt abdominal injury in the pregnant patient: detection with US. *Radiology* 2004; 233: 463–70.
- Brown MA, Sirlin SB, Farahmand N, et al. Screening sonography in pregnant patients with blunt abdominal trauma. *J Ultrasound Med* 2005; 24: 175–81.
- Goldman SM, Wagner LK. Radiologic ABCs of maternal and fetal survival after trauma: when minutes may count. *RadioGraphics* 1999; 19: 1349–57.
- Stalberg K, Haglund B, Axelsson O, et al. Prenatal x-ray exposure and childhood brain tumours: a population-based case-control study on tumour subtypes. *Br J Cancer* 2007; 97: 1583–7.
- Harvey EB, Boice JD Jr, Honeyman M, et al. Prenatal x-ray exposure and childhood cancer in twins. *N Engl J Med* 1985; 312: 541–5.
- Otake M, Schull WJ. Radiation-related brain damage and growth retardation among the prenatally exposed atomic bomb survivors. *Int J Radiat Biol* 1998; 74: 159–71.
- American College of Obstetricians and Gynecologists Committee Opinion #299: Guidelines for diagnostic imaging during pregnancy. 2004.
- Katz VL, Dotters DJ, Droegemueller W. Perimortem cesarean delivery. *Obstet Gynecol* 1986; 68: 571–6.
- Lopez-Zeno JA, Carlo WA, O'Grady JP, et al. Infant survival following delayed postmortem cesarean delivery. *Obstet Gynecol* 1990; 76: 991–2.
- Katz V, Balderston K, DeFreest M. Perimortem Cesarean delivery: were our assumptions correct? *Am J Obstet Gynecol* 2005; 192: 1916–20.

Pelvic Fractures

Matthew O. Dolich

Summary of Evidence and Recommendations			
Question	Answer	Level of evidence	Grade of recommendation
When is pelvic angiography and embolization indicated?	Contrast extravasation on CT. Hypotension with pelvic fracture and absence of extrapelvic injury.	IIb	B
Does extraperitoneal pelvic packing aid in hemostasis?	Probably, in selected cases	IV	C
Should rFVIIa be given routinely to facilitate hemostasis?	No, there is inadequate evidence to support routine use. Prophylactic use in the elective setting does not diminish blood loss.	IV IIb	D B
Is fecal diversion mandatory in all patients with open pelvic fractures?	No. Fecal diversion should be considered in patients with rectal or perineal wounds.	IIa	B
Is plain radiography of the pelvis necessary in all blunt trauma patients?	No. In stable patients undergoing CT scanning, plain pelvic x-ray adds little information.	IIIb	B
What is the optimal timing for operative pelvic fixation?	3–7 days postinjury	IIc	B
Abbreviation: CT, computed tomography.			

INTRODUCTION

Pelvic fractures are reported to account for 3% of all skeletal injuries and approximately 5% of trauma patients requiring hospitalization (1). Pelvic fractures may occur by a variety of different mechanisms, including motor vehicle collisions, pedestrian accidents, falls, and crush injuries. Pelvic fractures may present with a wide spectrum of severity, ranging from relatively minor pubic ramus fractures to significant open book or vertical shear type injuries with exsanguinating hemorrhage or large soft tissue wounds. Associated extrapelvic injuries are common, and the clinician is not infrequently faced with a complex decision process in a multiply injured, unstable patient. This chapter reviews the literature regarding diagnostic and therapeutic measures of particular interest to the trauma/acute care surgeon and provides recommendations based on the available evidence.

WHICH PATIENTS WITH PELVIC FRACTURES WARRANT EARLY ANGIOGRAPHY WITH EMBOLIZATION?

Whereas most patients with pelvic fractures have an initial presentation of hemodynamic stability with relatively little

blood loss, retroperitoneal hemorrhage causing hemodynamic instability does occur in a significant subgroup. A number of arterial and venous branches course along the internal surfaces of the sacrum and ilium; these structures may be disrupted following blunt fracture of the pelvis. Traditional methods for early detection of intracavitary hemorrhage such as focused assessment with sonography in trauma (FAST) and diagnostic peritoneal lavage (DPL) lack sensitivity for retroperitoneal pelvic hemorrhage. Clinical suspicion for pelvic fracture–associated retroperitoneal hemorrhage should increase in the hemodynamically unstable blunt trauma patient with an unremarkable chest x-ray, a negative FAST examination, and uninjured extremities. Although many authors indicate that more than 80% of pelvic fracture–associated hemorrhage is venous in origin, little scientific evidence exists to support this statement. Thus, the exact role of pelvic arteriography continues to evolve.

Several studies have examined the role of contrast-enhanced computed tomography (CT) in the detection of arterial hemorrhage in blunt pelvic trauma and in predicting which patients might derive benefit from pelvic angiography and embolization. Cerva et al. (2) retrospectively reviewed 30 patients with pelvic fracture who underwent both CT and pelvic angiography and found that contrast extravasation or “blush” on CT had 84% sensitivity, 85%

specificity, and 90% accuracy for prediction of arterial injury or hemorrhage on angiography. A subsequent study by Stephen and colleagues (3) found contrast extravasation on CT to have 80% sensitivity and 98% specificity for arterial hemorrhage on subsequent angiography. Positive predictive value of a contrast blush was 80%, and negative predictive value was 98%. Pereira and colleagues (4) performed a retrospective study of 290 patients with pelvic fracture who underwent contrast-enhanced CT; contrast extravasation was noted in 4.5%. More than two-thirds of the patients with contrast extravasation had evidence of hemodynamic instability, and all of these patients underwent therapeutic embolization. Overall sensitivity, specificity, and accuracy of CT for identifying patients requiring embolization were 90%, 98.6%, and 98.3%, respectively.

More recently, Brasel and colleagues (5) retrospectively reviewed their experience with 604 patients with pelvic fracture who underwent contrast-enhanced CT. In this study, patients with contrast extravasation had a higher mean injury severity score (24.5 versus 18.3, $p < 0.001$) and higher mortality (24% versus 6%, $p < 0.001$). However, therapeutic angioembolization was required in 33% of patients without contrast extravasation on CT. One possible explanation for this observation is transient arterial hemorrhage that had ceased during performance of the CT scan.

Miller et al. (6) examined the utility of clinical signs of ongoing hemorrhage for prediction of therapeutic angioembolization of arterial injury. Thirty-five patients with hypotension attributable to pelvic fracture were retrospectively evaluated. One or more episodes of hypotension following resuscitation with ≤ 2 units of packed red blood cells had 73% positive predictive value for arterial bleeding requiring embolization. The authors concluded that in the absence of other sources of hemorrhage, the clinical finding of inadequate response to resuscitation should prompt early pelvic angiography.

Recommendation: Patients with evidence of extravasation on contrast-enhanced CT of the pelvis should undergo urgent pelvic angiography and embolization (Grade B). However, absence of contrast extravasation should not preclude consideration of angiography, because bleeding may be transient in nature. Patients with hemodynamic instability, pelvic fracture, and no obvious extrapelvic source of hemorrhage warrant consideration of pelvic angiography.

WHAT IS THE ROLE OF EXTRAPERITONEAL PELVIC PACKING IN HEMODYNAMICALLY UNSTABLE PATIENTS WITH PELVIC FRACTURES?

Current management of patients with hemodynamic instability related to hemorrhage from pelvic fracture has generally focused on mechanical stabilization of the pelvis and angiographic embolization of arterial hemorrhage. However, the belief that most pelvic hemorrhage is venous in origin coupled with the success of damage-control packing techniques has generated renewed interest in pelvic packing as an adjunctive maneuver for control of pelvic hemorrhage. Extraperitoneal packing is accomplished via a lower midline incision with division of the skin, subcutaneous tissue, and anterior rectus sheath. The preperitoneal space is entered, and blunt dissection is used to fully develop an extraperitoneal "pocket" that extends from the symphysis

pubis to the sacroiliac joint. Three or four laparotomy pads are placed on each side, and the midline incision is closed. The procedure may be followed by mechanical stabilization of the pelvis, laparotomy, or angiography as needed. Packs are generally removed after 24–48 hours, when hemodynamic stability has been achieved. Although the technique has achieved modest utilization in Europe (7), it had not generated much interest in North America until 2005, when a preliminary report by Smith and colleagues (8) described two blunt trauma patients with pelvic fracture–associated hemorrhage who underwent extraperitoneal packing and survived to hospital discharge.

In a larger, more recent study, Tötterman et al. (9) published a retrospective review of 18 pelvic trauma patients who underwent extraperitoneal pelvic packing as part of an institutional protocol for control of massive pelvic hemorrhage. Thirty-day survival was 72%, and the authors reported a significant increase in systolic blood pressure on completion of pelvic packing ($p = 0.002$). Only one of the nonsurvivors was felt to have died of exsanguination rather than associated injury. Interestingly, angiography performed after pelvic injury was positive for arterial injury in 80% of patients.

Based largely on the aforementioned studies and their own clinical experience, Cothren and colleagues (10) adopted a clinical pathway for hemodynamically unstable patients with pelvic fracture that included aggressive use of extraperitoneal pelvic packing in addition to mechanical stabilization and angiographic embolization. Twenty-eight patients underwent pelvic packing during a 1.5-year period, and the mortality rate was 25%, which the authors felt was lower than expected for the injury severity in the group. Of note, no deaths were attributed to exsanguination from pelvic hemorrhage.

Recommendation: Although there are no prospective data, the technique of extraperitoneal pelvic packing appears to be a useful adjunct in hemodynamically unstable patients with suspected or actual pelvic fracture–associated hemorrhage. Limited retrospective studies support the concept of using extraperitoneal packing to achieve tamponade before or after mechanical stabilization (Grade C).

WHAT IS THE ROLE OF RECOMBINANT ACTIVATED FACTOR VIIA IN PATIENTS WITH PELVIC FRACTURE ASSOCIATED HEMORRHAGE?

Recombinant activated factor VIIa (rFVIIa) is a novel hemostatic agent currently approved for use in patients with hemophilia or factor VII deficiency. rFVIIa increases the rate of fibrin clot formation by thrombin generation in addition to activating factor X by adherence to activated platelets. In nonhemophilic patients, rFVIIa has been shown to decrease blood loss and has been used as an adjunct for hemostasis in the setting of coagulopathy. Successful use of rFVIIa has been described in liver transplantation (11), retropubic prostatectomy (12), obstetrical hemorrhage (13,14), aortic aneurysm repair (15), and spine surgery (16). Use of rFVIIa was first reported in the setting of trauma in 1999, when it was administered to a soldier who sustained a gunshot wound with massive hemorrhage (17). Since that time, rFVIIa has seen increased use in trauma-related hemorrhage and coagulopathy, and prospective studies are

under way. Concern does exist, however, about the possibility of thrombotic complications associated with the use of rFVIIa.

Specific experience with rFVIIa in pelvic fracture-associated hemorrhage is limited to small case series and one prospective trial. Williams et al. (18) described military use of rFVIIa in a soldier with an anteroposterior compression fracture of the pelvis and ongoing hemorrhage despite mechanical stabilization, exploratory laparotomy, and aortic cross-clamping. The patient survived, and the authors observed an improvement in diffuse bleeding with rFVIIa administration. Udy and colleagues (19) reported two cases of complex blunt pelvic trauma with hemorrhage and hemodynamic instability not responsive to conventional resuscitation. Both patients were observed to respond to a single 4.8mg dose of rFVIIa and survived to hospital discharge. A subsequent series of three patients with open pelvic fracture and significant soft tissue injury was reported by Overdevest and Heetveld (20). Patients received one or two 90µg/kg doses of rFVIIa during the course of resuscitation; two of the three patients survived despite high injury severity (mean Injury Severity Score = 52).

In an attempt to better examine the effect of rFVIIa, Raobaikady and colleagues (21) conducted a double-blind, randomized, placebo-controlled trial of prophylactic rFVIIa administration in 48 patients with pelvic and acetabular fractures undergoing semi-elective reconstructive surgery. Perioperative blood loss was the same in the rFVIIa and placebo groups. There were no differences in blood component administration, volume resuscitation requirements, operating time, and hospital length of stay between the two groups, and no thromboembolic events were observed in either group. The authors concluded that in the setting of semi-elective pelvic reconstruction, prophylactic use of rFVIIa does not decrease the volume of perioperative blood loss.

Recommendation: Although intuitively appealing, the use of rFVIIa in the setting of acute pelvic fracture-associated hemorrhage is supported by a limited number of anecdotal reports and small case series. There is inadequate evidence to support its routine use (Grade D). Prophylactic use of rFVIIa in elective reconstruction of pelvic and acetabular fractures does not diminish perioperative blood loss (Grade B).

WHAT IS THE ROLE OF FECAL DIVERSION IN OPEN PELVIC FRACTURES?

Open pelvic fracture is an uncommon clinical entity typically associated with high-energy blunt mechanisms and crush injuries. Historically, clinicians have voiced concern about communication of open perineal wounds with pelvic fractures generating an unacceptably high rate of osteomyelitis and pelvic sepsis. The practice of routine performance of a diverting colostomy in patients with open pelvic fractures arose largely based on this concern. However, few studies exist that provide scientific support for this practice, and the available data are further compromised by a lack of clearly defined criteria for defining the anatomy and severity of open pelvic fractures. For example, most studies are of a heterogeneous patient population that includes full-thickness rectal injuries, vaginal tears, perineal wounds, buttock lacerations, and groin wounds.

Raffa and Christensen (22) retrospectively reviewed 16 patients with open pelvic fracture, and observed a high rate of sepsis and death in patients managed without colostomy, or in those who underwent delayed colostomy. This observation led the authors to strongly recommend fecal diversion in all patients with open fractures of the pelvis. One of the first large retrospective studies of open pelvic fracture was performed by Richardson et al. in 1982 (23). Thirty-seven patients were treated at a single center, and 27 (73%) underwent diverting colostomy. The authors noted a correlation between wound location and infection. No patients with anterior wounds developed an infection irrespective of fecal diversion, whereas infection was common with perineal wounds (43% in the colostomy group, 100% in patients in whom colostomy was not performed). Wounds of the buttock region fell into an intermediate category, with no infections in the colostomy group and 67% infection rate in those not receiving a colostomy. Infectious complications also increased when colostomy was delayed for more than 48 hours, and all three patients who underwent fecal diversion more than 72 hours after admission developed infections. No p-values were reported, making determinations of statistical significance difficult.

Apparently contradictory results were obtained by Faringer and colleagues (24), who retrospectively reviewed their experience with 33 open pelvic fracture patients. Although their overall mortality rate was relatively low (15%), wound infections occurred more commonly in the colostomy group than in those without fecal diversion (31% versus 19%). This finding prompted the authors to suggest a more selective policy of fecal diversion in the setting of open pelvic fracture.

Jones et al. (25) performed a multicenter, retrospective analysis of 39 patients who sustained open pelvic fractures. Overall mortality in the series was 25%, and associated extrapelvic injuries were present in 97% of patients. Of the eight patients who developed sepsis, seven had rectal injuries, one did not. Although the authors did not define the term "sepsis," the association with rectal injury was statistically significant ($p < 0.001$). The presence of a rectal tear ($p = 0.12$) and delay in performance of diverting colostomy ($p = 0.16$) showed nonsignificant trends toward correlation with mortality.

More recently, Pell and colleagues (26) performed a retrospective analysis of 14 patients with open pelvic fractures treated at a single center. Nine patients (64%) with nonperineal wounds did not undergo fecal diversion, and five (36%) with perineal wounds underwent colostomy. No patients with anterior wounds and an intact fecal stream developed pelvic sepsis. The authors concluded colostomy might not be necessary in all patients with open pelvic fractures, particularly those with anterior wounds.

A systematic review of fecal diversion in preventing infection in open pelvic fracture was performed by Lunsjo and Abu-Zidan (27). When the available data were pooled, no significant reduction in the rate of infectious complications was noted when colostomy was performed (38% infection rate in the colostomy group versus 35% in the noncolostomy group, $p = 0.86$). Similarly, no significant benefit for sepsis-related mortality was noted those patients undergoing fecal diversion (15% for the colostomy group versus 9% for the noncolostomy group, $p = 0.35$).

Recommendation: Diverting colostomy is not mandatory in all patients with open pelvic fractures. Selective application of fecal diversion in patients with rectal injuries or perineal wounds may be justified (Grade B).

IS PLAIN RADIOGRAPHY OF THE PELVIS NECESSARY IN STABLE PATIENTS WITH BLUNT TRAUMA TO THE TORSO?

Current Advanced Trauma Life Support (ATLS) guidelines indicate that plain x-rays of the pelvis should be obtained in most patients sustaining blunt trauma to the torso (28). This policy is intended to facilitate diagnosis of pelvic fracture early in the course of evaluation of blunt trauma victims. However, the utility of this practice has recently been called into question, as CT of the abdomen and pelvis is obtained in the majority of hemodynamically stable patients with significant blunt torso trauma. Proponents of eliminating plain radiographs of the pelvis cite the superior sensitivity, specificity, and accuracy of CT for fractures of the pelvis and find little clinical significance in the slight delay added by transportation to the CT scanner.

Guillamondequi and colleagues (29) performed a retrospective review of 686 patients with blunt trauma undergoing CT of the abdomen and pelvis. Three hundred eleven (45%) had plain x-rays of the pelvis performed. The false-negative rate for pelvic radiography was 32%, and of the patients with a positive pelvic x-ray, 55% were noted to have additional fractures or a higher injury grade on CT scan.

In a more recent retrospective review of 129 stable blunt trauma patients, Kessel (30) found that CT diagnosed 36% more pelvic fractures than plain radiography, with CT findings leading to pelvic angiography in 15%. In this study, the authors found that plain x-rays of the pelvis did not alter management.

Obaid and colleagues (31) performed a retrospective review of 174 trauma patients who underwent both CT and plain radiography of the pelvis. The false-negative rate for plain x-ray in this study was 22%, with 51% of patients underdiagnosed by plain x-ray. Additionally, they found that pelvic fracture patients with hypotension or transfusion requirements in the emergency department were more likely to require an angiogram (17% versus 0%, $p < 0.0001$) and therapeutic embolization (9% versus 0%, $p < 0.001$). The authors concluded that plain radiographs of the pelvis are of little value in hemodynamically stable patients, but that plain x-ray may have continued utility as a screening tool in unstable patients or those requiring blood transfusion.

Recommendation: In settings where multidetector CT is readily available, plain radiography of the pelvis adds little information and may be safely omitted in the majority of hemodynamically stable blunt trauma patients. Plain pelvic x-ray appears to have a continued role in triaging unstable patients or those requiring early blood transfusion (Grade B).

WHAT IS THE OPTIMAL TIMING FOR OPERATIVE PELVIC STABILIZATION?

Controversy persists regarding the optimal timing of operative fixation of the pelvis. Proponents of an aggressive

policy of early operative stabilization cite decreased blood loss, improved hemodynamics, decreased resuscitation requirements, and diminished pain. However, pelvic stabilization is frequently a long, technically demanding procedure that may represent a "second hit" (after the initial trauma) that in turn increases the risk of multiple organ dysfunction syndrome (MODS). This concern, coupled with the relative success of damage control surgical techniques for abbreviating operations in unstable trauma patients, has generated increased interest in delaying definitive pelvic fixation until well after the initial resuscitation period.

Probst and colleagues (32) examined the relationship between timing and duration of operative pelvic stabilization on outcome. They retrospectively analyzed 290 patients with pelvic ring fractures undergoing operative stabilization. They observed that late operation (>three days after admission) was associated with lower rates of MODS, renal failure, and death as compared to early (day 0) or intermediate (days 1–3) operation ($p < 0.025$). Long procedures (>three hours) were associated with a significantly higher incidence of hepatic dysfunction, but the length of the procedure did not correlate with MODS incidence or mortality. Additional delay of surgery does not appear to provide further benefit. In a retrospective review of 151 pelvic fracture patients, Connor et al. (33) found that patients undergoing operative fixation within one week of injury had fewer pulmonary complications, reduced hospital length of stay, and reduced cost of care as compared to patients undergoing delayed surgery.

Recommendation: Pelvic fractures should be repaired after the patient is fully resuscitated. Optimal timing of operative repair appears to be between three and seven days postinjury (Grade B). Further delay may increase pulmonary complications and cost, and therefore should be considered only when extrapelvic injuries or physiologic status preclude surgery within the first week.

REFERENCES

1. Mucha P, Farnell MB. Analysis of pelvic fracture management. *J Trauma* 1984; 24: 379–86.
2. Cerva DS, Mirvis SE, Shanmuganathan K, et al. Detection of bleeding in patients with major pelvic fractures: value of contrast-enhanced CT. *Am J Roentgenol* 1996; 16: 131–5.
3. Stephen DJ, Kreder HJ, Day AC, et al. Early detection of arterial bleeding in acute pelvic trauma. *J Trauma* 1999; 47: 638–42.
4. Pereira SJ, O'Brien DP, Luchette FA, et al. Dynamic helical computed tomography scan accurately detects hemorrhage in patients with pelvic fracture. *Surgery* 2000; 128: 678–85.
5. Brasel KJ, Pham K, Yang H, et al. Significance of contrast extravasation in patients with pelvic fracture. *J Trauma* 2007; 62: 1149–52.
6. Miller PR, Moore PS, Mansell E, et al. External fixation or arteriogram in bleeding pelvic fracture: initial therapy guided by markers of arterial hemorrhage. *J Trauma* 2003; 54: 437–43.
7. Ertel W, Keel M, Eid K, et al. Control of hemorrhage using c-clamp and pelvic packing in multiply injured patients with pelvic ring disruption. *J Orthop Trauma* 2001; 15: 468–74.
8. Smith WR, Moore EE, Osborn P, et al. Retroperitoneal packing as a resuscitation technique for hemodynamically unstable patients with pelvic fractures: report of two representative cases and a description of technique. *J Trauma* 2005; 59: 1510–14.

9. Tötterman A, Madsen JE, Skaga NO, et al. Extraperitoneal pelvic packing: a salvage procedure to control massive traumatic pelvic hemorrhage. *J Trauma* 2007; 62: 843–52.
10. Cothren CC, Osborn PM, Moore EE, et al. Preperitoneal pelvic packing for hemodynamically unstable pelvic fractures: a paradigm shift. *J Trauma* 2007; 62: 834–42.
11. Hendriks HG, Meijer K, De Wolf JT, et al. Reduced transfusion requirements by recombinant factor VIIa in orthotopic liver transplantation: a pilot study. *Transplantation* 2001; 71: 402–5.
12. Friederich PW, Henny CP, Messelink EJ, et al. Effect of recombinant activated factor VII on perioperative blood loss in patients undergoing retropubic prostatectomy: a double-blind placebo-controlled randomized trial. *Lancet* 2003; 361: 201–5.
13. Segal S, Shemesh IY, Blumenthal R, et al. Treatment of obstetric hemorrhage with recombinant activated factor VII (rFVIIa). *Arch Gynecol Obstet* 2003; 268: 266–7.
14. Bouwmeester FW, Jonkhoff AR, Verheijen RH, et al. Successful treatment of life-threatening postpartum hemorrhage with recombinant activated factor VII. *Obstet Gynecol* 2003; 101: 1174–6.
15. Wahlgren CM, Swedenborg J. The use of recombinant activated factor VII to control bleeding during repair of a suprarenal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2003; 26: 221–2.
16. Kaw LL, Coimbra R, Potenza BM, et al. The use of recombinant factor VIIa for severe intractable bleeding during spine surgery. *Spine* 2004; 29: 1384–7.
17. Kenet G, Walden R, Eldad A, et al. Treatment of traumatic bleeding with recombinant factor VIIa. *Lancet* 1999; 354: 1879.
18. Williams DJ, Thomas G, Pambakian S, et al. First military use of activated factor VII in an APC-III pelvic fracture. *Injury* 2005; 36: 395–9.
19. Udy A, Vaghela M, Lawton G, et al. The use of recombinant activated factor VII in the control of hemorrhage following blunt pelvic trauma. *Anaesthesia* 2005; 60: 613–16.
20. Overdevest GM, Heetveld M. Open pelvic fractures: experience with recombinant factor VIIa, degloving, and bowel injury. *Injury* 2007; 38: 384–91.
21. Raobaikady R, Redman J, Ball AS, et al. Use of activated recombinant coagulation factor VII in patients undergoing reconstruction surgery for traumatic fracture of the pelvis or pelvis and acetabulum: a double-blind, randomized, placebo-controlled trial. *Br J Anaesth* 2005; 94: 586–91.
22. Raffa J, Christensen NM. Compound fractures of the pelvis. *Am J Surgery* 1976; 132: 282–6.
23. Richardson JD, Harty J, Amin M, et al. Open pelvic fractures. *J Trauma* 1982; 22: 533–8.
24. Faringer PD, Mullins RJ, Feliciano PD, et al. Selective fecal diversion in complex open pelvic fractures from blunt trauma. *Arch Surg* 1994; 129: 958–63.
25. Jones AL, Powell JN, Kellam JF, et al. Open pelvic fractures: a multicenter retrospective analysis. *Orthop Clin North Am* 1997; 28: 345–50.
26. Pell M, Flynn WJ, Seibel RW. Is colostomy always necessary in the treatment of open pelvic fractures? *J Trauma* 1998; 45: 371–3.
27. Lunsjo K, Abu-Zidan FM. Does colostomy prevent infection in open blunt pelvic fractures? A systematic review. *J Trauma* 2006; 60: 1145–8.
28. *Advanced Trauma Life Support for Doctors*, 7th edition. Chicago: American College of Surgeons, 2004.
29. Guillaumondequi OD, Pryor JP, Gracias VH, et al. Pelvic radiography in blunt trauma resuscitation: a diminishing role. *J Trauma* 2002; 53: 1043–7.
30. Kessel B, Sevi R, Jeroukhimov I, et al. Is routine portable pelvic x-ray in stable trauma patients always justified in a high technology era? *Injury* 2007; 38: 559–63.
31. Obaid AK, Barleben A, Porral D, et al. Utility of plain film pelvic radiographs in blunt trauma patients in the emergency department. *Am Surg* 2006; 72: 951–4.
32. Probst C, Probst T, Gaensslen A, et al. Timing and duration of initial pelvic stabilization after multiple trauma in patients from the German trauma registry: is there an influence on outcome? *J Trauma* 2007; 62: 370–7.
33. Connor GS, McGwin G, MacLennan PA, et al. Early versus delayed fixation of pelvic ring fractures. *Am Surg* 2003; 69: 1019–23.

An Evidence-Based Approach to Extremity Vascular Trauma

Terence O’Keeffe

Summary of Clinical Scenarios and Evidence-Based Recommendations		
Question	Answer	Grade
Can a diagnosis of vascular injury be adequately made by physical exam supplemented with ABI?	Physical exam with ABI is more than 90% sensitive for the presence of vascular injury.	B
Is CTA adequate for diagnosis of vascular injury or is invasive angiography always required?	In centers with the technical expertise, CTA is comparable to conventional angiography.	B
Should knee dislocation still be treated as a special circumstance—is routine angiography necessary?	Routine investigation is not required following knee dislocation in the presence of a normal exam.	B
Is there a role for the nonoperative management of vascular injuries?	Minor abnormalities, e.g., intimal flaps, may be safely observed with a low risk of complications.	C
What is the role of endovascular treatment (stenting) in the management of acute vascular injuries?	Although stenting is technically feasible, there is insufficient evidence to recommend this approach due to the lack of long-term follow-up.	C
What role should intravascular shunting for damage control vascular surgery play in the management scheme for vascular injuries?	Evidence suggests that shunting may improve outcomes in damage control vascular surgery.	C
Should the ATLS recommendations for the use of tourniquets be revised?	There is insufficient evidence from civilian studies at this time to change the current ATLS recommendations.	D
Following repair of an acute vascular injury should fasciotomies be performed prophylactically or should we measure compartment pressures?	There is insufficient evidence to recommend either prophylactic fasciotomies in all patients or to recommend specific screening protocols.	C
Abbreviations: ABI, ankle-brachial index; ATLS, Advanced Trauma Life Support; CTA, computed tomography angiography.		

INTRODUCTION

The use of evidence-based guidelines in trauma surgery has been challenging for many reasons, one of the most important being that by its very nature the emergent treatment required for many traumatic injuries does not lend itself to randomized controlled trials. Even observational studies are plagued by the poor follow-up that is seen in many trauma centers. Despite this, there is a growing body of clinical trials and evidence on which to base both diagnostic and therapeutic decisions in the acutely injured trauma patient.

Vascular surgery has changed dramatically over the past decade, and this includes the diagnosis and management of acute traumatic vascular injuries. Despite the relative homogeneity of the patient injuries, the literature is comprised of studies with small numbers, incomplete or varying definitions of injuries and complications (certainly none that are generally accepted as standard definitions), questionable gold standards, and very importantly in the setting of trauma—extremely limited patient follow-up. This makes the interpretation of the accrued data much more difficult.

In this chapter, the most recent data from the last ten years regarding the diagnosis and management of acute traumatic vascular injuries are presented, which has been divided into relevant clinical questions, with recommendations based on the most recent evidence.

CAN A DIAGNOSIS OF VASCULAR INJURY BE ADEQUATELY MADE BY PHYSICAL EXAM SUPPLEMENTED WITH ABI?

Following the recognition in the 1990s that mandatory angiography was not required for penetrating wounds in close proximity to vessels, the role of physical examination in evaluating the presence or absence of vascular injury has been more closely scrutinized (1,2).

In a study from the University of Florida Health Sciences Center in 1998, Dennis and colleagues found that after adopting a policy of physical exam alone for asymptomatic penetrating extremity wounds, only 1.3% of patients presented following discharge with a need for vascular repair (3). These patients all presented within a

week, and went on to have surgical repair without long-term sequelae. However, all patients were initially observed in the hospital for a full 24 hours, and follow-up was possible in only 29% of patients who had only undergone a physical examination.

An additional prospective trial in 1999 examined the accuracy of physical examination alone in proximity penetrating extremity trauma. There were 4 missed injuries out of 421, with a sensitivity of 92% for injury and a specificity of 95% (4). The authors concluded that examination alone was a good screening modality for patients with these types of injuries.

There is considerably more data on the use of the ankle-brachial pressure index (ABI) as an adjunct to physical diagnosis in the setting of vascular trauma; however, the two largest papers were both performed prior to the time limit of this review in 1991 and 1996 and dealt mostly with penetrating extremity injuries (1,5). Nevertheless, they both concurred that an ABI of less than 0.9 had a 75–87% sensitivity and a specificity of greater than 95% for the presence of vascular injury in this setting.

In blunt vascular injury, most of the data comes from studies of popliteal artery injuries due to knee trauma, which are dealt with in greater detail in a later section on knee dislocations. In a prospective study from 2004, researchers used an ABI cut-off value of 0.9 as a screening tool for angiography or immediate surgical exploration depending on clinical condition (6). An ABI of 0.9 was found to be 100% sensitive and specific for the diagnosis of arterial injury. In follow-up of 38 patients whose initial ABI was >0.9, there were no delayed signs of vascular compromise, after an average follow-up of 19 months. Physical exam with ABI was felt to be an accurate screening tool. No direct comparisons have yet been performed between physical exam alone and physical exam with ABI.

Summary: Physical examination alone can accurately detect hard signs of vascular injury. The ABI is easily performed and may improve the accuracy of the physical examination. Physical examination with or without ABI is adequate as a screening tool for blunt or penetrating vascular injury. Level of evidence IIb. Strength of recommendation: B.

IS CTA ADEQUATE FOR DIAGNOSIS OF VASCULAR INJURY, OR IS INVASIVE ANGIOGRAPHY ALWAYS REQUIRED?

As more and more facilities have access to multichannel computed tomography (CT) scanners, and the analysis software continues to improve, CT angiography (CTA) as an initial diagnostic modality for arterial injury has been increasingly promoted as the modality of choice.

In 1999, Soto and colleagues published a study of 45 consecutive patients where CTA was performed prior to conventional angiography (7). Two patients were excluded due to nondiagnostic images being obtained secondary to bullet fragments. Using two fellowship-trained radiologists blinded to the clinical results, there were no false positives, two false negatives for one radiologist, and no false reads for the second radiologist. The sensitivity and specificity for their consensus interpretation was 100%.

The authors followed this study in 2001 with a prospective study of 139 patients where CTA was used as the only initial evaluation in these patients (8). A small number of patients (3.6%) had inadequate quality images and required formal angiography. In four patients, the CTA was inaccurate—three false negative and one false positive result, for an overall sensitivity of 95.1% and specificity of 98.7%. After a mean follow-up of five months, no additional lesions were diagnosed in the 73 patients with normal CTA exams at presentation. Initial CTA was able to guide appropriate treatment in 93.5% of cases. However, this study did not include angiography as a gold standard for all patients, and the facility had 24-hour in-house radiologists.

Another prospective trial was published in 2006 from Reiger and colleagues in Austria (9). They performed CTA on a four-channel CT scanner on 87 patients clinically suspected of an arterial injury. They used a mixed gold standard of operative findings, angiography if required, and clinical and radiologic follow-up. Sixty-two lesions were diagnosed in 55 patients and confirmed at surgery. Prospective sensitivity was 95%, with a specificity of 87%. Two patients required angiography. There were no missed injuries reported at follow-up, although the length of follow-up was not reported.

A number of retrospective reports have also now been published: Busquets in 2004, Rieger as well as Inaba in 2006, Iezzi in 2007, and by Peng in 2008 (9–13). The first report detailed 97 CTA studies in 95 patients, of which 70% were from blunt trauma. Seventy-two studies were normal, and the 25 abnormal studies were compared with angiography, surgery, or both as their gold standard. There were no false positives. Sixty-two patients had no work-up other than CTA, with no missed injuries identified after a mean follow-up of eight months in 84% of patients. Sensitivity and specificity were therefore both 100%. In the article by Rieger et al., 87 patients underwent CTA using a four-channel CT scanner, with again a mixed gold standard of surgery, formal angiography, and/or clinical and radiologic follow-up. They reported prospective sensitivity and specificity of 95% and 87% with an accuracy of 93%, with no appreciable differences between the two radiologists reviewing the images. They stated that no anatomic injury was found in patients who did not require surgery. Nine findings were misclassified, all of which related to the presence of absence of vascular spasm.

The study by Inaba and colleagues retrospectively evaluated 63 examinations performed in 59 patients. There was one nondiagnostic study due to retained bullet fragments, although fully 19% of scans possessed artifact from bullets, due to 45% of these patients suffering penetrating injuries. Confirmatory angiography was performed on this occasion and found to be negative. Twenty-two lesions were diagnosed by CTA, 19 confirmed in the operating room, and the other 3 managed nonoperatively. Three of these patients underwent both CTA and conventional angiography with 100% concordance of findings. No missed injuries were found subsequently in patients with normal CTA, although follow-up was short at 48 days. These authors quoted a sensitivity and specificity of 100% for this modality.

In Iezzi et al.'s retrospective analysis of 47 patients over a 34-month period from a single institution, all CT scans were technically adequate. There were two false

positive exams and one false negative study. Like previous studies, the gold standard was a composite of conventional angiography, surgery, and clinical follow-up. Sensitivity was 96%, and specificity was 90% (13).

Peng reported their experience over a five-year period, with 38 patients undergoing a CTA, with 17 abnormal scans. All findings were confirmed at surgery and there were no false negatives or missed injuries. However, they did not specify a gold standard (12).

Summary: The data suggest that CTA is a highly useful screening tool for detecting vascular injury. However, significant technical expertise is required that may not be available in all centers and may limit its widespread applicability. Use of CTA as a screening tool for vascular injury: Level of evidence IIb. Strength of recommendation: B.

SHOULD KNEE DISLOCATION STILL BE TREATED AS A SPECIAL CIRCUMSTANCE—IS ROUTINE ANGIOGRAPHY NECESSARY?

Acute dislocation of the knee was previously thought to be a special circumstance because of a quoted injury prevalence rate of 20–30% to the popliteal artery, with a concomitant high rate of amputation if restoration of flow takes longer than eight hours (14).

As recently as 1997, some authors were still insisting that mandatory imaging of the popliteal artery was necessary, but in 2001 Miranda and colleagues presented the results of a prospective study of physical exam without routine angiography for knee dislocations (15,16). In their protocol, patients were admitted for a minimum of 23 hours with serial exams every 4–6 hours. Patients presenting with or developing hard signs of vascular injury had angiography performed and underwent surgery as indicated. There were 35 patients over their 10-year study period. Six patients (17%) presented with hard signs of injury and underwent immediate surgery. Two patients developed a loss of pulses during their admission, which was detected by serial physical exam. They underwent angiography, of which one was normal, with the other patient requiring a surgical repair. The remaining 27 patients had both a normal initial exam and a normal exam at discharge. At a mean follow-up of 13 months, 12 of these 27 patients (44%) were available for follow-up and reported no problems. The authors concluded physical examination alone was entirely reliable and accurate in the setting of knee dislocation.

Martinez et al. reported on 21 patients in 2001 with knee dislocations, and of the 9 patients with a normal pulse exam, only 1 had an abnormal arteriogram, which was an intimal flap that was subsequently managed nonoperatively (17).

A retrospective analysis of 20 years of knee dislocations was published by Abou-Sayed and colleagues in 2002, detailing their experiences with 53 knee dislocations or knee fractures (18). In this study, angiography was performed at the discretion of the attending surgeon, but they found that 79% of this group did not require surgical repair. Of the 26 limbs that were not investigated by angiography, in only two cases was surgery necessary, and this was evident from clinical examination (a nearly complete amputation in one case, and frank arterial hemorrhage in the other case). In the other 24 limbs, no intervention was required. They concluded physical examination had a 100% negative

predictive value and that angiography is unnecessary in an extremity with a normal admission neurovascular status.

Also in 2002, Barnes and colleagues performed a meta-analysis to evaluate the diagnostic accuracy of the pulse examination in detecting surgical arterial lesions associated with knee dislocation (19). He identified seven articles from 1979 to 2001 and extracted data on 284 knee dislocations. Based on these pooled data, it was calculated that abnormal pedal pulses presented a sensitivity of 0.79 and a specificity of 0.91 for vascular injury. Although they accepted that their study had limitations, the authors recommended that angiography still be used liberally in patients with knee dislocations. However, the prospective study by Miranda was not included in their analysis because it was published after their cut-off date.

As previously mentioned, a study by Mills et al. in 2004 further refined physical examination with the addition of the ABI. They reported on a prospective study where all patients with knee dislocation underwent pulse examination as well as having the ABI calculated using a Doppler probe (6). All patients with an ABI of 0.9 or higher had their knee immobilized and were then admitted for serial examination. Patients with an ABI of less than 0.9 underwent angiography or immediate surgical exploration as indicated. An ABI of less than 0.9 had a 100% sensitivity and specificity for the 11 patients with an arterial injury in this study. In contrast, no patient ($n = 27$) with an ABI of greater than 0.9 manifested evidence of vascular injury, neither as an inpatient nor at follow-up of an average of 19 months. In their series, physical exam alone had a sensitivity of 91% and a specificity of 89%. They concluded that routine angiography is not necessary for accurate diagnosis of a vascular injury, and that the ABI should be considered an extension of the physical examination for a patient with a knee dislocation.

The largest series ever reported was published in 2004 by Stannard and colleagues, and it reported on 138 knees treated using a protocol of selective angiography in a prospective, single-center study (20). The prevalence of arterial injury was only 7% (9 patients) with a total of 17 patients undergoing angiography, despite a normal physical exam. Out of these 17 patients, 15 had normal findings, 2 had mild spasm, and there was one intimal tear, which was treated nonoperatively. The authors quoted physical exam (without use of ABI) as having a sensitivity of 100% and a specificity of 99%.

A further report in 2004 on 57 knee dislocations in 55 patients again found no missed vascular injuries in the 32 patients who had a normal physical examination, although the gold standard was a composite of angiography and clinical follow-up (angiogram in 13 and follow-up in 19) (21). The incidence of vascular injury in their study was higher at 21%. This study used physical exam with the addition of the ABI. One fasciotomy was performed for compartment syndrome without evidence of vascular injury. They quoted a lower sensitivity of 71% (13 patients with a normal exam had no injury on angiography) with a specificity of 100%.

Finally, a 10-year review of 39 patients at another U.S. center in 2005 again concluded that routine angiography is unnecessary in patients with a normal physical exam after reduction of the knee dislocation, although in their review, 2 patients with a normal exam and minor

angiographic findings required fasciotomy (22). In light of this, although they quoted a sensitivity of 100%, the specificity was reduced to 58%.

Summary: Routine angiography in the setting of knee dislocation is unnecessary if a normal examination is present (including normal ABIs). Physical examination alone is sufficient in knee dislocations: Level of evidence IIb. Strength of recommendation: B.

IS THERE A ROLE FOR THE NONOPERATIVE MANAGEMENT OF VASCULAR INJURIES?

As diagnostic technologies have become more advanced, there has been an increase in the ability to detect minor vascular trauma. The original surgical tenet that all angiographic abnormalities must be surgically explored and repaired has been re-examined. The best study for this approach came from Dennis and colleagues, who compared a group of 43 patients who had angiographic abnormalities but with patent distal vessels, no extraluminal extravasation >2cm in size and without manifestations of hard signs of vascular injury (3). They were observed in hospital for 24–48 hours before discharge. Four of these patients (9%) re-presented with clinical deterioration within one month of injury and underwent immediate surgical repair without subsequent morbidity or problems during long-term follow-up. Clinical and duplex ultrasound follow-up in a further 23 patients did not reveal any abnormalities, bar a single patient with mild residual narrowing of the superficial femoral artery. Mean follow-up was nine years. Follow-up was also made in a group of 78 out of 287 patients who had been evaluated for vascular trauma by clinical exam alone, and there were no reports of vascular symptoms in this sample of 29% of the group of patients after a mean follow-up of five years.

A study from the pediatric population by Lazarides et al. reported on seven patients (all aged under seven years) with vascular trauma of iatrogenic or blunt etiology treated using intravenous heparin. None of these patients required subsequent operation, although follow-up varied from only one month to eight years (23). There are also other reports in the literature that detail nonoperative treatment of intimal flaps treated successfully with anticoagulation (18,24).

Summary: Minor vascular injuries (e.g., small intimal flaps) that do not compromise the distal blood supply may be safely treated nonoperatively if a period of close observation can be performed, although additional outpatient follow-up should be part of this algorithm. Nonoperative management of vascular injuries is appropriate in certain cases: Level of evidence IIIb. Strength of recommendation: C.

WHAT IS THE ROLE OF ENDOVASCULAR TREATMENT (STENTING) IN THE MANAGEMENT OF ACUTE VASCULAR INJURIES?

With the increased expertise that has been gained in the use of vascular stent grafting in both aortic and extremity vessels, it was only a matter of time before these devices were used to repair vessels that had been acutely injured. The first publications that described the use of stents in

arterial trauma were case reports concerning their use in the following arteries: axillary, subclavian, brachial, popliteal, and posterior tibial (25–29).

In a series from Xenos and colleagues from 2003, 12 patients out of 27 had an endovascular repair for traumatic injury (30). Only 3 out of the 27 patients had suffered an iatrogenic insult in this series. There were no periprocedural complications, and all stent grafts were placed successfully. Blood loss and procedure times were reduced for endovascular procedures as compared to surgical repair. One stent graft occluded after nine months, and bypass grafting was necessary, whereas all 11 patients with open surgical repair had patent interposition grafts at one year. The authors concluded that endovascular techniques are an alternative approach to treatment of subclavian or axillary injury and result in shorter operative time and less blood loss. Short-term patency was similar to that obtained from surgical repair.

White and colleagues published the results of a multicenter trial on the use of covered stents for the treatment of acute arterial trauma in 2006 (31). They enrolled 62 patients over the course of six years, but of these 46 patients were treated for iatrogenic injuries. There were only nine confirmed cases of use in traumatic injuries—seven for blunt trauma and two penetrating. Thirty-three patients had iliac injuries, 11 in the femoral artery and 18 upper extremity injuries. The average age for the entire cohort was 61.6 years, which is much higher than the average trauma patient. Most of the vessel injuries were successfully treated with stenting (93.5%), with four failures occurring in the treatment of arteriovenous fistulas (which gave a 75% success rate for this indication). Success rates for exclusion of endoleak fell to 88.4% at six months and 85.3% at one year with 69% of patients following up at one year. Success was lowest in those patients with femoral intervention at 62.3%. Success rates were not analyzed separately for iatrogenic and noniatrogenic injuries, and no data was given regarding amputations. The authors compared their results with the results of a literature search covering surgical repair of injured iliac arteries and concluded that endovascular treatment reduced operative complications and perioperative and late mortality compared to standard surgical repair. However, they provided no analysis or comparison on the severity of the injuries in these groups.

Piffaretti et al. reported on a series of 10 patients with peripheral arterial injuries treated by endovascular techniques in 2007 (32). Their primary success rate was 100%. After a mean follow-up of 16 months (range 3–60 months), only one patient required repeat intervention for stent graft thrombosis, which was reestablished with thrombolysis and angioplasty. No patients were lost to follow-up, and all others were asymptomatic.

Summary: With the inclusion of iatrogenic injuries in most series, which are likely to be less severe and more easily controlled, it is difficult at this time to make strong recommendations on the efficacy of endovascular repair for acutely injured vessels. Stenting is often technically feasible with good short-term results, although due to lack of the long-term data on the safety and efficacy of this approach, it should not be the procedure of first choice. Endovascular treatment as a therapy for vascular trauma: Level of evidence IV. Strength of recommendation: C.

WHAT ROLE SHOULD INTRAVASCULAR SHUNTING FOR DAMAGE CONTROL VASCULAR SURGERY PLAY IN THE MANAGEMENT SCHEME FOR VASCULAR INJURIES?

The principle of damage control surgery has been extended from using this technique in major abdominal trauma into the area of major extremity vascular trauma, particularly in the polytrauma patient, and recent experiences in military surgery have shown that the principles of damage control can be successfully employed in the early operative management of severe vascular trauma (33). The principle of abbreviated surgery has been advanced by the use of temporary intraluminal arterial (and venous) shunting. Shunts may be of various types, depending on the resources available, and can usually be managed without systemic anticoagulation. This restoration of blood flow by temporary shunting can allow time for orthopedic repair or transfer to another center for further stabilization prior to definitive repair.

The first described use was in a case report in 1971, but since then there have been a number of case series using this approach (34). A report from 1999 described using intraluminal shunts in probably the most common circumstance encountered, which is combined musculoskeletal and vascular injuries. In the seven cases described, surgeons were able to insert the shunts successfully in these patients, which was followed by repair of their orthopedic injuries. The shunts were removed at the same operation, being in situ for an average of 185 minutes (range 90–390 minutes). No shunt thrombosis was reported (35). A further case series of seven patients from Thailand in 2002 reported similar results, although the authors additionally reported using a shunt in a venous injury as well as the arterial system (36).

Granchi and colleagues described a group of 19 patients who had temporary shunts placed for either damage control or combined orthopedic and vascular injuries (37). Mortality was high at 37% overall, with an average Injury Severity Score of 15. No patient received heparin, and all shunts remained patent, with the longest time in situ of 52 hours. There were three amputations, two early and one delayed, with significant residual limb morbidity among survivors. The authors concluded that shunting was feasible without anticoagulation with patency maintained for at least 52 hours.

Hossny and colleagues studied the use of routine popliteal artery shunting in cases of blunt arterial trauma (38). He compared seven patients treated in this fashion and compared them to historical controls. There was a significant reduction in mean intraoperative ischemic times between groups, as would be expected. Four out of 7 patients who underwent shunting required fasciotomy (57%), compared to 9 out of 10 (90%) of the nonshunted group. Four out of 10 patients (40%) required amputation in the nonshunted group, whereas no patient required an amputation in the group that underwent routine shunting. Hospital stay and number of procedures were also lower in the shunted group.

However, the most extensive experience in the use of vascular shunts has once again been collected through the military experiences in the Iraq conflict. A number of

reports have been published detailing the results of the use of shunts, the first of which was by Rasmussen and colleagues (33). They found that shunts had been used in 30/126 (24%) of cases, and all but 2 had been placed in lower level surgical facilities prior to transfer. Nineteen of 22 (86%) proximal shunts were patent at time of surgical exploration, but only 1/8 (12%) of the distal shunts remained patent. Only 2 limbs out of 30 required amputation, a 93% limb salvage rate. The authors discussed the poor patency rates for distal shunts and concluded at best they did not harm, because distal embolectomy and reconstruction with subsequent limb salvage was possible at their facility. Additional military reports have since confirmed the utility of this approach, and this technique remains a valuable tool in approaching major vascular extremity trauma (39,40).

Summary: Vascular shunts for damage control vascular surgery are highly useful and can allow for combined venous/arterial repair. Ischemia times are lower and patency rates are high without anticoagulation, although definitive repair should still be performed as soon as possible. Use of vascular shunts as an adjunct in major vascular extremity trauma: Level of evidence IIIb. Strength of recommendation: C.

SHOULD THE ATLS RECOMMENDATIONS FOR THE USE OF TOURNIQUETS BE REVISED?

The use of tourniquets in civilian extremity trauma has generally been frowned upon. The 7th edition of the Advanced Trauma Life Support manual states “tourniquets should *not* be used (except in unusual circumstances such as traumatic amputation of an extremity)” (41). The Advanced Trauma Life Support manual has been recently revised, and the 8th edition now reads “Although controversial, the use of a tourniquet may occasionally be life-saving and/or limb-saving in the presence of ongoing hemorrhage uncontrolled by direct pressure”. There has been renewed interest in these devices due to the high-velocity nature of the injuries sustained by members of the armed forces in Iraq, for example, improvised explosive devices, shrapnel, and high-velocity gunshot wounds.

Provisional reports from Iraq suggested that pre-hospital tourniquet use was associated with improved hemorrhage control. Beekley and colleagues reported on 166 patients with a major vascular extremity injury or traumatic amputation (42). Sixty-five percent of patients with tourniquets had hemorrhage control on arrival, as opposed to 11% without tourniquets. The average time the tourniquet was applied was 70 minutes. There were no differences in secondary amputation rates or mortality between groups. Analysis of the seven deaths estimated that four of these patients could have been saved with adequate tourniquet placement.

In a prior study from Israel in 2003, Lakstein and colleagues reported on 91 soldiers treated with tourniquets with 78% overall effectiveness, considered if “absolute control of hemorrhage distal to the injury site was achieved.” They were 94% effective in the upper limb and 71% effective in the lower limb (43). However, they showed that up to 47% of the applications were not indicated. Furthermore, they identified seven limbs in five patients with neurologic

complications; ischemic times in these patients ranged from 109 to 187 minutes. No limbs were lost as a result of tourniquet application.

Anecdotal reports on tourniquet use in Iraq have also found their way into the media and have led to calls for all soldiers in the field to be supplied with “modern tourniquets.” Over 750,000 tourniquets have been supplied to the military in Iraq, despite few objective data on their efficacy and anecdotal evidence of continued application in unnecessary cases (44). There are no civilian data at this time on which to base any recommendations.

Summary: There is a lack of civilian data on tourniquet use from which to make recommendations, and the different nature of the injuries experienced by military personnel may not allow extrapolation to civilian trauma. At this time no definite recommendation can be made for general use. Use of tourniquets for exsanguinating extremity hemorrhage: Level of evidence IIIb. Strength of recommendation: D.

FOLLOWING REPAIR OF AN ACUTE VASCULAR INJURY, SHOULD FASCIOTOMIES BE PERFORMED PROPHYLACTICALLY OR SHOULD WE MEASURE COMPARTMENT PRESSURES?

The data regarding the use of prophylactic fasciotomy in patients who have undergone emergent vascular repair is patchy at best. There has never been a randomized trial comparing routine prophylactic fasciotomy to a policy of careful clinical exam and/or measurement of compartment pressures.

Abouezzi and colleagues published the largest series of the last decade on the subject of fasciotomies in 1998 (45). They analyzed 163 vascular injuries to the extremities and found that 45 patients (28%) required fasciotomy, with the highest rates noted in combined arterial and venous injuries and the lowest rates for isolated venous injuries (31.6% versus 15.2%). There was also a higher rate of fasciotomy in popliteal vessels injury compared with other locations. Seven of the 45 fasciotomies performed were delayed, 5 following failure of vascular repair and 2 for the onset of clinical compartment syndrome. The authors suggested that the presence of a combined vascular injury does not by itself necessitate routine fasciotomy, and they advocated a policy of selective use of this procedure based on objective criteria, such as venous stump monitoring and assessment of compartment pressures.

A review by Ulmer in 2002 attempted to assess whether published studies support basing the diagnosis of compartment syndrome of the lower leg on clinical findings (46). Only four studies met inclusion criteria and using a likelihood ratio methodology, he reported a sensitivity of 13–19% and a specificity of 97% for clinical findings to diagnose acute compartment syndrome. He concluded that clinical features of compartment syndrome are more useful in their absence than confirming the diagnosis if they are present. Using pain, paresthesias, pain with passive stretch, and paresis as the exam findings, the estimated prevalence of compartment syndrome was 25% with one finding present, rising to 93% if three factors were present, although he cautioned that this was based on limited data.

There has been some interest in near-infrared spectroscopy as a noninvasive method of detecting extremity compartment syndrome, but despite some promising early work, this has not translated into clinical practice at this time (47,48).

Kosir and colleagues described an aggressive screening approach to the diagnosis of acute lower extremity compartment syndrome (ALECS) in the work in 2007 (49). All high-risk trauma patients admitted to their intensive care unit (ICU) were screened using a comprehensive physical exam, which included measurement of lower leg circumference, pain assessment, and vascular and neurologic examination. Compartment pressures were measured when the physical exam was suspicious or unreliable. Subsequent screening was performed every 4 hours during the first 48 hours of admission. They screened 45 patients who met inclusion criteria out of 428 patients admitted to the ICU over a six-month period. Nine (20%) of these screened positive for lower extremity compartment syndrome and underwent four-compartment fasciotomies with clinical findings consistent at operation with ALECS. The mortality in this subgroup was 67%, compared to 17% in the group without compartment syndrome. No clinically significant ALECS developed in the group that was not screened.

The authors identified base deficit, lactate, and transfusion requirement as factors that were increased in patients who went on to develop ALECS. Also, no cases developed after 18 hours using this protocol, and thus they reduced their screening period to 24 hours. The authors recommended that in light of the inaccuracy of the physical examination, similar screening protocols to the one they described should be used by all high-volume trauma centers.

Summary: There is a paucity of good-quality data on which to base recommendations. In the absence of a good prospective clinical trial to identify which patients need to have this procedure performed and under what circumstances, clinical experience and frequent reexamination (with or without pressure monitoring) are the only tools that will adequately detect this syndrome. Prophylactic fasciotomies are necessary following vascular repair: Level of evidence: IIb/IIIa. Strength of recommendation: C.

CONCLUSIONS

Although certain questions regarding vascular trauma appear to have been definitively answered, clearly the vast majority of the vascular literature is fraught with limited patient numbers, varying definitions of injuries and complications, questionable gold standards, and limited follow-up. Accurate evidence-based guidelines are therefore difficult to formulate. In light of the small numbers of patients seen at any one center, it may be that the only way forward will be to organize multicenter cooperative trials to answer some of the remaining questions, such as the utility and safety of stenting for acute vascular injuries.

Until then, I have attempted to synthesize and summarize the recent accumulated evidence relating to the management of acute vascular injuries. I hope that a similar review in another 10 years' time will be able to draw on studies of a higher quality to make more definitive recommendations.

Summary of Studies Reviewed Showing Level of Evidence and Quality

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Abou-Sayed	18	2002	IIIb	Angiography versus clinical exam	RCS	3 months	Limb salvage, changes in management dictated by angiography
Abouezzi	45	1998	IV	Fasciotomy (primary versus secondary) versus no fasciotomy	CC	NR	Fasciotomy or limb amputation
Barnes	19	2002	IIa	Abnormal versus normal pedal pulses	MA	NR	Presence of arterial injury
Beekley	42	2006	IIIb	Tourniquet use versus no tourniquet use	RCS	NR	Bleeding control, amputation rates, mortality
Busquets	10	2004	IIIb	CTA compared to conventional angiography or surgical findings	RCS	8 months	Presence of arterial injury
Chambers	39	2006	IIb	Ligation versus primary repair versus shunting	RCS	NR	Complications, need for amputation
Clouse	40	2007	IIb	Shunt versus no shunts	PCS	NR	Shunt patency, early limb salvage
Dennis	3	1998	IIb	Proximity angiography versus clinical examination for 24 hours	PCS	5 years	Re-presentation with symptoms of arterial insufficiency
Gonzalez	4	1999	IIb	Observation for 24 hours versus operation versus angiography	PCS	1 week	Presence of significant arterial injury
Granchi	37	2000	IV	Patients with intraluminal arterial shunts placed	CS	NR but 17/21 patients	Shunt time
Hollis	22	2005	IV	Angiography versus clinical exam	CS	NR	Angiographic findings
Hossny	38	2004	IV	Routine shunting versus no shunting	CC	NR	Ischemic time, amputation and complication rates
Iezzi	13	2007	IIIb	CTA compared to conventional angiography or surgical findings	RCS	30 days	Accuracy of CTA
Inaba	11	2006	IIIb	CTA compared to aggregate gold standard: operation, follow-up, or angio	RCS	Mean 48 days	Accuracy of CTA
Johansen	1	1991	IIb	ABI with clinical exam versus angio or operation	PCS	5 days to 2 weeks	Accuracy of physical exam with ABI
Klineberg	21	2004	IIIb	Knee dislocations, normal versus abnormal physical exam	RCS	NR	Arterial injury versus no arterial injury
Kosir	49	2007	IIb	Lower extremity compartment syndrome versus no compartment syndrome	PCS	NR	Fasciotomy rate, limb loss, mortality
Lakstein	43	2003	IIIb	Tourniquet use versus no tourniquet use	RCS	NR	Ischemic time, effectiveness of tourniquet
Lazarides	23	2006	IV	Operative versus nonoperative treatment	CS	NR, 1 month to 8 years	Long-term outcome of arterial trauma
Lonn	27	2005	IV	Stents for arterial trauma	CS	NR, 10 months to 4 years	Long-term outcome of stenting
Martinez	17	2001	IV	Pulse status versus angiogram	CS	3 months	Presence of arterial injury
Mills	6	2004	IIb	Physical exam and ABI: >0.9 versus <0.9	PCS	19 months	Presence of arterial injury
Miranda	16	2002	IIb	Physical exam, normal versus abnormal pulses	PCS	19 months, 13 months	Presence of arterial injury, complications
Nassoura	5	1996	IIb	ABI versus angiography	PCS	NR	Presence of arterial injury
Peng	12	2008	IIIb	CTA compared to conventional angiography	RCS	Mean 4 weeks	Presence of arterial injury
Piffaretti	32	2007	IV	Endovascular repair compared to surgical repair	CS	Mean 16 months	Primary technical success in stent placement, device complications
Rasmussen	33	2006	IIIb	Distal versus proximal shunts	RCS	NR	Patency, complication rates, early limb amputation rates
Reber	35	1999	IV	Shunts for combined vascular and musculoskeletal trauma	CS	Range 2–24 months	Median ischemic time, limb loss
Rieger	9	2006	IIIb	CTA compared to aggregate gold standard: operation, follow-up, or angio	RCS	NR	Accuracy of CTA in detecting arterial injury
Rozycki	24	2003	IIIb	Hard signs, shunts, shock and mangled extremities, delayed diagnosis	RCS	NoR	Survival, fasciotomy, complications, and limb loss

(Continued)

Summary of Studies Reviewed Showing Level of Evidence and Quality (Continued)

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Soto	7	1999	Ilb	CTA compared directly to conventional angiography	PCS	Variable; 24 hours to 10 months	Accuracy of CTA in detecting arterial injury
Soto	8	2001	Ilb	CTA compared to aggregate gold standard: operation, follow-up, or angio	PCS	Median 4.7 months	Accuracy of CTA in detecting arterial injury
Sriussadaporn	36	2002	IV	Shunting versus no shunting in complex extremity injuries	CS	6 months	Shunt time, limb amputation rates
Stannard	20	2004	Ib	Normal versus abnormal physical exam	PCS	6 months for 116/134 injuries	Presence of arterial injury
Ulmer	46	2002	IIla	Presence or absence of compartment syndrome	MA	Variable; 6–14 months	Sensitivity, specificity of clinical findings
White	31	2006	IV	High-risk patients with vascular lesions, older patients with traumatic arterial injuries	PIT	Variable; 6–26 months	Early and late exclusion success, patency, adverse events, and mortality
Xenos	30	2003	IIlb	Axillary or subclavian arteries treated by open or endovascular repair	RCS	1 year	Early and late exclusion success, patency, adverse events, and mortality

Abbreviations: ABI, ankle-brachial index; CC, case control (retrospective); CS, case series (retrospective); CTA, computed tomography angiography; MA, meta-analysis; NR, not reported; PCS, prospective cohort study; PIT, prospective nonrandomized interventional trial; RCS, retrospective cohort study.

REFERENCES

- Johansen K, Lynch K, Paun M, et al. Non-invasive vascular tests reliably exclude occult arterial trauma in injured extremities. *J Trauma* 1991; 31: 515–59; discussion 519–22.
- Britt LD, Weireter LJ, Cole FJ. Newer diagnostic modalities for vascular injuries: the way we were, the way we are. *Surg Clin North Am* 2001; 81: 1263–79, xii.
- Dennis JW, Frykberg ER, Veldenz HC, et al. Validation of nonoperative management of occult vascular injuries and accuracy of physical examination alone in penetrating extremity trauma: 5- to 10-year follow-up. *J Trauma* 1998; 44: 243–52; discussion 242–3.
- Gonzalez RP, Falimirski ME. The utility of physical examination in proximity penetrating extremity trauma. *Am Surg* 1999; 65: 784–9.
- Nassoura ZE, Ivatury RR, Simon RJ, et al. A reassessment of Doppler pressure indices in the detection of arterial lesions in proximity penetrating injuries of extremities: a prospective study. *Am J Emerg Med* 1996; 14: 151–6.
- Mills WJ, Barei DP, McNair P. The value of the ankle-brachial index for diagnosing arterial injury after knee dislocation: a prospective study. *J Trauma* 2004; 56: 1261–5.
- Soto JA, Munera F, Cardoso N, et al. Diagnostic performance of helical CT angiography in trauma to large arteries of the extremities. *J Comput Assist Tomogr* 1999; 23: 188–96.
- Soto JA, Munera F, Morales C, et al. Focal arterial injuries of the proximal extremities: helical CT arteriography as the initial method of diagnosis. *Radiology* 2001; 218: 188–94.
- Rieger M, Mallouhi A, Tauscher T, et al. Traumatic arterial injuries of the extremities: initial evaluation with MDCT angiography. *Am J Roentgenol* 2006; 186: 656–64.
- Busquets AR, Acosta JA, Colon E, et al. Helical computed tomographic angiography for the diagnosis of traumatic arterial injuries of the extremities. *J Trauma* 2004; 56: 625–8.
- Inaba K, Potzman J, Munera F, et al. Multi-slice CT angiography for arterial evaluation in the injured lower extremity. *J Trauma* 2006; 60: 502–6; discussion 506–7.
- Peng PD, Spain DA, Tataria M, et al. CT angiography effectively evaluates extremity vascular trauma. *Am Surg* 2008; 74: 103–7.
- Iezzi R, Cotroneo AR, Pascali D, et al. Multi-slice CT (MSCT) angiography for assessment of traumatic lesions of lower limbs peripheral arteries. *Emerg Radiol* 2007; 14: 389–94.
- Perron AD, Brady WJ, Sing RF. Orthopedic pitfalls in the ED: vascular injury associated with knee dislocation. *Am J Emerg Med* 2001; 19: 583–8.
- Gable DR, Allen JW, Richardson JD. Blunt popliteal artery injury: is physical examination alone enough for evaluation? *J Trauma* 1997; 43: 541–4.
- Miranda FE, Dennis JW, Veldenz HC, et al. Confirmation of the safety and accuracy of physical examination in the evaluation of knee dislocation for injury of the popliteal artery: a prospective study. *J Trauma* 2002; 52: 247–51; discussion 251–2.
- Martinez D, Sweatman K, Thompson EC. Popliteal artery injury associated with knee dislocations. *Am Surg* 2001; 67: 165–7.
- Abou-Sayed H, Berger DL. Blunt lower-extremity trauma and popliteal artery injuries: revisiting the case for selective arteriography. *Arch Surg* 2002; 137: 585–9.
- Barnes CJ, Pietrobon R, Higgins LD. Does the pulse examination in patients with traumatic knee dislocation predict a surgical arterial injury? A meta-analysis. *J Trauma* 2002; 53: 1109–14.
- Stannard JP, Sheils TM, Lopez-Ben RR, et al. Vascular injuries in knee dislocations: the role of physical examination in determining the need for arteriography. *J Bone Joint Surg Am* 2004; 86A: 910–15.
- Klineberg EO, Crites BM, Flinn WR, et al. The role of arteriography in assessing popliteal artery injury in knee dislocations. *J Trauma* 2004; 56: 786–90.
- Hollis JD, Daley BJ. 10-year review of knee dislocations: is arteriography always necessary? *J Trauma* 2005; 59: 672–5; discussion 675–6.
- Lazarides MK, Georgiadis GS, Papas TT, et al. Operative and nonoperative management of children aged 13 years or younger with arterial trauma of the extremities. *J Vasc Surg* 2006; 43: 72–6; discussion 76.
- Rozycki GS, Tremblay LN, Feliciano DV, et al. Blunt vascular trauma in the extremity: diagnosis, management, and outcome. *J Trauma* 2003; 55: 814–24.
- Valentin MD, Tulsyan N, James K. Endovascular management of traumatic axillary artery dissection—a case report

- and review of the literature. *Vasc Endovascular Surg* 2004; 38: 473–5.
26. Molloy S, Jacob S, Buckenham T, Taylor RS. Technical report: percutaneous repair of an acute traumatic subclavian artery occlusion. *Eur J Vasc Endovasc Surg* 2001; 21: 75–6.
 27. Lonn L, Delle M, Karlstrom L, et al. Should blunt arterial trauma to the extremities be treated with endovascular techniques? *J Trauma* 2005; 59: 1224–7.
 28. Papavassiliou VG, Dervisis CI, Argitis VP, et al. Endovascular repair of a traumatic popliteal arteriovenous fistula. *Vasa* 2006; 35: 53–5.
 29. Halabi AR, Kandzari DE. The thrill is gone: catheter-based exclusion of a posttraumatic arteriovenous fistula with a covered stent graft. *Cath Cardiovasc Interv* 2005; 66: 27–33.
 30. Xenos ES, Freeman M, Stevens S, et al. Covered stents for injuries of subclavian and axillary arteries. *J Vasc Surg* 2003; 38: 451–4.
 31. White R, Krajcer Z, Johnson M, et al. Results of a multicenter trial for the treatment of traumatic vascular injury with a covered stent. *J Trauma* 2006; 60: 1189–95; discussion 1195–6.
 32. Piffaretti G, Tozzi M, Lomazzi C, et al. Endovascular treatment for traumatic injuries of the peripheral arteries following blunt trauma. *Injury* 2007; 38: 1091–7.
 33. Rasmussen TE, Clouse WD, Jenkins DH, et al. The use of temporary vascular shunts as a damage control adjunct in the management of wartime vascular injury. *J Trauma* 2006; 61: 8–12; discussion 12–15.
 34. Eger M, Golcman L, Goldstein A, et al. The use of a temporary shunt in the management of arterial vascular injuries. *Surg Gynecol Obstet* 1971; 132: 67–70.
 35. Reber PU, Patel AG, Sapio NL, et al. Selective use of temporary intravascular shunts in coincident vascular and orthopedic upper and lower limb trauma. *J Trauma* 1999; 47: 72–6.
 36. Sriussadaporn S, Pak-art R. Temporary intravascular shunt in complex extremity vascular injuries. *J Trauma* 2002; 52: 1129–33.
 37. Granchi T, Schmittling Z, Vasquez J, et al. Prolonged use of intraluminal arterial shunts without systemic anticoagulation. *Am J Surg* 2000; 180: 493–6; discussion 496–7.
 38. Hossny A. Blunt popliteal artery injury with complete lower limb ischemia: is routine use of temporary intraluminal arterial shunt justified? *J Vasc Surg* 2004; 40: 61–6.
 39. Chambers LW, Green DJ, Sample K, et al. Tactical surgical intervention with temporary shunting of peripheral vascular trauma sustained during Operation Iraqi Freedom: one unit's experience. *J Trauma* 2006; 61: 824–30.
 40. Clouse WD, Rasmussen TE, Peck MA, et al. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. *J Am Coll Surg* 2007; 204: 625–32.
 41. American College of Surgeons Committee on Trauma. *Advanced Trauma Life Support*, 8th edition. Chicago: American college of surgeons, 2004.
 42. Beekley A, Sebesta J, Blackburne L, et al. Pre-hospital tourniquet use in operation Iraqi freedom: effect on hemorrhage control and outcomes. Western Trauma Association, Big Sky, MT, 2006.
 43. Lakstein D, Blumenfeld A, Sokolov T, et al. Tourniquets for hemorrhage control on the battlefield: a 4-year accumulated experience. *J Trauma* 2003; 54(5 Suppl): S221–S225.
 44. Beekley AC, Starnes BW, Sebesta JA. Lessons learned from modern military surgery. *Surg Clin North Am* 2007; 87: 157–84, vii.
 45. Abouezzi Z, Nassoura Z, Ivatury RR, et al. A critical reappraisal of indications for fasciotomy after extremity vascular trauma. *Arch Surg* 1998; 133: 547–51.
 46. Ulmer T. The clinical diagnosis of compartment syndrome of the lower leg: are clinical findings predictive of the disorder? *J Orthop Trauma* 2002; 16: 572–7.
 47. Arbabi S, Brundage SI, Gentilello LM. Near-infrared spectroscopy: a potential method for continuous, transcutaneous monitoring for compartmental syndrome in critically injured patients. *J Trauma* 1999; 47: 829–33.
 48. Gentilello LM, Sanzone A, Wang L, et al. Near-infrared spectroscopy versus compartment pressure for the diagnosis of lower extremity compartmental syndrome using electromyography-determined measurements of neuromuscular function. *J Trauma* 2001; 51: 1–8, discussion 8–9.
 49. Kosir R, Moore FA, Selby JH, et al. Acute lower extremity compartment syndrome (ALECS) screening protocol in critically ill trauma patients. *J Trauma* 2007; 63: 268–75.

Surgery of Upper Extremity

Howard Wang, Patrick Schaner and David Sahar

Clinical Questions		
Question	Answer	Strength
How are common soft tissue infections, such as human or animal bites, flexor tenosynovitis, and hand abscess, treated and are the current empiric antibiotic used based on clinical evidence?	Bacteriology of animals and humans are studied and general guidance is given regarding antibiotic coverage however this may miss a significant amount of organism.	B
When is it appropriate to operate on scaphoid fractures and what are the diagnostic techniques employed?	No significant improvement of operative treatment over nonoperative treatment but may have decreased time to return to work. No significant improvement of MRI over CT currently in the diagnosis of scaphoid fractures.	B
What are the indications for replantation of digits and extremities?	Large retrospective reviews confirming successful outcomes in 70–87% of patients	C
What are the indications for release of forearm compartment syndrome, hand compartment syndrome, and acute carpal tunnel syndrome?	Pressure within 20 mmHg of diastolic cause ischemic muscle necrosis, and success of treatment is both time and pressure dependent.	C
What are the current options to treat flexor and extensor tendon injuries?	Most hand surgeons would operate when laceration is >50% of flexor tendon. Early improved function with dynamic splinting up to 6 months, then no difference.	C
How are common fractures of the hand, such as phalanx fractures, boxer's fractures, bennett fractures, Rolando fractures, treated?	Closed reduction or open reduction of fractures may be attempted, the technique must be adjusted for the individual fracture with the goal of preservation of function through stabilizing an adequate reduction.	C
What do you do with a fingertip amputation that is too distal for replantation?	Defects smaller than 1 cm ² can be allowed to heal by secondary intent, otherwise, a composite graft or local flap can be used instead.	C
Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.		

HOW ARE COMMON SOFT TISSUE INFECTIONS, SUCH AS HUMAN OR ANIMAL BITES, FLEXOR TENOSYNOVITIS, AND HAND ABSCESS, TREATED, AND ARE THE CURRENT EMPIRIC ANTIBIOTIC USED BASED ON CLINICAL EVIDENCE?

Infections of the hand can occur due to bites of different animals, including humans. This chapter concentrates mostly on human, dog, and cat bites. In terms of human bites, the mechanism can include intentional bites of different parts of the body or when the teeth penetrate skin due to an unintentional mechanism. One widely talked about mechanism is really not a bite per se but an injury sustained during a punch called a fight bite. Closed-fist punch of another individual can result in breaking of the skin and can penetrate through to the extensor sheath and down to bone. The issues to pay particular attention to is when a hand is in the clenched position during a punch and the relationship of the skin, tendon, and bone is in a different position than when the fingers are fully extended. Thus,

when you examine the patient (usually in the fully extended position), realize that injured structures that are underneath the skin (such as the extensor tendon) may not lie directly underneath the skin opening when the hand is examined in the clenched position. The majority of bites are from pet dogs and cats; only a small minority of them are from rabid animals. However, due to the significant consequence of rabies (near 100% mortality), all animal attacks should be reported to animal control and the animal either observed for 10 days or euthanized and the brain examined for Negri bodies.

Regardless of the mechanism, general principles of infection control should be observed. Although most bites are polymicrobial, antibiotic selection is initially empiric and based on the most common organisms found in the mouth. This may include *Staphylococcus species*, *Eikenella corrodens*, and *anaerobes* for humans. A broad-spectrum antibiotic such as Unasyn or Augmentin is usually the first line of therapy. Dog or cat bites, like human bites, are generally polymicrobial with the concern of *Pasteurella species*. First-line antibiotic treatment is similar to human bites and generally

a broad-spectrum agent can be used. Clindamycin is effective for animal bites for those allergic to penicillin. Tetanus prophylaxis and rabies prevention should also be considered.

If the wound is relatively superficial, generous washing and cleansing may be all that is needed. Deeper and more complex bites may require operative intervention and debridement of necrotic tissue. If purulence exists, cultures are sent. Any underlying structures that may be injured, such as the extensor mechanism in clenched fist injuries, should be explored and repaired operatively. Patients should be placed on antibiotics and the hand splinted in safe position and elevated for comfort in more severe cases. Daily dressing changes or staged return to the operating room (OR) for repeated washouts and debridements should be considered if initial control cannot be achieved due to heavy contamination or necrosis. Also, any definitive repairs of tendons and underlying structure may be delayed in these situations. Specific repair of tendon injuries is beyond the scope of this chapter.

Other hand infections may arise due to puncture injuries, especially in those who are immunocompromised, such as diabetics. Flexor tenosynovitis can occur when infection affects the flexor tendon mechanism of the digit. This presentation depends on how long the infection has been present. The classic sign of flexor tenosynovitis is Kanavel's sign: pain on extension of digit, flexed position of digit, fusiform swelling of digit, and tenderness along the flexor sheath. Early infection, less than 24 hours since onset, can be successfully managed medically: antibiotics, elevation, and splinting. However, once the infection has progressed, surgical drainage along with antibiotics may be needed. In all but the most severe infections, drainage can be accomplished through the placement of an irrigation catheter at the A1 pulley (distal palmar crease) with a counterincision and drain left at the A5 pulley [volar distal interphalangeal (DIP) joint]. Irrigation of the sheath is then accomplished using normal saline. The catheter may be left and irrigation attempted on the floor for the next 24–48 hours. The hand is splinted and elevated while antibiotics are started. This allows for continuous irrigation and repeated wash-out of the wound without the need to return to the OR. More severe infections may still require the use of classic Brunner's incisions for opening of the entire digit for adequate drainage (1,2).

Other forms of hand infections that can occur, such as an abscess or felon that needs to be drained as any other abscess in the body. The only specific issues to pay attention to are the types of incisions made (in the case of a felon) and the different hand spaces such as the midpalmar space. Paying attention to these anatomical separations will help guide the surgical exploration. The common theme to all infections, however, is the choice of antibiotic usage. Cultures are taken, and therapy is guided by speciation and the sensitivities, but prior to this, a good 48–72 hours may go by with empiric therapy. Thus, what evidence is there that our choice of antibiotic is correct? A study in the *New England Journal of Medicine* in 1999 attempted to look at the bacteriology of dog and cat bites. Although *Pasturella* was commonly implicated, many other bacteria, some unexpectedly so, were isolated. This prospective study involved a total of 107 patients (3). However, multiple studies throughout the years all demonstrate one thing:

animal bite bacteriology is not consistent, and although amoxicillin/clavulanate can cover most of the infections, it may not be effective for a significant minority of patients (4–6). In terms of human bites, although *E. corrodens* is one that is cited, in truth, the human oral flora is more complex than the oral flora of animals. *S. aureus* is generally the most common infectious organism (7–9). Most articles, however, agree that most bites result in multiple bacteria flora being introduced. Thus, this is the inherent difficulty of antibiotic choice: any empiric therapy may potentially miss myriad bacteria that are present in the mouth of animals or humans. Furthermore, one would suspect that region by region, there may be differences in bacteria flora of oral cavities, although this is not documented. Given these circumstances, antibiotic treatment for a hand infection is correct only a majority of the time if based on the most common bacteria across species, *Staph*. Thus, clinical follow-up remains crucial in making sure that the choice of antibiotic is appropriate.

Answer: Bacteriology of animals and humans are studied and general guidance is given regarding antibiotic coverage, however, this may miss a significant amount of organism. Recommendation grade: B.

WHEN IS IT APPROPRIATE TO OPERATE ON SCAPHOID FRACTURES, AND WHAT ARE THE DIAGNOSTIC TECHNIQUES EMPLOYED?

Scaphoid fracture of the wrist is one of the most common fractures clinicians will manage. Unfortunately, it is also a relatively difficult fracture to manage, because imaging studies can often miss it. Traditionally, scaphoid fractures were treated nonoperatively with a long-arm cast for up to 10–14 weeks. However, the complication of scaphoid non-union can be difficult to treat. Recent advances have led to improvements in both the understanding of the vascular anatomy as well as imaging studies that can aid in the diagnosis and subsequent management of these fractures.

The presenting symptom of these fractures, of course, is a perceived injury to the wrist with “snuff box” tenderness along the radial portion of the wrist. Imaging studies generally start with plain wrist views, which may show a fracture. However, this is not always the case. In terms of radiological diagnosis of a scaphoid fracture, the population of greatest interest is the patient that presents with wrist pain yet plain films are inconclusive. Three different imaging modalities can supercede a plain film's ability to diagnose scaphoid fractures. Part of the difficulty is that usually the *minority* of patients with suspected occult scaphoid fractures actually turn out to have one. Computed tomography (CT) scan and magnetic resonance imaging (MRI) are potential considerations, as well as bone scanning. Recent literature has looked at MRI and CT and has not definitely concluded that one is better than the other (10,11). Furthermore, when comparing MRI to bone scan, there is a lack of evidence of MRI superiority (12). Thus, although there has been recent enthusiasm of MRI and perhaps with advancement of imaging technology studies will show its superiority, current literature cannot definitely state the superiority of one modality over the other. Thus, given the potential cost of MRI, CT or bone scan may still be acceptable alternatives to MRI and adjunct to plain films

in diagnosing occult fractures. The one potential benefit of MRI is being able to see surrounding soft tissue and vasculature better. Nevertheless, current evidence-based recommendations cannot conclude the superiority of one second-line radiographic study over the other.

The traditional treatment for nondisplaced scaphoid fractures is nonoperative. The downside of this treatment is that it requires long-term immobilization of the extremity and the potential nonunion. The likelihood of nonunion can be related to the fracture's position relative to the inherent blood supply. Accordingly, because the blood supply of the scaphoid bone goes from a distal to proximal direction fractures of the proximal pole are much more likely to develop a nonunion. Though recent advances in internal fixation have simplified the technical operative management of scaphoid fractures, prospective, randomized trials have failed to show any significant benefit to early fixation using this new screw technology (13,14). In addition, there seems to be a lack of consensus regarding the use of different casts for nonoperative treatment of these fractures (15). There is some evidence, however, that internal fixation leads to a more rapid return to work and possible earlier union as evidenced radiographically (16,17).

Answer: No significant improvement of operative treatment over nonoperative treatment but may have decreased time to return to work. No significant improvement of MRI over CT is noted in the diagnosis of scaphoid fractures. Recommendation grade: B.

WHAT ARE THE INDICATIONS FOR REPLANTATION OF DIGITS AND EXTREMITIES?

Indications

- Thumb
- Multiple digits
- Single digit distal to flexor digitorum profundus (FDP) insertion
- Upper extremity and palm/wrist forearm
- Proximal to elbow if a sharp amputation
- Almost any amputation in a child

Contraindications

- Crushed /mangled parts
- Multilevel amputation
- Prolonged ischemia time
- Medical comorbidities
- Life-threatening injuries

Relative Contraindications

- Single digit in an adult
- Heavy contamination
- Self-mutilation
- Avulsion

The first thumb revascularization was reported by Kleinert and Kasdan (18) in 1965. Komatsu and Tamai made digital replantation a reality in 1965, and the first thumb replant was later reported by Komatsu and Tamai in 1968 (19).

Replantation capability is a requirement of every Level I trauma center, and the function of an appropriately replanted limb is usually better than a prosthesis (20).

However, having the ability to replant all or part of an extremity does not always make it the right choice. Despite the upper limb replant success rates of 70–87%, you must develop a personalized plan for each individual patient and evaluate the potential risks and benefits of replantation in each case (21–23). This is a very tough decision because an upper extremity, specifically a hand, have very different and very personal meanings and utility to each individual. For instance, a concert pianist may not be able to tolerate the loss of even a single fingertip and be willing to undergo months of rehab to save it. On the other hand, a laborer who must work to feed his family may prefer a revision amputation and the quickest possible recovery and return to productive employment.

Because replantation requires considerable more time, skill, and effort and a significantly prolonged rehabilitation period, we must take the probability of success into consideration. Although there is some debate about the criteria for replantation, there is a much greater chance of success in a young, healthy patient with a clean, sharp amputation and with minimal ischemia time. The person's handedness, occupation, smoking history, and ability to follow up must also be taken into consideration. Remember, success must be measured by the restoration of a functional limb or appendage, not just adequate perfusion. However, most will agree that any of the aforementioned criteria can be relaxed when it comes to replanting a patient who is a child (24).

The amount of ischemia that can be tolerated is directly proportional to the amount of muscle present in the amputated segment. Though much longer times have been reported anecdotally, the recommended limits are up to 12 hours of warm ischemia time and 24 hours cold for digits and up to 6 hours of warm ischemia and 12 hours cold for more proximal major replants (25). The proper packaging of a part for potential replant includes placing the part in moist gauze and a plastic bag that can then be submerged in ice water.

Do not let the amputation of a limb or partial limb prevent you from doing an adequate trauma intake. Your patient still requires an Advanced Trauma Life Support (ATLS) approach to avoid missing a significant concomitant process. Only after the patient has been cleared from a trauma standpoint can you focus on the limb at hand. Do a thorough exam testing neurovascular status and functionality of the proximal retained portion. Be sure to radiologically evaluate the proximal retained as well as the distal amputated segment. Once the decision to replant has been made, do not waste any time. If you are waiting for an OR, start to dissect out and tag the neurovascular pedicles as well as any tendons. Once your patient arrives in the OR after thorough evaluation, irrigation, and debridement, you will similarly tag the retained proximal portion of the limb. The process of replantation then proceeds with bony fixation, arterial repair, venous repair, tendon repair, and finally nerve repair. In cases of more proximal injuries, you may need to provide a conduit for a vascular shunt to limit the ischemic time while appropriate bony fixation is performed prior to final arterial and venous anastomosis (26).

Nowadays with the advent of composite tissue transplantation and technical advances of cyborg prosthesis, we must force ourselves to remember the goal of replantation versus revision amputation and possible prosthesis which is the restoration or creation of a functional, aesthetically pleasing extremity.

Answer: Large retrospective reviews confirming successful outcomes in 70–87% of patients for replantation. Recommendation grade: C.

WHAT ARE THE INDICATIONS FOR RELEASE OF FOREARM COMPARTMENT SYNDROME, HAND COMPARTMENT SYNDROME, AND ACUTE CARPAL TUNNEL SYNDROME?

Compartment syndrome is a surgical emergency and a high index of suspicion is necessary to avoid costly sequelae, such as resultant contracture and loss of function. A compartment syndrome exists when interstitial pressures are greater than tissue perfusion pressures, which leads to nerve and muscle ischemia and eventual contractures. In the upper extremity it is most often caused by crush injuries, reperfusion, and fractures and can be iatrogenic in the form of cast constriction, poor limb positioning, access-related arterial trauma, and anticoagulation.

Injuries that can cause compartment syndrome do so by either decreasing compartment volume via constriction or increasing compartment content. Casts, restrictive dressings, crushing injuries can all decrease volume while bleeding, venous obstruction, reperfusion, and snakebites (to name a few) can increase compartment content. Supracondylar fractures are well-known causes of Volkmann ischemic contractures at the humerus that can damage the median nerve, brachial artery, and vein.

The diagnosis of compartment syndrome is clinical, and the main symptom is pain out of proportion to the supposed injury, especially pain on passive stretch of the involved muscles. The patient will typically have a tense, swollen area of concern. Be very careful because once an actual decrease in sensation followed by pallor and pulselessness appear, the compartment is clearly ischemic. Thus, you must have a high index of suspicion because only early diagnosis and treatment can avoid ischemic injury and its resultant sequelae.

Hand-held tonometry devices such as the Stryker Intracompartmental Monitoring System, as well as A-line set-ups that can be fashioned in the intensive care setting can be used to measure compartment pressures. Although the diagnosis of compartment syndrome is predominantly clinical, compartment pressures have little role in the awake, cooperative patient. However, if your physical diagnosis is inconclusive, traditionally, a reading of 40–45 mmHg is indicative of a compartment syndrome in need of a fasciotomy. Be careful because in a hypotensive patient there can be compromise at even lower values (typically readings within 30 mm of the systolic pressure or 20 mm of diastolic pressure will also compromise the compartment) (27). This was shown in a canine model depicting ischemic muscle necrosis pathologically at these lower values (28).

In the forearm, the volar compartment is most commonly affected. The volar compartment houses the flexor and pronator muscles: FDP, flexor pollicis longus (FPL), pronator quadratus, flexor carpi ulnaris (FCU), palmaris longus, flexor carpi radialis (FCR), flexor digitorum superficialis (FDS), and the pronator teres. In addition, the volar compartment contains the median nerve, the ulnar nerve, and the deep branch of the radial nerve. The dorsal compartment and the mobile wad can also be affected. The

dorsal compartment contains the extensors: the supinator, abductor pollicis longus, and extensor indices, extensor carpi ulnaris (ECU), extensor digiti minimi (EDM), extensor digitorum, and anconeus. The mobile wad is comprised of the extensor carpi radialis longus (ECRL), extensor carpi radialis brevis (ECRB), and brachioradialis muscles. In the wrist and hand, the carpal tunnel can be involved. Thus, every distal radius fracture must be evaluated for acute carpal tunnel syndrome; even if you have a closed fracture, this additional diagnosis can upgrade the case to a surgical emergency. In addition, the thenar muscles, hypothenar muscles, and the four dorsal and three volar interossei of the hand can be affected.

Once you have made the diagnosis, timing is critical. Only 12 hours separates the onset of muscle weakness and pain on passive stretch and hypoesthesia from complete necrosis of muscle fibers (29). In addition, Sheridan and Matsen found that when fasciotomy was performed within 12 hours of the onset of compartment syndrome, normal function could be expected in up to 68% of patients (30). In all of the above-mentioned areas, the treatment remains the same: emergent fasciotomy. This procedure was first shown to prevent the sequelae of ischemic contracture in 1926 (31). Once the area in question is opened, the muscle is inspected for viability, any obviously necrotic tissue is debrided, and the wounds are left open for potential delayed primary versus secondary closure.

Answer: Pressure within 20 mmHg of diastolic cause ischemic muscle necrosis, and success of treatment is both time and pressure dependent. Recommendation grade: C.

WHAT ARE THE CURRENT OPTIONS TO TREAT FLEXOR AND EXTENSOR TENDON INJURIES?

Hand Flexor Tendon Injuries

Injuries to flexor tendon are commonly caused by lacerations and punctures (32). Partial flexor tendon injury management has been controversial. Evidence for improved function has been reported for both operative (33,34) and nonoperative management with early mobilization (35–38). Complications of unrepaired partial laceration include rupture, triggering, and tendon flap formation with entrapment. Successful nonoperative management of major partial tendon lacerations up to 95% has been reported previously (35,39). There are no randomized prospective studies indicating when a partial laceration should be safely observed. However, there is a consensus among hand surgeons for operative repair of partial flexor tendon injuries involving more than 50% of the tendon substance (40).

In nonoperative management, patients are placed on dorsal blocking splint with wrist in 10° flexion. Early guarded active motion is initiated on the first day after surgery. Splint is removed at four weeks, and resistance exercise is started with normal activity at six weeks (38).

Although complete laceration of flexor tendons do not require emergent resolution, it should be repaired within 3 weeks to avoid proximal tendon end swelling, muscle fibrosis, and tendon contraction (41,42). Incisions are designed to maximize exposure of tendons and associated bony injuries while avoiding ischemia of flaps and long-term contracture. Bruner zigzag incision is commonly employed to minimize neurovascular injury and stay

lateral to the flexor creases. Injuries should be repaired in the following order: bone and joints, tendons, and neurovascular structures. Expanding A2 and A4 pulleys compromises biomechanics of flexor tendons and should be avoided (43). If damaged, A2 pulley should be reconstructed with free tendon graft.

Tendon lacerations should be repaired in two layers (44): core and epitendinous. Modified Kessler technique is the most common for core sutures using 4–0 polyester, whereas 6–0 monofilament sutures are used for epitendinous repair. You will find placement of core sutures much easier if you first run the back wall of the epitendinous suture to aid in coaptation prior to placing the core strands and eventually complete the epitendinous closure.

Immediately postop, the wrist should be placed in splint at 20° and metacarpophalangeal (MCP) joint at 70° (45). Because mobilized tendons heal faster and stronger, rehabilitation postrepair entails graded early passive motion and advancing to active motion. The two likely postrepair time points for rupture are 5–10 days (tendon strength weakens for several days postop before strengthening) and 6 weeks (when strengthening exercises are initiated) and thus should be monitored closely during these periods.

Hand Extensor Tendon Injuries

Because classification of extensor tendon lacerations into eight zones by Kleinert and Verdan in 1993, significant advances have occurred in our understanding of the anatomy and physiology of these injuries (46). Patient compliance is critical to final outcome. Closed Zone I (Mallet finger) and Zone III (central slip) injuries are generally treated nonoperatively. Mallet fingers are splinted continuously for six weeks with aluminum foam splint or stack splint. Limited (30°) active flexion of DIP is then initiated with FDP block and increased to 60° by eight weeks. Resistive exercises are initiated at 10 weeks. A success rate of 80% is reported with this method of treatment.

Although central slip injuries (Zone III) may initially retain full extension via lateral bands, herniation of the head of the proximal phalanx through the central slip and volar migration of the lateral bands leads to a Boutonniere deformity over time. Thus, injuries to the central slip should be promptly treated either with a splint if closed or primarily repaired if open. Nonoperative management includes six weeks of complete extended immobilization of the proximal interphalangeal (PIP) joint. After six weeks, 30° of flexion is allowed with volar block with increased range of motion over time. Resistive exercises are initiated after 10 weeks.

In open extensor injuries over dorsal hand, complete and partial open lacerations over 50% are repaired primarily. Postoperatively, patients are placed in a volar positioning splint with passive extension for three weeks. After week 4, active flexion is initiated followed by graded resistive exercises. A dynamic extension splint is also used for allowing limited active flexion and passive extension. In a prospective, randomized, controlled study of 32 patients by Mowlavi et al. (47) an improved functional outcome is seen at four, six, and eight weeks, but not six months when compared to static splinting. Dynamic therapy should be reserved only to select and motivated patients with the

desire for early return of function. Furthermore, Giessler et al.'s (48) prospective randomized study of dynamic extension splinting for extensor indicis proprius (EIP) to extensor pollicis longus (EPL) transfer failed to show improved rehabilitation.

Answer: Most hand surgeons would operate when laceration is >50% of flexor tendon. Early improved function with dynamic splinting up to six months, then no difference. Recommendation grade: C.

HOW ARE COMMON FRACTURES OF THE HAND, SUCH A PHALANX FRACTURES, BOXER'S FRACTURES, BENNETT FRACTURES, ROLANDO FRACTURES, TREATED?

Fractures of the phalanges are one of the most common fractures in the body. In general, immobilization should be limited to four weeks. Immobilization exceeding four weeks results in total active motion loss to 66% of normal, compared to 80% when immobilization is limited to less than four weeks (49). Tuft and nondisplaced shaft fractures are mostly treated in closed fashion with splinting for three to four weeks. If the nail bed is injured, it should be repaired.

Accurate reduction is crucial in proximal and distal phalanx fractures to restore normal function. There are multiple ways of fixating fractures of the phalanx, and each has its merits. The method of choice often depends on the comfort of the surgeon and the type of fracture. Kirschner wires (K-wires) are a simple way to obtain closed reduction of the phalanx. They can very easily and quickly allow the surgeon to obtain reduction in simple transverse shaft fractures. However, as one gets into the area of oblique fractures or fractures involving the condyle, K-wires may not be adequate, and an open reduction technique may need to be applied. This may include lag screws or plating. This general theme is repeated in fractures of other areas of the hand. The key really is if an accurate reduction can be obtained and function can be preserved. If so, any technique is used to hold that reduction in place until the bone heals (50).

An important factor in managing metacarpal head fracture is angulation of the fractured segment. The clinical consequence one is trying to prevent is scissoring of the fingers. The index and long fingers may tolerate 20–30°, whereas the ring and little finger (boxer's fracture) can tolerate 50–70° of angulation depending on individual patient. In metacarpal shaft fractures, 15° of apex dorsal angulation is tolerated in index and long fingers, and 40° of angulation maybe tolerated in ring and small fingers. Long oblique fractures are generally treated surgically. Up to 5 mm of shortening is tolerated in shaft fractures. In metacarpal base fractures, the ring and little fingers can tolerate 10–15° of angulation, whereas only 5° of angulation is tolerated in index and long fingers. The repeated theme here is once again that an adequate reduction has to be achieved for function to be preserved. In the fifth metacarpal, for example, severe angulation of the reduction is well tolerated in many cases and still preserves function. Thus, although adequate reduction is important, the most important factor in the hand really is its functional preservation (51,52).

Extra-articular thumb metacarpal base fractures are commonly treated with a thumb spica cast for four weeks.

Up to 30° of angulation is tolerated due to carpometacarpal (CMC) joint mobility. Intra-articular base fractures include Bennett and Rolando-type fractures, which require operative intervention. Bennett fracture, involving fracture of the volar-ulnar aspect of the metacarpal base, may be treated with closed reduction and percutaneous pinning when less than 1 mm step-off is present. With a worse prognosis than a Bennett fracture, a Rolando fracture is a comminuted intra-articular base of the thumb metacarpal fracture. Closed reduction and internal fixation with multiple K-wires or open fixation can be attempted in both inherently unstable fractures. It is not entirely clear whether open reduction is better than closed reduction. However, the severity of comminution of the fracture may make a closed reduction harder. Nevertheless, in these fractures as well as all the fractures discussed, in the end an adequate reduction that gives the best functional outcome is the goal of any surgery (51–55).

Answer: Closed reduction or open reduction of fractures may be attempted; the technique must be adjusted for the individual fracture with the goal of preservation of function through stabilizing an adequate reduction. Recommendation grade: C.

WHAT DO YOU DO WITH A FINGERTIP AMPUTATION THAT IS TOO DISTAL FOR REPLANTATION?

This question often confronts the surgeon in the emergency room. The patient shows up with a small pulp of fingertip no longer attached to the finger. We specifically deal with situations where no critical structure such as bone is exposed. When there is exposure of underlying structures, some sort of flap closure or possible shortening of the digit should be considered. However, we look at the option of either composite graft replantation of the tip (if available) or conservative treatment (healing by secondary intent). Both have been attempted for small distal amputation of the fingertip pulp. The conventional wisdom is that anything 1 cm² or smaller can be allowed to heal by secondary intent. For anything larger, one may need to try to reattach the tip without revascularization because it is essentially impossible at the very tip of the finger using a composite graft. Local flaps can be attempted if the tip is not available for replantation (56–59).

Answer: Defects smaller than 1 cm² can be allowed to heal by secondary intent, otherwise, a composite graft or local flap can be used instead. Recommendation grade: C.

Levels of Evidence

Subject	Year	Ref.	Level	Strength	Findings
Bacteriology of animal bites	1999	3	IIB	B	Complex mix of bacteria including <i>Pasteurella</i>
Compare cast immobilization with internal fixation in nondisplaced scaphoid fractures and MRI to CT	2008, 2001	14, 17, 10	IA IIB IIC	B	Percutaneous screws allow faster return to work, no long-term benefit of internal fixation
Upper limb replantation success	1977, 1982, 1989	21–23	IIC	C	Large retrospective reviews confirming successful outcomes in 70–87% of patients
Compartment syndrome	1975, 1976	27, 30	IIC	C	Pressure within 20 mmHg of diastolic cause ischemic muscle necrosis, and success of treatment is both time and pressure dependent
When lacerations should be repaired; compare dynamic with static splinting for extensor tendon injury	2001, 2005, 2008	40, 47, 48	III, IIB	C	Most hand surgeons would operate when laceration is >50% of flexor tendon, early improved function with dynamic splinting up to 6 months, then no difference
How are common fractures of the hand, such as phalanx fractures, boxer's fractures, bennett fractures, Rolando fractures, treated?	1994, 2007	54, 51	IIC IIC	C	Closed reduction or open reduction of fractures may be attempted, the technique must be adjusted for the individual fracture with the goal of preservation of function through stabilizing an adequate reduction
What do you do with a fingertip amputation that is too distal for replantation?	1993, 2003	56, 58	IIC IIC	C	Defects smaller than 1 cm ² can be allowed to heal by secondary intent, otherwise, a composite graft or local flap can be used instead

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

REFERENCES

- Weinzweig J. Plastic surgery secrets: the hand and upper extremity. In: NWeinzweig N, ed., Infection of the Hand. Philadelphia: Hanley and Belfus Medical Publishers, 1999; 506–5.
- Thorne CH. Grabb and Smith's plastic surgery: hand. In: Chao JJ, Morrison BA, eds., Infections of the Upper Limb. Philadelphia: Lippincott Williams & Wilkins, 2007; 817–25.
- Talan DA, Citron DM, Abrahamian FM, et al. Bacteriologic analysis of infected dog and cat bites. Emergency Medicine Animal Bite Infection Study Group. N Engl J Med 1999; 14: 340: 85–92.
- Meyers B, Schoeman JP, Goddard A, et al. The bacteriology and antimicrobial susceptibility of infected and non-infected dog bite wounds: fifty cases. Vet Microbiol 2008; 127: 360–8.
- Ordog GJ. The bacteriology of dog bite wounds on initial presentation. Ann Emerg Med 1986; 15: 1324–9.
- Goldstein EJ, Citron DM, Finegold SM. Dog bite wounds and infection: a prospective clinical study. Ann Emerg Med 1980; 9: 508–12.

7. Callaham M. Controversies in antibiotic choices for bite wounds. *Ann Emerg Med* 1988; 17: 1321–30.
8. Dellinger EP, Wertz MJ, Miller SD, et al. Hand infections. Bacteriology and treatment: a prospective study. *Arch Surg* 1988; 123: 745–50.
9. Brook I. Microbiology of human and animal bite wounds in children. *Pediatr Infect Dis J* 1987; 6: 29–32.
10. Memarsadeghi M, Breitenseher MJ, Schaefer-Prokop C, et al. Occult scaphoid fractures: comparison of multidetector CT and MR imaging—initial experience. *Radiology* 2006; 240: 169–76.
11. Jenkins PJ, Slade K, Huntley JS, et al. A comparative analysis of the accuracy, diagnostic uncertainty and cost of imaging modalities in suspected scaphoid fractures. *Injury* 2008; 39: 768–74.
12. Beeres FJ, Rhemrev SJ, den Hollander P, et al. Early magnetic resonance imaging compared with bone scintigraphy in suspected scaphoid fractures. *J Bone Joint Surg Br* 2008; 90: 1205–9.
13. Dias JJ, Wildin CJ, Bhowal B, et al. Should acute scaphoid fractures be fixed? A randomized controlled trial. *J Bone Joint Surg Am* 2005; 87: 2160–8.
14. Vinnars B, Pietreanu M, Bodestedt A, et al. Nonoperative compared with operative treatment of acute scaphoid fractures. A randomized clinical trial. *J Bone Joint Surg Am* 2008; 90: 1176–85.
15. Yin ZG, Zhang JB, Kan SL, et al. Treatment of acute scaphoid fractures: systematic review and meta-analysis. *Clin Orthop Relat Res* 2007; 460: 142–51.
16. Arora R, Gschwentner M, Krappinger D, et al. Fixation of nondisplaced scaphoid fractures: making treatment cost effective. Prospective controlled trial. *Arch Orthop Trauma Surg* 2007; 127: 39–46.
17. Bond CD, Shin AY, McBride MT, et al. Percutaneous screw fixation or cast immobilization for nondisplaced scaphoid fractures. *J Bone Joint Surg Am* 2001; 83A: 483–8.
18. Kleinert HE, Kasdan ML. Anastomosis of digital vessels. *J Ky Med Assoc* 1965; 63: 106–8.
19. Komatsu S, Tamai S. Successful replantation of a completely cut-off thumb: case report. *Plast Reconstr Surg* 1968; 374.
20. Peacock K, Tsai TM. Comparison of functional results of replantation versus prosthesis in a patient with bilateral arm amputation. *Clin Orthop* 1987; 214: 153.
21. Morrison WA, O'Brien BM, MacLeod AM. Evaluation of digital replantation: a review of 100 cases. *Orthop Clin NA* 1977; 8: 295.
22. Tamai S. 20 years experience of limb replantation: review of 293 upper extremity replants. *J Hand Surg* 1982; 7: 549.
23. Tark KC, Kim YW, Lee YH, et al. Replantation and revascularization of hands: Clinical analysis and functional results of 261 cases. *J Hand Surg* 1989; 14A: 17.
24. Koul AR, Cyriac A, Khaleel V, et al. Bilateral high upper limb replantation in a child. *Plas Recon Surg* 2004; 113: 1734–8.
25. Wei FC, Chang YL, Chen HC, et al. Three successful digital replantations in a patient after 84, 86, and 94 hours of cold ischemia time. *Plas Recon Surg* 1988; 82: 346–50.
26. Davins M, Llagostero S, Llamas C, et al. Role of temporary arterial shunt in the reimplantation of a traumatic above-elbow amputation. *Vascular* 2007; 15: 176–8.
27. Whitesides TE, Haney TC, Morimoto K, et al. Tissue pressure measurements as a determinant of the need for fasciotomy. *Clin Orthop* 1975; 113: 43–51.
28. Matava MJ, Whitesides TE Jr, Seiler JG 3rd, et al. Determination of the compartment pressure threshold of muscle ischemia in a canine model. *J Trauma* 1994; 37: 50–8. <http://www.ncbi.nlm.nih.gov/pubmed/8028059>
29. Miller HH, Welch CS. Quantitative studies on the time factor in arterial injuries. *Ann Surg* 1949; 130: 428–38.
30. Sheridan GW, Matsen FA 3rd. Fasciotomy in the treatment of the acute compartment syndrome. *J Bone Joint Surg Am* 1976; 58A: 112. <http://www.ncbi.nlm.nih.gov/pubmed/1249096>
31. Jepson PN. Ischemic contraction. Experimental study. *Ann Surg* 1926; 84: 785–95.
32. Pennington G, Gary Pennington MD, Robert Jacoby, et al. Flexor tendon injuries. In: first hand News: Topics in Upper Extremity Care, vol. 5, no. 2. Louisville, KY: Christine M. Kleinert Institute for Hand and Micro Surgery, 1993, 1–4.
33. Kleinert HE, Kalisman M, Steyers CM. Complications in flexor tendon injuries. In: Boswick JA, ed., *Complications in Hand Surgery*. Philadelphia: WB Saunders, 1986, 19–28.
34. Kleinert HE. Should an incompletely severed tendon be sutured? Commentary. *Plast Reconstr Surg* 1976; 57: 236.
35. Wray RC, Holtmann B, Weeks PM. Clinical treatment of partial tendon lacerations without suturing and with early motion. *Plast Reconstr Surg* 1977; 59: 231–4.
36. Wray RC Jr, Weeks PM. Treatment of partial tendon lacerations. *Hand* 1980; 12: 163–6.
37. McGeorge DD, Stilwell JH. Partial flexor tendon injuries: to repair or not. *J Hand Surg* 1992; 17B: 176–7.
38. Al-Qattan MM, Clarke HM, Bowen V. Conservative management of transverse partial flexor digitorum profundus tendon lacerations in zone 2. *Can J Plast Surg* 1995; 3: 157–60.
39. Al-Qattan MM. Conservative management of zone II partial flexor tendon lacerations greater than half the width of the tendon. *J Hand Surg* 2000; 25A: 1118.
40. McCarthy DM, Boardman ND III, Tramaglini DM, et al. Clinical management of partially lacerated digital flexor tendons: a survey of hand surgeons. *J Hand Surg* 1995; 20A: 273–5.
41. Kleinert HE, Cash SL. Management of acute flexor tendon injuries in the hand. *Instr Course Lect* 1985; 34: 361.
42. Wang ED. Tendon repair. *J Hand Ther* 1998; 11: 105.
43. Barton NJ. Experimental study of optimal location of flexor tendon pulleys. *Plast Reconstr Surg* 1969; 43: 125.
44. McCarthy DM, Boardman ND, Tramaglini DM, et al. Clinical management of partially lacerated digital flexor tendons: a survey of hand surgeons. *J Hand Surg (Am)* 1995; 20: 273.
45. Matloub HS, Dzwierzynski WW, Erickson S, et al. Magnetic resonance imaging scanning in the diagnosis of zone II flexor tendon rupture. *J Hand Surg (Am)* 1996; 21: 451.
46. Kleinert HE, Verdan C. Report of the Committee on Tendon Injuries (International Federation of Societies for Surgery of the Hand). *J Hand Surg (Am)* 1993; 8: 794.
47. Mowlavi A, Burns M, Brown RE. Dynamic versus static splinting of simple zone V and zone VI extensor tendon repairs: a prospective, randomized, controlled study. *Plast Reconstr Surg* 2005; 115: 482.
48. Giessler GA, et al. Early free active versus dynamic extension splinting after extensor indicis proprius tendon transfer to restore thumb extension: a prospective randomized study. *J Hand Surg (Am)* 2008; 33: 864–8.
49. Strickland JW, Steichen JB, Kleinman WB, et al. Phalangeal fractures: factors influencing digital performance. *Orthop Rev* 1982; 11: 39–50.
50. Kawamura K, Chung KC. Fixation choices for closed simple unstable oblique phalangeal and metacarpal fractures. *Hand Clin* 2006; 22: 287–95.
51. Van Aaken J, Kämpfen S, Berli M, et al. Outcome of boxer's fractures treated by a soft wrap and buddy taping: a prospective study. *Hand (NY)* 2007; 2: 212–17.
52. Ali A, Hamman J, Mass DP. The biomechanical effects of angulated boxer's fractures. *J Hand Surg (Am)* 1999; 24: 835–44.
53. Lutz M, Sailer R, Zimmermann R, et al. Closed reduction transarticular fixation versus open reduction internal fixation in the treatment of Bennett's fracture dislocation. *J Hand Surg (Br)* 2003; 28: 142–7.

54. Timmenga EJ, Blokhuis TJ, Maas M, et al. Long-term evaluation of Bennett's fracture. A comparison between open and closed reduction. *J Hand Surg (Br)* 1994; 19: 373-7.
55. Foster RJ, Hastings H II. Treatment of Bennett, Rolando, and vertical intraarticular trapezial fractures. *Clin Orthop Relat Res* 1987; 214: 121-9.
56. Mennen U, Wiese A. Fingertip injuries management with semi-occlusive dressing. *J Hand Surg (Br)* 1993; 18: 416-22.
57. Fox JW IV, Golden GT, Rodeheaver G, et al. Nonoperative management of fingertip pulp amputation by occlusive dressings. *Am J Surg* 1977; 133: 255-6.
58. Heistein JB, Cook PA. Factors affecting composite graft survival in digital tip amputations. *Ann Plast Surg* 2003; 50: 299-303.
59. Martin C, del Pino JG. Controversies in the treatment of fingertip amputations. *Clin Orthop* 1998; 353: 63-73.

Lower Extremity Injury

Hany Bahouth and Doron Norman

Grade Recommendation		
Subject	Findings	Grade recommendation
How well do clinical findings aid in the diagnosis of CS of the lower extremity?	Clinical findings are poor predictors of compartmental for the diagnosis of lower extremity have to be defined.	C
Which compartmental pressure measurement method is optimal method for diagnosis of acute lower leg CS?	It is unclear what the value of optimal method of measuring compartmental syndrome.	C
The optimal method for screening and diagnosing CS.	No recommendation on this subject.	C
Is it safe to use tourniquets in major lower extremity trauma?	Tourniquet use appears indicated on the battlefield when required for hemorrhage control for limited time intervals. Civilian use of tourniquets is not generally recommended.	C
Is damage control justified for the orthopedic care of multiple trauma patients?	Damage control orthopedic is recommended in severely injured multiple trauma patients.	B
When should antibiotics be used in the setting of open lower extremity fracture?	No prophylactic antibiotics are required for open fractures resulting from low-velocity civilian gunshot wounds that do not require open reduction and internal fixation. In the setting of open extremity fractures, no more than 24 hours are required postoperatively.	B
What is the optimal time from injury to long bone fracture stabilization in the multiple trauma patient?	There is no difference in survival in polytrauma patients who undergo early or late long bone fracture stabilization. It is unclear whether timing of bone fracture stabilization impacts outcome in the setting of chest or brain injury.	C
What is the best method for prediction of amputation after severe lower extremity injuries?	There is no predictive scale that can be used with confidence to determine whether to amputate or attempt to salvage a mangled lower extremity. Scoring systems should be used only as guides to supplement the surgeon's clinical judgment and experience.	C
Abbreviation: CS, compartment syndrome.		

INTRODUCTION

Acute lower extremity trauma is very common health problem. According to the Health Care Cost and Utilization Project, more than 746,000 people in 2003 were hospitalized for lower limb fractures (1). Due to the increasing use of the safety devices in vehicles, trauma caregivers are managing more severely injured survivors with catastrophic lower extremity injuries.

HOW WELL DO CLINICAL FINDINGS AID IN THE DIAGNOSIS OF COMPARTMENT SYNDROME OF THE LOWER EXTREMITY?

Compartment syndrome (CS) is defined as an increase in pressure within confined anatomic space, resulting in ischemic changes to the encompassed tissues (2). Vascular impairment leads to decreased tissue oxygenation, and if persistent,

cellular death will follow. Nervous and muscular tissues appear the most sensitive to ischemia. The incidence of CS is 7.3 per 100,000 in men and 0.7 per 100,000 in women (3). Fractures are the most common etiology, and the most common location for CS is the lower leg. It is reported to occur in 1–10% of all tibial fractures (4). Clinical findings (pain, paresthesia, pain with passive stretch, and paresis) have a low sensitivity (13–19%) and low positive predictive value (11–15%) (5) for the diagnosis of the lower extremity CS.

Answer: Clinical findings are poor predictors of compartmental syndrome of the lower extremity (grade C).

WHICH COMPARTMENT PRESSURE MEASUREMENT METHOD IS OPTIMAL FOR THE DIAGNOSIS OF ACUTE LOWER LEG CS?

The utility of compartment pressure in the diagnosis of CS and subsequent need for fasciotomy is controversial.

Various methods of measuring compartment pressures have been described (5–9). In a prospective observational study over six months (10), Koiser et al. evaluated 45 patients who were admitted to a trauma intensive care unit and met one or more of the risk factors for CS, which included pulmonary artery catheter-directed shock resuscitation, open or closed tibial shaft fracture, major vascular injury below the aortic bifurcation, abdominal CS, or pelvic or lower extremity crush injury. Initial screening included a comprehensive physical examination and compartment pressure measurements (anterior and deep posterior compartments) when physical examination was suspicious or unreliable. Subsequent examination was performed every 4 hours for 48 hours. A difference of less than 30 mmHg between the diastolic blood pressure and the measured compartment pressure mandated four compartment fasciotomies. During this time period, the incidence of acute lower leg CS in the screened patients was 20%. No limb loss was subsequently reported in this group of patients. The authors conclusion was that aggressive screening in high risk patients may provide some diagnostic insights. No other screening protocols for the diagnosis of the acute lower extremity CS were found in the English literature.

Answer: It is unclear what the value or optimal method of measuring compartmental pressure (grade C).

IS IT SAFE TO USE TOURNIQUETS IN MAJOR LOWER EXTREMITY TRAUMA?

Since the first description of tourniquets in the seventeenth century, their use has remained of uncertain benefit. The controversy exists on a number of tourniquet-related issues; the indications for tourniquet use, the optimal type of tourniquet, timing of application and removal; and finally who should apply the device (11). Experiments in World War I revealed that tourniquet use was not without potential risks. Observations in World War II suggested that misuse or inadequate assessment was dangerous, and therefore the standard of care was exclusive use in patients with obvious arterial bleeding (12). In Iraq today, tourniquets are used liberally (12–14).

Three recent studies regarding the use of military tourniquets have given us a greater understanding of potential utility. The Norwegian military in Iraq in 1991 (15) reported on 68 patients who suffered traumatic amputations. Patients were compared during two different time spans. During the first time period, tourniquets were liberally used. In the second, wounds were managed by removing the tourniquet early and replacing it with a tight elastic bandage. The mortality in the first group was 17% (3/18) but decreased in the second group to 2% (1/50). The transfusion requirements in the first group were 56% versus 27% in the second. The conclusion of the authors was that the use of tourniquet for traumatic amputations was ineffective and potentially dangerous. However, we feel the difference may be exclusively related to the severity of injury. The second study is from the Israeli Defense Force Medical Services (16), where 110 tourniquets were applied to 91 casualties; 53% were judged to have been applied properly, 78% (71% for the lower limbs) were felt to be effective, and 53% were thought to have been clinically indicated. They concluded

that the use of field tourniquet was justified. Finally, the 31st U.S. Combat Support Hospital in Iraq (17) studied 166 matched patients with significant extremity injuries. Sixty-seven patients who received prehospital tourniquets were compared to 99 who did not. Twenty-three percent of tourniquets were ineffective at controlling bleeding. The amputation rate was 42% in the tourniquet group and 26% in the nontourniquet group ($p < 0.04$). Tourniquet use was felt to have resulted in the unnecessary loss of 2% of limbs. The use of tourniquet is generally not recommended beyond the setting of traumatic amputation with uncontrollable hemorrhage (U.S. Army Survival Manual) (18).

Answer: Tourniquet use appears indicated on the battlefield when required for hemorrhage control for limited time intervals. Civilian use of tourniquets is not generally (grade C).

IS DAMAGE CONTROL JUSTIFIED FOR THE ORTHOPEDIC CARE OF MULTIPLE TRAUMA PATIENTS?

Rotondo et al. (19) found a remarkable salvage rate of over 70% in a limited number of patients treated with damage control for abdominal vascular injury and massive shock, hypothermia, and acidosis. Since then, the damage control approach to unstable trauma patients has gained widespread use in other trauma fields (chest, vascular, urology) along with orthopedic injuries. Damage control orthopedic intervention appears to be a suitable alternative to definitive orthopedic surgery (i.e., open reduction, internal fixation) for patients at high risk of developing post-traumatic systemic complications such as adult respiratory distress syndrome (ARDS) and multiple organ failure. The orthopedic damage control approach in lower extremity trauma includes

1. External fixation and temporary soft tissue coverage at open fracture sites.
2. Distal perfusion of the injured extremity with temporary intraluminal shunting.
3. Liberal use of fasciotomy in the setting of ischemia.

External fixation (EF) is a viable alternative to attain temporary rigid stabilization in patients with multiple injuries. It is rapid, with negligible blood loss, and can be followed by intramedullary nailing (IMN) when the patient is stabilized (20). In one retrospective study, investigators tracked the clinical course of adult trauma patients admitted with femur fractures who were treated with EF versus IMN. The patients treated with EF were more seriously injured and less physiologically stable than those treated with standard IMN. The authors' conclusion was that immediate EF followed by early closed medullary nailing is a safe method for treating femoral shaft fractures in badly injured patients (20).

Pape and colleagues (21) assessed the impact of time on femur shaft fractures repair in 514 multiple blunt trauma patients. They demonstrated a significant increased incidence of ARDS in patients during the damage control era when they were submitted to primary intramedullary stabilization of the femur shaft when compared with EF. They also noted a decrease in the relative percentage of patients who developed ARDS, 54.6% to 26.4% (damage control

orthopedic, DCO) when primary IMN was performed, which decreased from 97.4% to 22.1% when primary EF was performed.

Importantly, in a systematic literature review conducted by the German Trauma Society, controlled trials were tested and failed to support a “generalized management strategy” (22). A total of 1,465 femur shaft fracture treatments in 8,057 trauma registry patients [age 19–35 years; Injury Severity Score (ISS) 14.9–23.5; 17.3% mortality] were treated initially (<24 hour) by EF, nail, or plate in 47.0%, 41.1%, and 11.9%, respectively. Despite large interhospital variability, EF was more likely with increasing severity of ISS, Glasgow Coma Score, thorax trauma, base excess, coagulation abnormalities, and initial probability of death. Although decision making is currently based on unvalidated criteria, anatomic and physiologic injury severity appears to influence the choice of management concept.

A prospective cohort controlled trial (23) in 409 patients with multitrauma, 75 (ISS of 37.3) required DCO surgery for 135 fractures, whereas 334 patients (ISS of 30.4) did not require immediate fracture fixation. Mean surgical time was 30–62 minutes (standard error of the mean, 3.5) for DCO. Duration of external fixation averaged 13.7 days (range, 3–46 days). Overall mortality in DCO patients was significantly lower than predicted by trauma and ISS (20% versus 39.3%), as it was in the 334 patients without immediate fracture fixation (29.5% versus 24.3%). In this study, DCO appears to reduce operation time and blood loss in the primary treatment period among severely injured patients compared with historical data. In addition, the authors found that DCO did not appear to be associated with an increased rate of procedure-related complications. They concluded that DCO with early and one-stage conversion seems to be a safe strategy of primary fracture treatment in patients with multiple injuries.

Answer: Damage control orthopedic is recommended in severely injured multiple trauma patients. Level II recommendation (grade B).

WHEN SHOULD ANTIBIOTICS BE UTILIZED IN THE SETTING OF OPEN LOWER EXTREMITY FRACTURE?

Open fractures require urgent surgical treatment to reduce the risk of infection. Failure to use prophylactic antibiotics and increased time from injury to initiation of antimicrobial agent and operative debridement are among the primary factors that increase the risk of infection. Gustilo et al. (25) were first to recognize that fracture location, mechanism, grade, and operative management are all independent roles in prevention of infection. In a double-blind prospective trial, Dellinger and colleagues randomized 248 patients with open fractures to receive one or five days of cefonicid sodium therapy or five days of cefamandole nafate therapy as part of the initial treatment. Rates of fracture-associated infections in the three groups were 10 (13%) of 79, 10 (12%) of 85, and 11 (13%) of 84, respectively. The 95% confidence limit for the difference in infection rates between the one-day group and the combined five-day groups was 0% to 8.3%. The actual difference was

0.2%. They concluded that a brief course of antibiotic administration was not inferior to a prolonged course of antibiotics for prevention of postoperative fracture-site infections (24).

Answer: Level I: No prophylactic antibiotics are required for open fractures resulting from low-velocity civilian gunshot wounds that do not require open reduction and internal fixation. In the setting of open extremity fractures, no more than 24 hours are required postoperatively (grade B).

WHAT IS THE OPTIMAL TIME FROM INJURY TO LONG BONE FRACTURE STABILIZATION IN THE MULTIPLE TRAUMA PATIENT?

The potential advantages of the early surgery for the long bone fracture stabilization (defined as <48 hours from injury) include increased patient mobilization and decreased pulmonary morbidity (fat emboli syndrome, pneumonia, ARDS), late septic sequelae, mortality, hospital length of stay, intensive care length of stay, and ventilator days. The known disadvantages of the early stabilization in polytrauma patients includes increased blood loss, fluid administration, surgical stress, fat embolism, possibly a greater likelihood of pulmonary complication risks, and mortality (26).

There have been concerns regarding the timing of long bone stabilization in patients with brain or chest injury. Problems with early fixation of long bones in patients with brain injury include secondary brain injury as a result of hypoxemia, hypotension, and/or complexity of controlling intracranial hypertension and increased fluid administration, which might exacerbate cerebral edema.

Answer: There is no difference in survival in polytrauma patients who undergo early or late long bone fracture stabilization. It is unclear whether timing of bone fracture stabilization impacts outcome in the setting of chest or brain injury. Level IIb recommendation (grade C).

WHAT IS THE BEST METHOD FOR PREDICTION OF AMPUTATION AFTER SEVERE LOWER EXTREMITY INJURIES?

Several limb salvage scoring systems have been devised to help clinicians determine when to attempt limb salvage or whether to perform early amputation. Level of the vascular injury, degree of bony injury, degree of muscular injury, and the warm ischemia time have been used to predict the outcome after lower extremity injury (27).

The Predictive Salvage Index (28) calculated score by dividing dermal, muscular, and bony damage into slight, moderate, or severe and counted one to three points, respectively. This score showed a sensitivity of 78% and specificity of 100%. Lange et al. showed in 1985 (29) that in patients with similar local injuries, the age, comorbidities, and social environment of the patients also play an important role in the outcome. In 1990, Helfet et al. (30) found Lange's absolute indications for amputation difficult to determine in certain patients. From the retrospective analysis of 26 severe injuries to the lower extremity with vascular injuries

(Gustilo Grade IIIC), four parameters were found significant: extent of the bone and soft tissue damage, time of ischemia, initial shock, and age of the patient. In 1994 McNamara et al. (31) published the Nerve Injury, Ischemia, Soft Tissue Injury, Skeletal Injury, Shock and Age score by retrospective evaluation of 24 patients with Grade IIIC injury. Bosse et al. (32) in a prospective study of 556 limbs found that all the lower extremity injury scoring systems have limited

usefulness and cannot be used as the sole criterion by which amputation decisions are made.

Answer: At present, there is no predictive scale that can be used with confidence to determine whether to amputate or attempt to salvage a mangled lower extremity. Scoring systems should be used only as guides to supplement the surgeon's clinical judgment and experience (grade C).

Levels of Evidence

Subject	Level of evidence	Grade recommendation	Findings
Clinical findings for the diagnosis of CS	IIb	B	The predictive value of the clinical findings for the diagnosis of CS of the lower extremity has to be defined.
The optimal method for the measurement of the compartment pressure	III	C	No recommendation for one of the screened methods.
The optimal method for screening and diagnosing CS	IIb	C	No recommendation on this subject.
The safety of tourniquet use	III	C	Appropriate use of tourniquets in the battlefield for a short time can be safe.
Justification for the damage control orthopedic	IIb	B	Damage control orthopedic is recommended in severely injured patients.
Antibiotic prophylaxis in open fractures	Ia	B	24 hours of first-generation cephalosporin agent is sufficient in Grade I open fracture.
The optimal time for long bone fracture stabilization	IIb	B	No difference in outcome between early and late stabilization.
The best scoring system for the clinical decision in mangled extremity	IIb	B	The scores are adjuncts tools to aid the clinician but are not a sole criterion.

Abbreviation: CS, compartment syndrome.

REFERENCES

- Coben JH, Steiner CA, Barret M, et al. Completeness of cause of injury coding in healthcare administrative database in the United states, 2001. *Inj Prev* 2006; 12: 199.
- Emmanuel K, et al. Diagnosis and management of extremity compartment syndromes: An orthopaedic perspective. *Am Surgeon* 2007; 73: 1199–209.
- McQueen MM, Gaston P, Court-Brown CM. Acute compartment syndrome: who is at risk? *J Bone Joint Surg Br* 2000; 82: 200–3.
- Elliot KGB, Johnstone AJ. Diagnosing acute compartment syndrome. *J Bone Joint Surg Br* 2003; 85: 625–32.
- Ulmer T. The clinical diagnosis of compartment syndrome of the lower leg: are clinical findings predictive of the disorder? *J Ortho Trauma* 2002; 16: 8: 572–7.
- Katz LM, Nauriyal V, Nagarj S, et al. Infrared imaging of trauma patients for detection of acute compartment syndrome of the leg. *CCM* 2008; 36: 6: 1756–61.
- Wilson SC, Varhas MS, Berson L, et al. A simple method to measure compartment pressures using an intravenous catheter. *Orthopedics* 1997; 20: 403–6.
- Gianotti G, Cohn SM, Brown M, et al. Utility of near infrared spectroscopy in the diagnosis of lower extremity compartment syndrome. *J Trauma* 2000; 48: 396–401.
- Arbabi S, Brundage SI, Gentilello LM. Near infrared spectroscopy: a potential method for continuous, transcutaneous monitoring for compartment syndrome in critically injured patients. *J Trauma* 1999; 47: 829–33.
- Koiser R, Moore F, Selby JH, et al. Acute lower extremity compartment syndrome screening protocol in critically ill trauma patients. *J Trauma* 2007; 63: 268–75.
- Thomas JW, Robert LM. Issues related to the use of tourniquet on the battlefield. *Mil Med* 2005; 270: 770–5.
- Welling DR, Burris DG, Hutton JE, et al. A balanced approach to tourniquet use: lessons learned and relearned. *J Am Coll Surg* 2006; 203: 107–15.
- Kam PC. Uses and precautions of tourniquets. *Surgery* 2005; 23: 76–7.
- Thomas JW, Robert LM. Issues related to the use of tourniquet on the battlefield. *Mil Med* 2005; 270: 770–5.
- Pillgram-Larsen J, Mellesmo S. Not a tourniquet but compressive dressing: experience from 68 traumatic amputations after injuries from mines. *Tidsskr Nor Laegeforen* 1992; 112: 2188–90.
- Lakstein D, Blumenfield A, Sokolow T, et al. Tourniquet for hemorrhage control in battlefield: a four year accumulated experience. *J Trauma* 2003; 54: S221–S225.
- Beekley AC, Sebesta JA, Mullinex P, et al. Tourniquet placement in Operation Iraqi Freedom. 31st CSH Database, 2005.
- American College of Surgeons Committee on Trauma. Advanced Trauma Life Support, 7th edition. Chicago: American College of Surgeons, 2004.
- Rotondo MF, Schwab CW, McGonigal MD, et al. Damage control: an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993; 35: 375–82.
- Scalea TM, Boswell SA, Scott JD, et al. External fixation as a bridge to intramedullary nailing for patients with multiple injuries and with femur fractures: damage control orthopedics. *J Trauma* 2002; 48: 613–62.
- Pape HC, Hildebrand F, Pertschy S, et al. Changes in the management of femoral shaft fractures in polytrauma patients: from early total care to damage control orthopedic surgery. *J Trauma* 2006; 53: 452–61.

22. Rixen D, Grass G, Sauerland S, et al. Polytrauma Study Group of the German Trauma Society. Evaluation of criteria for temporary external fixation in risk-adapted damage control orthopedic surgery of femur shaft fractures in multiple trauma patients: "evidence-based medicine" versus "reality" in the trauma registry of the German Trauma Society. *J Trauma* 2005; 59: 1375–95.
23. Taeger G, Ruchholtz S, Waydhas C. Damage control orthopedics in patients with multiple injuries is effective, time saving, and safe. *J Trauma* 2005; 59: 408–15.
24. Dellinger EP, Caplan ES, Weaver LD, et al. Duration of preventive antibiotic administration for open extremity fractures. *Arch Surg* 1988; 123: 333–9.
25. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. *J Bone Joint Surg* 1976; 58A: 453–8.
26. The EAST Practice Management Guidelines Work Group; Dunham CM, Bosse MJ, Clancy TV, et al. Practice management guidelines for the optimal timing of long bone fracture stabilization in polytrauma patients. *J Trauma* 2001; 50: 958–67.
27. Gregory RT, Gould RJ, Peclet M, et al. The mangled extremity syndrome (MES): a severity grading system for multisystem injury of the extremity. *J Trauma* 1985; 25: 1147–50.
28. Howe HR Jr, Poole GV Jr, Hansen KJ, et al. Salvage of lower extremities following combined orthopedic and vascular trauma. A predictive salvage index. *Am Surg* 1987; 53: 205–8.
29. Lange RH, Bach AW, Hansen ST Jr, et al. Open tibial fractures with associated vascular injuries: prognosis for limb salvage. *J Trauma* 1985; 25: 203–8.
30. Helfet DL, Howey T, Sanders R, et al. Limb salvage versus amputation. Preliminary results of the Mangled Extremity Severity Score. *Clin Orthop Rel Res* 1990; 256: 80–6.
31. McNamara MG, Heckman JD, Corley FG. Severe open fractures of the lower extremity: a retrospective evaluation of the Mangled Extremity Severity Score (MESS). *J Orthop Trauma* 1994; 8: 81–7.
32. Boss MJ, Mackenzie EJ, Kellam JF, et al. A prospective evaluation of the clinical utility of the lower extremity injury severity scores. *J Bone Joint Surg Am* 2001; 83: 3–14.

Limb Salvage for the Mangled Extremity

Gabriel E. Burkhardt and Todd E. Rasmussen

Summary of Recommendations			
Question	Answer	Level of evidence	Grade
Which management strategies improve ischemia and reperfusion injury following traumatic extremity injury?	1. Damage control techniques aid in limb salvage after life-threatening trauma.	IIIb	C
	2. Large vessel venous injuries should be repaired when feasible.	IIIb	C
	3. Temporary vascular shunts are safe and fewer amputations are performed in patients with severely mangled extremities.	IIb	B
Is there a difference in limb salvage strategies in the setting of upper versus lower extremity injury?	1. Limb salvage rate exceeds 90% in upper extremities, but poor functional outcomes	IV	D
	2. The rate of upper extremity amputation is higher in the setting of complex wartime injury.	IV	D
What prehospital adjuncts are available that impact limb salvage following traumatic extremity injury?	1. Tourniquets are life-saving when placed appropriately and do not adversely impact limb salvage.	IIb	B
	2. Hemostatic agents effectively control hemorrhage.	*	*
What contemporary strategies in skeletal reconstruction impact limb salvage following traumatic injury?	1. Definitive stabilization (intramedullary nail) within 24 hours of injury in stable patients.	Ib	A
	2. Early external fixation followed by intramedullary nail in unstable patients.	Ib	A
	3. Early antibiotic coverage continued for 3 days from time of injury.	Ib	A
How do advances in soft tissue wound management strategies impact limb salvage following traumatic injury?	1. Frequent and adequate debridement is a critical component of soft tissue wound closure.	IIb	B
	2. Negative-pressure wound therapy decreases infection rates and hastens time to wound closure.	IIIb	C
	3. Complex reconstruction of soft tissue defects should occur within 72 hours of injury and by experienced subspecialists.		
How do injury patterns impact decision making regarding extremity salvage?	1. Severe soft tissue injuries, nerve injuries and vascular injuries influence decision to amputate but no difference in functional outcome	Ib	A
	2. Limb salvage rates associated with wartime extremity injuries are comparable to that reported in civilian literature	IIIb	C
Which extremity severity scores predict limb salvage and functional outcome?	1. No scoring system accurately predicts limb salvage or functional outcome	Ib	A
What are the costs of reconstruction and quality of life?	1. There is no significant difference in functional outcome between limb salvage and amputation.	Ib	A
	2. Limb salvage is associated with more operations, longer recovery time, and more than twice the cost than amputation.	Ib	A

INTRODUCTION

The patient exposed to limb-threatening trauma presents the surgeon with a complex array of early and critical challenges that persist well beyond the time of injury. Although the multifaceted and emergent nature of this injury pattern has precluded the highest levels of clinical study, evidence-based guidelines can be discerned from available clinical reviews, case series, and general clinical consensus. From

the multitude of published literature on this topic, several strategies have been advocated to simplify the process and minimize the morbidity and mortality from extremity trauma. The objective of this chapter is to identify and expand on evidence-based strategies that influence treatment decisions aimed at maximizing functional recovery following traumatic extremity injury.

Across the spectrum of extremity injury, the mangled lower extremity requires the greatest attention. The term

mangled extremity describes a limb in which at least three of the four components (soft tissue, nerve, bone, vessel) are severely injured (1). Whereas *limb salvage* is defined as an attempt to restore structure and neurovascular function to a mangled extremity, often the decision of whether to repair or to perform an amputation hinges not only on the feasibility but also on the anticipated functional outcome. These decisions are frequently made in the context of additional associated life-threatening injuries. Although substantial advances have been made in reconstructive techniques that have created opportunities to address both life- and limb-threatening injuries, heroic measures for limb salvage do not necessarily provide superior quality of life and limb outcomes even if reconstructive efforts produce a viable limb (2–5).

Primary amputation is defined as an extremity amputation that is performed at the original operation for injury (i.e., in which limb salvage efforts were not pursued). In some cases, a primary amputation may offer the patient an expedited and superior functional outcome (6,7). A *secondary amputation* is defined as an extremity amputation that takes place following any attempt for limb salvage (i.e., following intent to treat or intent to salvage). Secondary amputation is further divided into *early* (an amputation within 30 days following the initial intent to salvage) and *late* (an amputation performed greater than 30 days following the initial intent to salvage). Whether early or late, a secondary amputation is performed at a subsequent operation when the measures to salvage a limb are deemed unsuccessful, futile, or detrimental to the patient.

Beyond initial stabilization of critically ill patients with injured extremities, and in addition to the complexity that operative intervention entails, an overarching factor that guides early decision making is selecting the course that will optimize functional recovery. An intricate limb repair that does not enable the patient to perform activities at a level comparable to a similar patient with a primary or secondary amputation does a disservice to the patient and poses an economic burden on health care resources (3,8,9). Although there is a paucity of high-level data that guides strategies in the treatment of the mangled extremity, this chapter poses eight relevant questions and recommendations to highlight the strongest clinical evidence on this challenging topic.

WHICH MANAGEMENT STRATEGIES REDUCE THE IMPACT OF ISCHEMIA AND REPERFUSION INJURY ON LIMB SALVAGE FOLLOWING TRAUMA?

In the setting of extremity vascular injury, the ability to save an injured limb is based in large part on the ability to restore adequate perfusion. Over 50% of patients with severe extremity injuries will have additional injuries, many of which are life-threatening (10,11). Treatment of a life-threatening torso, head, or neck injury takes priority over definitive repair of an extremity vascular injury, leaving the limb at high risk for amputation as the negative impact of ischemic time is increased (5,12).

Although placement of an autologous vein interposition graft is the most common and often ideal form of repair, it is a time-consuming endeavor that is not feasible in the setting of coagulopathy, acidosis, and hypothermia.

In the setting of life-threatening polytrauma, successful application of damage control techniques are based on early recognition of pending patient demise with adjustment of the operative plan. Damage control strategies for extremity arterial and venous injuries include abbreviated lateral vessel repair, placement of a temporary vascular shunt, and vessel ligation with or without performance of a primary amputation.

Many consider vessel ligation a technique of last resort, but as demonstrated over 50 years ago by DeBakey and Simeone in a series of 2,471 vascular injuries treated during World War II, ligation of a major extremity vessel does not uniformly lead to amputation (13). The introduction of *selective vessel ligation* in the setting of extremity vessel injuries reduced the amputation rate from nearly 100% to 49%. Another example of the concept of selective vessel ligation rests in an analysis of patients with brachial artery injury that demonstrated a twofold difference in amputation rates depending on whether the artery was ligated above (55%) or below (26%) the profunda brachii artery. A similar relationship in the rates of lower extremity amputation has been reported for femoral artery injuries: 81% lower extremity amputation rate if the ligation is above the profunda femoris artery versus 55% if ligation occurs below the profunda femoris artery.

Venous ligation is generally better tolerated than arterial ligation. Though the direct impact of venous ligation on amputation rates has been reported to be low, ligation of large lower extremity vessels has been found to result in thrombosis, significant venous hypertension, and postphlebotic syndrome (14,15). Injuries resulting from high-energy mechanisms, particularly those resulting from explosive devices or high-velocity gunshot wounds, strip collateral venous drainage from the extremity potentiating lifestyle-limiting venous hypertension (16). In the largest post-Vietnam War review of venous injuries, Fox and associates reported a retrospective analysis of 82 patients with 103 extremity venous injuries due to combat injuries (15). In this 2008 study, 63% of extremity venous injuries were treated by ligation and the remaining 37% were repaired. Importantly, this study reported an 84% midterm patency of venous repair and showed that patients with extremity vein repair did not experience a higher incidence of pulmonary embolus than those treated with venous ligation. All patients in this landmark report developed postinjury edema of the extremity, and there was a trend toward increased deep vein thrombosis (DVT) rate (14% versus 7%) and phlegmasia (2% versus 0%) in the group treated by venous ligation (16).

Another tool that can be used in the setting of vascular injury is the temporary vascular shunt (TVS). These devices are used routinely during the performance of carotid endarterectomy but have also been used as a damage control adjunct as a means of quickly restoring perfusion to an extremity in the setting of vascular injury. Large animal studies by Dawson et al, demonstrated the safety and efficacy of TVS in restoring distal perfusion during hemorrhagic shock (17). In this model, TVS remained patent and functioning for nearly 24 hours without systemic hepatic injury. Several retrospective clinical series have also reported the short-term efficacy of TVS in the setting of extremity vascular injury, the most recent and largest being a report from the Air Force Theater Hospital on Balad AB,

Iraq (18–21). This series demonstrated that although shunts placed in smaller, more distal arteries and veins are more likely to thrombose, there is no adverse impact on limb salvage (20). Gifford et al. have recently reported the impact of TVS on long-term limb salvage in a case-control study of 125 patients with severe extremity injuries (22). In this sentinel report there were more early amputations performed in the control than the TVS group (13% versus 3%; $p = 0.04$); however, after nearly two years of follow-up there was no significant difference in the amputation rate (17% versus 23%; $p = 0.42$). After adjusting for a mangled extremity severity score (MESS) greater than 8, the TVS group had a significantly lower risk of amputation [hazard ratio (HR) = 0.43; $p = 0.04$]. Outcomes data such as these suggest that TVS does not cause harm in the setting of extremity vascular injury and likely extends the window of opportunity for limb salvage.

Recommendations

1. Arterial ligation may be used as a damage control maneuver, understanding that there is an increased incidence of extremity amputation.
2. Large vessel venous injuries should be repaired when feasible.
3. Temporary vascular shunts are an effective damage control adjunct, and the long-term impact on amputation is most beneficial in the subset of patients with mangled extremities (MESS ≥ 8) (Level of evidence: IIIb. Grade C recommendation).

IS THERE A DIFFERENCE IN LIMB SALVAGE STRATEGIES IN THE SETTING OF UPPER VERSUS LOWER EXTREMITY INJURY?

Although severe extremity injuries are less common in the upper extremity, the complex and important function of the hand presents unique considerations that require modification in management strategies. Because of the relative smaller size and increased collateralization, ligation of upper extremity vascular injuries is better tolerated than those of the lower extremity (13,14). Conversely, interwoven tendons and nerves of the upper extremity play an integral role in arm, hand, and digit function and require more meticulous debridement and repair. Finally, the relative paucity of soft tissue in the upper compared to the lower extremity makes coverage of nerve and vascular repairs more challenging in many cases.

Civilian literature, consisting of smaller case series describing blunt and penetrating injuries, reports a very high rate of upper limb salvage (95%) (23,24). Even in the setting of combined neural and vascular trauma, after repair and nearly four years of rehabilitation, 87% of patients showed improvement as assessed by the American Medical Association's standardized disability impairment scale (24).

In contrast, wartime injuries to the upper extremity are high-energy wounds often with penetrating, blast, and burn components. In this setting, upper extremity injuries are associated with more extensive soft tissue, nerve, and bone destruction. Data in two separate reports from the global war on terrorism demonstrated that upper extremity amputation rates in wartime may be as high as 10%,

perhaps reflecting attempts to salvage more severely injured upper extremities than those in the civilian setting (25,26). Despite high upper extremity limb salvage rates reported by Rich et al. from the Vietnam Vascular Registry, nearly 75% of patients with mangled upper extremities report significant long-term disability (16). This is especially the case for proximal upper extremity injuries, which frequently involve the axillary structures including the brachial plexus.

Recommendations

1. Limb salvage rates are higher for upper extremities than lower extremities in setting of civilian trauma.
2. The rate of upper extremity amputation is higher in the setting of complex wartime injury (Level of evidence: IV. Grade D recommendation).
3. Three-quarters of patients with upper extremity injury report significant functional disability in the long term (Level of evidence: IIIb. Grade C recommendation).

WHAT PREHOSPITAL ADJUNCTS ARE AVAILABLE THAT IMPACT LIMB SALVAGE FOLLOWING TRAUMATIC EXTREMITY INJURY?

Tourniquets have been used as an adjunct for extremity hemorrhage control for over 100 years and have been reintroduced during military conflicts as a life-saving measure while preparing for transport from the battlefield (27–29). Uncontrolled hemorrhage remains a leading cause of preventable battlefield death and the second most common cause of death for civilian trauma (11). During each recent major conflict, attention has been directed to the proper design, application, and utility of tourniquets (30). A recent randomized control trial evaluating the effectiveness of seven different self-applied tourniquets suggests that only the Combat Application Tourniquet, the Emergency and Military Tourniquet, and the Special Operations Forces Tactical Tourniquet were effective in eliminating Doppler evidence of distal arterial signal after self-application to the thigh and proximal arm (31). Subsequently, over 275,000 of these commercially designed tourniquets have been issued for use on the battlefields of Iraq and Afghanistan (32).

A prospective review of tourniquet usage at a combat support hospital in Baghdad was conducted to evaluate potential adverse events associated with tourniquet usage (33). Of 232 patients with tourniquets in place, no limbs were lost as a result of tourniquet use. There were many secondary outcomes investigated, including fasciotomy, DVT, pain, and nerve palsy. However, the only complications reported were transient nerve palsies in 2%. Nonetheless, improperly applied tourniquets may cause increased hemorrhage when placed above a venous injury, and properly placed tourniquets cause significant pain if left in place for extended periods of time. It is a current consensus that the efficacy of tourniquet use on the battlefield is inversely related to the time in which it takes for the tourniquet to be evaluated, loosened, or removed by a surgical team.

An additional prehospital adjunct that has gained attention is the topical hemostatic agent designed to stop bleeding from large proximal arterial and venous injuries. In addition to standard pressure dressings, there are two component agents (zeolite and chitosan) approved for military use (34). Studies supporting the safety and efficacy

of these agents have been based on large animal work, which suggests that zeolite dressings significantly reduce blood loss after large vessel laceration and uncontrolled hemorrhagic shock. Alam et al. compared the mortality and blood loss after the application of five hemostatic agents to an iliac injury in a swine model of uncontrolled hemorrhage (35). Animals in the zeolite group demonstrate a statistically significant mortality benefit; no animals died in the zeolite group, whereas mortality rates in the remaining treatment groups ranged from 28% in the chitosan group to 100% in the untreated group. Although the hemostatic properties of the zeolite dressing appears promising, the associated exothermic reaction causes tissue damage that may complicate wound healing or cause thrombosis. Despite concern and anecdotal reports that topical hemostatic agents may compromise the ability to perform vascular reconstruction and limb salvage there are no studies that support this line of thinking.

Recommendations

1. Tourniquets should be placed early and above arterial extremity injuries and remain in place until further resuscitation and evaluation by qualified teams (Level of evidence: IIb. Grade B recommendation).
2. Chemical hemostatic agents limit life-threatening blood loss in select extremity injury patterns at the expense of thermal tissue injury (based on animal studies).

WHAT STRATEGIES IN SKELETAL RECONSTRUCTION IMPACT LIMB SALVAGE FOLLOWING TRAUMATIC INJURY?

Like vascular injuries, patients with skeletal injuries will benefit most from primary definitive stabilization. Similarly, definitive stabilization is often time-consuming and represents an additional physiologic burden for the patient. Principles of damage control for orthopedic injuries include external fixation with delayed intramedullary nailing (IMN) of long bone fractures (36,37). Initial small randomized multicenter trials conducted by the European Polytrauma Study on the Management of Femur Fractures demonstrated that patients with severe polytrauma [Injury Severity Score (ISS) 22] and femur fractures exhibited a significantly greater cytokine response following early IMN versus external fixation followed by delayed IMN (38). These findings were not corroborated when the same group randomized 165 patients across 10 European centers to receive either early IMN or external fixation (EF) followed by delayed IMN (39). Regression analysis of the most severely injured patients (ISS 32 versus 24) with thorax injuries (Abbreviated Injury Score [AIS] 2.8) suggests a lower risk of pulmonary complications and sepsis if treated with early EF rather than early IMN. Conversely, stable patients did not benefit from a two-staged repair (e.g., EF followed by delayed IMN). In fact, in this less severely injured group, EF followed by delayed IMN was associated with nearly double the intensive care unit hours (212 versus 133) and nearly triple the ventilator hours (142 versus 66), although neither was statistically significant.

Open fractures carry a significantly higher incidence of infection than closed fractures (52% versus 4%,

respectively) and Gram-negative bacterial infections are over three times more common in the setting of an open extremity fracture (39). Gustilo and colleagues classified open lower extremity fracture patterns based on wound size, presence of contamination, degree of soft tissue injury, and associated vascular injuries (40). In his series of 511 patients, those with open fractures and associated vascular injuries (Gustilo Class IIIC) had a 41% chance of developing either an infection or requiring a secondary amputation (40).

Recommendations

1. Severely injured patients with long bone fracture benefit from early external fixation followed by IMN.
2. Less severely injured patients are best served with definitive stabilization in the form of IMN within the first 24 hours of injury (Level of evidence: Ib. Grade A recommendation).
3. Due to increased incidence of wound-related sepsis after open fractures, Gram-negative coverage should be provided in addition to a first-generation cephalosporin for three days from the time of initial evaluation (Level of evidence: Ib. Grade A recommendation).

HOW DO ADVANCES IN SOFT TISSUE WOUND MANAGEMENT STRATEGIES IMPACT LIMB SALVAGE?

Severe lower extremity trauma is often associated with extensive soft tissue loss. Large soft tissue wounds create an independent physiologic burden on the patient in the form of insensible fluid loss, infection, and metabolic demands during healing. Among the most commonly employed tools used to manage extremity soft tissue wounds are the negative-pressure vacuum-assisted closure device (VAC, KCI, San Antonio, Texas), tissue flaps, free-tissue transfers, and skin grafts.

VAC therapy (using reticulated open cell foam) acts to remove interstitial fluids containing inflammatory cytokines that suppress the proliferative phase of wound healing and bacteria. Negative-pressure wound therapy also reduces capillary afterload, which increases local circulation, and a properly sealed system decreases the burden of external contamination (41–43). The applications of VAC therapy are extensive, and the techniques especially effective when placed over properly debrided, well-vascularized tissues such as muscle and subcutaneous fat. Several case series have demonstrated that the use of the VAC device decreases the time to wound closure or coverage with a skin graft without the aid of tissue flaps (43–45).

Use of VAC therapy has been extensive in the management of wartime extremity injury and has become standard in some phase of nearly all soft tissue wounds. Leininger et al. reported in 2006 on a series of local patients injured in Iraq with large soft tissue wounds (46). In this study, a strict wound management strategy that included repeat debridement, irrigation, initiation of delayed primary closure, and VAC changes in the operating room resulted in no wound complications or skin graft failures. Each patient in this series received definitive wound treatment at a Level III surgical hospital from one group of surgeons using one uniform wound management strategy. Leininger et al.'s results were confirmed and extended

by Peck et al. a year later in a report describing the utility of VAC therapy in the complete management of soft tissue wounds associated with extremity vascular injury (63).

For those extremity wounds with extensive devitalized tissues, a rotational flap or free tissue transfer may be delivered in to a clean wound bed to aid in definitive wound closure. An analysis of the timing of tissue transfer after extremity trauma was completed by Godina in 1986 (47). This multicenter retrospective series included 532 patients receiving free-flap transfer early (within 72 hours of injury), delayed (between 72 hours and 3 months of injury), or late (between 3 months and 12 years of injury). Those patients undergoing delayed free tissue transfer had significantly higher rate of wound infections (delayed: 18% versus early: 2%) and the average hospitalization was over four times as long (130 days versus 27 days). The author also highlighted the steep learning curve associated with the microsurgical reconstruction of free tissue transfers as failures occurred in 26% of the first 100 flaps and only 4% of the last 100.

The value of surgical expertise in tissue reconstruction is particularly relevant in light of the decreasing use of free tissue transfers for complex extremity injuries. A retrospective review of 290 Gustilo Grade III injuries collected from 1992 to 2003 reports a decrease in free tissue transfers from 20% in the first four years of the study, 11% in the second four years, and 5% in the most recent four years (48). A reciprocal increase in the use of skin grafts and delayed primary closure was noted over the same interval (22% in the first four years of the study and 49% in the last four years of the study). No significant difference was noted in secondary amputation or wound infection rates in this study.

Recommendations

1. Frequent and adequate surgical debridement is paramount in the preparation of extremity soft tissue wounds.
2. Negative-pressure wound therapy (VAC) as a standard surgical adjunct that aids in the management of extremity injury is associated with low infection rates and decreased time to closure or coverage with skin graft (Level of evidence: IIb. Grade B recommendation).
3. When necessary, reconstruction of wounds using free tissue transfers should occur early and be performed by experienced subspecialists (Level of evidence: IIIb. Grade C recommendation).

HOW DO PATIENT AND INJURY CHARACTERISTICS IMPACT DECISION MAKING REGARDING EXTREMITY SALVAGE?

Six factors that influence the initial decision to amputate or attempt limb salvage are:

1. Physiologic reserve of the patient
2. Extent and severity of associated injuries
3. Nature of the extremity injury
4. Preinjury functional status
5. The presence of significant comorbidities
6. Access to adequate resources during rehabilitation.

Authors of the Lower Extremity Assessment Project (LEAP) assessed the relationships among these factors and the functional outcome after extremity reconstruction and limb salvage or amputation (2,49–52). LEAP is a multicenter prospective study of 600 patients with severe lower extremity injury who underwent either amputation or reconstruction. Results from this important study have shown that factors associated with the injury itself are the most significant in influencing the decision to amputate (51). Specifically, muscle injury, arterial and/or deep venous injury, and absence of plantar sensation are three factors shown to be associated with a fivefold risk of amputation (2,49,51).

To address the absence of plantar sensation as an indication for extremity amputation, three groups of patients were selected based on the absence of plantar sensation on initial evaluation and successful limb salvage (group 1), the absence of plantar sensation and amputation (group 2), and the presence of plantar sensation and limb salvage (group 3) (50). There was no difference in functional outcomes between the groups, and approximately half (55%) of the entire cohort had normal plantar sensation after two years.

These studies found no difference in functional outcome from either group based on injury characteristics or presence of a limb. In fact, subset analysis suggests that the factors most likely to influence functional outcome are related to preinjury social characteristics, such as level of education, income level, and access to health care (2,49,61,62).

Similar findings are reported by Sohn and associates for a cohort of 153 patients wounded during Operation Iraqi Freedom (10). In contrast to participants in LEAP, who were 16–69-year-old civilians, the injured troops in Sohn's study were young (mean 23 years), were otherwise healthy, and had sustained greater percentages of high-energy complex wounds. On initial presentation, a quarter were hypotensive and 80% had a base deficit ≥ 6 . The median military ISS of the cohort was 13, all of which suggest a significant physiologic derangement as a result of their injuries. Despite the extent of these injuries, the authors report an 80% early limb salvage rate, which is comparable to that observed in LEAP (83%) (2,10).

Recommendations

1. Patient factors most highly correlated with extremity amputation are severe soft tissue injury, nerve injury, and vascular injury in descending order (Level of evidence: Ib. Grade A recommendation).
2. Limb salvage rates associated with complex wartime extremity injuries are similar to those reported in the civilian trauma literature (Level of evidence: IIIb. Grade C recommendation).

WHAT IS THE ROLE OF MANGLED EXTREMITY SCORES AND INDICES ON DECISION MAKING IN LIMB SALVAGE?

Based on data from the previously mentioned studies and others, factors have been identified that influence functional outcome after limb salvage. To guide the decision-making process during initial and early management of patients

with severe extremity trauma, scoring systems have been developed that incorporate several of these factors. An ideal mangled extremity scoring system needs to be simple to implement during the initial evaluation, based on readily available information, and able to predict limb salvage and functional outcome. Unfortunately, no single scoring system has been designated as ideal, and as a result, several options are now available. Among the most common are the MESS; the Predictive Salvage Index (PSI); the Limb Salvage Index (LSI); the Nerve Injury, Ischemia, Soft Tissue Injury, Skeletal Injury, Shock, and Age of Patient Score (NISSSA); and the Hannover Fracture Scale-98 (HFS-98).

The most commonly reported scoring system, the MESS, was derived by Johansen and associates from the initial retrospective and subsequent prospective outcomes of 52 patients, 21 of whom underwent an amputation (53). Factors considered in the calculation of a score include:

1. Presence or absence of skeletal/soft tissue injury (graded 1–4)
2. Presence or absence of limb ischemia (graded 1–3)
3. Presence or absence of shock (graded 0–2)
4. Patient age (graded 0–2).

Each variable is graded and the individual scores added to provide a score from 2 to 11. The authors of the MESS recognize limb ischemia as time-dependent and suggest limb ischemia scores be doubled if perfusion has not been restored within six hours of injury. The authors of the MESS found that a score ≥ 7 predicted amputation with 100% accuracy and scores < 6 also predicted limb salvage in all cases (53). Interestingly, patients with significant peripheral nerve deficits were excluded from the study because they were assumed to require amputation. Larger prospective trials with long-term follow-up have not successfully duplicated the results of the MESS report (10,54,55). The MESS and scoring systems like it tend to have high specificities with low scores accurately able to predict limb salvage. However, the sensitivity of these metrics is lacking because their ability to predict amputation in the setting of high scores is variable (i.e., low positive predictive values).

Less commonly used scoring systems are available, each more complex than the MESS. Examples include the PSI, developed by Howe et al., which includes the level of arterial injury, the degree of bone injury, the degree of muscle injury, and the time to surgery (56). A score greater than or equal to 8 should be predictive of need for amputation. The LSI, designed by Russell et al., measures seven components, including artery, deep vein, nerve, bone, skin, muscle, and warm ischemia time (57). Again variables are graded and an additive score ≥ 6 predicts the need for amputation. The NISSSA, developed by McNamara and colleagues in 1994, contains six variables, including nerve injury, ischemia, soft tissue injury, skeletal injury, shock, and patient age (58). Amputations are recommended with scores ≥ 11 . The HFS-98 proposed in revised form by Krettek et al. is the most complex and involves the determination of fracture type, the degrees of bone loss, periosteal stripping, skin injury, muscle injury, wound contamination, local circulation, systemic circulation, and neurologic function (59). The scoring system is designed to be employed during the initial operation by the operating surgeon and

ranges from 0 to 22 with a score ≥ 11 being predictive of amputation.

In the most comprehensive evaluation of extremity injury scoring metrics to date, the designers of LEAP applied the criteria for each of the above listed scoring systems to the 407 patients in their study group with the intent to evaluate long-term functional outcomes after attempted limb salvage (55). In this important part of the LEAP report, there was found to be no correlation between any of the injury severity scores and reported functional outcome at either 6 or 24 months.

Recommendations

1. Mangled extremity severity scoring systems have limited predictive value in terms of the need for amputation.
2. No scoring system is able to reliably predict functional outcome (Level of evidence: 1b. Grade A recommendation).

WHAT IS THE FINANCIAL COST OF EXTREMITY RECONSTRUCTION VERSUS EARLY AMPUTATION AND THE IMPACT ON QUALITY OF LIFE?

Extremity injury presents a significant physical and emotional burden for the patient as well as an economic challenge for the health care system, acute and long-term. Several groups have evaluated the costs associated with pursuit of limb salvage as opposed to early amputation and placed these in relation to functional outcomes (5,7,20,31,48,60). There are significant differences in the length of hospital stay, need for rehospitalization, number of operations, and length of time to return to work in patients receiving primary amputation versus those with limb salvage. In nearly every report, these variables are significantly greater for groups after limb salvage (5,17,31). As an example, Bondurant and colleagues reported that patients who required a secondary amputation remained in the hospital more than twice as long as those who underwent primary amputation (53 versus 22 days) (8). Patients in limb salvage groups also require a significantly greater number of operations than those receiving primary amputation (19% versus 5%) (49). Nearly half of patients in both groups (limb salvage and primary amputation) failed to return to work within 24 months following injury, illustrating the persistent morbidity associated with severe extremity injury (5,17,31,49). Finally, Bondurant and colleagues documented the fiscal cost of secondary versus early primary amputation by showing an increase in the number of operations (2 versus 7) and doubling of hospital costs (\$28,964 versus \$53,462 in 1988 dollars) in the secondary amputation group (8).

In a notable finding, LEAP demonstrated no difference in quality of life between patients with primary amputation and those with successful limb salvage at two years (49). Using the validated, self-reporting questionnaire called the Sickness Impact Profile, which assesses 12 categories of function including ambulation, mobility, body care, social interaction, ability to work and others, LEAP failed to show improved quality of life in those with successful limb salvage following severe extremity injury at 24 months (7). These findings may be attributable to the increasing quality of prosthetics as well as the social and financial support

required for optimal care and rehabilitation following limb salvage attempts.

Recommendations

1. There is no significant difference in functional outcome after limb salvage versus amputation following severe extremity injury.
2. There is a significant economic, health care, and rehabilitation cost associated with limb salvage (Level of evidence: Ib. Grade A recommendation).

REFERENCES

1. Gregory RT, Gould RJ, Peclet M, et al. The mangled extremity syndrome (M.E.S.): a severity grading system for multisystem injury of the extremity. *J Trauma* 1985; 25: 1147–50.
2. Bosse MJ, MacKenzie EJ, Kellam JF, et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. *N Engl J Med* 2002; 347: 1924–31.
3. Fern KT, Smith JT, Zee B, et al. Trauma patients with multiple extremity injuries: resource utilization and long-term outcome in relation to injury severity scores. *J Trauma* 1998; 45: 489–94.
4. Holbrook TL, Anderson JP, Sieber WJ, et al. Outcome after major trauma: 12-month and 18-month follow up results from the Trauma Recovery Project. *J Trauma* 1999; 46: 765–71.
5. Katzman SS, Dickson K. Determining the prognosis for limb salvage in major vascular injuries with associated open tibial fractures. *Orthop Rev* 1992; 21: 195–9.
6. Purry NA, Hannon MA. How successful is below-knee amputation for injury? *Injury* 1989; 20: 32–46.
7. Quirke TE, Sharma PK, Boss WK Jr, et al. Are type IIIC lower extremity injuries an indication for primary amputation. *J Trauma* 1996; 40: 992–6.
8. Bondurant FJ, Cotler HB, Buckle R, et al. The medical and economic impact of severely injured lower extremities. *J Trauma* 1988; 28: 1270–3.
9. Dischinger PC, Read KM, Kufera JA, et al. Consequences and costs of lower extremity injuries. *Annu Proc Assoc Adv Automot Med* 2004; 48: 339–53.
10. Sohn VY, Arthurs ZM, Herbert GS, et al. Demographics, treatment, and early outcomes in penetrating vascular combat trauma. *Arch Surg* 2008; 143: 783–7.
11. Starnes BW, Beekley AC, Sebesta JA, et al. Extremity vascular injuries on the battlefield: tips for surgeons deploying to war. *J Trauma* 2006; 60: 432–42.
12. Clarke P, Mollan RA. The criteria for amputation in severe lower limb injury. *Injury* 1994; 25: 139–43.
13. Debaeky ME, Simeone FA. Battle injuries of the arteries in World War II: an analysis of 2471 cases. *Ann Surg* 1946; 123: 534–7.
14. Timberlake GA, Kerstein MD. Venous injury: to repair or ligate, the dilemma revisited. *Am Surg* 1995; 61: 139.
15. Quan R, Gillespie R, Stuart R, et al. The effect of vein repair on the risk of venous thromboembolic events: a review of more than 100 traumatic military venous injuries. *J Vasc Surg* 2008; 47: 571–7.
16. Rich NM, Mattox KL, Hirschberg A. *Vascular Trauma*, 2nd edition. New York: McGraw-Hill, 2004, pp 3–73, 353–92.
17. Dawson D, Putnam AT, Light JT, et al. Temporary vascular shunts to maintain limb perfusion after arterial injury: an animal study. *Trauma* 1999; 47: 64–71.
18. Clouse WD, Rasmussen TE, Peck MA, et al. In-theater management of vascular injury: 2 years of the Balad Vascular Registry. *J Am Coll Surg* 2007; 204: 625–32.
19. Chambers LW, Green DJ, Sample K, et al. Tactical surgical intervention with temporary shunting of peripheral vascular trauma sustained during Operation Iraqi Freedom: one unit's experience. *J Trauma* 2006; 61: 824–30.
20. Rasmussen TE, Clouse WD, Jenkins DH, et al. The use of temporary vascular shunts as a damage control adjunct in the management of wartime vascular injury. *Trauma* 2006; 61: 8–12.
21. Taller J, Kamdar JP, Greene JA, et al. Temporary vascular shunts as initial treatment of proximal extremity vascular injuries during combat operations: the new standard of care at echelon II facilities? *J Trauma* 2008; 65: 595–603.
22. Gifford S, Rasmussen TE, Adinian R, et al. Improved long-term outcomes following temporary vascular shunting for wartime vascular injury: a case control analysis from the GWOT vascular initiative. Presented at the American Association of Surgery for Trauma Maui, Hawaii, 2008.
23. Joshi V, Gregory EJ, Harding GE, et al. Determination of functional outcome following upper extremity arterial trauma. *Vasc Endovascular Surg* 2007; 41: 111–14.
24. Manford JD, Garard CL, Kline DG, et al. Management of severe vascular and neural injury of the upper extremity. *J Vasc Surg* 1998; 27: 43–9.
25. Clouse WD, Rasmussen TE, Perstein J, et al. Upper extremity vascular injury: a current in-theater wartime report from Operation Iraqi Freedom. *Ann Vasc Surg* 2006; 20: 431–4.
26. Weber MA, Fox CJ, Adams E, et al. Upper extremity arterial combat injury management. *Perspect Vasc Surg Endovasc Ther* 2006; 18: 141–5.
27. Fox CJ, Starnes BW. Vascular surgery on the modern battlefield. *Surg Clin N Am* 2007; 87: 1193–211.
28. Fox CJ, Gillespie DL, O'Donnell SD, et al. Contemporary management of wartime vascular trauma. *J Vasc Surg* 2005; 41: 638–44.
29. Lakstien D, Blumfield A, Sokolov T, et al. Tourniquets for hemorrhage control on the battlefield: a 4-year accumulated experience. *J Trauma* 2003; 54: S221–S225.
30. Welling DR, Burris DG, Hutton JE, et al. A balanced approach to tourniquet use: lessons learned and relearned. *J Am Coll Surg* 2006; 203: 106–15.
31. Walters TJ, Wenke JC, Kauvar DS, et al. Effectiveness of self-applied tourniquets in human volunteers. *Prehosp Emerg Care* 2005; 9: 416–22.
32. Rasmussen TE, Clouse WD, Jenkins DH, et al. Echelons of care and the management of wartime vascular injury: a report from the 332nd EMDG/Air Force Theater Hospital, Balad Air Base, Iraq. *Perspect Vasc Surg Endovascular Ther* 2006; 18: 91–9.
33. Kragh JF, Walters TJ, Baer DG, et al. Practical use of emergency tourniquets to stop bleeding in major limb trauma. *J Trauma* 2008; 64: S38–S50.
34. Pusateri AE, Holcomb JB, Kheirabadi BS, et al. Making sense of the preclinical literature on advanced hemostatic products. *J Trauma* 2006; 60: 674–82.
35. Alam HB, Uy GB, Miller D, et al. Comparative analysis of hemostatic agents in a swine model of lethal groin injury. *J Trauma* 2003; 54: 1077–82.
36. Rixen D, Grass G, Sauerland S, et al. Evaluation of criteria for temporary external fixation in risk-adapted damage control orthopedic surgery of femur shaft fractures in multiple trauma patients: “evidence-based medicine” versus “reality” in the trauma registry of the German Trauma Society. *J Trauma* 2005; 59: 1375–95.
37. Scalea TM, Boswell SA, Scott JD, et al. External fixation as a bridge to intramedullary nailing for patients with multiple injuries and with femur fractures: damage control orthopedics. *J Trauma* 2000; 48: 613–21.
38. Pape HC, Grimme K, Van Griensven M, et al. Impact of intramedullary instrumentation versus damage control for

- femoral fractures on immunoinflammatory parameters: prospective randomized analysis by the EPOFF Study Group. *J Trauma* 2003; 55: 7–13.
39. Pape HC, Rixen D, Morley J, et al. Impact of the method of initial stabilization for femoral shaft fractures in patients with multiple injuries at risk for complications (borderline patients). *Ann Surg* 2007; 246: 149–57.
 40. Gustilo RB, Mendoza RM, Willimas DN. Problems in the management of type III severe open fractures: a new classification of type III open fractures. *J Trauma* 1984; 24: 742–6.
 41. Georgiadis GM, Behrens FF, Joyce MJ, et al. Open tibial fractures with severe soft-tissue loss. Limb salvage compared with below-the-knee amputation. *J Bone Joint Surg Am* 1993; 75: 1431–41.
 42. Pirela-Cruz MA, Machen MS, Esquivel D. Management of large soft-tissue wounds with negative pressure therapy—lessons learned from the war zone. *J Hand Ther* 2008; 21: 196–202.
 43. DeFranzo AJ, Argenta LC, Marks MW, et al. The use of vacuum-assisted closure therapy for the treatment of lower-extremity wounds with exposed bone. *Plastic Reconstr Surg* 2001; 108: 1184–91.
 44. Herscovici D Jr, Sanders RW, Scaduto JM, et al. Vacuum-assisted wound closure (VAC therapy) for the management of patients with high-energy soft tissue injuries. *J Ortho Trauma* 2003; 17: 683–8.
 45. Geiger S, McCormick F, Chou R, et al. War wounds: lessons learned from Operation Iraqi Freedom. *Plast Reconstr Surg* 2008; 122: 146–53.
 46. Leininger BE, Rasmussen TE, Smith DL, et al. Experience with wound VAC and delayed primary closure of contaminated soft tissue injuries in Iraq. *J Trauma* 2006; 61: 1207–11.
 47. Godina M. Early microsurgical reconstruction of complex trauma of the extremities. *Plast Reconstr Surg* 1986; 78: 285–92.
 48. Parrett BM, Matros E, Pribaz JJ, et al. Lower extremity trauma: trends in the management of soft-tissue reconstruction of open tibia-fibula fractures. *Plast Reconstr Surg* 2006; 117: 1315–22.
 49. Bosse MJ, MacKenzie EJ, Kellam JF, et al. A prospective evaluation of the clinical utility of the lower-extremity injury-severity scores. *J Bone Joint Surg Am* 2001; 83A: 3–14.
 50. Bosse MJ, McCarthy ML, Jones AL, et al. The insensate foot following severe lower extremity trauma: an indication for amputation? *J Bone Joint Surg Am* 2005; 87: 2601–8.
 51. MacKenzie EJ, Bosse MJ, Kellam JF, et al. Factors influencing the decision to amputate or reconstruct after high-energy lower extremity trauma. *J Trauma* 2002; 52: 641–9.
 52. Treiman RL, Doty D, Gaspar MR. Acute vascular trauma: a fifteen year study. *J Surg* 1966; 111: 469–73.
 53. Johansen K, Daines M, Howey T, et al. Objective criteria accurately predict amputation following lower extremity trauma. *J Trauma* 1990; 30: 568–72; discussion 572–3.
 54. Jurkovich G, Mock C, MacKenzie E, et al. The Sickness Impact Profile as a tool to evaluate functional outcome in trauma patients. *J Trauma* 1995; 39: 625–31.
 55. Ly TV, Trivison TG, Castillo RC, et al. The LEAP Study Group. Ability of lower-extremity injury severity scores to predict functional outcome after limb salvage. *J Bone Joint Surg Am* 2008; 90: 1738–43.
 56. Howe HR Jr, Poole GV Jr, Hansen KJ, et al. Salvage of lower extremities following combined orthopedic and vascular trauma. A predictive salvage index. *Am Surg* 1987; 53: 205–8.
 57. Russell WL, Sailors DM, Whittle TB, et al. Limb salvage versus traumatic amputation. A decision based on a seven-part predictive index. *Ann Surg* 1991; 213: 473–80; discussion 480–1.
 58. McNamara MG, Heckman JD, Corley FG. Severe open fractures of the lower extremity: a retrospective evaluation of the Mangled Extremity Severity Score (MESS). *J Orthop Trauma* 1994; 8: 81–7.
 59. Krettek C, Seekamp A, Kontopp H, et al. Hannover Fracture Scale '98—re-evaluation and new perspectives of an established extremity salvage score. *Injury Int J Care Injured* 2001; 32: 317–28.
 60. Hierner R, Betz AM, Comtet JJ, et al. Decision making and results in subtotal and total lower leg amputations: reconstruction versus amputation. *Microsurgery* 1995; 16: 830–9.
 61. MacKenzie EJ, Bosse MJ, Pollak AN, et al. Long-term persistence of disability following severe lower-limb trauma. Results of a seven-year follow-up. *J Bone Joint Surg Am* 2005; 87: 1801–9.
 62. MacKenzie EJ, Bosse MJ, Kellam JF, et al. Factors influencing the decision to amputate or reconstruct after high-energy lower extremity trauma. *J Trauma* 2002; 52: 641–9.
 63. Peck MA, Clouse WD, Cox MW, et al. The complete management of extremity vascular injury in a local population: a wartime report from the 332nd Expeditionary Medical Group/Air Force Theater Hospital, Balad Air Base, Iraq. *J Vasc Surg* 2007; 45: 1197–205.

Critical Questions in Support of the Burned Patient

Steven E. Wolf

Clinical Questions and Recommendations		
Question	Answer	Recommendation grade
What is the optimal resuscitation method following severe burn?	Parkland or modified Brooke formula with isotonic crystalloid	C
How is burn depth best determined?	Laser Doppler imaging	B
When is the optimal time for burn wound excision?	First 48 hours after injury	B
How is blood loss best minimized during burn excision procedures?	Tourniquets, topical thrombin, and fibrin sealant	B
How is burn wound infection effectively minimised?	Early excision and grafting, topical antimicrobials	B
What is the best method of ventilation after smoke inhalation injury to minimize lung complications?	High-frequency percussive ventilation	C

INTRODUCTION

Burn care has advanced dramatically in the past 50 years, to the point that a young person with almost any injury might be expected to survive. Most of these advances were reached through intensive research, both on the bench and at the bedside. The days of conservative wound management and wait-and-see critical care has given way to goal-directed fluid management, early excision and grafting of burn wounds for wound closure, and aggressive organ support. Primary advances, therefore, have been in the areas of resuscitation, wound care, prevention of infection, and critical care. In the future, long-term outcomes will most likely be improved by better rehabilitation and scar management.

Even with these advances, important questions still arise about what exactly the advances have been and how should these be considered in decision for patient treatment, particularly in those with severe burns. Most define burns of greater than 20% of the total body surface area (TBSA) to be severe, with real risk of mortality and other poor outcomes. In this chapter, I consider the relevant questions in the severely burned of exactly how much fluid to give and when in the first 24 hours after injury, when to go to the operating theatre and how to manage the patient when there, how to reduce infectious complications, and how to manage a relevant pulmonary complication peculiar to this population. Each of these questions is vitally important in outcomes.

WHAT IS THE OPTIMAL RESUSCITATION METHOD FOLLOWING SEVERE BURN?

Current guidelines outlining the resuscitation of severely burned patients were developed over thirty years ago, and the most commonly used are the Parkland formula (1) and modified Brooke formulas (2). Each of these were developed in preclinical studies and then were trialed in patients without contemporaneous controls (Class V evidence); evidence to support their use was simply success of the formulae. Both of these formulae make recommendations for the first 24 hours after injury and are crystalloid-based with no provision for colloid during this time period. This notion is based on the finding that fluid given in the first 24 hours escapes from the intravascular space into the interstitium regardless of its molecular size, thus the purported advantage of colloid to expand the intravascular space is lost during this time period (2). This led Pruitt to state that “in early burn resuscitation, colloid is no more than expensive salt water” (3). Many studies exist that examine alterations or adjustments in resuscitation protocols that may lead to improved outcomes; however, none are definitive and none have replaced the tried-and-true standards (4).

In the past several years, many adjuncts to resuscitation of the severely burned have been suggested, some with supporting data. These include the use of fluids other than isotonic crystalloid such as hypertonic saline (Class V) (5) and the colloids albumin (Class V) (6), pentastarch (Class II) (7), and plasma (Class II) (8). In the case of hypertonic saline,

one Class III study showed increased mortality and renal failure with the use of this modality, and thus it is not in common use (9). Of these agents, perhaps plasma shows the most promise with the findings of improved base deficit and abdominal pressures in a Class II study. Other proposed adjuncts include infusion of high-dose antioxidants such as vitamin C (10) (Class II) and use of plasma exchange (11) (Class III) or continuous hemofiltration (12) (Class IV). Although each of these studies provides compelling evidence that perhaps these treatments may improve resuscitation in the severely burned, none of them are in the worldwide standard of care; common use remains only in specific centers. Large-scale trials are required to provide findings generalizable to broad practice.

In the future, I expect a shift from the Parkland and Brooke formulae as the recognition of better and more frequent monitoring is better established. Perhaps the best way to resuscitate the severely burned will be to define a starting dose of a defined fluid, then adjust therapy based on response, possibly with the use of decision support technology with allocations for expected biologic responses over time (13). Currently the outcome measured to define response is urine output, but this also may change in the future.

Answer: The available data and established expert opinion favor crystalloid resuscitation with lactated Ringer's solution infused at 2–4 ml/kg/% TBSA burned with one-half given in the first 8 hours after injury, and the second in the subsequent 16 hours (grade C recommendation). Adjuncts such as the use of plasma in resuscitation (grade B) and high-dose vitamin C (grade B) hold the most promise for advances in the field but are not established standard of care.

HOW IS BURN DEPTH BEST DETERMINED?

Wound depth determination is critical to the decision to operate in burned patients. This is based on the notion that deep partial-thickness burns and full-thickness burns will not heal in a timely fashion, and therefore are best treated with prompt excision and grafting. Central to this idea is the ability to properly discern wound depth such that the decision to operate is made only in those with real need, that is, those with partial-thickness burns that will heal with conservative therapies are not subjected to skin grafting. Typically, this is done through clinical assessment by an expert examiner, however, this method has only 60–80% accuracy in well-done descriptive studies using histologic analysis from biopsy of the wound as the standard (14). This method is therefore insufficient.

Many alternative methods have been tested to evaluate wound depth (15), the most promising of which is the laser Doppler. This technology images blood flow using laser Doppler assessment of moving red blood cells to detect vascularity and thus viability. Images are collected of normal and burned skin; normal skin has a moderate level of blood flow, whereas superficial burns have significantly increased blood flow associated with increased local inflammation. Deep partial-thickness burns and full-thickness burns have significantly decreased blood flow. Images can be obtained at any time after injury with reasonable accuracy (>90% sensitivity and specificity with wound biopsies and requirement for surgery) (16). Several trials

testing this modality have been performed, all of which confirm the superiority of laser Doppler imaging to clinical assessment (Class II). The greatest usefulness is in those wounds that are not clearly superficial and are not clearly full-thickness. Even with this evidence, most still rely on clinical assessment until the technology is more widespread.

Answer: The preponderance of the evidence suggests that burn depth is best determined by laser Doppler imaging to the exclusion of clinical assessment (grade B recommendation). For wounds in doubt, this technology should be considered.

WHEN IS THE OPTIMAL TIME FOR BURN WOUND EXCISION?

Deep partial- and full-thickness burns require excision and grafting for timely closure. Cope and others first espoused early excision and grafting for treatment of the acutely burned in the 1940s (17), initially as a means of accelerating time to healing (18). These initial efforts led to the practice followed by most burn centers, which is to excise the majority of the wound within the first week after injury. The question that arises is precisely when should these procedures be performed in this time frame? Is there some benefit to performing these procedures in the first day after injury compared to a week or more later? Unfortunately, the answer to these questions has not been addressed in a prospective randomized controlled trial, so we are left with lesser evidence to make a determination.

Herndon and Parks in 1986 compared two groups of patients with massive burns (mean >70% TBSA) treated in their center over a four-year period; some underwent complete excision and grafting within 48 hours of admission, and others underwent serial excision and grafting over a period of several weeks. They found that mortality was not different, however, wound closure was 33% more rapid in the early excision group, which was associated with a similar decrease in length of hospital stay (Class III) (19). The group in Seattle had the similar findings in a related study with a significant decrease in burn wound sepsis (Class III) (20). These data indicate that early excision and grafting decrease burn wound infections and length of stay without effects on mortality. To further refine whether excision and grafting done within the first 48 hours compared to sometime in the first week was beneficial, a group in Galveston compared patients who were admitted to the hospital within the first day of injury and underwent excision and grafting within 48 hours of injury compared to those who were admitted later associated with long-distance transport with excision and grafting over 48 hours after injury. They found that excision greater than 48 hours after injury was associated with a higher incidence of invasive wound infection and sepsis and longer total length of hospital stay (21), which is in agreement with the earlier studies (Class III). A recent meta-analysis of all studies in this regard showed a significant reduction in mortality for early excision in those *without* inhalation injury (22).

Answer: The optimal time for burn wound excision is within 48 hours of injury to minimize infectious wound complications and expedite length of hospital stay (grade B recommendation).

HOW IS BLOOD LOSS BEST MINIMIZED DURING BURN EXCISION PROCEDURES?

It is well known that blood loss is common during burn wound excision and grafting procedures. Reported blood loss is from 0.3 to 1.0 cc/cm² excised, and in one study was best predicted by larger body size, higher wound bacterial counts, wound area excised, and operative time (23). Given then that approximately 0.5 cc will be lost per 1 cm² excised, a normal sized man with a 50% TBSA burn excision will be predicted to lose 5,000 cc of blood, or 10 units. Therefore, the issue at hand is obvious.

Blood loss can be reliably measured in the burned patient by calculating the change in hemoglobin concentration during the operation and the amount of blood that was replaced during and after the operation. To determine whether a technique to decrease blood loss was effective, this number should proportionally decrease in relation to the surface area excised. Reported techniques to decrease blood loss during burn surgery include the use of tourniquets for extremity injuries (Class II in favor) (24), subcutaneous clamping of donor sites with vasoconstrictors (Class III showing no benefit) (25), thrombin spray to excised areas and donor sites (Class II in favor) (26), or fibrin spray to excised areas and donor sites (Class II in favor) (27). In practice, burn surgeons use a combination of these techniques to attempt to minimize transfused blood products. Other considerations, such as timing of surgery (less blood loss early in the course), also have merit (Class III in favor) (28).

Answer: Burn wound excision is a bloody business. Efforts to decrease bleeding should include the use of tourniquets on the extremities (class B recommendation) and topical thrombin and/or fibrin sealant (class B recommendation). No particular fibrin or thrombin product has been found to be definitively superior to another.

HOW IS BURN WOUND INFECTION EFFECTIVELY MINIMIZED?

Burn wound infection is common in the severely burned due to loss of innate defense associated with the skin, the rich pabulum of the denatured protein comprising eschar, and relative burn-induced immune suppression. These three conditions combine to result in the occurrence of invasion of microorganisms into remaining viable tissue as the established criterion for this diagnosis. Organisms typically causing burn wound infection are of a wide spectrum, from Gram positives and negatives to opportunistic fungi and viruses.

Burn wound infection, therefore, can be minimized in two ways. The first is early excision and grafting for wound closure to reestablish the skin barrier and remove the culture medium of the eschar. We have already seen that early excision of the wound in deep partial- and full-thickness burns is associated with decreased incidence of wound infection (Class III evidence), and another study showed that wounds excised more than six days from injury had increased bacterial counts, which was associated with an increased rate of graft loss (Class III evidence) (29). The second is to provide topical antimicrobial therapy directly to the wound, which was shown with Class III

evidence to be beneficial in burn wounds between 40% and 80% TBSA (30), or systemic antibiotics, which has almost no supportive evidence in the literature yet is a common practice. Antimicrobial selection should be for a broad spectrum agent effective against Gram-positives, Gram-negatives, and fungus. This is typically achieved topically with the use of a silver-containing agent, such as silver sulfadiazine, silver ion-containing dressings, or alternating use of highly effective soaks and salves such as 5% sulfamylon and/or Dakin's and Domboro's solutions.

Answer: Burn wound infection is most effectively minimized through the aggressive early use of excision and grafting for wound closure (grade B recommendation) and judicious use of topical antimicrobials (grade B recommendation). Systemic antibiotics are commonly used with no supporting evidence in the literature.

WHAT IS THE BEST METHOD OF VENTILATION AFTER SMOKE INHALATION INJURY TO MINIMIZE LUNG COMPLICATIONS?

The diagnosis of inhalation injury is generally made by a history of being in an enclosed space with smoke, physical findings of soot in the airway or perioral/perinasal burns, high concentrations of carbon monoxide in the blood, and evidence on bronchoscopy of erythema, edema, loss of epithelium, and/or carbonaceous secretions. Prudent medical practice dictates early intubation to secure the airway of patients with significant inhalation injury, particularly in those with coexistent significant cutaneous burns, before significant edema of the airway develops during resuscitation. With the diagnosis of inhalation injury, the actual damage to the airway and lung is variable ranging from some mild irritation of the upper airways to full-thickness burns of the upper and lower airways.

Many modes of ventilation are available for patients intubated with inhalation injury from standard methods used daily in all patient groups to very specialized modes used primarily in this population. These include conventional volume-controlled mechanical ventilation, high-frequency percussive ventilation (HFPV), high-frequency oscillatory ventilation (HFOV), or permissive hypercapnia in association with conventional ventilation. The best studied of these modes is HFPV (31), which was first shown to improve rates of pneumonia and improve survival compared to historic controls (32) (Class IV). The survival data were confirmed by another study with contemporaneous nonrandomized controls in burns >40% TBSA (Class III) (33). However, the only randomized controlled study in this population showed only early improvements in oxygenation but no demonstrable improvement in survival or other clinical outcomes (Class II) (34). Though some of the early data are compelling, no firm clinical evidence with properly controlled trials exists for the superiority of high-pressure release ventilation over conventional ventilation.

Other modes reported in the literature for inhalation injury include HFOV and permissive hypercapnia with conventional ventilation. HFOV was found to improve oxygenation when used as a salvage technique, with the conclusion that it can be used effectively for this use in this population (Class V) (35). A similar report was made for the use of permissive hypercapnia, with no

controls, and the conclusion was that this mode can be used safely (36).

Other newer modes of ventilatory support have been reported recently in other populations, most particularly airway pressure release ventilation (37). No reports of its effectiveness in those with inhalation injury are extant.

Answer: No ventilator strategy has been found to be definitively superior to another in the condition of inhalation injury. HFPV has shown the most promise, however, with some Class III and IV studies showing benefit. At the current time, this is the recommended mode of ventilation until more definitive trials are completed (grade C recommendation).

CONCLUSION

Data exist in the literature to support the use of many therapies to improve the lot of the severely burned, however, most of these methods have not been rigorously tested. The highest grade of recommendation for these central questions for burn care is only at the Class II level for the quality of evidence, and thus only grade B recommendations can be made. Well-defined and -conducted trials are required to provide further answers to these questions, in particular method of resuscitation, timing of burn excision and grafting, and optimal method of ventilation in those with smoke-induced lung injury.

Levels of Evidence for Answers

Subject	Year	Ref.	Level of evidence	Findings
Plasma for burn resuscitation	2005	8	II	Plasma-based resuscitation decreases volume-infused and abdominal pressures
High-dose vitamin C and burn resuscitation	2000	10	II	Vitamin C use is associated with significantly less volume and improved clinical outcomes
Early (<48 hours) excision and grafting	2002	21	III	Early excision is associated with less wound colonisation and decreased length of hospital stay
Mode of ventilation for inhalation injury	2002	34	III	No superiority

REFERENCES

- Baxter CR. Physiological response to crystalloid resuscitation of severe burns. *Ann NY Acad Sci* 1968; 150: 874–83.
- Pruitt BA, Mason AD, Moncrief JA. Hemodynamic changes in the early post-burn patient: the influence of fluid administration and of a vasodilator (hydralazine). *J Trauma* 1971; 11: 36–46.
- Pruitt BA. Protection from excessive resuscitation: “pushing the pendulum back”. *J Trauma* 2000; 49: 567–8.
- Cartotto RC, Innes M, Musgrave MA, et al. How well does the Parkland formula estimate actual fluid resuscitation volumes. *J Burn Care Rehab* 2002; 23: 258–65.
- Monafo WW. The treatment of burn shock by the intravenous and oral administration of hypertonic lactated saline solution. *J Trauma* 1970; 10: 575–86.
- Cochran A, Morris SE, Edelman LS, et al. Burn patient characteristics and outcomes following resuscitation with albumin. *Burns* 2007; 33: 25–30.
- Waxman K. Hemodynamic and oxygen transport effects of pentastarch in burn resuscitation. *Ann Surg* 1989; 209: 341–5.
- O'Mara MS, Slater H, Goldfarb IW, et al. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. *J Trauma* 2005; 58: 1011–18.
- Huang PP, Stucky FS, Dimick AR, et al. Hypertonic sodium resuscitation is associated with renal failure and death. *Ann Surg* 1995; 221: 543–54; discussion 554–7.
- Tanaka H. Reduction of resuscitation fluid volumes in severely burned patients using ascorbic acid administration: a randomized, prospective study. *Arch Surg* 2000; 135: 326–31.
- Kravitz M, Warden GD, Sullivan JJ, et al. A randomized trial of plasma exchange in the treatment of burn shock. *J Burn Care Rehab* 1989; 10: 17–26.
- Chung KK, Juncos LA, Wolf SE, et al. Continuous renal replacement therapy improves survival in severely burned military casualties with acute kidney injury. *J Trauma* 2008; 64(2 Suppl): S179–S185; discussion S185–S187.
- Alvarado R, Chung KK, Cancio LC, et al. Burn resuscitation. *Burns* 2008.
- Pape SA, Skouras CA, Byrne PO. An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth. *Burns* 2001; 27: 233–9.
- Hemington-Gorse SJ. A comparison of laser Doppler imaging with other measurement techniques to assess burn depth. *J Wound Care* 2005; 14: 151–3.
- Jeng JC, Bridgeman A, Shivanian L, et al. Laser Doppler imaging determines need for excision and grafting in advance of clinical judgment: a prospective blinded trial. *Burns* 2003; 29: 665–70.
- Cope O, Langohr JL, Moore FD, et al. Expeditious care of full thickness burn wounds by surgical excision and grafting. *Ann Surg* 1947; 125: 1–22.
- Burke JF, Bondoc CC, Quinby WC. Primary burn excision and immediate grafting: a method shortening illness. *J Trauma* 1974; 14: 389–95.
- Herndon DN, Parks DH. Comparison of serial debridement and autografting and early massive excision with cadaver skin overlay in the treatment of large burns in children. *J Trauma* 1986; 26: 149–52.
- Gray DT, Pine RW, Harnar TJ, et al. Early surgical excision versus conventional therapy in patients with 20 to 40 percent burns. A comparative study. *Am J Surg* 1982; 144: 76–80.
- Xiao-Wu W, Herndon DN, Spies M, et al. Effects of delayed wound excision and grafting in severely burned children. *Arch Surg* 2002; 137: 1049–54.
- Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. *Burns* 2006; 32: 145–50.
- Hart DW, Wolf SE, Beauford RB, et al. Determinants of blood loss during primary burn excision. *Surgery* 2001; 130: 396–402.

24. O'Mara MS, Goel A, Recio P, et al. The use of tourniquets in the excision of unexsanguinated extremity burn wounds. *Burns* 2002; 28: 684–7.
25. Barret JP, Dziewulski P, Wolf SE, et al. Effect of topical and subcutaneous epinephrine in combination with topical thrombin in blood loss during immediate near-total burn wound excision in pediatric burned patients. *Burns* 1999; 25: 509–13.
26. Prasad JK, Taddonio TE, Thomson PD. Prospective comparison of a bovine collagen dressing to bovine spray thrombin for control of haemorrhage of skin graft donor sites. *Burns* 1991; 17: 70–1.
27. Nervi C, Gamelli RL, Greenhalgh DG, et al. A multicenter clinical trial to evaluate the topical hemostatic efficacy of fibrin sealant in burn patients. *J Burn Care Rehab* 2001; 22: 99–103.
28. Desai MH, Herndon DN, Broemeling L, et al. Early burn wound excision significantly reduces blood loss. *Ann Surg* 1990; 211: 753–9; discussion 759–62.
29. Barret JP, Herndon DN. Effects of burn wound excision on bacterial colonization and invasion. *Plast Reconstr Surg* 2003; 111: 744–50; discussion 751–2.
30. Brown TP, Cancio LC, McManus AT, et al. Survival benefit conferred by topical antimicrobial preparations in burn patients: an historical perspective. *J Trauma* 2004; 56: 863–6.
31. Cioffi WG, Graves TA, McManus WF, et al. High-frequency percussive ventilation in patients with inhalation injury. *J Trauma* 1989; 29: 350–4.
32. Cioffi WG, Rue LW, Graves TA, et al. Prophylactic use of high-frequency percussive ventilation in patients with inhalation injury. *Ann Surg* 1991; 213: 575–80; discussion 580–2.
33. Hall JJ, Hunt JL, Arnoldo BD, et al. Use of high-frequency percussive ventilation in inhalation injuries. *J Burn Care Res* 2007; 28: 396–400.
34. Reper P, Wibaux O, Van Laeke P, et al. High frequency percussive ventilation and conventional ventilation after smoke inhalation: a randomised study. *Burns* 2002; 28: 503–8.
35. Cartotto RC, Ellis S, Gomez M, et al. High frequency oscillatory ventilation in burn patients with the acute respiratory distress syndrome. *Burns* 2004; 30: 453–63.
36. Sheridan RL, Kacmarek RM, McEtrick MM, et al. Permissive hypercapnia as a ventilatory strategy in burned children: effect on barotrauma, pneumonia, and mortality. *J Trauma* 1995; 39: 854–9.
37. Varpula T, Valta P, Niemi R, et al. Airway pressure release ventilation as a primary ventilatory mode in acute respiratory distress syndrome. *Acta Anaesthes Scand* 2004; 48: 722–31.

Burn Wound Management

Joseph H. Shin, Antonio Jorge V. Forte and Renato Freitas

Clinical Questions		
Question	Answer	Grade of recommendation
What substance is the most useful agent for fluid resuscitation in the patient with the acute burn and how should it be administered?	Crystalloid: Parkland formula	A
What, if any, are the indications for the use of the antibiotics in burn patients?	Systemic: none Topical: yes; silver sulfadiazene, mafenide	A
When and what form of initial debridement is necessary? What is the best method of burn wound excision?	Early excision and grafting (excluding inhalational injury)	A
What is the best choice of definitive treatment: Autograft? Allograft? Integra?	Autograft; select skin replacements depending on clinical indication	B
What is the best ancillary treatment to prevent scar contracture or keloids?	Silicone sheeting, pressure garments (15 mmHg)	B

INTRODUCTION

Burn wounds present some of the most significant challenges in the entire field of wound management. Burn injuries may range from easily managed minor skin wounds to exceedingly complex and devastating burns affecting form and function. The prognosis and management of these injuries varies based on the etiology and extent of the thermal energy imparted to the patients as well as the location and depth of penetration of the thermal source.

Irrespective of the variations in thermal source and energy, though, there are consistent patterns of the care of burn wound injuries that have been demonstrated to provide more satisfactory outcomes. The initial management of burns and triage of patients has been well documented in the criteria established by the Committee on Trauma of the American College of Surgeons and the American Burn Association regarding transfer to a burn center. The burn patient is and should be assumed to be a trauma patient. The initial work-up and evaluation should proceed as usual for the trauma patient. Special consideration for the burn patient center on immediate airway management regarding potential for inhalation injuries and the need for attention to airway problems unique to the burn patient (smoke, carbon dioxide, carbon monoxide, as well as airway burns). Burn injury, unlike penetrating or blunt trauma, necessitates a differential and generally more aggressive fluid management based specifically on the nature and extent of the thermal injury to the skin. The exact method of fluid resuscitation may vary and will be addressed. Proper perfusion

to the skin and end organs and at the same time a limitation in the extreme edema associated with resuscitation may have a direct impact on the wound. This is particularly true given that edema may have a critical impact on the development of the three zones of the burn wound: (1) hyperemia, (2) stasis, and (3) coagulation.

Regardless of where the care of these patients is provided, there are critical issues regarding both early and late management of the burn wound. Assuming resuscitative maneuvers are successful in the acute phase, long-term morbidity can be minimized with early excision, grafting, and early mobilization and therapy. This has become a generalized and accepted principle in the care of the burn patient but is sometimes difficult to fully implement inasmuch as gauging the extent of injury maybe challenging. At the same time, the advent of a variety of additional skin replacements have extended the armamentarium of the surgeon caring for the burn patient. In principle, the burn wound is essentially an open wound. The management, just as in resuscitation, is not functionally different. It is, however, governed by the protean physiologic response and the dramatic nature of the loss of barrier function and its implication from an immunologic standpoint. Overall, though, the outlook for patients has improved in that the presence of specialized burn centers as well as newer modalities of treatment continue to be developed and provide hope for the significantly injured burn patients.

The following questions will hopefully guide management in this group of patients.

WHAT SUBSTANCE IS THE MOST USEFUL AGENT FOR FLUID RESUSCITATION IN THE PATIENT WITH THE ACUTE BURN AND HOW SHOULD IT BE ADMINISTERED?

The extent of fluid resuscitation should be guided by the depth and extent of the burn wound and injury. In general fluid resuscitation is not usually necessary in most patients with burns less than 20 % of total body surface area (TBSA). The rule of nines is an effective gauge of the extent of injury of the TBSA in adult or teen patients and is critical in determining the total volume of fluid resuscitation. Currently three options exist with regards to the option for fluid resuscitation products. These include (1) crystalloid, (2) colloid, and (3) hypertonic saline.

Of these three options, by far the most popular and currently taught method is to utilize crystalloid resuscitation given in the manner of the Parkland formula. This formula uses lactated Ringer's solution and provides 4cc/kg/% TBSA administered over 24 hours. Fifty percent of this solution should be administered over 8 hours and the remaining volume in 16 hours. Adequacy of fluid resuscitation is assessed by hourly urine output measurements and is expected to be a minimum of 30cc/hour. Mitra et al. retrospectively studied the data of 49 patients, comparing fluid resuscitation volumes with the amount predicted by the Parkland formula. They state that fluid resuscitation volumes significantly higher than those predicted by the Parkland formula can be given, because their patients presented minimal clinically evident complications and mortality similar to that in other centers (1).

Colloid resuscitation, primarily in the form of albumin (5% albumin solution administered as 0.1ml/kg/% TBSA) but also fresh frozen plasma as well as dextran, has been a point of controversy because it has been suggested that this fluid is more effective in preventing extravasation and fluid leak by increasing intravascular oncotic pressure and driving interstitial fluid toward the vascular space. Despite this theory, there has been little adaptation of this form of resuscitation inasmuch as it has also been demonstrated that colloid or protein may leak into the interstitial space, potentially aggravating tissue edema. It has therefore been generally accepted that colloid may be more beneficial after the initial 24 hours as the patient is stabilized.

In 2005, O'Mara et al. published a prospective and randomized study of 31 patients receiving either crystalloid or colloid resuscitation whose intra-abdominal pressure was measured (2). Despite no difference at the time of admission, patients resuscitated with plasma received significantly less volume than the crystalloid group and maintained an intra-abdominal pressure below the threshold of complications of intra-abdominal hypertension, which appears to be a direct result of the decrease in volume required. However, Liberati et al. reviewed 32 trials in 2006 and found no evidence that human albumin replacing blood in burn patients provides survival advantage over saline. Fluid replacement with saline solution should be the mainstay therapy because of albumin's cost (3).

In pediatric patients, Greenhalgh et al. demonstrated in a prospective and randomized trial that the maintenance of albumin levels with large burns is unnecessary, with no differences in complication rates, mortality, tolerance to tube feedings, or ventilatory support in previously healthy

children who suffer severe burns and receive adequate nutrition (4).

Bunn et al. reviewed seventy studies in 2008 and found no strong evidence that a certain colloid solution is more effective or safe than any other (5). However, the authors could not rule out clinically significant differences between colloids, because the confidence intervals (CIs) were wide. Therefore, larger trials of fluid therapy are needed if clinically significant differences in mortality are to be detected or excluded. Finally, Perel and Roberts reviewed 63 studies in 2008 found no evidence from randomized controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with burns or following surgery (6). Colloids are also more expensive than crystalloids, and their use was not associated with an improvement in survival.

Hypertonic saline has also been utilized and touted as beneficial in the acute phase of the burn for much the same reason as colloid, with an eye toward reducing the total volume of fluid but supporting the cardiac output. Despite this theory, in 1989, Gunn and colleagues designed a prospective and randomized trial to analyze fluid, electrolyte, and physiologic parameters during burn resuscitation with the use of hypertonic saline or lactated Ringer's solution in patients with an average TBSA of 36.7% (7). Because it was not possible to demonstrate decreased fluid requirements, improved tolerance of feedings, or decrease in percent weight gain, the researchers concluded that there is no advantage of hypertonic saline solution over conventional therapy with lactated Ringer's solution. Great care and extremely close monitoring of the patient is required with this form of resuscitation because the development of hyponatremia can be rapid.

Regarding plasma exchange, Kravitz et al. in 1989 randomly assigned 22 adult patients to one of two groups. Both groups received standard fluid resuscitation, but only the study group underwent plasma exchange during the second eight-hour period after the burn. This procedure did not fundamentally change the course of burn shock in this cohort (8).

In summary: The use of crystalloid resuscitation in the form of lactated Ringer's solution given in the manner prescribed and known as the Parkland formula is likely the most effective. As with all forms of resuscitation, end organ perfusion, easily measured as urine output, is the most effective and simple gauge of the extent of resuscitation (grade A).

WHAT, IF ANY, ARE THE INDICATIONS FOR THE USE OF THE ANTIBIOTICS IN BURN PATIENTS?

Despite the fact that infection and burn wound sepsis is the major cause of death in burn patients, there is no role for the systemic administration of prophylactic antibiotics in the patient with the acute burn wound. The burn wound prior to excision has an intact eschar in most instances, which has no vascular supply. Hence, systemic antibiotics have little capacity to penetrate into the wound. Its use has little benefit at providing protection against either cellulites or the dreaded burn wound sepsis. Their early use though may clearly select resistant bacterial strains. In 2004, Ugburo et al. carried out a prospective study on 61 patients to

assess the role of systemic antibiotic prophylaxis in the control of burn wound infection (9). The subjects were randomly distributed into three groups: Group 1 ($n = 21$) received ampicillin and cloxacillin, group 2 ($n = 20$) received erythromycin tablets and intravenous gentamicin, and a control group ($n = 20$) received no systemic chemoprophylaxis. All burn wounds were initially treated and dressed similarly. Wound colonization was determined from surface wound swab cultures. All burn wounds that showed signs of infection were biopsied and the specimen sent for culture and histopathological studies. The colonization time in days for the groups was 2.90 ± 0.92 , 3.15 ± 0.77 , and 3.05 ± 0.83 for groups 1 and 2 and the control, respectively. *Staphylococcus aureus* was the predominant organism identified in the surface swab from contaminated wounds. Wound infection was seen in 5.70 ± 1.70 , 5.75 ± 1.62 and 5.6 ± 1.90 days for group 1, group 2, and the control group, respectively. There was no significant difference between wound infection time of control and group 1, nor any difference between the control and group 2 ($p > 0.05$). The most common organism, identified by wound biopsy culture, infecting burn wounds in all the groups was *Pseudomonas aeruginosa* followed by *S. aureus*. A significant difference between the treatment groups and the control ($p < 0.05$) was noted with regard to the percentage of infected wounds that grew *P. aeruginosa*, compared to those that grew *S. aureus*. Last, the authors state that systemic antibiotic prophylaxis is of no value in controlling burn wound infection in patients managed in surgical wards and may favor *P. aeruginosa* in the burn wounds.

The use of topical antibiotics delivered at the wound site itself, often placed directly on the eschar, prior to excision has been demonstrated to be effective at preventing colonization of the burn wound. In 1990, Livingston et al. prospectively studied 52 patients who were treated with tangential excision and split-thickness skin grafting. Their study demonstrated that topical antimicrobial agents reduce infection-related skin graft loss in patients with medium-sized (20–40% TBSA) burns and that neomycin plus bacitracin may be associated with rapid emergence of drug-resistant organisms, whereas silver nitrate may not (10). They reported that infection in the area of graft loss was caused by antibiotic-resistant organism of yeast in 50% of the group treated with lactated Ringer's solution only. No graft infections were caused by resistant bacteria or yeast in their patients treated with silver nitrate.

Options for topical antibiotic treatment include silver nitrate, silver sulfadiazine, mafenide acetate, and for smaller wounds agents such as mupirocin, bacitracin, or polymixin B. Of all of the agents, the most used of these topical agents is silver sulfadiazine (11–13). Early burn wounds generally are at risk for Gram-positive organisms, and this is also useful for this spectrum. The advantages are easy application, lack of pain, and compatibility with most treatment forms. The major limitation is poor eschar penetration and potential development of neutropenia and bone marrow suppression. Currently, silver nitrate is less frequently utilized because of the messiness of its use, potential for pain, and rarely methemoglobinemia.

Mafenide is exceedingly beneficial in those patients who have extensive eschar for whom penetration is critical. Exposed or burned skin on cartilage in areas such as the

ear may benefit from mafenide use, though its application is often limited by the extreme pain on immediate administration (13). Mafenide may be beneficial in Gram-negative infections as well.

Lesser topical agents such as bacitracin and polymixin have little role in the management of the large acute burn wound. Mupirocin, though, can be beneficial if methicillin-resistant *S. aureus* infection is identified. Its use should be limited to culture positive cases.

Fungal infection is seen late but may be associated with the use of broad spectrum antibiotics. The use of such without a clear indication is to be condemned as associated mortality with fungal infections may exceed 30%.

In summary: There is no role for systemic prophylactic antibiotics in the acute burn patient. The complications of resistance as well as lack of penetration of the burn wound should preclude its use. The use of topical agents is clearly well documented, and the choice of agents is closely dependent on the clinical setting. In general, silver sulfadiazine is an excellent first-line choice in most patients. As with any treatment, the complications of the treatment need to be carefully assessed as they may add to the morbidity of the patient's condition (grade A).

WHEN AND WHAT FORM OF INITIAL DEBRIDEMENT IS NECESSARY? WHAT IS THE BEST METHOD OF BURN WOUND EXCISION?

In 1986, Chicarilli et al. proposed the feasibility of performing early major escharectomy in patients with thermal burns ranging from 30% to 70% of TBSA without increasing the surgical risk, when compared to patients treated with conventional staged excision (14). In a randomized, prospective study of 50 patients, Thompson et al., in 1987, reported the decrease in mortality with early excision in patients with burns greater than 50% TBSA and no inhalation injury. However, they explained their finding by age differences alone (15). In another randomized and prospective study from 1989, Herndon et al. affirmed that mortality from burns without inhalation injury was significantly decreased by early excision from 45% to 9% in patients who were 17–30 years of age ($p < 0.025$), although no differences in mortality could be identified between therapies in adult patients older than 30 years of age or with a concomitant inhalation injury (16). The authors also showed that children with similar large burns treated by early excision experienced a significant increase in mortality with increasing burn size and with concomitant inhalation injury ($p < 0.05$). In 1999, Subrahmanyam conducted a prospective and randomized trial with 50 patients and affirmed that early tangential excision and skin grafting was clearly superior to expectant treatment using topical honey in patients with moderate burns regarding skin graft take and functional and cosmetic results (17).

Finally, in 2006, Ong et al. conducted a meta-analysis of 441 articles, 15 of which were randomized controlled trials, to evaluate whether early excision and grafting is better or equivalent to the conservative treatment of burns in both children and adults with minor or major burns (18). They found a significant reduction in mortality with early excision of burns when compared with traditional treatment only in patients without inhalational injury, with a

pooled relative risk (RR) of 0.36 and 95% CI (0.2 to 0.65). The length of hospital stay in days was also significantly shorter in the early excision group (standardized mean difference of -8.89 and a 95% CI of -14.28 to -3.5). However, the blood transfusion requirement was significantly higher in the early excision group, and no conclusive evidence was found regarding the differences between the groups in terms of duration of sepsis, wound healing time, and skin graft take.

O'Mara et al., in 2002, prospectively assessed 10 patients with bilateral extremity burns (19). The extremities were randomized, and tourniquet was applied to one of the legs. They found that the use of the tourniquet in the unexsanguinated extremity reduced blood loss without affecting graft take.

Regarding the evolving technology available for burn wound debridement, Gravante et al. prospectively studied 87 patients randomly divided in two homogeneous groups: One underwent traditional escharectomy and the Versajet hydrosurgery system (Smith & Nephew, London) was used on the other (20). The authors demonstrated that all patients received adequate debridement, but with the use of the Versajet, the procedure was faster ($p < 0.05$) and subjectively more precise in obtaining the correct plane.

In summary: Early excision and grafting is better or equivalent to the conservative treatment of burns in adults with minor or major burns (without inhalational injury). Early excision in children with concomitant inhalational injury may also be associated with a higher mortality, depending on the size of the burn. To this date, there are no strong data available in the current literature regarding the advantage of tangential or fascial excision over the other. Both have been successfully used, and their choice is left to surgeon's personal preference and comfort (grade A).

WHAT IS THE BEST CHOICE OF DEFINITIVE TREATMENT: AUTOGRAFT? ALLOGRAFT? INTEGRA?

Several bioengineered skin substitutes are currently available. Biobrane is a biosynthetic dressing composed of a knitted nylon mesh that is bounded to a thin silicone membrane and coated with porcine polypeptides. TransCyte is a temporary biosynthetic covering composed of a semipermeable silicone membrane and newborn human fibroblast cells cultured on porcine collagen-coated nylon mesh. Dermagraft is a bioabsorbable polyglactin mesh seeded with allogeneic neonatal fibroblasts. Integra is composed of two layers: a bovine collagen-based dermal analog, which integrates with the patient's own cells, and a temporary epidermal silicone sheet that is peeled away as the wound heals. Apigraft is a bilayered living skin equivalent composed of type I bovine collagen and allogeneic keratinocytes and fibroblasts obtained from neonatal foreskin. Autologous cultured skin for burns consists of the harvested and cultured keratinocytes and fibroblasts obtained from biopsy samples, which are prepared for grafting onto full-thickness burn sites. Allogenic cultured skin consists of keratinocytes and fibroblasts obtained from allogenic epidermal human cells, which are cultured and applied (21).

In 1988, Heimbach et al. coordinated an 11-center prospective randomized clinical trial with 139 burn sites on

106 patients with a mean burn size of 46.5% of TBSA (22). Patients received either artificial dermis or the investigator's usual skin grafting material. At the end, they concluded that artificial dermis allows early wound closure with as good take as allograft; when combined with an epidermal graft, it provides a permanent cover that is at least as satisfactory as skin grafting techniques and uses donor grafts that are thinner and leave donor sites that heal faster.

In 2007, Branski et al. organized a longitudinal pediatric clinical trial to assess the use of Integra in the management of severe full-thickness burns of more than 50% TBSA (23). Twenty children were randomized to be treated with either Integra or autograft-allograft technique. No statistically significant difference was found when compared the following parameters in both groups: burn size ($70 \pm 5\%$ versus $74 \pm 4\%$ TBSA), mortality (40% versus 30%), and length of stay (41 ± 4 versus 39 ± 4 days). In the short term, resting energy expenditure significantly decreased ($p < 0.01$), and serum levels of constitutive proteins significantly increased ($p < 0.03$) in the Integra group compared with controls. Moreover, the authors found a significant increase in bone mineral content and density at two years, as well as improved scarring in terms of height, thickness, vascularity, and pigmentation at one and two years in the Integra group. Additionally, the coverage with Integra does not bear the risk of cadaver skin-associated antigenicity and cross-infection, nor does it increase the risk associated with harvesting large autograft.

In 2007, Pham et al. reviewed 20 randomized controlled trials and suggested that Biobrane, TransCyte, Dermagraft, Apligraf, autologous cultured skin, and allogeneic cultured skin were at least as safe as biological skin replacements or topical agents/wound dressings (21). However, the safety and efficacy of Integra could not be adequately demonstrated. For the management of partial thickness burns, the evidence suggested Biobrane, TransCyte, Dermagraft, and allogeneic cultured skin, were at least as efficacious as topical agents/wound dressings or allograft. In addition, the efficacy of autologous cultured skin for the management of full-thickness burns could not be proven based on the prior studies.

In summary: To date, autografting with either partial-thickness skin or full-thickness skin from the patient still represents the gold standard in the care of the burn patient. The rapid expansion in the use and indications of skin substitutes clearly shows specific benefits in certain indications but cost remains a significant issue (grade B).

WHAT IS THE BEST ANCILLARY TREATMENT TO PREVENT SCAR CONTRACTURE OR KELOIDS?

Once the acute phase of the patient's burn wound management is completed, the extent and form of the scarring remains the critical determinant of the quality of life in many cases. Contractures as well as the development of keloids and hypertrophic scars represent one of the most challenging areas for management of burn wounds. Adjunctive therapies are many. Their effectiveness often difficult to gauge as the manifestations of scarring are protean.

O'Brien and Pandit in 2006 conducted a systematic review of 15 trials, involving 615 people, comparing adhesive silicon gel sheeting with control, non-silicon gel sheeting,

silicon gel plates with added vitamin E, laser therapy, triamcinolone acetonide injection, and nonadhesive silicon gel sheeting. Some studies suggest that silicon gel sheeting might reduce the incidence of hypertrophic scarring in patients (RR 0.46, 95% CI 0.21 to 0.98), and produced a statistically significant reduction scar thickness (RR -1.99, 95% CI -2.13 to -1.85) and color amelioration (RR 3.05, 95% CI 1.57 to 5.96); these studies were highly susceptible to bias (24). Therefore, the researchers concluded that there is weak evidence of a benefit of silicon gel sheeting as a prevention method for abnormal scarring in high-risk individuals.

In 1998, Patino et al. carried out a prospective and randomized study of 30 pediatric patients who had hypertrophic scarring following dermal wounds in more than 30% TBSA. They used a modified Vancouver Burn Scar Assessment Scale to determine the characteristics of the scar before and after the implementation of massage therapy, which consisted of a 10-minute massage session per day. The study failed to demonstrate any appreciable effects of massage therapy on the vascularity, pliability, and height of the hypertrophic scar studied, although there were reports of a decrease in pruritus in some patients (25).

Finally, a prospective clinical trial, performed by Kerckhove et al. in 2005, aimed to investigate the influence of two different levels of compression on erythema and thickness of burn scars and examine the association between erythema and thickness. To measure the scar erythema and thickness, a colorimeter and an echographic evaluation

with high-frequency ultrasound were used, respectively, at the first, second, and third month of treatment. Scars that were treated with garments from a “normal” compression class did score significantly better for thickness compared to the “low” compression class (26). The difference in thickness was most evident at one month. Thereafter no further significant improvement between the treatments over time could be obtained. This difference for erythema was not statistically significant. Positive correlations were found between erythema and thickness values in the first, second, and third month. However, changes in erythema and thickness only correlated significantly after the first month. After three months of treatment, this pattern of change in both parameters correlated with a high level of significance. Therefore, the authors suggest that pressure garments that deliver a pressure of at least 15mmHg tend to accelerate scar maturation. In addition, they propose that measurements of scar thickness can be used to predict changes of the erythema.

In summary: Options for scar, hypertrophic scar, and keloid management are challenging to evaluate because of the heterogeneity of the patient’s problem and scar type. It appears that there may be some benefit from the use of silicon sheeting as well as pressure garments given a sufficient pressure (15mmHg) (grade B).

The management of the burn patient is one of the most challenging of all areas in surgery. It tests the skill and dedication of a large team in managing one of the most devastating injuries afflicting the trauma patient.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Choice of fluids for resuscitation	2007	6	IIA	A	The use of crystalloid is necessary and adequate for resuscitation, and colloids presented no additional advantage.
Use of systemic and topical antibiotics	1990, 2004	9, 10	IIA, IIA	A	Systemic antibiotics have no value on burn wound infection prophylaxis, and topical antibiotics that should be used include silvadene and mafenide.
Timing and technique for debridement	2006	18	IIA	A	Early excision and grafting is beneficial and recommended.
Definitive treatment and artificial skin	2007	21	IIB	B	Autograft is the recommended option. Skin replacements can be used depending on clinical indication.
Ancillary treatment to prevent keloids or scar contracture	2006, 2005	24, 26	IIB, IIB	B	Pressure garments with tension higher than 15 mmHg are recommended. There is weak evidence of silicon gel’s benefit.

REFERENCES

- Mitra B, Fitzgerald M, Cameron P, et al. Fluid resuscitation in major burns. *ANZ J Surg* 2006; 76: 35–8.
- O’Mara MS, Slater H, Goldfarb IW, et al. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. *J Trauma* 2005; 58: 1011–18.
- Liberati A, Moja L, Moschetti I, et al. Human albumin solution for resuscitation and volume expansion in critically ill patients. *Intern Emerg Med* 2006; 1: 243–5.
- Greenhalgh DG, Housinger TA, Kagan RJ, et al. Maintenance of serum albumin levels in pediatric burn patients: a prospective, randomized trial. *J Trauma* 1995; 39: 67–73.
- Bunn F, Trivedi D, Ashraf S. Colloid solutions for fluid resuscitation. *Cochrane Database Syst Rev* 2008; 1: CD001319.
- Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev* 2007; 4: CD000567.
- Gunn ML, Hansbrough JF, Davis JW, et al. Prospective, randomized trial of hypertonic sodium lactate versus lactated

- Ringer's solution for burn shock resuscitation. *J Trauma* 1989; 29: 1261–7.
8. Kravitz M, Warden GD, Sullivan JJ, et al. A randomized trial of plasma exchange in the treatment of burn shock. *J Burn Care Rehab* 1989; 10: 17–26.
 9. Ugboro AO, Atoyebi OA, Oyenyin JO, et al. An evaluation of the role of systemic antibiotic prophylaxis in the control of burn wound infection at the Lagos University Teaching Hospital. *Burns* 2004; 30: 43–8.
 10. Livingston DH, Cryer HG, Miller FB, et al. A randomized prospective study of topical antimicrobial agents on skin grafts after thermal injury. *Plast Reconstr Surg* 1990; 86: 1059–64.
 11. Caruso DM, Foster KN, Blome-Eberwein SA, et al. Randomized clinical study of Hydrofiber dressing with silver or silver sulfadiazine in the management of partial-thickness burns. *J Burn Care Res* 2006; 27: 298–309.
 12. Atiyeh BS, Costagliola M, Hayek SN, et al. Effect of silver on burn wound infection control and healing: review of the literature. *Burns* 2007; 33: 139–48.
 13. Monafó WW, West MA. Current treatment recommendations for topical burn therapy. *Drugs* 1990; 40: 364–73.
 14. Chicarilli ZN, Cuono CB, Heinrich JJ, et al. Selective aggressive burn excision for high mortality subgroups. *J Trauma* 1986; 26: 18–25.
 15. Thompson P, Herndon DN, Abston S, et al. Effect of early excision on patients with major thermal injury. *J Trauma* 1987; 27: 205–7.
 16. Herndon DN, Barrow RE, Rutan RL, et al. A comparison of conservative versus early excision. Therapies in severely burned patients. *Ann Surg* 1989; 209: 547–52.
 17. Subrahmanyam M. Early tangential excision and skin grafting of moderate burns is superior to honey dressing: a prospective randomised trial. *Burns* 1999; 25: 729–31.
 18. Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. *Burns* 2006; 32: 145–50.
 19. O'Mara MS, Goel A, Recio P, et al. The use of tourniquets in the excision of unexsanguinated extremity burn wounds. *Burns* 2002; 28: 684–7.
 20. Gravante G, Delogu D, Esposito G, et al. Versajet hydro-surgery versus classic escharectomy for burn débridement: a prospective randomized trial. *J Burn Care Res* 2007; 28: 720–4.
 21. Pham C, Greenwood J, Cleland H, et al. Bioengineered skin substitutes for the management of burns: a systematic review. *Burns* 2007; 33: 946–57.
 22. Heimbach D, Luterma A, Burke J, et al. Artificial dermis for major burns. A multi-center randomized clinical trial. *Ann Surg* 1988; 208: 313–20.
 23. Branski LK, Herndon DN, Pereira C, et al. Longitudinal assessment of Integra in primary burn management: a randomized pediatric clinical trial. *Crit Care Med* 2007; 35: 2615–23.
 24. O'Brien L, Pandit A. Silicon gel sheeting for preventing and treating hypertrophic and keloid scars. *Cochrane Database Syst Rev* 2006; 1: CD003826.
 25. Patiño O, Novick C, Merlo A, et al. Massage in hypertrophic scars. *J Burn Care Rehabil* 1999; 20: 268–71.
 26. Van den Kerckhove E, Stappaerts K, Fieuws S, et al. The assessment of erythema and thickness on burn related scars during pressure garment therapy as a preventive measure for hypertrophic scarring. *Burns* 2005; 31: 696–702.

Inhalation Injury

Leopoldo C. Cancio

Clinical Questions: Inhalation Injury		
Question	Answer	Recommendation grade
What are the indications for endotracheal intubation?	Early prophylactic airway control is indicated for most symptomatic patients with II and for patients with extensive burns during initial resuscitation.	C
What are the indications for tracheostomy?	Tracheostomy is an option for long-term airway management and may facilitate pulmonary toilet.	C
What diagnostic procedures should be performed?	A presumptive diagnosis can be made on clinical grounds, supplemented by fiber optic laryngoscopy. Definitive diagnosis requires bronchoscopy.	B
What mode of mechanical ventilation is most effective?	High-frequency percussive ventilation improves ventilation and oxygenation and may reduce pneumonia and mortality.	C
What IV fluid strategies improve outcome?	Avoid under- or over-resuscitation. II patients frequently require larger volumes for burn shock resuscitation, but no evidence supports initiation of resuscitation at higher infusion rates.	C
What drugs improve outcome?	Inhaled heparin may prevent obstructing clots and casts.	C
How is CO poisoning diagnosed?	Coximetry (measurement of COHb and MetHb levels) should be performed in patients with II.	D
What treatment is safe and effective for CO poisoning?	100% oxygen should be given to all patients with CO poisoning until the COHb is normal (<5%).	D
What is the role for HBOT?	HBOT is an option for patients with CO poisoning to prevent delayed neurocognitive syndrome.	C
What treatments are safe and effective for cyanide?	Hydroxocobalamin should be considered for patients with known or suspected cyanide poisoning.	C
Should II patients be transferred to a burn center?	Consultation with the regional burn center should be performed on admission.	D
<i>Note:</i> The reader is cautioned that, for example, recommendations concerning airway management, treatment of CO poisoning, and burn center referral are considered standard of care in the United States despite the cited levels of evidence. <i>Abbreviations:</i> CO, carbon monoxide; COHb, carboxyhemoglobin; HBOT, hyperbaric oxygen therapy; II, inhalation injury; MetHb, methemoglobin.		

INTRODUCTION

Smoke inhalation injury (II) occurs in about 10% of patients admitted to burn centers and greatly increases postburn pneumonia and mortality risk, especially at the mid-range of age and burn size (1,2). Acute care surgeons frequently provide initial care to patients with II. This chapter reviews the evidence for current standards of care in the treatment of these patients. The acute care surgeon, faced with a patient with severe II, must address the following questions:

- What are the indications for endotracheal intubation and for tracheostomy in patients with II?
- What diagnostic procedures should be performed in patients with suspected II?
- What mode of mechanical ventilation is most effective for these patients?
- What drugs and fluid management strategies, if any, improve outcome?
- What immediate treatments are safe and effective for metabolic asphyxiation, for example, by carbon monoxide or cyanide?
- Should patients with II be transferred to a burn center?

An understanding of the pathophysiology and availability of techniques for the effective management of II has only developed over the past 50 years. II can be classified into three types, based on the anatomic location of the lesion. (1) Upper airway injuries are those caused primarily by thermal injury to the mouth, oropharynx, and larynx. (2) Lower airway and parenchymal injuries are

those tracheal, bronchial, and alveolar injuries caused by the passage of the chemical and particulate constituents of smoke past the glottis. (3) Metabolic asphyxiation is the process by which smoke constituents (carbon monoxide, cyanide) or their byproducts (methemoglobinemia due to oxidation of hemoglobin by, e.g., nitrogen dioxide) impair oxygen delivery to and/or consumption by the tissues. All three types of II may coexist in a given patient, whose care may be further complicated by cutaneous thermal injury or mechanical trauma. However, unless otherwise specified, the phrase “inhalation injury” usually means “lower airway and parenchymal injury.”

In conducting this review, the primary methodology was a PubMed search for all English-language publications for 1966–2008 with the key words “smoke inhalation injury” or “burns, inhalation,” limited to clinical trial, randomized controlled trial, meta-analysis, or practice guideline. The reader is cautioned that although the level of evidence is low for some recommendations, many of these are considered the current standard of care in the United States. These include prophylactic intubation of symptomatic II patients, provision of 100% oxygen to patients with CO poisoning, and burn center consultation for II patients.

WHAT ARE THE INDICATIONS FOR ENDOTRACHEAL INTUBATION AND FOR TRACHEOSTOMY IN PATIENTS WITH II?

The indications for intubation include decreased mental status from inhalation of metabolic asphyxiants (see following discussion) or from other injuries, airway obstruction caused by II or generalized postburn edema, and pulmonary failure from subglottic II. The evidence in favor of early intubation of patients with II is primarily that gained by hard experience, rather than that derived from randomized controlled trials (RCTs). Direct thermal injury to the upper airway (to include the larynx, oropharynx, mouth, and tongue) causes edema formation, which may progress within minutes or hours to complete airway obstruction. Orotracheal intubation of such patients after the onset of obstruction is often impossible, and immediate cricothyroidotomy should then be considered. To avoid that scenario, prophylactic intubation is appropriate. Premedication for direct laryngoscopy should be performed with an appreciation for the fact that many patients with burns and II are hypovolemic and may become profoundly hypotensive on induction of anesthesia. The primary risk associated with prophylactic intubation in these patients is catastrophic loss of the airway, especially during transport. Thus, cotton ties (0.5-inch umbilical “tape”), rather than adhesive tape, is used to secure the endotracheal tube circumferentially around the patient’s neck. Second, the tube may become obstructed in patients with copious mucus production. This may be prevented by frequent (hourly or more) suctioning.

The presence of concomitant skin burns compounds airway swelling and increases the risk of airway obstruction. While II directly damages the airway, cutaneous thermal injury causes generalized edema throughout the body, including the airway. In fact, Zak et al. showed that some children with scald injuries and no II whatsoever required endotracheal intubation, in particular when age <2.8 years and burn size >19% of the total body surface area (TBSA) (3).

In adults, we recommend prophylactic endotracheal intubation for burn patients with greater than 40% TBSA burns until the resuscitation period is complete (first 48 hours)—even when II is absent.

Not all patients with smoke exposure require endotracheal intubation. Of 96 patients with isolated II (no skin burns) from a subway fire in Korea in 2003, only 7 were intubated (4). In another retrospective study, of 41 patients who underwent fiber optic laryngoscopy (FOL), 8 were intubated. Soot in the mouth, facial burns, body burns, edema of the true vocal cords, and edema of the false vocal cords were associated with the decision to intubate (5). FOL can be used as a screening tool in a multiple-casualty incident (6). In questionable cases, we recommend awake transnasal FOL as a quick way of assessing laryngeal patency. We use a bronchoscope for this purpose as it also permits evaluation of the subglottic airway (see following discussion).

Tracheostomy

Whether and when to perform tracheostomy for patients with II continues to be debated. In a 1989 report, there were 74 deaths among 99 patients who underwent tracheostomy—including 7% due to lost airway and 4% to massive hemorrhage (7). More recently, in a retrospective review of 38 burned children, tracheostomy was performed a mean of 3.9 days after admission. Indications included expectation of prolonged ventilation (63%), acute respiratory distress syndrome (ARDS, 13%), or partial occlusion of endotracheal tube (24%). The operation led to improvements in compliance and in oxygenation ($\text{PaO}_2\text{-to-FiO}_2$ ratio, PFR). Twenty-three were performed through neck burns. There were no surgical site infections, tracheostomy-related deaths, or tracheal stenoses (8). In another retrospective study, 98 burned children underwent mechanical ventilation for at least 7 days (mean 19.7 ventilator days). Two of these required tracheostomy. At a mean follow-up time of 2.9 years, subglottic stenosis was noted in only one patient (9). In a prospective trial in adult burn patients, an early predictor of ventilator dependence was used to select patients for study. Then patients were randomized to early tracheostomy (day 4, $n = 21$) or tracheostomy if still intubated at two weeks (day 15, $n = 23$). There was no difference in length of stay, ventilator days, survival, or pneumonia (10). In brief, in both adults and children, the route of intubation seems less important than avoidance of high peak inspiratory pressures and high cuff pressures. Our practice is to perform tracheostomy at 14 days for those patients who remain ventilator-dependent. The principal caveat is that earlier tracheostomy may be necessary for pulmonary toilet. Facilitating pulmonary toilet may be life-saving in patients with severe II when they begin to slough the airway mucosa, bleed into the airway, and form obstructing clots and casts; this may begin within a few days of injury.

We and others frequently perform bedside percutaneous tracheostomy in these patients (11). However, caution should be employed when considering the percutaneous route for patients with copious purulent or bloody secretions, as may be the case in severe II. For these patients, open tracheostomy may be safer.

Answer: Early prophylactic airway control is indicated for most symptomatic patients with II and for patients with extensive burns during initial resuscitation (Grade C

recommendation). Tracheostomy is an option for long-term airway management and may facilitate pulmonary toilet (Grade C recommendation).

WHAT DIAGNOSTIC PROCEDURES SHOULD BE PERFORMED IN PATIENTS WITH SUSPECTED II?

Definitive diagnosis of the presence or absence of II before transferring a patient to a burn center is not necessary; it is sufficient to identify the patient at risk for airway and breathing problems and to protect the airway. For this purpose, FOL, history and physical, and carboxyhemoglobin levels (if available) suffice. Mechanism of injury, signs, symptoms, and physical examination provide clues to the presence of II but not diagnostic certainty. Shirani et al. in a retrospective study of 1,058 patients, 373 of whom had II by fiber optic bronchoscopy (FOB) and/or xenon-133 lung scans, generated the following equation to predict the presence of II:

$$P(\text{II}) = e^k / (1 - e^k),$$

where $k = -4.4165 + 1.61$ (closed space)
 $+ 1.77$ (facial burn) $+ 0.0237$ (TBSA, %)
 $+ 0.0268$ (age, years).

P ranges from 0 to 1; values for closed space and facial burn are 0 (absent) or 1 (present). In other words, patients with a history of injury in a closed space, facial burns, large burn sizes, and/or advanced age are more likely to have II (1). Other historical clues to diagnosis include loss of consciousness at the fire scene and the presence of noxious fumes at the fire. In Clark et al.'s retrospective review of the presenting symptoms of 805 patients with burns and II (12), classic signs of airway obstruction (stridor, voice change, dyspnea) were frequently absent.

FOB

FOB has been called a gold standard for the diagnosis of II (13). Several authors have developed grading schemes for severity of injury based on FOB that may correlate with outcome (14–16). FOB may disclose hyperemia, edema, necrosis, pallor, varying amounts of carbonaceous material (soot) in the airways, copious or no secretions, and/or progressive sloughing of the mucosa. Finally, FOB may be falsely negative if performed immediately after injury in patients with burn shock. A repeat FOB 24–48 hours later may be more revealing (17).

Imaging

Aside from FOB, radiographic and nuclear medicine techniques have been used to diagnose II. Most patients with II have a normal chest radiograph on initial presentation. The percentage of abnormal initial radiographs in patients with II ranges from 8% to 73% in various retrospective series. Thus, a normal chest radiograph cannot be used to rule out II (12,18–21). Bronchial thickening, perivascular fuzziness or cuffing, alveolar or interstitial pulmonary edema, consolidation, and atelectasis have been reported.

Other imaging technologies used to diagnose II include computed tomography (CT) scans (12,22–24), Xe-133 ventilation scans (17,25–27), and aerosolized technetium-99m complexed to diethylenetriaminepentaacetate

(Tc-99m-DPTA) scans (28,29). These methods are mainly used as research tools.

Answer: A presumptive diagnosis of II and a decision to transfer to a burn center can be made on clinical grounds, but definitive diagnosis requires FOB and/or advanced imaging techniques (Grade B recommendation).

WHAT MODE OF MECHANICAL VENTILATION IS MOST EFFECTIVE FOR PATIENTS WITH II?

Despite the acute respiratory management in acute respiratory distress syndrome (ARMA) trial conducted by ARDSnet, which showed that lower tidal volumes are associated with improved survival, this question is unanswered; ARMA excluded patients with burns in excess of 30% TBSA (30). There is reason to believe that the ARMA results may not be fully applicable to patients with II. The principal cause of hypoxemia in ARDS induced by pulmonary contusion, systemic injury, or sepsis is alveolar flooding and an increase in true shunt. In II chemical damage to the small airways predominates and causes an increase in ventilation-perfusion mismatch manifested by an increase in blood flow to poorly ventilated lung segments (31). As small airways obstruction progresses, atelectasis followed by consolidation and pneumonia ensue. Thus, treatment of II patients, in contrast to other forms of ARDS, should focus not only on avoiding ventilator-induced lung injury but also on actively providing pulmonary toilet and recruiting and stabilizing collapsed alveoli.

This is the rationale for the use of high-frequency percussive ventilation by means of the Volumetric Diffusive Respiration (VDR-4) ventilator (Percussionaire, Sandpoint, ID). This device is different from high-frequency jet or oscillation ventilators. It combines both subtidal, high-frequency (e.g., 400–1,000 breaths per minute) and tidal, low-frequency (e.g., 0–20 breaths per minute) ventilation. With the VDR-4, gas exchange at lower peak and mean airway pressures occurs as a result of a variety of mechanisms, including more turbulent flow and enhanced molecular diffusion (32,33). Unique to the VDR-4, the high-frequency, flow-interrupted breaths effect dislodgement of debris and cause its retrograde expulsion out of the airways. For this reason, we partially deflate the endotracheal tube cuff (to a minimal leak level) and frequently suction the oropharynx, as plugs and secretions in II patients can be copious. Finally, VDR-4, like airway-pressure release ventilation (APRV, also known as bilevel ventilation), enables spontaneous ventilation throughout the inspiratory and expiratory phases. In most cases, this improves patient-ventilator synchrony, and as in APRV may have other beneficial effects on gas distribution and respiratory muscle strength. The chief disadvantage of the VDR-4 is the extra training required of nurses and respiratory therapists in its operation.

Cioffi and colleagues described 54 II patients treated with VDR-4 during 1987–90 and compared observed mortality and pneumonia rates to those predicted by data from the recent past, in which conventional ventilation was employed (12–15 ml/kg tidal volumes). The VDR-4 was associated with a reduction in mortality from 43% (predicted) to 19% (observed) and with a reduction in pneumonia from 46% (predicted) to 26% (observed) (34). Rodeberg and colleagues used VDR-4 as salvage therapy

for 48 thermally injured pediatric patients and noted that VDR-4 was more effective than conventional volume-control ventilation at performing gas exchange at lower peak airway pressures (35). Reper et al. randomized 35 burn patients to VDR-4 or conventional ventilation on admission and observed increased PFRs in the VDR-R group (36). Carman et al. also conducted an RCT in which 64 thermally injured children were randomized to VDR-4 or pressure-control ventilation. VDR-4 improved PFR at lower peak airway pressures (37). Most recently, Hall and colleagues retrospectively compared 92 patients with II treated with the VDR-4 to 130 well-matched concurrent patients with II treated with conventional ventilation. VDR-4 was associated with a significant decrease in mortality in those patients with burn size less than 40% TBSA (38).

The publication by Cioffi et al. led to our adopting the VDR-4 for treatment of II patients at the U.S. Army Burn Center. Future studies should be prospective and adequately powered to detect differences in mortality (33). Currently, we are conducting a prospective, randomized trial of VDR-4 versus low-tidal-volume conventional ventilation in burn patients requiring mechanical ventilation.

Answer: In comparison to conventional mechanical ventilation, high-frequency percussive ventilation improves ventilation and oxygenation in patients with II and may reduce pneumonia and mortality (Grade C recommendation).

WHAT DRUGS AND FLUID MANAGEMENT STRATEGIES, IF ANY, IMPROVE OUTCOME IN PATIENTS WITH II?

Patients with isolated II rarely have prodigious fluid resuscitation requirements. It is well known, however, that the addition of II to cutaneous burns greatly increases the fluid resuscitation requirements during the first 48 hours postburn (39). In one study, patients resuscitated with the modified Brooke formula (which predicts 2 ml/kg/TBSA burned as the lactated Ringer's dose for the first 24 hours actually received over 5 ml/kg/TBSA burned (40). Efforts to anticipate this response by starting patients out on higher infusion rates are likely to result in increased complications of volume overload (41). On the other hand, fluid restriction does not protect the lungs or improve outcome. For example, Herndon and coauthors demonstrated an increase in lung lymph flow (indicating increased microvascular permeability) in fluid-restricted sheep with combined II and burns (42). Thus, resuscitation of patients with combined II and burns should be conducted with close attention to providing neither too much nor too little fluid by hourly attention to endpoints, such as the urine output.

Inhaled Heparin

Despite research that has greatly improved our understanding of the pathophysiology of II (43), pharmacologic options for II treatment remain limited. Inhaled heparin is one important addition. Desai et al. reported a reduction in reintubation rates and in mortality (from 19% to 4%) in burned children treated with inhaled heparin and N-acetylcysteine in comparison with recent historical controls (44). On the other hand, Holt and colleagues reviewed their experience with inhaled heparin and N-acetylcysteine in adults with II.

There were no differences in ventilator days or mortality between those who received it and those who did not (45). The divergent results of the two studies may be due to the fact that children, with smaller airways and endotracheal tubes, are more vulnerable to airway obstruction (46). Because obstructing clots and casts are a common life-threatening problem after II, and because this therapy is inexpensive and does not cause systemic anticoagulation, we routinely provide nebulized heparin to all II patients, beginning on admission and continuing as long as they are intubated and the airways remain friable. Traber's group has taken this concept a step further in their ovine model of combined burn and II, providing both intravenous recombinant human antithrombin (ATIII) and inhaled heparin. This resulted in not only improved lung function and reduced airway obstruction but also decreased edema and inflammation. These provocative data suggest that ATIII, in addition to enhancing airway patency in combination with heparin, also exerts anti-inflammatory effects (47).

Other Drugs

Inhaled nitric oxide, by improving blood flow to well-ventilated lung segments, modestly improves oxygenation following II (48). In a case series, Sheridan et al. noted an improvement in PFR of 28% and a decrease in pulmonary arterial pressure of 8% after 24 hours of inhaled nitric oxide in patients with burns and II (49). Although RCTs of inhaled NO in this patient population are not available, we deliver it, if necessary, via the VDR-4 ventilator to occasional patients with severe oxygenation failure (50).

Previously, intravenous corticosteroids were often used to treat patients with II. Levine and colleagues conducted an RCT in which intravenous dexamethasone was compared to placebo. There was no difference in mortality or in pulmonary complications (51). In a review of survivors of two Las Vegas hotel fires with isolated II, the use of intravenous dexamethasone did not influence ARDS or pneumonia rates (52). Because pneumonia is the most common cause of death in patients with burns and II (1,53), the immunosuppressive effects of corticosteroids are to be avoided except in those patients who are adrenally insufficient or who (rarely) have refractory bronchospasm. Bronchodilators such as albuterol, with or without N-acetylcysteine, are routinely given to intubated II patients.

Prophylactic antibiotics have not been shown to prevent infection in II or burn patients. Especially when hospitalized for weeks to months, these patients are at risk of colonization and infection with multiple-drug-resistant organisms; this risk increases with indiscriminant antibiotic exposure. On the other hand, they are also at high risk for pneumonia, which greatly increases postburn mortality (1,54). Compounding the problem is the fact that burn injury alone causes a hyperdynamic systemic inflammatory response syndrome, characterized by many of the same signs and symptoms of sepsis. Thus, elevated temperature or white blood cell count do not correlate well with systemic infection (55), and other clinical indicators (e.g., hyperglycemia, tachypnea, tube-feeding intolerance) must be sought. Early institution of broad spectrum antibiotics, an aggressive diagnostic approach to include bronchoalveolar lavage, and rapid tailoring of the regimen to match organism sensitivities are crucial.

Answer: Fluid resuscitation of patients with II should be carefully titrated to physiologic endpoints, such as adequacy of urine output (range 30–50 ml/hour in adults), avoiding both fluid excess and fluid restriction (Grade C recommendation). Inhaled heparin may prevent obstructing clots and casts in patients with II at low risk and cost (Grade C recommendation).

WHAT IMMEDIATE TREATMENTS ARE SAFE AND EFFECTIVE FOR METABOLIC ASPHYXIACTION BY CARBON MONOXIDE OR CYANIDE?

Along with smoke, patients may inhale compounds that impair oxygen delivery to or utilization by the tissues. Chief among these is carbon monoxide (CO). CO is produced by the partial combustion of carbon-containing compounds such as cellulose (e.g., wood, paper, coal, charcoal), natural gases (methane, butane, propane), and petroleum products. CO poisoning is a common cause of death at fire scenes (56,57), and is a leading cause of non-fire-related fire deaths in the United States (58). In addition to combining with hemoglobin to form carboxyhemoglobin (COHb) with an affinity 200 times that of oxygen, CO also impairs mitochondrial function and causes brain injury by pathways involving oxidative stress, inflammation, and excitatory amino acids (59). The organs most vulnerable to CO poisoning are those most affected by oxygen deprivation, namely, the cardiovascular system and the brain. Currently, the diagnosis requires measurement of arterial COHb levels using a coximeter; the PaO_2 in these patients is frequently normal or high, and a standard two-wavelength pulse oximeter will falsely provide a high SpO_2 reading even with COHb levels in the lethal range ($\geq 50\%$), because it cannot discriminate between COHb and oxygenated hemoglobin (60). The half-life of COHb is a function not of the FiO_2 but of the PaO_2 , which in II patients may be quite variable even at an FiO_2 of 100%. In one retrospective study of 240 patients, the COHb half-life of patients treated with 100% oxygen was 74 minutes $\pm$ 25 SD (range 26–148 minutes) (61).

The mainstay of treatment is 100% oxygen by nonrebreather mask or endotracheal tube until the COHb level is less than 5% (62) or for 6 hours (63). Controversy surrounds the use of hyperbaric oxygen therapy (HBOT) to treat these patients. Although HBOT accelerates the clearance of CO beyond that achieved by 100% oxygen at one atmosphere, the main rationale is prevention of a delayed neurocognitive syndrome. This features memory loss and other cognitive defects with onset 2–28 days after exposure and is thought to be caused by binding of CO to brain mitochondrial cytochromes and by other mechanisms (63,64). In an important RCT, Weaver and colleagues provided HBOT to symptomatic patients with COHb exposure, consisting of three treatments over 24h, beginning less than 24 h after exposure. There was a decrease in the neurocognitive syndrome from 46% to 25% at six weeks. Of note, COHb levels were normal by the time of HBOT in these patients (65). Loss of consciousness and higher COHb levels ($\geq 25\%$) were factors associated with successful HBOT, that is, prevention of the syndrome (66). The Cochrane group reviewed six RCTs of HBOT for prevention of neurological sequelae. Four studies showed no benefit, two did show benefit, and the pooled analysis showed no benefit. Because of design flaws, and so on, they concluded that the efficacy of HBOT in this setting

is uncertain (67). The American College of Emergency Physicians published a clinical policy in 2008 stating that Level C data support HBOT as an “option” in CO poisoning and that its use is not mandated (68).

In the special case of the patient with burns, II, and CO poisoning, there is almost no evidence concerning the use of HBOT. Heimbach and colleagues described a case series of 10 such patients treated with HBOT. Several significant problems complicated HBOT: aspiration, seizures, progressive hypovolemia, and so on. This experience points to the difficulty inherent in transporting hemodynamically unstable patients with burn shock and II to an HBOT chamber and providing care in the chamber. Furthermore, the data suggest that HBOT for prevention of delayed neurocognitive syndrome need not begin until the 23rd hour after exposure (69). Consequently, we do not routinely provide HBOT to patients during resuscitation from burn shock.

Cyanide

Hydrogen cyanide (CN) is produced by the combustion of materials such as plastics, foam, paints, wool, and silk. It impairs cellular utilization of oxygen by binding to the terminal cytochrome on the electron transport chain, causing lactic acidosis, and potentially elevated mixed venous oxygen saturation. The half-life in the human body is about one hour.

The role of CN in fire deaths and the prevalence of CN poisoning in patients with II is less clear than that of CO. In their review of 364 fire deaths in New Jersey, Barillo et al. found that 195 (55%) had lethal COHb levels ($\geq 50\%$), whereas 31 (9%) had lethal CN levels (i.e., $>3\text{ mg/L}$). Only 8 (2%) had high CN and low COHb levels (56). On the other hand, Baud et al. obtained CN and COHb levels at the scene of residential fires in Paris. The mean CN level in 66 II patients who lived was $21.6\text{ }\mu\text{mol/L}$ (0.6 mg/L), and in 43 who died it was $116\text{ }\mu\text{mol/L}$ (3 mg/L). CN was linearly correlated with COHb and with plasma lactate. Plasma lactate levels above 10 mmol/L were a sensitive indicator of a toxic CN level $>40\text{ }\mu\text{mol/L}$ (1 mg/L) (70). Thus, CN may be a significant factor in a variable percentage of II patients.

Diagnosis of CN poisoning is difficult because a rapid assay is not available; CN and CO poisoning share many features, including signs and symptoms related to the central nervous and cardiovascular systems (71). Three types of antidote are available for CN. The Cyanide Antidote Kit in the United States contains amyl nitrite for inhalation, and sodium nitrite and sodium thiosulfate for IV injection. The nitrites oxidize hemoglobin to methemoglobin, which chelates CN. Sodium thiosulfate combines with CN to form thiocyanate, which is excreted in the urine. We do not recommend the use of nitrites in patients with II and suspected CN poisoning. They can cause severe hypotension and the methemoglobin does not transport oxygen (72). This is problematic, particularly in patients with burn shock and impaired oxygen transport and utilization from CO and CN. Certainly, nitrites should not be used in II victims without knowledge of the COHb and methemoglobin levels (73). Sodium thiosulfate is a safer alternative, but the onset is slow (74).

Recently, hydroxocobalamin (a form of vitamin B12) has become available in the United States as the Cyanokit for IV injection. This drug is well tolerated and rapidly chelates CN. A prospective uncontrolled observational trial in Paris documented a 67% survival rate in 69 II patients

with decreased mental status and $CN \geq 39 \mu\text{mol/L}$ who received hydroxocobalamin at the fire scene. No side effects were attributed to the antidote (75). Although we recognize that most studies demonstrate CN toxicity in a minority of II patients, now that a safe and effective antidote to CN is available we believe it would be reasonable to administer hydroxocobalamin IV to II patients with signs and symptoms suggestive of CN poisoning, such as persistent lactic acidosis, unexplained loss of consciousness, and so on (71).

Methemoglobinemia

Methemoglobinemia is another life-threatening syndrome of metabolic asphyxiation that is rarely seen in II patients. Certain smoke constituents, such as nitric oxide (NO) and nitrogen dioxide (NO_2), oxidize hemoglobin to methemoglobin (MetHb), a species that is incapable of carrying oxygen. This problem may also be caused by several drugs, including nitrites, or topical anesthetics such as benzocaine. As with COHb, a two-wavelength pulse oximeter cannot distinguish MetHb and falsely gives SpO_2 readings in the 80s. Patients with high levels of MetHb may have chocolate brown-colored blood and, if light-skinned, central cyanosis. Diagnosis is by cooximetry, and treatment consists of IV methylene blue, preferably in consultation with a poison control center or similar (76).

It is likely that COHb, CN, and/or MetHb act additively such that toxicity occurs at lower individual levels when more than one toxin is present. However, there are limited data on such combined effects (77).

Answer: Cooximetry (measurement of COHb and MetHb levels) should be performed in patients with II (Grade D recommendation). One hundred percent oxygen should be given to all patients with known or suspected COHb poisoning until the COHb is normal (less than 5%) (Grade D recommendation). HBOT is an option for patients with COHb poisoning for prevention of the delayed neurocognitive syndrome (Grade C recommendation). Hydroxocobalamin treatment should be considered for patients with known or suspected cyanide poisoning (Grade C recommendation).

SHOULD PATIENTS WITH II BE TRANSFERRED TO A BURN CENTER?

II is one of the American Burn Association criteria for burn center referral (78). Although we are not aware of

prospective data comparing the outcomes of II patients treated in burn centers versus those treated elsewhere, many of the modalities mentioned in this chapter are not routinely available outside of burn centers—including, most important, the expertise of respiratory therapists and other health care professionals with the experience to provide optimal care to patients with this highly lethal injury. Certainly, smoke-exposed patients with an unremarkable physical examination, alert mental status, and normal blood gases and COHb levels may safely be discharged home (79). For all those II patients requiring admission, we recommend at a minimum prompt consultation with the regional burn center.

Answer: Consultation with the regional burn center should be performed on admission of a patient with II (Grade D recommendation).

CONCLUSION

The advances described in this chapter, along with general improvements in the care of burn patients, have resulted in a significant reduction in mortality following II since the 1942 Coconut Grove fire (80). Still, II remains a significant independent predictor of postburn death (81). A recent American Burn Association State of the Science symposium identified four priorities for II research: (1) diagnosis and grading of severity of injury, (2) therapeutics (mechanical ventilation, extracorporeal life support, drugs, role of tracheostomy), (3) long-term outcomes, and (4) basic science mechanisms (82). Randomized, controlled, multicenter trials, in particular, are needed to address these unsolved issues.

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Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Long-term airway management	2002, 2004	8–10	IV	C	Both endotracheal intubation and tracheostomy may be equally safe for long-term airway management.
Diagnosis of II	2004, 2007	14, 15	IIb	B	Fiber optic bronchoscopy permits diagnosis of II and grading of severity.
Best mode of mechanical ventilation	1991, 2007	34, 38	IIIb	C	High-frequency percussive ventilation may reduce pneumonia and mortality in II.
Pharmacologic therapy	1998, 2008	44, 45	IIIb	C	Inhaled heparin may improve outcome in II.
HBOT for carbon monoxide	2005	67	IIa(–)	C	HBOT may reduce incidence of delayed neurocognitive syndrome. Role in burn patients undefined.
Antidote for cyanide	2007	75	II	C	Hydroxocobalamin is safe and may be effective for CN poisoning in II.

Abbreviations: HBOT, hyperbaric oxygen therapy; II, inhalation injury.

REFERENCES

- Shirani KZ, Pruitt BA Jr, Mason AD Jr. The influence of inhalation injury and pneumonia on burn mortality. *Ann Surg* 1987; 205: 82–7.
- Tredget EE, Shankowsky HA, Taerum TV, et al. The role of inhalation injury in burn trauma. A Canadian experience. *Ann Surg* 1990; 212: 720–7.
- Zak AL, Harrington DT, Barillo DJ, et al. Acute respiratory failure that complicates the resuscitation of pediatric patients with scald injuries. *J Burn Care Rehabil* 1999; 20: 391–9.
- Cha SI, Kim CH, Lee JH, et al. Isolated smoke inhalation injuries: acute respiratory dysfunction, clinical outcomes, and short-term evolution of pulmonary functions with the effects of steroids. *Burns* 2007; 33: 200–8.
- Madnani DD, Steele NP, de Vries E. Factors that predict the need for intubation in patients with smoke inhalation injury. *Ear Nose Throat J* 2006; 85: 278–80.
- Goh SH, Tiah L, Lim HC, et al. Disaster preparedness: experience from a smoke inhalation mass casualty incident. *Eur J Emerg Med* 2006; 13: 330–4.
- Jones WG, Madden M, Finkelstein J, et al. Tracheostomies in burn patients. *Ann Surg* 1989; 209: 471–4.
- Palmieri TL, Jackson W, Greenhalgh DG. Benefits of early tracheostomy in severely burned children. *Crit Care Med* 2002; 30: 922–4.
- Kadilak PR, Vanasse S, Sheridan RL. Favorable short- and long-term outcomes of prolonged translaryngeal intubation in critically ill children. *J Burn Care Rehabil* 2004; 25: 262–5.
- Saffle JR, Morris SE, Endelman L. Early tracheostomy does not improve outcome in burn patients. *J Burn Care Rehabil* 2002; 23: 431–8.
- Gravvanis AI, Tsoutsos DA, Iconomou TG, et al. Percutaneous versus conventional tracheostomy in burned patients with inhalation injury. *World J Surg* 2005; 29: 1571–5.
- Clark WR, Bonaventura M, Myers W. Smoke inhalation and airway management at a regional burn unit: 1974–1983. Part I: diagnosis and consequences of smoke inhalation. *J Burn Care Rehabil* 1989; 10: 52–62.
- Anonymous. Evidence-based surgery. *J Am Coll Surg* 2003; 196: 306–12.
- Endorf FW, Gamelli RL. Inhalation injury, pulmonary perturbations, and fluid resuscitation. *J Burn Care Res* 2007; 28: 80–3.
- Chou SH, Lin SD, Chuang HY, et al. Fiber-optic bronchoscopic classification of inhalation injury: prediction of acute lung injury. *Surg Endosc* 2004; 18: 1377–9.
- Bingham HG, Gallagher TJ, Powell MD. Early bronchoscopy as a predictor of ventilatory support for burned patients. *J Trauma* 1987; 27: 1286–8.
- Hunt JL, Agee RN, Pruitt BA Jr. Fiberoptic bronchoscopy in acute inhalation injury. *J Trauma* 1975; 15: 641–9.
- Hantson P, Butera R, Clemessy JL, et al. Early complications and value of initial clinical and paraclinical observations in victims of smoke inhalation without burns. *Chest* 1997; 111: 671–5.
- Teixidor HS, Rubin E, Novick GS, et al. Smoke inhalation: radiologic manifestations. *Radiology* 1983; 149: 383–7.
- Wittram C, Kenny JB. The admission chest radiograph after acute inhalation injury and burns. *Br J Radiol* 1994; 67: 751–4.
- Lee MJ, O'Connell DJ. The plain chest radiograph after acute smoke inhalation. *Clin Radiol* 1988; 39: 33–7.
- Park MS, Cancio LC, Batchinsky AI, et al. Assessment of severity of ovine smoke inhalation injury by analysis of computed tomographic scans. *J Trauma* 2003; 55: 417–27.
- Koljonen V, Maisniemi K, Virtanen K, et al. Multi-detector computed tomography demonstrates smoke inhalation injury at early stage. *Emerg Radiol* 2007; 14: 113–16.
- Gore MA, Joshi AR, Nagarajan G, et al. Virtual bronchoscopy for diagnosis of inhalation injury in burnt patients. *Burns* 2004; 30: 165–8.
- Moylan JA Jr, Wilmore DW, Mouton DE, et al. Early diagnosis of inhalation injury using 133 xenon lung scan. *Ann Surg* 1972; 176: 477–84.
- Agee RN, Long JM III, Hunt JL, et al. Use of ¹³³xenon in early diagnosis of inhalation injury. *J Trauma* 1976; 16: 218–24.
- Schall GL, McDonald HD, Carr LB, et al. Xenon ventilation-perfusion lung scans. The early diagnosis of inhalation injury. *JAMA* 1978; 240: 2441–5.
- Clark WR, Grossman ZD, Ritter-Hrncirik C, et al. Clearance of aerosolized ^{99m}Tc-diethylenetriaminepentaacetate before and after smoke inhalation. *Chest* 1988; 94: 22–7.
- Lin WY, Kao CH, Wang SJ. Detection of acute inhalation injury in fire victims by means of technetium-99m DTPA radioaerosol inhalation lung scintigraphy. *Eur J Nucl Med* 1997; 24: 125–9.
- Anonymous. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med* 2000; 342: 1301–8.
- Shimazu T, Yukioka T, Ikeuchi H, et al. Ventilation-perfusion alterations after smoke inhalation injury in an ovine model. *J Appl Physiol* 1996; 81: 2250–9.
- Krishnan JA, Brower RG. High-frequency ventilation for acute lung injury and ARDS. *Chest* 2000; 118: 795–807.
- Salim A, Martin M. High-frequency percussive ventilation. *Crit Care Med* 2005; 33: S241–S245.
- Cioffi WG Jr, Rue LW III, Graves TA, et al. Prophylactic use of high-frequency percussive ventilation in patients with inhalation injury. *Ann Surg* 1991; 213: 575–82.
- Rodeberg DA, Housinger TA, Greenhalgh DG, et al. Improved ventilatory function in burn patients using volumetric diffusive respiration. *J Am Coll Surg* 1994; 179: 518–22.
- Reper P, Wibaux O, Van Laeke P, et al. High frequency percussive ventilation and conventional ventilation after smoke inhalation: a randomised study. *Burns* 2002; 28: 503–8.
- Carman B, Cahill T, Warden G, et al. A prospective, randomized comparison of the Volume Diffusive Respirator vs conventional ventilation for ventilation of burned children. 2001 ABA paper. *J Burn Care Rehabil* 2002; 23: 444–8.
- Hall JJ, Hunt JL, Arnoldo BD, et al. Use of high-frequency percussive ventilation in inhalation injuries. *J Burn Care Res* 2007; 28: 396–400.
- Navar PD, Saffle JR, Warden GD. Effect of inhalation injury on fluid resuscitation requirements after thermal injury. *Am J Surg* 1985; 150: 716–20.
- Lund T, Goodwin CW, McManus WF, et al. Upper airway sequelae in burn patients requiring endotracheal intubation or tracheostomy. *Ann Surg* 1985; 201: 374–82.
- Pruitt BA Jr. Protection from excessive resuscitation: "Pushing the pendulum back" [editorial; comment]. *J Trauma* 2000; 49: 567–8.
- Herndon DN, Traber DL, Traber LD. The effect of resuscitation on inhalation injury. *Surgery* 1986; 100: 248–51.
- Cancio LC. Current concepts in the pathophysiology and treatment of inhalation injury. *Trauma* 2005; 7: 19–35.
- Desai MH, Mlcak R, Richardson J, et al. Reduction in mortality in pediatric patients with inhalation injury with aerosolized heparin/N-acetylcysteine therapy. *J Burn Care Rehabil* 1998; 19: 210–12.
- Holt J, Saffle JR, Morris SE, et al. Use of inhaled heparin/N-acetylcysteine in inhalation injury: does it help? *J Burn Care Res* 2008; 29: 192–5.

46. Zak AL, Harrington DT, Barillo DJ, et al. Acute respiratory failure that complicates the resuscitation of pediatric patients with scald injuries [see comment]. *J Burn Care Rehabil* 1999; 20: 391-9.
47. Enkhbaatar P, Esehie A, Wang J, et al. Combined anticoagulants ameliorate acute lung injury in sheep after burn and smoke inhalation. *Clin Sci (Lond)* 2008; 114: 321-9.
48. Ogura H, Saitoh D, Johnson AA, et al. The effect of inhaled nitric oxide on pulmonary ventilation-perfusion matching following smoke inhalation injury. *J Trauma* 1994; 37: 893-8.
49. Sheridan RL, Hurford WE, Kacmarek RM, et al. Inhaled nitric oxide in burn patients with respiratory failure. *J Trauma* 1997; 42: 629-34.
50. Cancio LC, Galvez E Jr, Jordan BS, et al. Delivery of nitric oxide by high-frequency percussive ventilation: system design and evaluation. *Clin Intensive Care* 2006; 17: 41-8.
51. Levine BA, Petroff PA, Slade CL, et al. Prospective trials of dexamethasone and aerosolized gentamicin in the treatment of inhalation injury in the burned patient. *J Trauma* 1978; 18: 188-93.
52. Robinson NB, Hudson LD, Riem M, et al. Steroid therapy following isolated smoke inhalation injury. *J Trauma* 1982; 22: 876-9.
53. Cancio LC, Reifenberg L, Barillo DJ, et al. Standard variables fail to identify patients who will not respond to fluid resuscitation following thermal injury: brief report. *Burns* 2005; 31: 358-65.
54. Edelman DA, Khan N, Kempf K, et al. Pneumonia after inhalation injury. *J Burn Care Res* 2007; 28: 241-6.
55. Murray CK, Hoffmaster RM, Schmit DR, et al. Evaluation of white blood cell count, neutrophil percentage, and elevated temperature as predictors of bloodstream infection in burn patients. *Arch Surg* 2007; 142: 639-42.
56. Barillo DJ, Goode R, Esch V. Cyanide poisoning in victims of fire: analysis of 364 cases and review of the literature. *J Burn Care Rehabil* 1994; 15: 46-57.
57. McGwin G Jr., Chapman V, Rousculp M, et al. The epidemiology of fire-related deaths in Alabama, 1992-1997. *J Burn Care Rehabil* 2000; 21: 75-3.
58. Anonymous. Carbon monoxide-related deaths—United States, 1999-2004. *MMWR Weekly* 2007; 56: 1309-12.
59. Thom SR. Hyperbaric-oxygen therapy for acute carbon monoxide poisoning. *N Engl J Med* 2002; 347: 1105-6.
60. Hampson NB. Pulse oximetry in severe carbon monoxide poisoning. *Chest* 1998; 114: 1036-41.
61. Weaver LK, Howe S, Hopkins R, et al. Carboxyhemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. *Chest* 2000; 117: 801-8.
62. Ilano AL, Raffin TA. Management of carbon monoxide poisoning. *Chest* 1990; 97: 165-9.
63. Piantadosi CA. Carbon monoxide poisoning. *N Engl J Med* 2002; 347: 1054-5.
64. Piantadosi CA, Sylvia AL, Jobsis-Vandervliet FF. Differences in brain cytochrome responses to carbon monoxide and cyanide in vivo. *J Appl Physiol* 1987; 62: 1277-84.
65. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med* 2002; 347: 1057-67.
66. Weaver LK, Valentine KJ, Hopkins RO. Carbon monoxide poisoning. Risk factors for cognitive sequelae and the role of hyperbaric oxygen. *Am J Respir Crit Care Med* 2007; 176: 491-7.
67. Juurlink DN, Buckley NA, Stanbrook MB, et al. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database of Systematic Reviews* 2005; 1: CD002041.
68. Wolf SJ, Lavonas EJ, Sloan EP, et al. Clinical policy: critical issues in the management of adult patients presenting to the Emergency Department with acute carbon monoxide poisoning. *Ann Emerg Med* 2008; 51: 138-52.
69. Grube BJ, Marvin JA, Heimbach DM. Therapeutic hyperbaric oxygen: help or hindrance in burn patients with carbon monoxide poisoning? *J Burn Care Rehabil* 1988; 9: 249-52.
70. Baud FJ, Barriot P, Toffis V, et al. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med* 1991; 325: 1761-6.
71. Baud FJ. Cyanide: critical issues in diagnosis and treatment. *Hum Exp Toxicol* 2007; 26: 191-201.
72. Hall AH, Kulig KW, Rumack BH. Suspected cyanide poisoning in smoke inhalation: complications of sodium nitrite therapy. *J Toxicol Clin Exp* 1989; 9: 3-9.
73. Kirk MA, Gerace R, Kulig KW. Cyanide and methemoglobin kinetics in smoke inhalation victims treated with the cyanide antidote kit. *Ann Emerg Med* 1993; 22: 1413-18.
74. Dart RC. Hydroxocobalamin for acute cyanide poisoning: new data from preclinical and clinical studies; new results from the prehospital emergency setting. *Clin Toxicol* 2006; 44: 1-3.
75. Borron SW, Baud FJ, Barriot P, et al. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. *Ann Emerg Med* 2007; 49: 794-801.
76. Hoffman RS, Sauter D. Methemoglobinemia resulting from smoke inhalation. *Vet Hum Toxicol* 1989; 31: 168-70.
77. Levin BC, Rechani PR, Gurman JL, et al. Analysis of carboxyhemoglobin and cyanide in blood from victims of the Dupont Plaza Hotel fire in Puerto Rico. *J Forensic Sci* 1990; 35: 151-68.
78. Anonymous. Guidelines for the operation of burn centers. In: *Resources for Optimal Care of the Injured Patient*. Chicago: Committee on Trauma, American College of Surgeons, 2006, 79-86.
79. Mushtaq F, Graham CA. Discharge from the accident and emergency department after smoke inhalation: influence of clinical factors and emergency investigations. *Eur J Emerg Med*; 11: 141-4.
80. Rue LW III, Cioffi WG, Mason AD, et al. Improved survival of burned patients with inhalation injury. *Arch Surg* 1993; 128: 772-80.
81. Cancio LC, Galvez E Jr., Turner CE, et al. Base deficit and alveolar-arterial gradient during resuscitation contribute independently but modestly to the prediction of mortality after burn injury. *J Burn Care Res* 2006; 27: 289-96.
82. Palmieri TL. Inhalation injury: research progress and needs. *J Burn Care Res* 2007; 28: 549-54.

Electrical, Cold, and Chemical Injuries

Stephanie A. Savage

Evidence Based Data for Electrical, Cold and Thermal Injuries		
Question	Answer	Grade of recommendation
Do all patients with electrical injury require continuous cardiac monitoring?	Patients with high-voltage injuries or a history of loss of consciousness, arrhythmia, or abnormal electrocardiogram at admission require monitoring.	B
What are the key prompts for upper arm fasciotomy after electrical injury?	Neurovascular compromise, increased compartment pressures, and persistent myonecrosis are indications for decompression.	C
What is the most effective method of rewarming following cold injury?	Rewarming should wait until there is no further risk of freezing, and rate depends on severity of injury.	C
What role do thrombolytics play in salvaging tissues damaged by the cold?	Thrombolytics should be reserved for those with a poor response to rewarming and evidence of diminished perfusion.	C
What is the role of endoscopy in managing patients with caustic ingestion?	Endoscopy should be reserved for symptomatic patients or those attempting suicide.	C
Is there any role for exogenous agents to prevent esophageal stricture after caustic ingestion?	Data on steroids are mixed; other agents may be useful but require more study.	B

INTRODUCTION

Traumatic injury to tissues is a common occurrence, and sequelae may range from the relatively benign to major functional alterations to death. By far the most common mechanisms include motor vehicle crashes, falls, gunshot wounds, and stabbings. Less common causes of injury can frequently be more difficult to treat, due to the lack of familiarity with the disease process, potential complications, and long-term derangements. Injuries resulting from electrical, cold, and chemical exposures fall into the latter category. In cases such as these, evidence-based medicine is a sound foundation on which to base practice decisions.

ELECTRICAL INJURIES

Electrical injuries account for 3–5% of burn unit admissions annually with a mortality rate approaching 40% (approximately 1,000 deaths annually) (1–3). Age distribution tends to be bimodal with the majority of injuries occurring in young children, from accidental contact with power sources, and in adults (3). In adult patients, electrocutions occur preferentially as a work-related injury, with electricians, line men, and construction workers displaying the most frequent occurrence. Due to gender distribution in these trades, occurrence favors males in their fourth and fifth decade (4–5).

Electrical injuries may be especially challenging for the trauma or burn surgeon to treat because external evidence of injury (entrance and exit wounds) frequently grossly under-represent the true extent of tissue damage. The severity of injury is determined by the magnitude of energy delivered, the resistance to current flow, duration of contact with the electric source, and the pathway through which the current travels (6–7). Mechanisms of tissue injury are varied and contribute to the difficulty of caring for these patients. The direct effect of the electric current on the tissue, especially cardiac, may result in asystole, ventricular fibrillation, or apnea, in cases of respiratory muscle spasm. Electrical current may be converted to thermal energy resulting in burns. Arcing, the transition of current across a charged space, may throw a patient, resulting in blunt injuries from falls. Tetanic contractions of muscles may also lead to fractures and the blunt disruption of soft tissues (1,8). At a cellular level, three major mechanisms can result in cellular death. Joule heating literally results in “frying” of tissues and disrupts the lipid bilayer. Electroporation, a process used in laboratories to introduce DNA into cells, causes the formation of temporary pores in the lipid bilayer. The influx of charged particles, especially calcium, can alter membrane gradients and lead to cellular apoptosis. Electroconformational denaturation results in a change in orientation of proteins that result in denaturation (3). All of these processes occur with electrical injury contributing

to tissue injury and death at the microscopic and macroscopic level.

Does Every Patient with an Electrical Injury Require a Comprehensive Cardiac Evaluation with Inpatient Monitoring?

With potential of injury to such varied systems as cardiac, respiratory, nervous, renal, ocular, and skeletal systems, many management conundrums arise. The pool of evidence-based data in the case of electrical injuries is primarily Grade II and III data. One of the most vexing questions in the care of patients who have been electrocuted is determining who needs admission with cardiac monitoring due to ongoing risk of potentially lethal arrhythmias. Due to uneven distribution of cardiac injury from current, with dead cells next to viable ones, cardiac manifestations of electrical injury may include arrhythmias and conduction abnormalities (1,9–10). In evaluating patterns of myocardial injury, horizontal current flows (as seen with entry in one hand and out the other) more commonly result in arrhythmias. Vertical current flow (for example, from head to toe as with a lightning strike) frequently causes direct myocardial damage. Low-voltage injuries are more likely to result in ventricular fibrillation, as opposed to asystole more commonly seen with high-voltage injuries (1). These are merely patterns, however, and each injury varies by patient and current factors. Patterns may be useful in guiding evaluation and treatment decisions.

In choosing who requires more intensive monitoring, a provider must determine whether a patient even requires admission. Low-voltage injuries, as expected, have a lesser rate of serious injury. If patients exposed to a low-voltage electric injury have no evidence of injury, discharge from the emergency room is a reasonable option (11). Purdue and Hunt proposed a series of criteria to determine whether patients require admission following electrical injury. These criteria include loss of consciousness at the scene or cardiac arrest in the field, a documented cardiac arrhythmia in the field, an abnormal electrocardiogram (ECG) (with broad criteria extending as far as bradycardia or tachycardia), or a separate indication for admission (11). However, the need for admission does not mandate continuous cardiac monitoring. Bailey, Gaudreault, and Thivierge looked at 134 patients presenting to 21 emergency departments over the course of four years. This study provided continuous cardiac monitoring to patients with specific risk factors, including a transthoracic current pathway, history of tetany related to the event, loss of consciousness, or an electricity source of greater than 1,000 volts. They determined that for low-voltage injuries, patients presenting in a normal sinus rhythm were unlikely to develop an arrhythmia related to the electrical injury during that hospital stay. Therefore, patients who were asymptomatic and had a normal ECG were candidates for discharge (6). A small Canadian study from 2005 looked at 10 patients with electrocutions deemed to be severe [electrocution and Injury Severity Score (ISS) >12]. They determined that all patients with documented circulation at the scene of injury survived to discharge, and none of the patients who presented in asystole survived to discharge, including one patient successfully resuscitated at the scene (4). Finally, Blackwell and Hayllar looked at 212 consecutive patients presenting to an Australian hospital

with low-voltage electrical injury. They detected no late rhythm abnormalities in patients who originally had normal ECGs. Much like Bailey and colleagues, the Australian group recommended continuous cardiac monitoring of patients with a history of loss of consciousness, documented arrhythmia, or abnormal ECG at presentation (12).

Cardiac enzyme panels [creatinine kinase (CK), CK-MB isoenzyme, and troponin] are commonly used in the inpatient setting to detect myocardial injury secondary to infarction. Is there any role for cardiac enzyme evaluation in electrical injuries? CK levels are frequently elevated in electrical injury due to diffuse muscle damage and therefore are not a very sensitive method by which to detect cardiac injury. Indeed, the average CK level following an electrical burn is 18,900 IU and is more useful in monitoring for rhabdomyolysis. As an entire panel, the cardiac enzymes are generally deemed not helpful in detecting myocardial injury or in evaluating for the risk of late arrhythmias (1,11).

Answer: The need for further monitoring depends on voltage and presenting complaints (Grade B evidence).

Based on the current evidence, the majority comprising Grade B data, recommendations for the management of electrical injuries include the following points. Low-voltage (<1,000 V) electrocutions with no history of arrhythmia and a normal ECG at presentation may be discharged without further evaluation. High-voltage injuries and/or those with abnormal ECG, a history of arrhythmia, or other indications for admission should be monitored with telemetry. Further evaluation then depends on the patient's symptoms.

What Is the Preferred Method to Monitor the Upper Extremities Following Electrocution, and What Are Key Prompts for Fasciotomy?

Management of upper extremity electrical burns is very common, as one or both hand(s) is typically the site of entry for the current. Alternating current sources, such as those routinely found in residential electrical injuries, can lead to tetanic contractions. Tetany may prevent release from the electrical source, resulting in a worse direct injury to contact site (hands) as well as systemically (5). Unfortunately, despite the frequent involvement of upper extremities, standard treatment algorithms are not common.

As with compartment syndromes for lower extremities or circumferential burns, standard signs of compartment syndrome should raise suspicion regarding the upper extremities. Entrance or exit wounds on the hands or arms and elevated CK levels should be the first clue. Class IIa evidence indicates that progressive neurologic dysfunction, evidence of vascular compromise, increased compartment pressures, and systemic deterioration from progressive myonecrosis are indications for decompressive fasciotomy. As in lower extremities, compartment pressures greater than 30 are also prompts for fasciotomy. Decompression should include both assessments of muscle viability as well as carpal tunnel release (11).

Mann et al. presented Class IIb evidence in the *Journal of Trauma* in 1996 to guide management of high-voltage injuries to the upper extremities. This algorithm proposed selective surgical management versus early aggressive surgical decompression. By using clinical variables such as

neurologic deterioration and general clinical deterioration due to worsening myonecrosis, the authors limited emergency decompression (within the first 24 hours) to 25.8% of severe upper extremity burns. Furthermore, the ultimate total amputation rate in this group was limited to 10% versus 45% in a series involving immediate decompression for all severe upper extremity burns. Mann et al. also noted that none of their amputations were related to missed injuries secondary to delayed exploration (13). Important to note is that a management algorithm, such as the one above, requires extremely close observation in a burn intensive care unit. Additional adjuncts such as Doppler evaluation or perfusion scans may add useful information but should not be relied upon to diagnose patients requiring decompression (11).

Answer: Decompression should be used selectively in upper extremity electrocutions (Grade C evidence).

Patients with severe upper extremity electrical injuries should not be decompressed merely as a matter of course. Rather, these patients should be admitted to a burn intensive care unit and monitored for progressive myonecrosis or neurologic compromise. In these specific cases, fasciotomies should include evaluation for muscle viability and carpal tunnel release.

COLD INJURIES

Frostbite is an old problem, especially in eras where adequate heating or protection from the elements was not the norm. Most at risk are two opposing groups of patients, the homeless and outdoor enthusiasts of winter sports. Vretenar et al. identified risk factors for cold injury. These include alcohol use, a history of psychiatric illness, vehicular trauma or failure, and drug abuse (14–15). Additional patient factors that may exacerbate injury include atherosclerotic disease, smoking, diabetes mellitus (due to risk of peripheral vascular disease), and a history of prior cold-related tissue injury (16). Men have a greater rate of cold-related injury with incidence approaching 10:1 (male:female), with men ages 30–49 most commonly affected. Injuries preferentially affect regions away from the core, where heat conservation occurs. Areas of frequent injury include the digits and hands, feet, nose, and ears (16).

Frostbite represents a more severe degree of tissue injury that typically leads to necrosis and some degree of tissue loss. As freezing of the tissues occurs, ice crystals form in extracellular fluids. These crystals damage cell membranes, resulting in altered concentration gradients with abnormal cellular electrolyte concentrations. Further temperature decreases result in intracellular ice crystal formation and cell death. Direct tissue freezing is not the only source of cell death, however. Endothelial injury and local tissue edema from the release of inflammatory mediators leads to occlusion of small vessels and sludging within vessels. Interruption of oxygen delivery also clearly results in tissue ischemia (16).

The degree of tissue loss is often hard to delineate at the time of the injury. Traditionally, frostbite has been described on a scale of first through fourth degree, similar to descriptive methods used to describe burn injuries. These classifications are impossible to make before rewarming occurs, and typically complete delineation of necrotic tissue

is not apparent until days to weeks later. A less specific but more accurate grading system is simply classifying frostbite wounds as superficial (encompassing first and second degree) or deep (third and fourth degree). Murphy et al. note this system to be more accurate at predicting clinical outcome than the degree system (16).

Hypothermia is the most life-threatening of the cold injury disorders, despite the lack of obvious external injury as seen in frostbite. As patients progress from mild hypothermia (32–35°C) to severe hypothermia (<28°C), systemic sequelae increase. Hypothermia causes decreased cardiac contractility. Combined with relative volume depletion due to fluid sequestration and cellular crystallization, patients with hypothermia experience decreased cardiac output and shock, which easily transitions to cardiac arrest. Additionally, hypothermia contributes to cardiac irritability, often resulting in intractable arrhythmias during attempts to resuscitate patients. Hypothermia leads to vasoconstriction and endothelial injury with sludging and vessel thrombosis. Cold diuresis results from inhibition of antidiuretic hormone and cold-induced glycosuria, further contributing to volume depletion (17). A further illustration of the deleterious effects of hypothermia can be seen with a modern example in the least obvious of locales. Reports of the impact of hypothermia on trauma patients from Operation Iraqi Freedom have emerged from military hospitals. These observational studies have found that lesser degrees of hypothermia are more deleterious than hypothermia found in the nontrauma civilian cohort. Arthurs et al. reclassified hypothermia in the military trauma subset and noted that hypothermia in trauma patients in-theater was an independent risk factor for the need for operative therapy. Clearly hypothermia is a component of the deadly triad, which includes acidosis and coagulopathy, and frequently results in mortality in trauma patients. In the report by Arthurs et al., they noted that no patient presenting to the 31st Combat Support Hospital with a temperature <32°C survived (18).

What Is the Most Effective Method of Rewarming, for Various Cold Injuries, to Preserve Tissue Viability and Function?

The obvious answer to the many threatening sequelae of cold injury is rewarming. The majority of evidence regarding rewarming following cold injury is Grade C or D. In cases of frostbite, warming should be accomplished as rapidly as possible in a water bath. Some authors recommend truly rapid rewarming, with 40–42°C water baths the most efficient in achieving tissue salvage (17). Only rewarming halts ice crystal formation, which contributes to cell death in frostbite. The most important aspect of rewarming, as noted in multiple citations, however, is that it should not occur until there is no further potential of refreezing. Refreezing may convert damaged but viable tissue more easily to frankly ischemic tissue (16–17,19–22). Rapid and repeated freeze-thaw cycles promote inflammatory response, resulting in increased production of arachidonic acid and thromboxane. These tenets are borne out by Grade B data from the 1980s. Aspiration of fluid blisters demonstrated high levels of inflammatory mediators, including prostaglandin F_{2α} and thromboxane B₂ (23). Limiting freeze-thaw cycles will limit production of these inflammatory mediators. However,

improved tissue survival and decreased amputation was demonstrated by Heggers et al. with the use of anti-inflammatory agents such as methimazole, aloe vera, aspirin, and methylprednisolone (24).

Hypothermia as a form of cold injury also mandates rapid rewarming as the primary modality of therapy. Because inappropriate rewarming can lead to reperfusion injury, it is important to minimize this risk while avoiding the pitfalls that accompany a hypothermic state—namely, cardiac irritability, respiratory depression, acidosis, and coagulopathy. Class IIb data using a swine model investigated the optimal rate of rewarming to improve outcome. In this uncontrolled hemorrhage model, optimal rewarming (defined as survival without significant neurological deficit) was achieved at 0.5°C/min (19). To this end, adjuncts may include active external methods, such as forced heated-air systems, simple active internal warming with heated intravenous fluids and warmed oxygen, or more complex internal warming with warmed gastric and cystic lavage (17). Cardiopulmonary bypass is the most aggressive option for rewarming in profoundly unstable patients (25). Vretenar et al. used cardiopulmonary bypass in 68 patients with core temperatures less than 28°C (61 were in cardiac arrest). The Level IIb data indicated 60% survival with the use of bypass with 32 patients having no neurologic sequelae (15).

Answer: Rewarming should wait until there is no further risk of freezing. The rate of rewarming depends on the severity of the injury (Grade C evidence).

Rewarming should not occur until there is no further risk of refreezing. For hypothermic patients, active rewarming to achieve a rate of 0.5°C/min is ideal. Cardiopulmonary bypass should be reserved for the profoundly hypothermic or in patients with cardiac manifestations. When used promptly, however, patients may achieve good neurologic outcomes.

What Is the Role of Thrombolytics in Salvaging Tissues Damaged via Cold Exposure?

The use of blood-thinning agents and thrombolytics is the area of most vigorous research in cold injury. Hypothermia contributes to intravascular sludging, which impairs delivery of oxygen and nutrients. During thaw cycles, endothelial damage may also contribute to thrombosis of small vessels resulting in tissue ischemia and necrosis (17). Most convincing is the Level IIb data from Twomy and colleagues in 2005. This group looked at 19 patients with severe frostbite who failed to improve with standard initial therapy of rapid rewarming and had no evident Doppler signal or perfusion on technetium-99m bone scan. Patients received either intravenous or intra-arterial tissue plasminogen activator (tPA) plus heparin. Of 174 digits deemed to be at risk, only 33 (19%) ultimately required amputation. Two patients developed bleeding complications (bleeding from an arterial puncture site and hematuria) and required cessation of therapy (11%) (22). A retrospective review (Level IV data) from Bruen et al. in 2007 found similar results. In this small series of patients, those receiving tPA therapy had a 10% amputation rate, whereas those treated without tPA had a digit amputation rate of 41% (20). tPA was delivered just proximally from the site of loss of perfusion, though Twomy et al. demonstrated equal efficacy with intra-arterial and intravenous infusion (20,22).

Answer: Thrombolytics should be reserved for those with poor response to rewarming and evidence of decreased perfusion (Grade C evidence).

Rapid rewarming is the mainstay of therapy for frostbite. In those with a poor response to rewarming who have evidence of diminished perfusion, the use of thrombolytics (in the form of tPA) with heparin should be considered, if there is no known bleeding risk.

CHEMICAL INJURIES

Injuries from chemical exposures are not common in the United States. The group at most routine risk for a caustic burn includes laborers. Examining work-related burn injuries from 1995 to 2004, only 5.8% of burns were chemical in nature as opposed to 45.8% electrical burns and 39.6% thermal burns (17). Despite the very serious nature of work-related chemical burns, with morbidity and loss of productivity, caustic ingestions are a far more common source of chemical burn seen by the emergency room and surgeons. Included in the category of accidental caustic burns seen routinely in hospitals would be those to the pulmonary system due to aspiration pneumonitis. Caustic ingestion occurs in a bimodal age distribution, and the severity of injury is often linked to the reason behind the ingestion. Caustic ingestions are seen frequently in young children who may mistake household cleaning items for beverages. Conversely, in adults, the most common cause of caustic ingestion is during a suicide attempt.

Overall, caustic ingestions in adults tend to be more severe due to the motivation of attempted suicide (26). These patients typically may ingest larger volumes and not seek evaluation for prolonged periods. The extent of tissue damage depends on multiple factors, including the type of agent (alkali or acid), the physical properties of the agent, agent concentration, duration of the contact, and volume of substance ingested (27–30). Solutions with a pH <2 or >12 tend to be highly corrosive, and solid or powdered forms may be more damaging due to the tendency to adhere to the mucosal surface (26). Alkali ingestion results in liquefactive necrosis with thrombosis of small vessels and local heat production compounding the injury. In a similar fashion, acids cause liquefactive necrosis with eschar formation. By four to seven days following the injury, mucosal sloughing begins. This allows the potential for bacterial invasion with a robust inflammatory response and deposition of granulation tissue. Tensile strength of tissue is low for the first three weeks and the inflammatory response and tissue sloughing renders tissues weakened starting at 48 hours. This increases the likelihood of perforation. Scar formation, which may begin as early as the second week following surgery, may result in esophageal shortening. A shortened esophagus has altered pressures at the lower esophageal sphincter, allowing increased acid reflux, which may exacerbate injuries (26).

Caustic ingestions in children are quite variable in degree of severity. Accidental ingestions are seen more commonly in developing countries, where household cleaners and other chemicals may be stored in reused containers, thereby leading children to think the contents are potable. Twenty-six percent of children with accidental ingestions

are ultimately found to have severe lesions and 1–5% of children with accidental ingestions ultimately develop a stenosis (30).

What Is the Optimal Role of Endoscopy in Evaluating and Treating Patients with Caustic Ingestions?

The degree of esophageal injury (though the stomach may be involved, too) is assessed with endoscopy and graded on a scale of 0–IIIb (27,30). With such a variability in degree of injury, how to best use endoscopy to manage these patients is an issue. The primary concern during endoscopy is not in detecting perforation, which may be diagnosed with other modalities, but in differentiating none to mild injury from severe injury, which then influences management. In a retrospective cohort study of 50 patients with caustic ingestions from 1988 to 2003 in Israel, the overall rate of stricture formation was 10%. However, patients with third-degree esophageal injuries had a 71% rate of stricture formation (27). In a series of 48 pediatric patients reported in Level IIb evidence from France, 26% of patients with accidental ingestions had severe lesions. However, this study found that all patients at risk for stenosis with severe lesions presented with symptoms (30). Predictive symptoms have included hematemesis and respiratory distress, however, no particular symptom was predictive of increased severity of esophageal lesion and thus risk of stenosis.

In light of these findings, children with accidental caustic ingestions who present asymptomatic likely do not require endoscopy and should merely be monitored. Due to intent to harm, all suicidal ingestions and patients presenting with symptoms should receive endoscopy for evaluation. Endoscopy should occur within the first 48 hours because after this time point, tensile strength is decreased and the risk of iatrogenic perforation increases (26). Additionally, endoscopy should not proceed past circumferential burns due to the increased risk of perforations at these points. Further evaluation of the gastrointestinal tract may occur with a barium study if necessary. Patients who are found to be free of injury may be immediately discharged. Subsequent management of patients with injury will depend on patient condition, injury severity, and physician practice. Though the use of nasogastric tubes to stent the esophagus and injury sites has been promulgated, some evidence indicates this may actually promote stricture formation. Zargar et al., in a prospective endoscopic evaluation of 81 patients with corrosive esophageal burns, determined that all patients with Grade 0–IIa burns recovered without sequelae. Further, approximately three-fourths of patients with IIb burns and all those with Grade IIIa and IIIb injuries ultimately developed esophageal stricture. These authors postulated that early resection of the most severe injuries (Grade IIIb) may improve outcome as defined by morbidity and mortality (31).

Answer: Endoscopy should be reserved for symptomatic patients or for ingestions secondary to suicidal intent (Grade C Evidence).

The majority of the evidence in caustic injuries falls somewhere within the realm of Grade C data. Endoscopy clearly has a role in the management of patients with caustic ingestions and should be used routinely for symptomatic patients or those with ingestion due to suicide

attempt. Results of endoscopy can then be used to determine prognosis and formulate a management plan.

Is There any Role for Exogenous Agents to Limit Damage After Chemical Ingestion or Aspiration Pneumonitis?

In light of the potentially serious effects of caustic damage to the esophagus and related organs, including the lungs, the obvious question is whether any intervention may mitigate or prevent negative long-term outcomes of these ingestions. The most commonly used modality to prevent stricture formation is steroids. Although some animal models have indicated a potential benefit, evidence in human subjects is mixed. A meta-analysis retrospective review of 361 patients with corrosive esophageal injury found a stricture rate of 19% in patients treated with steroids (40–60 mg/day intravenous) and antibiotics versus 40% stricture rate in those not receiving steroids (32). However, a randomized control trial of 60 children suffering caustic ingestions and treated with steroids (2 mg/kg/day intravenous) versus no steroids found no decrease in stricture rate with the use of steroids (33). The only firm recommendation regarding the use of steroids in caustic ingestion patients is that antibiotics should be given concurrently with steroids to mitigate the immunosuppressive effect (26).

In an effort to develop agents that may prevent the formation of esophageal stricture without the detrimental issues of immunosuppression and decreased tissue strength, some research effort has been turned to halofuginone. Halofuginone is an alkaloid plant derivative that has been demonstrated to be effective in suppression of collagen synthesis and inhibition of collagen type 1 α gene expression. In a prospective, randomized control trial of 11 rats, Arbell et al. demonstrated a 73% esophageal patency rate in animals treated with halofuginone (delivered orally) as compared to 11% patency in untreated controls. Though obviously limited to a small study population, the results are thought-provoking. Indeed, halofuginone has been routinely used in veterinary practice for caustic ingestions, so the use in humans has potential with further study (34). Finally, animal protocols exist demonstrating decreased stricture formation with the use of such adjuncts as heparin, epidermal growth factor, sucralfate, and caffeic acid phenethyl ester. Though no human evidence exists with these substances, they show promise as a new direction of study (30).

Finally, though typically not secondary to accidental or purposeful ingestion, caustic injury secondary to aspiration pneumonitis is an intensive care unit challenge that continues to plague clinicians. Following aspiration, one-third of patients will develop severe pulmonary symptoms, and up to 22% are at risk of acute respiratory distress syndrome (ARDS) with the associated morbidity and mortality. Aspiration may result in a profound inflammatory response, with activation of cytokines including tumor necrosis factor (TNF) α , interleukin-1, and interleukin-8. Attempts to modulate the development of ARDS increasingly focus on anti-inflammatory agents and immunomodulators. Pawlik et al. examined the role of pentoxifylline, which inhibits the release of TNF α , in limiting the development of ARDS following aspiration. In this animal model ($n = 24$), animals receiving pentoxifylline had significantly improved oxygenation, less atelectasis, and less evidence

of inflammation on computed tomography than animals in the untreated group. Mortality was also significantly less in the treated group. These results are directly opposite to findings in the ARDSnet trial using lisofylline, a pentoxifylline derivative. However, method of drug administration and ventilatory methods were quite different between the studies, making direct comparison between them studies difficult (35).

Answer: Steroids may be helpful when given with antibiotics, though data are mixed. Other promising agents require more study (Grade B evidence).

Adjuncts minimize the formation of esophageal stricture are less defined. The most evidence exists regarding the use of steroids, though significant morbidities may occur. Nevertheless, if steroids are incorporated, they should be

used in conjunction with antibiotics. Additional agents are promising in animal studies but require more analysis in human trials.

CONCLUSION

Injuries secondary to electricity, cold exposure, and caustic ingestions are uncommon. Subsequent to this, the library of evidence-based data is somewhat limited. As with all injuries, the most effective management is prevention. However as discussed in this chapter, there are a variety of topics undergoing scientific investigation. The results, as outlined, should be used to guide decision making and management when these injuries are encountered.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Findings
Cardiac monitoring	2005	4	IIIb	Patients with vitals at the scene primarily survive to discharge.
Cardiac monitoring	2007	6	IIIa	In low-voltage injuries, normal ECG at admission make subsequent dysrhythmia unlikely.
Cardiac monitoring	1986	10	IIIb	Monitoring after high-voltage injury should be based on loss of consciousness, documented arrhythmia, or abnormal ECG.
Cardiac monitoring	2006	11	IIa	All patients with electrical injury should receive an ECG. Low-voltage injuries with normal ECG, consider discharge.
Cardiac monitoring	2002	12	IIb	Asymptomatic patients with normal ECGs do not require cardiac monitoring.
Upper extremity management	2006	11	IIa	Decompression should be prompted by neurologic dysfunction, vascular compromise, increased compartment pressures, and systemic myonecrosis.
Upper extremity management	1996	13	IIIa	Decompression should be chosen if the patient is symptomatic. Routine decompression leads to greater tissue loss.
Rewarming	2006	19	IIb	Long-term survival and function is influenced by rate of reversal of profound hypothermia.
Rewarming	1981	23	IIIb	Frostbite injury is in part due to inflammatory mediators, as seen in frostblister fluid.
Thrombolytics in frostbite	2005	22	IIb	tPA and heparin in selected patients is safe and reduces rate (versus predicted) of digit amputation.
Thrombolytics in frostbite	1987	24	IIb	Progressive dermal ischemia in frostbite may be diminished by the use of inflammatory inhibitors.
Endoscopy and caustic ingestion	2001	30	IIb	Endoscopy is not recommended for asymptomatic children after caustic ingestion.
Endoscopy and caustic ingestion	1991	31	IIb	Early endoscopy is a safe and reliable diagnostic tool.
Agents to prevent chemical injury	1992	32	IIa	Steroids may be useful in preventing strictures in patients with second- and third-degree esophageal injury.
Agents to prevent chemical injury	1990	33	IIb	Steroids have no effect in children; development of stricture after caustic ingestion related to severity of injury.
Agents to prevent chemical injury	2005	34	IIb	Halofuginone increases esophageal patency and animal survival after caustic injury in rats.
Agents to prevent chemical injury	2005	35	IIb	Pentoxifylline given after aspiration pneumonitis improves oxygenation and survival if administered in a set manner.

Abbreviations: ECG, electrocardiogram; tPA, tissue plasminogen activator.

REFERENCES

- Sples C, Trohman RG. Narrative review: electrocution and life-threatening electrical injuries. *Ann Intern Med* 2006; 145: 531–7.
- Maghsoudi H, Adyani Y, Ahmadian N. Electrical and lightning injuries. *J Burn Care Res* 2007; 28: 255–61.
- Tuttnauer A, Mordzynski SC, Weiss YG. Electrical and lightning injuries. *Contemp Crit Care* 2006; 4: 1–10.
- Laupland KB, Kortbeek JB, Findlay C, et al. Population-based study of severe trauma due to electrocution in the Calgary health region, 1996–2002. *Can J Surg* 2005; 48: 289–92.
- Fordyce TA, Kelsh M, Lu ET, et al. Thermal burns and electrical injuries among electric utility workers, 1995–2004. *Burns* 2007; 33: 209–20.
- Bailey B, Gaudreault P, Thivierge R. Cardiac monitoring of high-risk patients after an electrical injury: a prospective multicentre study. *Emerg Med J* 2007; 24: 348–52.

7. Part 10.9: electric shock and lightning strikes. *Circulation* 2005; 112(Suppl IV): 154–5.
8. Li M, Hamilton W. Review of autopsy findings in judicial electrocutions. *Am J Forens Med Pathol* 2005; 26: 261–7.
9. Pham TN, Gibran NS. Thermal and electrical injuries. *Surg Clin N Am* 2007; 87: 185–206.
10. Purdue GF, Hunt JL. Electrocardiographic monitoring after electrical injury: necessity or luxury. *J Trauma* 1986; 26: 166.
11. Arnoldo B, Klein M, Gibran NS. Practice guidelines for the management of electrical injuries. *J Burn Care Res* 2006; 27: 439–47.
12. Blackwell N, Hayllar J. A three year prospective audit of 212 presentations to the emergency department after electrical injury with a management protocol. *Postgrad Med J* 2002; 78: 283–5.
13. Mann R, Gibran N, Engrav L, et al. Is immediate decompression of high voltage electrical injuries to the upper extremity always necessary. *J Trauma* 1996; 40: 584–9.
14. Koljonen V, Andersson K, Mikkonen K, et al. Frostbite injuries treated in the Helsinki area from 1995 to 2002. *J Trauma* 2004; 57: 1315–20.
15. Vretenar DF, Urschel JD, Parott JC, et al. Cardiopulmonary bypass resuscitation for accidental hypothermia [review]. *Ann Thorac Surg* 1994; 58: 895–8.
16. Murphy JV, Banwell PE, Roberts AHN, et al. Frostbite: pathogenesis and treatment. *J Trauma* 2000; 48: 171–8.
17. Biem J, Koehncke N, Classen D, et al. Out of the cold: management of hypothermia and frostbite. *Can Med Assoc J* 2003; 168: 305–11.
18. Arthurs Z, Cuadrado D, Beekley A, et al. The impact of hypothermia on trauma care at the 31st Combat Support Hospital. *Am J Surgery* 2006; 191: 610–14.
19. Alam HB, Rhee P, Honma K, et al. Does the rate of rewarming from profound hypothermic arrest influence the outcome in a swine model of lethal hemorrhage? *J Trauma* 2006; 60: 134–46.
20. Bruen KJ, Ballard JR, Morris SE, et al. Reduction of the incidence of amputation in frostbite injury with thrombolytic therapy. *Arch Surg* 2007; 142: 546–53.
21. McGillion R. Frostbite: case report, practical summary of ED treatment. *J Emerg Nurs* 2005; 31: 500–2.
22. Twomey JA, Peltier GL, Zera RT. An open-label study to evaluate the safety and efficacy of tissue plasminogen activator in treatment of severe frostbite. *J Trauma* 2005; 59: 1350–5.
23. Robson MC, Heggors JP. Evaluation of hand frostbite blister fluid as a clue to pathogenesis. *J Hand Surg (Am)* 1981; 6: 43–7.
24. Heggors JP, Robson MC, Manavalen K, et al. Experimental and clinical observations on frostbite. *Ann Emerg Med* 1987; 16: 1056–62.
25. Chughtai TS, Gilardino MS, Fleiszer DM, et al. An expanding role for cardiopulmonary bypass in trauma. *Can J Surg* 2002; 45: 95–103.
26. Ramasamy K, Gumaste VV. Corrosive ingestion in adults. *J Clin Gastroenterol* 2003; 37: 119–24.
27. Arevalo-Silva C, Eliashar R, Wohlgelernter J, et al. Ingestion of caustic substances: a 15 year experience. *Laryngoscope* 2006; 116: 1422–6.
28. Wedler V, Guggenheim M, Moron M, et al. Extensive hydrofluoric acid injuries: a serious problem. *J Trauma* 2005; 58: 852–7.
29. Mattos GM, Lopes DD, Mamede RCM, et al. Effect of time of contact and concentration of caustic agent on generation of injuries. *Laryngoscope* 2006; 116: 456–60.
30. Lamireau T, Rebouissoux L, Denis D, et al. Accidental caustic ingestion in children: is endoscopy always mandatory? *J Pediatr Gastroenterol Nutr* 2001; 33: 81–4.
31. Zargar SA, Kuchhar R, Mehta S, et al. The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. *Gastrointest Endosc* 1991; 37: 165–9.
32. Howel Dalsey WC, Hartsell FW, et al. Steroids for the treatment of corrosive esophageal injury. A statistical analysis of past studies. *Am J Emerg Med* 1992; 10: 421–5.
33. Anderson KD, Rouse TM, Randolph JG. A controlled trial of corticosteroids in children with corrosive injury of the esophagus. *New Engl J Med* 1990; 323: 637–40.
34. Arbell D, Udassin R, Koplewitz BZ, et al. Prevention of esophageal strictures in a caustic burn model using halofuginone, an inhibitor of collagen type I synthesis. *Laryngoscope* 2005; 115: 1632–5.
35. Pawlik MT, Schreyer AG, Ittner KP, et al. Early treatment with pentoxifylline reduces lung injury induced by acid aspiration in rats. *Chest* 2005; 127: 613–21.

Evidence-Based Wound Care Management

David Sahar and Howard Wang

Clinical Questions in Wound Care Management		
Question	Answer	Grade of recommendation
Factors affecting wound healing?	Infection, hypoxemia, foreign body, radiation	B
Does preoperative smoking affect wound healing?	Yes, it increases risk of infection and ischemia	B
What is mechanism of accelerated wound healing in NPWT?	Decrease edema, increase blood flow, micromechanical forces, removal of effluent and bacteria	B
Does NPWT affect healing time or cost?	It appear to affect healing time, but no strong evidence for cost	B
How does acellular dermal replacement affect wounds in burn and reconstructive surgery?	Acellular dermal replacement decreases hypertrophic scars and contracture. It also reduces donor site morbidity.	B
Is HBO beneficial to ischemic or irradiated flaps?	Although intuitive, there is no convincing evidence that HBO improves survival of ischemic or irradiated flaps	C
What are effective treatments against keloid and hypertrophic scar?	Excision and intralesional triamcinolone injection. Radiation for refractory and selected cases.	B
Abbreviations: HBO, hyperbaric oxygen therapy; NPWT, negative-pressure wound therapy.		

The management of chronic, complicated, and slow-healing wounds is a significant challenge in medicine today. The body's response to acute tissue injury is to minimize morbidity and restore function. Acute injury is followed by overlapping orchestrated molecular and cellular events leading to either complete healing or development of a chronic wound. Healing occurs immediately after inciting injury has occurred through three overlapping phases: inflammatory, proliferative, and maturation phase. Paramount to preparation of wound for healing is adequate debridement. Once large, open wounds are cleared of non-viable tissues, the healing process may be hastened by providing optimal wound environment using several methods depending on the wound size, depth, vascularity, and so on. In the late 1970s and 1980s, the concept of moist wound care became standard treatment as opposed to drying the wound prior to this era. Despite treatment with the best suited wound care products, it may be difficult to heal some chronic wounds. To heal these difficult wounds, advance wound care products, such as negative pressure, hyperbaric oxygen therapy, composite, and interactive wound care products, are used before reconstruction using local, regional, or distant flaps is considered. Many variables play in ensuring a timely wound healing with

minimal complications. Current management of these variables are met with varying levels of evidence.

WHAT ARE COMMON FACTORS ADVERSELY AFFECTING WOUND HEALING?

Infection is a common cause of delayed wound healing. Colonization of bacteria beyond 10^5 per gram of tissue or presence of beta-hemolytic *Streptococcus* induces continued inflammation to clear the wound of infection and result in delayed wound healing (1). Once healed, infected wounds are prone to excessive scarring and keloid formation. Wound hypoxemia, caused by atherosclerosis, wound tension, anemia, or cardiac failure, can impair fibroblast activity when tissue oxygen level is below 35mmHg (2). Smoking causes relative hypoxemia by vasoconstriction and reducing perfusion. Diabetes mellitus thickens capillary basement membranes and decreases wound perfusion microenvironment (3). It also impairs phagocytic function and prolongs inflammation, leading to delayed healing. Ionizing radiation effects G2 through M phase of cell cycle of rapidly dividing cell populations. Albumin levels of $<2\text{g/dl}$ is associated with delayed healing and wound

dehiscence (4). Improving nutrition alone has significant effect in closure of chronic wounds. Old age, mineral deficiency, and certain medications (e.g., doxorubicin) also have detrimental effect on wound healing. Aside from burdening patients and families with managing daily care and causing associated morbidities, chronic open wounds may lead to squamous cell carcinoma (5). Cancer in the context of chronic wound has been described in variety of wounds, including burns, pressure soars, osteomyelitis, venous stasis ulcers, and hidradenitis.

Recommendation: Infection, smoking, diabetes, radiation, and poor nutrition all impact wound healing negatively (Grade B recommendation).

HOW MUCH DOES PREOPERATIVE SMOKING CESSATION AFFECT POSTOPERATIVE WOUND HEALING?

Smoking has long been suspected of negatively impacting the process of wound healing. Even with most advanced technology of today, smoking may delay, complicate, or fail wound healing. Mosely and Finseth for the first time demonstrated the detrimental effect of smoking on healing of hand wounds in 1977 (6). Since that time, the negative effect of smoking on wound healing has been accepted, and patients are routinely advised against smoking, specially perioperatively.

In an attempt to quantify risk of smoking on surgically created wounds, 916 flaps and full-thickness grafts were studied by Goldminz and Bennett (7) in whom some degree of necrosis was present. Current smokers of one pack per day or more were three times more likely to develop necrosis. Former smokers and low-level smokers (less than one pack per day) had no significant increase in necrosis compared to nonsmokers. However, once tissue necrosis developed, the median percent of necrosed area was three times that of a nonsmoker, regardless of number of packs per day smoked.

A randomized clinical trial by Sorensen et al. (8) studied 78 patients studied lateral sacral incisional biopsy sites. After two weeks of observation, the wound infection rate was 12% in smokers and 2% in never-smokers ($p < 0.05$). Wound infection was significantly lower in abstinent smokers compared with continuous smokers.

In a prospective study of 50 patients, Bartsch et al. (9) studied the effect of nicotine on breast reduction. Cotinine, a metabolite of nicotine, was measured in urine of patients preoperatively and on postoperative day 4. Impaired wound healing was noted in 40% of smokers, compared with 16% of nonsmokers. Smokers with higher cotinine concentration were more likely to develop impaired wound healing. Chat et al. (10) studied the affect of smoking abstinence during perioperative period in breast reduction in 173 patients. As expected, smokers were more likely to develop wound healing problems compared with nonsmokers (55.4% versus 33.7%, $p < 0.05$). More important, when they stopped smoking prior to operation, it made a difference. Wound healing impairment in patients who stopped smoking > four weeks prior to operation was 33.3%, in those who stopped < four weeks it was 52.6%, and in those who persisted until the operation it was 67.7%.

Recommendation: Smoking may delay, complicate, or cause failure of wound healing (Grade B recommendation).

WHAT IS THE MECHANISM OF ACCELERATED WOUND HEALING USING SUBATMOSPHERIC PRESSURES?

Evidence in favor of negative-pressure wound therapy (NPWT) has been mounting over the past decade as this mode of therapy has become ubiquitous in hospitals as well as outpatient settings with mobile units. The device consist of polyurethane or polyvinyl alcohol porous open-cell sponge that is applied to the wound and covered with occlusive dressing to sustain negative pressure in the local wound environment. A tube connecting the sponge with a vacuum pump maintains subatmospheric pressure in continuous or intermittent fashion. The sponge dressing is changed approximately every two days until the desired effect is obtained.

A variety of mechanisms of action has been proposed for clinical effects seen on wounds through NPWT. A major mechanism includes reduction of tissue edema and thus improved oxygenation and nourishment of cells (11). However, wounds with minimal fluid excretion have been known to improve in healing with NPWT (12). Studies show an increase in blood flow to the wound with NPWT, which may explain increased rate of granulation tissue formation (13). Given that stretched cells in the presence of growth factors are prone to proliferation and induction of angiogenesis, micromechanical forces on individual wound cells is another possible mechanism of improved wound healing (12,14). Wound effluent, including neutrophil degradation products, which are suctioned out during NPWT, inhibit wound healing, and thus its removal by NPWT would enhance the process of wound healing (15). Drawing soft tissues together may minimize retraction of wound edges and promotion of wound closure (16). Although reducing infectious load has been advocated based on animal studies (13), retrospective human studies is less convincing (17).

Recommendation: The mechanism of action of NPWT is likely multifactorial, including edema reduction, increasing blood flow, mechanical stimulation of cells, reducing inhibitory wound exudates, and potentially reducing bacterial load (Grade B recommendation).

DOES NPWT AFFECT HEALING TIME? IS IT COST-EFFECTIVE?

A review of Cochrane randomized controlled clinical studies by Evans and Land (18) comparing NPWT with standard of care dressing changes in 2001 was an attempt to determine efficacy of NPWT. Endpoints included complete wound healing, rates of change in wound surface area, and percentage of wound healed during study time frame. Of the eight studies, only two met inclusion criteria (19–21) totaling 34 patients. Joseph et al. assessed 24 patients with chronic wounds including pressure, dehiscence, trauma, venous stasis, or radiation wounds. Half of these patients received NPWT with continuous suction (125mmHg) changed every two days, and the other half received standard normal saline dressing changes. This study reported significant reduction in wound volume in NPWT group (78% versus 30%, $p = 0.038$). McCallon et al. assessed only 10 patients with diabetic foot ulcers. Satisfactory healing was obtained sooner with NPWT (22.8 versus 42.8 days).

At an endpoint of two weeks, reduction in wound surface area was noted to have changed greatest with NPWT (28.4% reduction versus 9.55% increase). These studies suffered from poor reporting of statistical analysis, low power and selection, attrition, and performance bias. Reviewers concluded that the data at hand were “weak” evidence in favor of NPWT and need for “well-designed, adequately powered, multi-centre RCTs to evaluate the contribution of (NPWT) to the healing of chronic wounds.”

More recently, randomized clinical trial by Armstrong et al. (21) of 162 patients with diabetic foot ulcers compared patients treated with NPWT and those treated with standard moist dressing. Over a 16-week period, more patients healed in NPWT group (56%) compared with standard therapy group (39%). The rate of wound healing was faster with NPWT as well as granulation tissue formation. Although differences were statistically significant, concerns over this study include low power and funding by manufacturer of the NPWT device. Apelqvist et al. (22) compared resource utilization and direct economical cost of healing diabetic foot wound between NPWT and moist wound therapy. A total of 162 patients were enrolled into a 16-week, multicenter randomized clinical trial. Although there was no difference between NPWT and moist wound therapy in inpatient hospital stays, NPWT fared better in that there were less surgical procedures (120 versus 43, $p < 0.001$), fewer outpatient visits (4 versus 11, $p = 0.044$), and lower costs (\$27,000 versus \$36,000) over an eight-week period in NPWT group. The effect of NPWT on split-thickness skin graft was studied by Moisidis et al. (23). With an endpoint of two weeks, the wounds were blindly examined and revealed improvement qualitatively (appearance) in NPWT, though there was no significant quantitative difference in graft take. However, as authors pointed out, low sample size and no long-term follow-up makes it difficult to extrapolate concrete recommendation from this particular study.

Recommendation: Evidence for NPWT decreasing wound healing time compared to wet to dry dressing exists, but the data are weak. Very few studies currently address the cost-effectiveness of the modality (Grade B recommendation).

HOW DOES ACELLULAR REPLACEMENT DERMIS AFFECT FINAL WOUND HEALING IN BURN AND RECONSTRUCTIVE SURGERY?

Although acellular replacement dermis was initially developed in the 1970s for coverage of burn wounds, its clinical application has widened dramatically in reconstructive surgery. The first use of acellular replacement dermis was reported by Burke et al. in 1981 on 10 burn patients (24). After FDA granting of license to the manufacturer in 1996, the first multicenter trial published in 2003 showed favorable outcome in function and patient satisfaction (25).

The bilayer matrix is a porous matrix of cross-linked bovine tendon collagen and glycosaminoglycan obtained from shark cartilage covered with semipermeable polysiloxane (silicone) layer. The 2-mm-thick collagen-glycosaminoglycan matrix provides a scaffold for dermal

regeneration via cellular invasion and capillary growth through 70–200 μ m pores (26). The silicone layer, which is removed generally in three weeks, controls water vapor loss, provides a flexible adherent covering, and adds strength to the bilayer system.

In the original case series by Burke et al. in 1981, the patients with artificially grafted dermis were described as closely resembling normal skin in palpation, elasticity, softness, and pliability. The conventionally meshed autograft was described to have hypertrophic scars in areas of interstices and feels stiff and thick to palpation without normal skin resilience. Although histologic biopsies of artificially grafted skins were shown to resemble normal skin with a “neodermis,” and the paper describes in detail the technique involved in placing the artificial dermis, the clinical evidence was weak.

Heimbach et al.’s 11-center prospective randomized trial including 139 sites on 106 patients with major burns (27). Acellular replacement dermis was compared with autograft, allograft, xenograft, or a synthetic dressing. Median take was reported to be 80%, compared with median take of all controls of 95%. A learning curve was noted with an improved take in centers reporting more than 10 patients. The donor site thickness mean was less than half in acellular replacement dermis grafts compared to control. Naturally, donor sites healed significantly faster. At the conclusion of the study, there was less hypertrophic scarring of artificial dermis, and more patients and surgeons preferred the artificial dermis to the control graft. Negative feedback from surgeons include second operation, less adequate drainage of serum and blood through the silastic solid sheet, and the seemingly poor resistance of the artificial dermis to infection. A multicenter study involving 216 burn injury patients by the same group confirmed safe and effective treatment modality in the hands of properly trained clinicians in burn centers (25).

A randomized case series of patients with at least 45% burn to body surface area by Peck et al. in 2002 (28) revealed an unusually high rate of infection (100%). The study was terminated early due to this ethical dilemma. Low sample size ($n = 7$) and poor design make it difficult to make conclusions regarding these results. In fact, their first conclusion was that they “lack sufficient experience with the device, and lack of expertise has resulted in failure.” Furthermore, immunosuppression in burns >45% total body surface area was suggested to play a role in contributing to increased rate of infection.

In addition to its utility in acute burn setting, acellular replacement dermis has been increasingly used in contracture release and reconstruction. Given scarcity of full-thickness skin graft for large areas of deep skin defects, dermal regeneration template has been advocated as a substitute for full-thickness skin graft, skin expansion, and even skin flaps in reconstructive surgery. Unfortunately, no randomized clinical trials have been reported to date in reconstructive application of acellular replacement dermis, though several studies examine its utility in this setting.

Dantzer et al. (29) reported their experience with artificial dermis in general plastic surgery as one of the first series. In their series of 31 patients, scar tissues or skin tumor were excised and replaced immediately with the acellular replacement dermis. Ultrathin autograft was

placed over the neodermis three weeks later. In every case, the coverage was described as flexible and nonadherent to deep tissue. Furthermore, the skin was uniform in color and texture. Frame et al. (30) further confirmed the utility of acellular replacement dermis in scar release in a multicenter evaluation retrospective study involving 89 patients and 127 contracture releases. Unfortunately, no control group was included in this study, and results were compared to reported studies on contracture release with split-thickness skin graft, full-thickness skin graft Z-plasty, skin flaps, and tissue expanders. Over three-quarters of the results were considered good or excellent in terms of range of motion or function by physicians. The recurrence rate was 25%, which is significantly better than split-thickness skin graft (62–80%).

Given the benefits of dermal regeneration template in reconstructive surgery and acceleration of wound healing by NPWT, it was only matter of time to combine the two methods to optimize management of deep and complex wounds. A retrospective case series presented by Molnar et al. (31) showed that NPWT applied over acellular replacement dermis would improve take as well as expedite tissue infiltration of the dermal template. In this series of eight patients, the authors used NPWT for an average of 7.25 days (almost 2 weeks less than standard therapy) over the acellular replacement dermis followed by split-thickness graft and reapplication of NPWT for another 4 days. Wounds included exposed bone, joint, and tendon. Acellular replacement dermis take was reported as 95%, and the take of autograft over neodermis was 93%, similar to original reports of Burke et al. Furthermore, splinting was not necessary due to NPWT sponges becoming firm with suction. Jeschke et al. improved artificial dermis take to 98% from 78% ($p = 0.003$) by adding fibrin glue prior to application of the dermal matrix and NPWT. This study also confirmed reduction of time for take (10 days versus 24 days). Thus NPWT combined with acellular replacement dermis would decrease healing time, simplify wound care, and potentially save significant resources.

Recommendation: Acellular replacement dermis appears to decrease hypertrophic scarring and lessening contractures, which benefits both burn surgery as well as reconstructive surgery. Furthermore, acellular replacement dermis allows the use of ultrathin skin grafts, which improves donor site morbidity (Grade B recommendation).

IS HBO THERAPY BENEFICIAL TO ISCHEMIC OR IRRADIATED FLAPS?

Hyperbaric oxygen therapy (HBO) was thought to hasten wound healing as early as 1965 when burns from a coal mine explosion were treated for CO poisoning (32). Although clinical efficacy of HBO has been demonstrated in variety of clinical problems, including diabetic foot ulcers (33), carbon monoxide toxicity (34), gas gangrene (35), and osteoradionecrosis of the mandible (36), definitive evidence supporting use of HBO in improving ischemic and irradiated flaps is less evident.

One of the earliest attempts to study the effect of HBO on ischemic flaps was by Perrins (37) in 1975. In this nonrandomized prospective study, ischemic flaps were treated with HBO between 2.0 and 3.0 atmospheres

of pressure. Of the 150 flaps per year performed in his institution, there was 4.5% failure rate. In contrast, retrospectively in previous five years in the same institution the failure rate was between 8.5% and 11.8%. However, the poor design made this study weak evidence in favor of HBO. Bowersox et al. (38) reviewed HBO for threatened failure of skin flaps between 1976 and 1983. Fifty-five percent were reported to heal completely, and an additional 34% showed marked improvement. Given lack of proper controls, the quality of data is questionable. In a study of 26 patients, Ueda et al. (39) studied effect of HBO on ischemic state of variety of flaps including Abbe, deltopectoral, cervical, sternocleidomastoid, and pectoralis major musculocutaneous flaps. Different surgical treatments and variable onset of treatment makes it difficult to draw conclusion from this data.

Postradiated tissue undergoing reconstruction is at significant risk for wound complications. HBO has been advocated in treatment of postradiated wounds. However, there is a paucity of evidence in favor of using HBO for these flaps. We need more studies to evaluate the role of HBO in breast reconstruction in radiated breasts.

Recommendation: Although HBO has been shown to be effective in a number of settings, there is paucity of convincing evidence for its use in reconstructive surgery. Flaps at risk for ischemia or postradiation continue to be treated with HBO, without any evidence from prospective randomized trials (Grade C recommendation).

WHAT ARE THE CURRENT EFFECTIVE TREATMENTS AGAINST FORMATION OF KELOID AND HYPERTROPHIC SCAR?

Opposite to the nonhealing end of the wound healing spectrum is keloid formation from excessive fibroblast activity and abnormally high collagen deposition. First described by ancient Egyptians (40), it remains a frustrating clinical problem. Normally after full-thickness dermal injury, matrix accumulates and scar forms. Initially the wound enters evolutionary phase marked by increase in height, firmness, and redness. This is followed by stability and finally involutional stage marked by flattening, softness, and paler. Keloid does not follow this normal pattern of wound healing and may develop directly after the initiating event or years from original trauma. Keloid is different clinically and histologically from hypertrophic scars, which exhibit similarities to normal wound healing but with prolonged time course and worse effect on form and function.

Although a variety of treatments are available for keloid and hypertrophic scar management, the mainstay remains to be surgical excision, steroid injection, pressure therapy, and occasionally radiation. Since the first description of surgical excision as a mode of therapy for keloid formation by Druit (41) in 1844, the futility of surgical excision alone has become apparent as initially noted by DaCosta (42) in 1903. Surgical excision alone simply replays the cascade of healing biology that previously led to keloid formation and potentially results in larger keloid. Recurrence rate of 40–100% (43) is expected when simple surgical excision is employed. In 1972, an era when no biological difference between keloid and

normal scar was known, Cosman and Wolff (44) published their results of a study after excision of keloids. Of the 18 patients they followed for an average period of 1.75 years, there were eight recurrences (44%) consistent with current consensus that half of keloids simply excised will recur.

Intralesional steroid injection remains first line of therapy for keloid (45). Although the use of steroids for treatment of keloid was first reported by Conway and Stark (46) in 1951, their systemic route of injection, photographs, and end results obtained did not impress the contemporary surgical community. Intralesional injection of triamcinolone for “dermatoses” was first described by Hollander (47). The frequently cited 1963 report by Murray (48) presented 87 patients treated with triamcinolone. However, he did not differentiate hypertrophic scars from keloid in this study. Overall, in the group treated with triamcinolone injection with excision and triamcinolone ointment massage postoperatively, 82% were reported as good or fair with better outcome in Caucasian population. He achieved similar results by addition of 800 roentgen units of x-ray therapy. In 1966, Griffith reported results of intralesional injection of 37 keloids in 29 patients. Fifty-one percent of keloids completely flattened out, and an additional 40% became much softer. All had relief of symptoms. Lesions that were not completely flattened had 15% recurrence rate on an average follow-up of 10.3 months. Of the 19 keloids that were excised in addition to injected with triamcinolone, he had only one recurrence in a 10–16-month average follow-up. Intralesional injection of triamcinolone was further confirmed by subsequent studies to have greater than 80% efficacy, typically 10 mg per centimeter of incision wound monthly (49–51).

The efficacy of radiation in treatment of keloid has been documented, but its use is limited due to risk of inducing malignancy. Radiation is contraindicated in pediatric populations and pregnant women as well as on sites with underlying visceral structures. In addition to excision, radiation has been shown to have 65–99% efficacy and consistently better than excision alone (52–56).

Other common methods of treatment for keloid include silicone gel and pressure therapy. Silicone gel, a cross-linked polymer of ethylsiloxane, has been shown to be efficacious in treatment of hypertrophic scars (57,58). Silicone gel is placed as a covering layer over wounds for 12–24 hours a day. Results are appreciated after four to six months of application. One study shows superiority of silicone gel over triamcinolone injection in treatment of hypertrophic scars (59). However, this has not been established in keloid treatment. Pressure therapy is a simple and cost-effective method of reducing keloid recurrence to less than 20% (60–65). This effect was shown as early as 1942 by Nason et al. in a controlled trial where recurrence of keloid was reduced from 67 to 18% (66). Other unconventional and less effective methods of keloid management include laser, intralesional injection of 5-fluorouracil, intralesional injection of interferon, topical and intralesional injection of vitamin A and its retinoid derivatives, and many more.

Recommendation: There is evidence in favor of intralesional triamcinolone injection of keloid scars with or without excision as the first line of therapy. Hypertrophic scar maybe managed with silicone gel and pressure therapy initially, though excision and triamcinolone injection maybe needed. Radiation is reserved for selected patient populations with lesions that are refractory to conventional therapy (Grade B recommendation).

Level of Evidence and Reference for Wound Care Management

Subject	Year	Ref.	Level	Strength	Findings
Factors affecting wound healing	1969, 1979, 1994, 2003	1–5	IIB	B	Infection, smoking, diabetes, radiation, and poor nutrition negatively affects wound healing.
Preoperative smoking effect on wound healing	1991, 2003, 2006, 2007	7–10	IIB	B	Smoking may delay, complicate and cause failure of wound healing.
Mechanism of accelerated wound healing in NPWT	1997, 2004, 1997, 2000, 1996, 2001	11–16	IIB	B	Multifactorial: edema reduction, increase blood flow, mechanical stimuli, reduce exudates, decrease bacterial load.
NPWT effect on healing time or cost	2004, 2001, 2000, 2001, 2005, 2008	13, 18–22	IIB	B	NPWT may decrease healing time and potentially cost.
Acellular dermal replacement effect on wounds in burn and reconstructive surgery	2004, 1994, 2003, 2002, 2001, 2004	23–25, 28–30	IIB	B	Acellular dermis decrease hypertrophic scars, lessens contracture in burn scars, and reduces donor site morbidity.
HBO therapy effect on ischemic or irradiated flaps	2000, 1975, 1986	36–38	IIIB	C	No convincing evidence that HBO helps ischemic or irradiate flaps.
Effective treatments against keloid and hypertrophic scar	1844, 1903, 1972, 1963, 1970	41, 42, 44, 47, 51	IIB	B	Excision, intralesional triamcinolone injection, silicone gel/pressure therapy, and radiation.

Abbreviations: HBO, hyperbaric oxygen therapy; NPWT, negative-pressure wound therapy.

REFERENCES

- Robson MC, Hegggers JP. Surgical infection. II. The beta-hemolytic streptococcus. *J Surg Res* 1969; 9: 289–92.
- Hunt TK, Zederfeldt B, Goldstick TK. Oxygen and healing. *Am J Surg* 1969; 118: 521–5.
- Goodson WHD, Hunt TK. Deficient collagen formation by obese mice in a standard wound model. *Am J Surg* 1979; 138: 692–4.
- Hill DP Jr, Cooper DM, Robson MC. Serum albumin is a poor prognostic factor for pressure ulcer healing in controlled clinical trials. *Wounds* 1994; 6: 174–8.
- Trent JT, Kirsner RS. Wounds and malignancy. *Adv Skin Wound Care* 2003; 16: 31–4.
- Mosely LH, Finseth F. Cigarette smoking: impairment of digital blood flow and wound healing in the hand. *Hand* 1977; 9: 97–101.
- Goldminz D, Bennett RG. Cigarette smoking and flap and full-thickness graft necrosis. *Arch Dermatol* 1991; 127: 1012–15.
- Sorensen LT, Karlsmark T, Gottrup F, et al. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. *Ann Surg* 2003; 238: 1–5.
- Bartsch RH, Weiss G, Kästenbauer T, et al. Crucial aspects of smoking in wound healing after breast reduction surgery. *J Plast Reconstr Aesthet Surg* 2007; 60: 1045–9.
- Chan LK, Withey S, Butler PE. Smoking and wound healing problems in reduction mammoplasty: is the introduction of urine nicotine testing justified? *Ann Plast Surg* 2006; 56: 358.
- Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment. Clinical experience. *Ann Plast Surg* 1997; 38: 563.
- Saxena VSM, Hwang C, Huang S, et al. Vacuum-assisted closure: microdeformations of wounds and cell proliferation. *Plast Reconstr Surg* 2004; 114: 1086.
- Morykwas MJ, Argenta LC, Shelton-Brown EI, et al. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg* 1997; 38: 553–62.
- Iwasaki H, Eguchi S, Ueno H, et al. Mechanical stretch stimulates growth of vascular smooth muscle cells via epidermal growth factor receptor. *Am J Physiol Heart, Circ Physiol* 2000; 278: H521–H529.
- Yager Dorne R, Zhang LY, Liang HX, et al. Wound fluids from human pressure ulcers contain elevated matrix metalloproteinase levels and activity compared to surgical wound fluids. *J Invest Derm* 1996; 107: 743–8, 1996.
- Fenn CH, Butler PE. Abdominoplasty wound-healing complications: assisted closure using foam suction dressing. *Br J Plast Surg* 2001; 54: 348–51.
- Weed T, Ratliff C, Drake DB. Quantifying bacterial bioburden during negative pressure wound therapy. *Ann Plast Surg* 2004; 52: 276–80.
- Evans D, Land L. Topical negative pressure for treating chronic wounds. *Brit J Plast Surg* 2001; 54: 238–42.
- Joseph E, Hamori CA, Bergman S, et al. A prospective randomized trial of vacuum assisted closure versus standard therapy of chronic nonhealing wounds. *Wounds* 2000; 12: 60–7.
- McCallon SK, Knight CA, Valiulus JP, et al. The effectiveness of vacuum assisted closure vs. saline moistened gauze in the healing of post-operative diabetic foot wounds. *Adv Wound Care* 2001.
- Armstrong DG, Lavery LA, Diabetic Foot study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet* 2005; 366: 1704–10. <http://www.ncbi.nlm.nih.gov/pubmed/16291063>
- Apelqvist J, Armstrong DG, Lavery LA, et al. Resource utilization and economic costs of care based on a randomized trial of vacuum-assisted closure therapy in the treatment of diabetic foot wounds. *Am J Surg* 2008; 195: 782–8. <http://www.ncbi.nlm.nih.gov/pubmed/16291063>
- Moisisdis E, Heath T, Boorer C, et al. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. *Plast Reconstr Surg* 2004; 114: 917–22.
- Burke JF, Yannas IV, Quinby WC, Jr, et al. Successful use of a physiologically acceptable artificial skin in the treatment of extensive burn injury. *Ann Surg* 1981; 1994: 413.
- Heimbach DM, Warden GD, Luterma A, et al. Multicenter postapproval clinical trial of Integra dermal regeneration template for burn patients. *J Burn Care Rehabil* 2003; 24: 42.
- Tompkins RG, Burke JF. Progress in burn treatment and the use of artificial skin. *World J Surg* 1990; 14: 819–24.
- Heimbach D, Luterma A, Burke J, et al. Artificial dermis for major burns: a multi-center randomized clinical trial. *Ann Surg* 1988; 208: 313–20.
- Peck MD, Kessler M, Meyer AA, et al. A trial of the effectiveness of artificial dermis in the treatment of patients with burns greater than 45% total body surface area. *J Trauma* 2002; 52: 971–8.
- Dantzer E, Braye EM. Reconstructive surgery using an artificial dermis (Integra): results with 39 grafts. *Br J Plastic Surg* 2001; 54: 659–64.
- Frame JD, et al. The use of a dermal regeneration template (Integra) for acute resurfacing and reconstruction of defects created by excision of giant hairy nevi. *Plast Reconstr Surg* 2004; 114: 162–8.
- Molnar JA, et al. Acceleration of Integra incorporation in complex tissue defects with subatmospheric pressure. *Plast Reconstr Surg* 2004; 113: 1339–46.
- Smith G, Sharp GR. Treatment of coal gas poisoning with oxygen at two atmospheres pressure. *Lancet* 1962; 1: 816–19.
- Faglia E, Favales F, Aldehgi A, et al. Adjunctive systemic hyperbaric oxygen therapy in treatment of severe prevalently ischemic diabetic foot ulcer: a randomized study. *Diabetes Care* 1996; 19: 1338.
- Weaver LK, Hopkins RO, Chan K, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med* 2002; 347: 1057.
- Hirn M. Hyperbaric oxygen in the treatment of gas gangrene and perineal necrotizing fasciitis. *Eur Surg Suppl* 1993; 570: 1.
- Curi MM, Dib LL, Kowalski LP. Management of refractory osteoradionecrosis of the jaws with surgery and adjunctive hyperbaric oxygen. *Int J Oral Maxillofac Surg* 2000; 29: 430.
- Perrins DJD. The effect of hyperbaric oxygen on ischemic skin flaps. In Grabb WC, Myers MB, eds., *Skin Flaps*. Boston: Little, Brown, 1975, 53.
- Bowersox JC, Strauss MB, Hart GB. Clinical experience with hyperbaric oxygen therapy in the salvage of ischemic skin flaps and grafts. *J Hyperbaric Med* 1986; 1: 141.
- Ueda M, Kaneda T, Takahashi H, et al. Hyperbaric oxygen therapy of ischemic skin flaps: clinical and experimental study. 9th Int Symp Underwater Hyperbaric Physiol UHMS 1987: 823.
- Breast JH. The Edwin Smith Surgical Papyrus, Vol. 1 (hieroglyphic translation and commentary). Chicago: University of Chicago Press, 1930, 403–6.
- Druit R. Modern Surgery. Philadelphia: Lea and Blanchard, 1844.
- DaCosta JC. Modern Surgery. Philadelphia: Saunders, 1903.
- Al-Attar A, Mess S, Thomassen JM, et al. Keloid pathogenesis and treatment. *Plast Reconstr Surg* 2006; 117: 286–300.

44. Cosman B, Wolff M. Correlation of keloid recurrence with completeness of local excision: a negative report. *Plast Reconstr Surg* 1972; 50: 163.
45. Mustoe TA, Cooter RD, Gold M, et al. International clinical recommendations on scar management. *Plast Reconstr Surg* 2002; 110: 560.
46. Conway H, Stark RB. ACTH in plastic surgery. *Plast Reconstruct Surg* 1951; 8: 354.
47. Hollander A. Intralesional injections of triamcinolone acetonide: a therapy for dermatoses. *Antibiotic Med Clin Therapy* 1961; 8: 78–81.
48. Murray RD. Kenalog and the treatment of hypertrophied scars and keloids in Negroes and whites. *Plast Reconstr Surg* 1963; 31: 275–80.
49. Ketchum LD, Smith J, Robinson DW, et al. The treatment of hypertrophic scar, keloid and scar contracture by triamcinolone acetonide. *Plast Reconstr Surg* 1966; 38: 209.
50. Ketchum LD, Robinson DW, Masters FW. Follow-up study on the treatment of keloids with triamcinolone acetonide. *Plast Reconstr Surg* 1971; 48: 256.
51. Griffith BH, Monroe CW, McKinney PA. Follow-up study on the treatment of keloids with triamcinolone acetonide. *Plast Reconstr Surg* 1970; 46: 145.
52. Darzi MA, Chowdri NA, Kaul SK, et al. Evaluation of various methods of treating keloids and hypertrophic scars: a 10-year follow-up study. *Br J Plast Surg* 1992; 45: 374.
53. Levy DS, Salter MM, Roth RE. Postoperative irradiation in the prevention of keloids. *Am J Roentgenol* 1976; 127: 509.
54. Borok TL, Bray M, Sinclair I, et al. Role of ionizing irradiation for 393 keloids. *Int J Radiat Oncol Biol Phys* 1988; 15: 865.
55. Klumppar DI, Murray JC, Anscher M. Keloids treated with excision followed by radiation therapy. *J Am Acad Dermatol* 1994; 31: 225.
56. Ragoowansi R, Cornes PG, Moss AL, et al. Treatment of keloids by surgical excision and immediate post-operative single-fraction radiotherapy. *Plast Reconstr Surg* 2003; 111: 1853.
57. Ahn ST, Monafo WW, Mustoe TA. Topical silicone gel for the prevention and treatment of hypertrophic scar. *Arch Surg* 1991; 126: 499.
58. Gold MH. A controlled clinical trial of topical silicone gel sheeting in the treatment of hypertrophic scars and keloids. *J Am Acad Dermatol* 1994; 30: 506.
59. Sproat JE, Dalcin A, Weitaue N, et al. Hypertrophic sternal scars: silicone gel sheet versus Kenalog injection treatment. *Plast Reconstr Surg* 1992; 90: 988.
60. Agrawal K, Panda KN, Arumugam A. An inexpensive self fabricated pressure clip for the ear lobe. *Br J Plast Surg* 1998; 51: 122.
61. Lawrence WT. Treatment of earlobe keloids with surgery plus adjuvant intralesional verapamil and pressure earrings. *Ann Plast Surg* 1996; 37: 167.
62. Brent B. The role of pressure therapy in management of earlobe keloids: preliminary report of a controlled study. *Ann Plast Surg* 1978; 1: 579.
63. Mercer DM, Studd DM. "Oyster splints": a new compression device for the treatment of keloid scars of the ear. *Br J Plast Surg* 1983; 36: 75.
64. Pierce HE. Postsurgical acrylic ear splints for keloids. *J Dermatol Surg Oncol* 1986; 12: 583.
65. Hurtado AJ, Crowther DS. Methyl methacrylate stent for prevention of postexcisional recurrent ear keloid. *J Prosthet Dent* 1985; 54: 245.
66. Nason KH. Keloids and their treatment. *N Engl J Med* 1942; 226: 883.

Viperidae Snakebite Envenomation

Steven Granger and Ronald Stewart

Clinical Questions		
Question	Answer	Grade of recommendation
First aid after pit viper snakebite?	Extremity/patient immobilization and immediate transport to a medical facility.	C
Should snake antivenin be administered?	1. Early/immediate administration of antivenom for symptomatic snakebite victims. 2. Asymptomatic patients may undergo a trial of initial observation. 3. Minimally symptomatic patients who suffered a confirmed copperhead envenomation may not require antivenom.	B
What antivenin should be used for pit viper snakebite?	Crotalidae polyvalent immune Fab (ovine) (CroFab; FabAV)	B
What is the dosing regimen for FabAV?	Initial dosing of six vials, repeated until control of venom effects then maintenance with two vials at 6, 12, and 18 hours. Redosing with six vials if worsening occurs during this 24-hour observation period.	C
When is surgical debridement indicated and are fasciotomies still needed after pit viper snake envenomation?	Early surgical debridement has no role in the treatment of envenomation. Debridement of necrotic tissue may be required after medical therapy. Fasciotomy should be performed for documented elevations in compartment pressures refractory to antivenom and conservative therapy.	C
Should antibiotics be administered after pit viper snake envenomation?	No	A

INTRODUCTION

This chapter addresses common questions surrounding pit viper (Viperidae) envenomations common to North America. Because envenomations are not reportable, and few maintain registries, the exact incidence is uncertain. Approximately 45,000 snakebites occur per year in the United States with 8,000 from venomous snakes and 5–15 associated deaths (1–4). To place this in perspective, Chippaux estimated 5,000 deaths in Central and South America and up to 125,000 worldwide (5).

The two clinically important families of venomous snakes in the North America include the Viperidae and Elapidae. A majority of these bites are from one of the three relevant Viperidae (subfamily crotalines or pit vipers), including the rattlesnake (genera *Crotalus* and *Sistrurus*), copperhead (*Agkistrodon contortrix*), and the cottonmouth water moccasin (*Agkistrodon piscivorus*). There are also three relevant elapids in the United States, including the Eastern coral snake (*Micrurus fulvius*), Texas coral snake (*Micrurus tener*), and the Sonoran coral snake (*Micrurus tener*) (1,6).

Envenomation from Viperidae and Elapidae are clinically different in terms of presentation and treatment.

These differences include the significant local findings and consequences of a Viperidae envenomation compared to the systemic consequences of Elapidae envenomation. Most envenomations evaluated by physicians in North America are caused by Viperidae. Most major medical centers where these bites occur have on hand stocks of antivenin, whereas the antivenin for Elapidae is usually available at regional repositories where these snakes are indigenous.

Clinically relevant questions surrounding pit viper bites include (1) initial type of first aid, (2) when (if ever) to administer antivenin therapy, (3) what type of antivenin to administer, (4) what initial dose of antivenin and whether redosing is indicated, (5) indications for surgical intervention including when (if ever) to employ fasciotomies, and (6) whether antibiotics should be administered.

WHAT INITIAL FIRST AID SHOULD BE ADMINISTERED AFTER A VENOMOUS SNAKEBITE?

Not all pit viper bites lead to envenomation. Most experts believe there is no envenomation in approximately 20% of bites. Severe envenomations are infrequent, depending on

the type of snake and the volume of venom injected. Initial first aid for snakebite has changed over the past 100 years. Historic treatments, based on anecdotal experience, included application of ice (cryotherapy), incision and suction on the wound by laypersons, tourniquets, and even electric shock therapy (1,7–10). Each of these therapies has the potential to create harm independently of the snakebite itself.

Current treatment efforts emphasize supportive measures, including removal of the victim and caregivers from danger/proximity to the snake and establishment of airway, breathing, and circulation. Additional proposed initial treatments include immobilization of the affected extremity at or below the level of the heart, placement of a compression dressing, application of suction on the wound with a commercially available venom extraction device within five minutes of envenomation, proximal placement of a lymphatic constriction band, and rapid transport to the nearest medical facility.

Data regarding use of an extraction device are sparse. Two recent studies have shown no clinically significant venom was extracted. Alberts and colleagues performed a prospective human trial where radioactively labeled mock venom was injected at a depth of 1 cm into the leg of human volunteers, followed in three minutes by application of a popular commercially available suction device. Only 2% of the mock venom was extracted, despite extracting a larger amount of “bloody fluid” (11). Bush and colleagues performed a controlled animal trial using real rattlesnake venom. Clinical endpoints were measured, including swelling and local effects. These authors concluded that the extractor did not reduce swelling but caused further injury in some subjects (12). Several small studies dating back to the 1960s had previously suggested benefit from these devices (13–15). Based on the lack of data showing efficacy and the potential for harm, suction device use for snakebites cannot be recommended (Level IIIb evidence, Grade C recommendation) (8,16–18).

Local and/or circumferential compression therapy is aimed at slowing the systemic absorption of crotaline venom. The theoretic advantage would be to delay serious systemic toxicity until arrival at a health care facility. Arterial tourniquets are not supported by any data or academic body because of the risk for limb ischemia (17,19). Insufficient data and concerns regarding uniform application of venous tourniquets and compression devices have similarly led to a lack of universal acceptance. However, some experimental data suggest these measures slow systemic absorption of venom or in most cases mock venom. The theoretic disadvantage to these methods is the trapping of venom locally. The pit viper venom, in particular, has significant local hemolytic/tissue effects. In an animal study injecting rattlesnake venom into the legs of a porcine model, Burgess and colleagues demonstrated how a constriction band delayed venom absorption without causing increased swelling (20). A slightly different technique, pressure-immobilization, has been demonstrated as effective in slowing the systemic absorption of a mock venom. This method employs pressure wrapping the extremity between 40 and 70 mmHg and splinting of the entire affected extremity (21,22). Conflicting animal data have suggested worsened local effects from these constriction devices as well as a possible bolus effect from venom on releasing the device (17,20,21,23,24). There are insufficient data and

potential harm with these devices, so routine use of constriction bands and pressure-immobilizing techniques cannot be recommended for pit viper envenomations (Level IIIb evidence, Grade C recommendation). In individual cases where a patient is suffering from systemic decompensation secondary to neurotoxic venom, use of a constriction device or compressive bandage may decrease the systemic effects of venom until a medical facility can be reached (17,24).

Simple extremity immobilization has been shown in several animal models to decrease lymphatic and subsequent systemic absorption of venom, which leads to an increase in the lethal dose of venom tolerated. Early work by Leopold et al. showed that simple immobilization of all four limbs in a rabbit model allowed an increase in the lethal dose of *Cadamanteus* venom that could be tolerated (15). Similarly, Snyder and colleagues showed an increase in the lethal dose of venom after immobilization, and Anker et al. showed slowed transit of radiolabeled isotope with extremity immobilization (Level IIIb evidence) (17,25–27). Patient and affected extremity immobilization may decrease the rate of systemic absorption of venom and has minimal associated risk (Grade C recommendation).

Although no specific studies have been performed, common sense suggests that rapid transport to a medical facility will likely provide improved care after snake envenomation—allowing more skilled supportive therapy, access to antivenin, and access to specialists when needed.

Answer: “Do no harm” first aid consisting of immobilization and rapid transit to a medical facility are recommended (IIIb evidence, Grade C recommendation). Suction devices, application of constrictive dressings, or tourniquets are not recommended (IIIb, Grade C recommendation).

SHOULD ANTIVENIN BE ADMINISTERED AFTER SUSPECTED PIT VIPER SNAKEBITE?

Multiple historic animal studies have shown that pretreatment or early postbite treatment with antivenin is effective at reducing morbidity and mortality. These same studies have mixed results when treatment is delayed past four hours from the envenomation (14,27–29). Data regarding the translation of these results to clinically relevant scenarios are lacking. One prospective randomized clinical trial has been performed in the United States. In 1963, Reid randomized patients admitted with pit viper envenomation to antivenin, steroids, and untreated controls. Patients with severe symptoms were excluded. The three groups differed only in less hemorrhagic complications in the antivenin-treated group, but did not differ in local swelling or tissue necrosis (30). Rojnuckarin et al. in 2006 published a randomized, double-blind, placebo-controlled trial of antivenin for green pit viper bites in Thailand. Twenty-eight patients with marked limb swelling but without coagulopathy were randomized to receive placebo versus antivenin. Plasma venom levels and affected extremity swelling were reduced in the antivenin group versus placebo. No difference in pain scores or outcomes was noted, leading these authors to conclude that general use of antivenin, in the absence of coagulopathy, was not warranted after green pit viper envenomation (31).

Determining the need for antivenin administration is complicated by the unpredictability of whether snakebite has occurred, is from a venomous snake, whether the strike

was envenoming, and whether the consequences/clinical course will be minor or severe, warranting antivenin. Definitive diagnosis requires experienced identification of the snake and clinical manifestations of envenomation. In the absence of snake identification, clinical signs and symptoms become the focus.

In the United States, absolute indications for antivenin administration have not been rigorously studied or established. Severity scores have been published that attempt to classify the severity of pit viper envenomation as a guide to directing therapy. These are often based on local, systemic, laboratory, and organ system involvement with some authors advocating no treatment in asymptomatic patients because up to 25% of confirmed bites may be venomous (1,6). Most cases of pit viper envenomation are associated with minimal morbidity, which ultimately may not warrant antivenin administration (32). Approximately 7–13% are classified as severe, including those with early presentation of life-threatening symptoms (33). The venom from copperheads is the least potent U.S. pit viper venom relative to that of rattlesnakes and water moccasins. Several authors have published experiences with conservative management of select pit viper snakebites and specifically mildly symptomatic copperhead envenomations (Level IV evidence) (6,30–32,34–36).

Answer: Early administration of antivenin appears most effective and should be employed when symptomatic snakebite victims present (IIb evidence, Grade C recommendation). Asymptomatic patients and those with mild symptoms after confirmed copperhead snakebites may be initially managed without antivenin when serial examinations and close observation can be rigorously performed (Grade C recommendation).

WHAT ANTIVENIN SHOULD BE USED FOR PIT VIPER SNAKEBITE?

Two antivenin choices are currently available to clinicians caring for patients who suffer pit viper envenomation in the United States: antivenin (ACP; Crotalidae) polyvalent (equine) and more recently approved Crotalidae polyvalent immune Fab (ovine) (CroFab; FabAV).

ACP was developed in 1954 and has been shown to be effective at treating pit viper envenomation in animal models and human subjects (27,29,37). ACP is isolated from horse serum and is associated with allergic reactions in up to 56% of recipients, ranging from mild hypersensitivity reactions to anaphylaxis and death (38). FabAV was released in 2001 for treatment of pit viper envenomations. Several studies have shown it to be more potent and with a safer side effect profile than previous reports of ACP. It has never been compared in a randomized fashion, but experience with FabAV suggests it is superior and safer than ACP (Level IIb evidence) (39–43).

Answer: FabAV appears to have fewer side effects and may be more efficacious than ACP at treating envenomation from U.S. pit vipers (Grade B recommendation).

WHAT DOSING REGIMEN SHOULD BE EMPLOYED FOR PIT VIPER ENVENOMATION?

The timing for administration and exact dosing has not been rigorously elucidated. Several prospective studies have

demonstrated a rebound phenomenon after FabAV administration that suggests redosing is often necessary (39,44). The exact initial dose and redosing interval is not known. Most authors who recommend antivenin after pit viper snakebite suggest initial immediate dosing of enough vials of FabAV to gain control of the effects of the envenomation, followed by regularly scheduled redosing. Dart and colleagues showed in two prospective studies that an initial dose of six vials was sufficient in 65% of patients with redosing of two vials every six hours for maintenance or redosing of four to six vials at any time that progression was apparent (Level IIIb evidence) (1,39). Lavonas and colleagues reviewed their experience with FabAV retrospectively for copperhead envenomations. Seventy-two percent of their treated patients required an initial dose of four vials to halt progression of swelling, and 18% suffered recurrent swelling. They report that during this same time period after release of FabAV, they treated 92% of copperhead snakebite victims without antivenin (43).

Answer: Initial dosing of six vials with repeated dosing until control of progression is witnessed, followed by redosing of two vials for maintenance at 6, 12, and 18 hours or six vials at any point that worsening of signs or symptoms is appreciated (Grade C recommendations). Symptomatic copperhead snakebite victims may require less antivenin than other crotalid envenomations (Grade D recommendation).

WHEN IS SURGICAL DEBRIDEMENT OR FASCIOTOMIES INDICATED AFTER PIT VIPER SNAKE ENVENOMATION?

Historically, early surgical debridement was thought to be effective in removing venom from the wound and was employed as a preferred treatment over (or adjunct treatment with) antivenin (27,45–47). Medical and surgical treatments have both been shown to be efficacious and are associated with potentially significant morbidity. Treatment for envenomation has evolved, with many authors that suggesting surgical debridement is rarely needed and with the improved safety profile of FabAV. Burch and colleagues published a series of 81 pit viper snakebite (mostly copperhead) patients who were managed without medical or surgical therapy (32). Numerous authors have noted that the vast majority of envenomations are superficial to the fascia, with the possible exception of the fingers, hand, and anterolateral lower leg, making compartment syndrome extremely rare. Nonetheless, clinical judgment cannot be eliminated because some patients do still suffer from severe envenomations and will develop necrosis and compartment syndromes requiring surgical debridement and fasciotomy (8). In a controlled animal study, Stewart and colleagues showed antivenin alone to provide the best control of local muscle necrosis over the surgical arm alone and the combined medical and surgical arm (47). In this animal model, it was very clear that fasciotomy and debridement led to the removal of viable muscle in those animals treated with antivenin. Authors of large series advocate antivenin, observation, and delayed minimal debridement of obviously necrotic tissue (Level IIb evidence) (18).

As with early aggressive surgical debridement, early fasciotomy was once recommended and employed after pit viper snakebite (46). Compartment syndrome has since

been found to be a rare but morbid complication after envenomation (8,48–50). A controlled animal study with intramuscular injections of venom, leading to elevated compartment pressures, clearly demonstrated that fasciotomy and debridement were associated with worse outcomes than antivenin (Level IIIb evidence) (47). In Hall and colleagues review of 1,257 snakebite cases, fasciotomy was performed in only 2 cases (8).

Answer: Antivenin alone is sufficient in almost all envenomations. Surgical debridement has no role in acute treatment of envenomation. Compartment fasciotomy may be indicated for the very rare patient with documented elevations in compartment pressures despite medical therapy (Grade C recommendation).

SHOULD ANTIBIOTICS BE ADMINISTERED AFTER PIT VIPER SNAKE ENVENOMATION?

Each animal's mouth has a unique resident flora, which may lead to infection following a bite. Prophylaxis after a bite from an animal is routine in some circumstances. Historically this was true after snakebite, which includes the proteolytic factors from venom causing local tissue destruction as well as bacterial flora from the snake's mouth. When infections do occur, they can be associated with significant morbidity. Kerrigan et al. performed a prospective randomized controlled trial to evaluate the need for antibiotics after pit viper snakebite. One hundred fourteen patients with local and/or laboratory evidence of pit viper envenomation were randomized over a three-year period. No difference in abscess rate was found between the two groups with an overall abscess rate of 7.8% (Level Ib evidence) (51). Prophylactic antibiotics have not been shown to decrease wound infection rates which have been reported at 3–8% after snakebite (Grade A recommendation) (51–53).

Answer: Prophylactic antibiotics after pit viper snakebite is not warranted (Grade A recommendation).

REFERENCES

- Gold BS, Dart RC, Barish RA. Bites of venomous snakes. *N Engl J Med* 2002; 347: 347–56.
- Watson WA, et al. 2002 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 2003; 21: 353–421.
- Watson WA, et al. 2003 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 2004; 22: 335–404.
- O'Neil ME, et al. Snakebite injuries treated in United States emergency departments, 2001–2004. *Wilderness Environ Med* 2007; 18: 281–7.
- Chippaux JP. Snake-bites: appraisal of the global situation. *Bull World Health Org* 1998; 76: 515–24.
- Juckett G, Hancox JG. Venomous snakebites in the United States: management review and update. *Am Fam Phys* 2002; 65: 1367–74.
- McCollough N. Evaluation of venomous snake bite in the southern United States from parallel clinical and laboratory investigations: development of treatment. *J Fla Med Assoc* 1963; 49: 959–67.
- Hall EL. Role of surgical intervention in the management of crotaline snake envenomation. *Ann Emerg Med* 2001; 37: 175–80.
- Meier J. *Handbook of Clinical Toxicology of Animal Venoms and Poisons*. Boca Raton, FL: CRC Press, 1995, 477.
- Dart RC, Gustafson RA. Failure of electric shock treatment for rattlesnake envenomation. *Ann Emerg Med* 1991; 20: 659–61.
- Alberts MB, Shalit M, LoGalbo F. Suction for venomous snakebite: a study of “mock venom” extraction in a human model. *Ann Emerg Med* 2004; 43: 181–6.
- Bush SP, et al. Effects of a negative pressure venom extraction device (extractor) on local tissue injury after artificial rattlesnake envenomation in a porcine model. *Wild Environ Med* 2000; 11: 180–8.
- Reitz CJ, et al. Evaluation of the enom Ex apparatus in the initial treatment of puff adder envenomation. A study in rabbits. *S Afr Med J* 1986; 69: 684–6.
- Ya P. Experimental evaluation of methods for the early treatment of snakebite. *Surgery* 1960; 47: 975–81.
- Leopold R. An evaluation of the mechanical treatment of snakebite. *Mil Med* 1957; 120: 414–16.
- Bush SP. Snakebite suction devices don't remove venom: they just suck. *Ann Emerg Med* 2004; 43: 187–8.
- McKinney PE. Out-of-hospital and interhospital management of crotaline snakebite. *Ann Emerg Med* 2001; 37: 168–74.
- Wingert WA, Chan L. Rattlesnake bites in southern California and rationale for recommended treatment. *West J Med* 1988; 148: 37–44.
- Gold BS, Wingert WA. Snake venom poisoning in the United States: a review of therapeutic practice. *South Med J* 1994; 87: 579–89.
- Burgess JL, Dart RC, Egen NB, Mayersohn M. Effects of constriction bands on rattlesnake venom absorption: a pharmacokinetic study. *Ann Emerg Med* 1992; 21: 1086–93.
- Sutherland SK, Coulter AR. Early management of bites by the eastern diamondback rattlesnake (*Crotalus adamanteus*): studies in monkeys (*Macaca fascicularis*). *Am J Trop Med Hyg* 1981; 30: 497–500.
- Sutherland SK, Coulter AR, Harris RD. Rationalisation of first-aid measures for elapid snakebite. *Lancet* 1979; 1: 183–5.
- Pearn J, Morrison J, Charles N, Muir V. First-aid for snakebite: efficacy of a constrictive bandage with limb immobilization in the management of human envenomation. *Med J Aust* 1981; 2: 293–5.
- Watt G, Padre L, Tuazon ML, et al. Tourniquet application after cobra bite: delay in the onset of neurotoxicity and the dangers of sudden release. *Am J Trop Med Hyg* 1988; 38: 618–22.
- Anker RL, Straffon WG, Loiselle DS, Anker KM. Retarding the uptake of “mock venom” in humans: comparison of three first-aid treatments. *Med J Aust* 1982; 1: 212–14.
- Anker RL, Straffon WG, Loiselle DS, Anker KM. Snakebite. Comparison of three methods designed to delay uptake of “mock venom.” *Aust Fam Physician* 1983; 12: 365–8.
- Snyder CC, Pickins JE, Knowles RP, et al. A definitive study of snakebite. *J Fla Med Assoc* 1968; 55: 330–7.
- Fischer F. Antivenin and antitoxin in the treatment of experimental rattlesnake venom intoxication (*Crotalus adamanteus*). *Am J Trop Med Hyg* 1962; 102: 75–79.
- Brubacher JR, Lachmanen D, Hoffman RS. Efficacy of Wyeth polyvalent antivenin used in the pretreatment of copperhead envenomation in mice. *Wild Environ Med* 1999; 10: 142–5.
- Reid H. Specific antivenin and prednisone in viper-bite poisoning: controlled trial. *Br Med J* 1963; 2: 1378–80.
- Rojnuckarin P, Chanthawibun W, Noiphrom J, et al. A randomized, double-blind, placebo-controlled trial of antivenom for local effects of green pit viper bites. *Trans R Soc Trop Med Hyg* 2006; 100: 879–84.

32. Burch JM, Agarwal R, Mattox KL, et al. The treatment of crotalid envenomation without antivenin. *J Trauma* 1988; 28: 35–43.
33. Litovitz TL, Klein-Schwartz W, Dyer KS, et al. 1997 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 1998; 16: 443–97.
34. Whitley RE. Conservative treatment of copperhead snakebites without antivenin. *J Trauma* 1996; 41: 219–21.
35. Acikalin A, Gokel Y, Kuvandik G, et al. The efficacy of low-dose antivenom therapy on morbidity and mortality in snakebite cases. *Am J Emerg Med* 2008; 26: 402–7.
36. Caravati EM. Copperhead bites and Crotalidae polyvalent immune Fab (ovine): routine use requires evidence of improved outcomes. *Ann Emerg Med* 2004; 43: 207–8.
37. Minton SA Jr. Polyvalent antivenin in treatment of experimental snake venom poisoning. *Am J Trop Med Hyg* 1954; 3: 1077–82.
38. Jurkovich GJ, Luterman A, McCullar K, et al. Complications of Crotalidae antivenin therapy. *J Trauma* 1988; 28: 1032–7.
39. Dart RC, Seifert SA, Boyer LV, et al. A randomized multicenter trial of crotalinae polyvalent immune Fab (ovine) antivenom for the treatment for crotaline snakebite in the United States. *Arch Intern Med* 2001; 161: 2030–6.
40. Corneille MG, Larson S, Stewart RM, et al. A large single-center experience with treatment of patients with crotalid envenomations: outcomes with and evolution of antivenin therapy. *Am J Surg* 2006; 192: 848–52.
41. Clark RF, McKinney PE, Chase PB, Walter FG, et al. Immediate and delayed allergic reactions to Crotalidae polyvalent immune Fab (ovine) antivenom. *Ann Emerg Med* 2002; 39: 671–6.
42. Consroe P, Egen NB, Russell FE, et al. Comparison of a new ovine antigen binding fragment (Fab) antivenin for United States Crotalidae with the commercial antivenin for protection against venom-induced lethality in mice. *Am J Trop Med Hyg* 1995; 53: 507–10.
43. Lavonas EJ, Gerardo CJ, O'Malley G, et al. Initial experience with Crotalidae polyvalent immune Fab (ovine) antivenom in the treatment of copperhead snakebite. *Ann Emerg Med* 2004; 43: 200–6.
44. Dart RC, Seifert SA, Carroll L, et al. Affinity-purified, mixed monospecific crotalid antivenom ovine Fab for the treatment of crotalid venom poisoning. *Ann Emerg Med* 1997; 30: 33–9.
45. Huang TT, Lynch JB, Larson DL, Lewis SR, et al. The use of excisional therapy in the management of snakebite. *Ann Surg* 1974; 179: 598–607.
46. Glass TG Jr. Early debridement in pit viper bites. *JAMA* 1976; 235(23k0): 2513–6.
47. Stewart RM, Page CP, Schwesinger WH, et al. Antivenin and fasciotomy/debridement in the treatment of the severe rattlesnake bite. *Am J Surg* 1989; 158: 543–7.
48. Grace TG, Omer GE. The management of upper extremity pit viper wounds. *J Hand Surg (Am)* 1980; 5: 168–77.
49. Curry SC, Kraner JC, Kunkel DB, et al. Noninvasive vascular studies in management of rattlesnake envenomations to extremities. *Ann Emerg Med* 1985; 14: 1081–4.
50. Garfin SR, Mubarak SJ, Davidson TM. Rattlesnake bites: current concepts. *Clin Orthop Relat Res* 1979; 140: 50–7.
51. Kerrigan KR, Mertz BL, Nelson SJ, Dye JD. Antibiotic prophylaxis for pit viper envenomation: prospective, controlled trial. *World J Surg* 1997; 21: 369–72; discussion 372–3.
52. Clark RF, Selden BS, Furbee B. The incidence of wound infection following crotalid envenomation. *J Emerg Med* 1993; 11: 583–6.
53. Kularatne SA, Kumarasiri PV, Pushpakumara SK, et al. Routine antibiotic therapy in the management of the local inflammatory swelling in venomous snakebites: results of a placebo-controlled study. *Ceylon Med J* 2005; 50: 151–5.

Evidence-Based Surgery: War Wounds

Lorne H. Blackbourne

Question Summary		
Question	Answer	Grade
Should tourniquets be used prehospital with exsanguinating extremity trauma?	Tourniquets are the most important prehospital life-saving maneuver for combat-injured patients.	B
What is the optimal work-up for abdominal, flank, and back fragmentation wounds from explosions?	CT scan should be used to evaluate for intraperitoneal penetration in hemodynamically stable patients.	C
Should hemostatic dressing be used on combat wounds?	Hemostatic agents, including HEMCON dressings, may provide additional benefit for hemostasis compared to cloth bandages.	C
How can large soft tissue injuries from explosions be treated?	After initial irrigation and debridement, Wound VAC negative-pressure dressings can be applied safely.	C
How should combat injured patients undergoing a massive blood transfusion be resuscitated?	FFP and PRBCs should be administered in a 1:1.4 ratio. This is clinically given as a simple 1:1 ratio.	B
How is a major vessel injury treated in an austere surgical environment?	Major vascular injuries are treated with a temporary shunt and fasciotomy prior to transfer to a higher level of care.	B
How can "over-resuscitation" be avoided in combat wounded undergoing global transport?	A simple burn flowsheet, documenting intravenous fluid rate and urine output can decrease over-resuscitation in burn patients	C
Abbreviations: CT, computed tomography; FFP, fresh frozen plasma; PRBCs, packed red blood cells.		

INTRODUCTION

War wounds offer unique challenges to the evidence-based practice. War wounds are often caused by explosions with multiple fragmentation wounds and large soft tissue injuries that have no correlate in civilian trauma (1). U.S. military combat wounded are evacuated over several continents and receive care at several surgical facilities during a long journey to the continental United States; see Figure 39.1 (2). Due to the many additional movements and multiple operations performed by different physicians during this process, there is ample opportunity for unique challenges not encountered in civilian trauma.

In addition to unique wounding patterns and global evacuation process that cannot be studied in the civilian trauma population, soldiers are considered to be a vulnerable study population. In addition, trauma patients are often unable to give consent by the nature of their trauma physiology. Thus, by default, all combat-related research is based on "waiver of consent" retrospective medical chart data collections or prospective observational studies. The confluence of unique wounding patterns with global patient evacuation without a civilian counterpart (where randomized, prospective studies might be performed) and the constraints of ethical research in the combat wounded results in evidence-based combat casualty information that is, at best, Level II data (3).

PREHOSPITAL COMBAT CASUALTY CARE

What Are the Potentially Preventable Causes of Death on the Battlefield?

A review of autopsy reports from combat deaths revealed that approximately 15% of soldiers killed in action were determined to be "potentially survivable" (4). Holcomb et al., in this assessment of special operation forces soldiers killed in action, found that compressible extremity hemorrhage was the most common potentially preventable cause of death (4). Other causes of potentially preventable death included loss of airway, compressible nonextremity hemorrhage, and tension pneumothorax.

What Battlefield Techniques Are Available to Combat Medics to Treat Potentially Preventable Deaths on the Battlefield?

Tourniquets

Shortly after the start of Operation Iraqi Freedom, several tourniquets were tested to maximize ways to save lives on the battlefield. Several windlass-type tourniquets were identified as adequate for use by nonmedical and medical military personnel alike (5). The prehospital use of tourniquets has been documented in retrospective reviews to be effective and life-saving with a very low rate of complications (6,7).

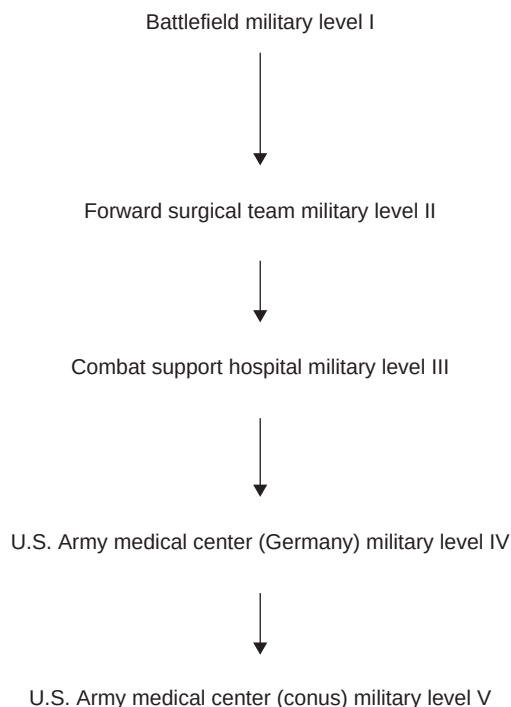


Figure 39.1 Combat-injured evacuation route. U.S. Army Medical Center (Continental United States) military level V.

Tension Pneumothorax

Early in the Global War on Terror, anecdotal evidence identified treatment of tension pneumothorax with needle decompression as inadequate using standard 14-gauge angiocatheters in combat wounded. A review of autopsy and computed tomography (CT) imaging demonstrated that many men and women have a chest wall thickness surpassing the length of standard 14-gauge angiocatheters (8). As a result, 14-gauge decompression catheters of ≥ 3.25 inches in length are now carried by combat medics and many first responders.

Hypotensive Resuscitation

Combat casualties are most often injured by a penetrating mechanism, and the evacuation times can vary greatly until surgical intervention. The U.S. military has adopted a minimal resuscitation policy (aka “hypotensive resuscitation”) with the goal of achieving a systolic blood pressure of approximately 90 mmHg based on civilian trauma data and animal research data documenting a rebleeding threshold (9,10). Hextend, a hetastarch-based colloid, or crystalloid are the recommended initial intravenous fluids to be used by combat medics, titrated to a clinical measurement of a systolic blood pressure of 90 mmHg based on a palpable weak or normal radial pulse and/or a normal mental status in patients without head injuries (11).

Chitosan Hemostatic Wound Dressings

In all previous conflicts, fabric gauze dressing and manual pressure were the exclusive tools and methods for

hemorrhage control. In 2005, the U.S. Army deployed a hemostatic chitosan-based dressing to every soldier. The chitosan dressing is made from chitin, a complex carbohydrate, and the dressing has been shown to be effective in hemorrhage control in several animal models (12). A retrospective case use analysis of the chitosan-based dressing (Hemcon) documented a 97% success rate for hemostasis in combat injured (13).

Recommendation: In mass casualties, tourniquets should be employed on all extremity wounds with significant bleeding that is not easily controlled with manual pressure. In patients in extremis with signs and symptoms of tension pneumothorax, prehospital personnel should use a needle that is ≥ 3.25 inches in length to decompress the pleural cavity. Prehospital personnel should administer intravenous fluids judiciously in patients with active hemorrhage who do not have brain injury. Hemostatic dressings should be considered by prehospital personnel if gauze dressing fails to stop bleeding from an injury that is not amenable to tourniquet placement.

WORK-UP OF PATIENTS WITH FRAGMENTATION WOUNDS

How Are Fragmentation War Wounds to the Abdomen, Flank, and Back Evaluated?

Explosion injuries account for the majority of combat wounds (14). These explosions result in most patients having multiple fragmentation wounds—often from head to toe. Although the classic method for the management of penetrating abdominal wounds has been exploratory laparotomy, in reality this cannot be done in the combat setting. Due to multiple casualties, operating rooms are often not available, making mandatory exploration untenable. Furthermore, although observation of penetrating injuries is often done at busy civilian Level I trauma facilities, the rapid evacuation of patients through multiple surgical facilities makes observation by the same surgeon an impossibility. In response to these limitations, the use of CT has revolutionized the care of the hemodynamically normal patient with multiple fragmentation wounds.

CT triage of the hemodynamically normal patient with multiple abdominal, flank, and/or back fragmentation wounds has allowed successful nonoperative management of these patients. Due to multiple fragments, pain and intramural hematomas the physical exam is unreliable with a sensitivity of 30.2% (15). Ultrasound was also found to have a low sensitivity of 11.7%, but with 100% specificity ($n = 4$) (15). CT had a high sensitivity of 97.8% for documenting intraperitoneal fragments and predicting the need for therapeutic laparotomy.

Recommendation: Patients with multiple fragmentation wounds to the abdomen, flank, and/or back with normal hemodynamics should undergo a CT scan for the evaluation of intraperitoneal fragments. Intraperitoneal fragments mandate surgical exploration, and absence of intraperitoneal fragments can safely allow observation. A negative ultrasound cannot safely rule out intraperitoneal injury, and these patients should undergo a CT scan.

COMBAT DAMAGE CONTROL RESUSCITATION

How Should Combat Injured Patients Undergoing a Massive Blood Transfusion Be Resuscitated?

Damage control resuscitation is the method of intravenous fluid resuscitation in massive transfusion [>10 units of packed red blood cells (PRBCs)/24 hours] for patients undergoing damage control surgery. Predictive factors for combat-related massive transfusion requirements include heart rate >105 beats per minute, pH <7.25 , systolic blood pressure <110 mmHg, hematocrit $<25\%$, and an international normalization ratio (INR) >1.5 on admission (16–17). The concept of damage control resuscitation is to replace the red blood cells, clotting factors, and platelets that the patient has lost with blood and blood components. Crystalloid administration is minimized with the goal of restoring the coagulation system and oxygen-carrying capacity, along with efforts to correct acidosis and hypothermia (18).

Borgman et al., in a retrospective review of combat wounded undergoing damage control surgery and requiring a massive transfusion, found that the increased use of fresh frozen plasma (FFP) in a PRBCs-to-FFP ratio of 1.4 was associated with a lower mortality rate when compared to patients receiving a higher ratio of PRBCs (19). Deciphering the reason for the lower mortality in patients with an increased FFP transfusion is unknown due to the fact that FFP contains both clotting factors and fibrinogen. This is further complicated by the fibrinogen/clotting factors contained in fresh whole blood, the fibrinogen in cryoprecipitate, and in the apheresis platelets used for transfusion in combat support hospitals. Stinger et al. in a retrospective review of the ratio of fibrinogen to red blood cells (RBCs) transfused in combat patients receiving a massive transfusion identified a decreased mortality rate in the patients receiving a higher ratio of fibrinogen to RBCs (20).

The role of FFP transfusion in patients not receiving a massive transfusion but requiring PRBC transfusion is currently undefined. A retrospective review by Spinella et al. revealed an association with survival for each unit of FFP transfused and a decrease in survival for each unit of PRBCs transfused in combat wounded receiving a transfusion of at least 1 unit of PRBCs (21).

While checking INR and platelet counts are the standard method for assessing coagulopathy in trauma patients, thrombelastography (TEG) has been shown to be a more accurate indicator of the need for blood products in combat wounded (22). TEG may play a significant role in damage control resuscitation in the near future.

Recommendation: In the patient with a combat injury requiring a massive transfusion, the patient should be transfused with PRBCs and FFP in a 1:1 ratio with minimal intravenous crystalloid.

COMBAT VASCULAR SURGERY

How Is a Major Vessel Injury Treated in an Austere Surgical Environment?

Approximately 60% of combat trauma admissions have major extremity injuries with vascular injury occurring in about 5% (23). Combat wounded seen at austere far forward surgical facilities undergo placement of a temporary vascular shunt until transfer to a more robust surgical facility (e.g., combat support hospital, military level II). On

retrospective reviews, the extremity vascular shunts placed in combat wounded had a patency rate of 78–86% with no documented amputation due to thrombosis of the vascular shunt (23,24).

Patients with prolonged extremity ischemia undergo a prophylactic extremity compartment fasciotomy. If a fasciotomy is undertaken, it is imperative to perform an adequate fasciotomy by fascial incision length that must include all involved compartments, because inadequate fasciotomy of combat wounded is associated with an increase in muscle excision and mortality (25). Delayed fasciotomy for extremity compartment syndrome was also associated with increased mortality and amputation rates in combat wounded in this retrospective review (25).

Recommendation: Patients with large vessel injury in an austere surgical environment with access to rapid evacuation to a more robust surgical capable facility should have a shunt placed and undergo definitive repair with saphenous vein at the receiving facility. Combat injured with major vascular injury to the extremities should undergo adequate compartment fasciotomy.

SOFT TISSUE WAR WOUND MANAGEMENT

How Can Large Soft Tissue Injuries from Explosions Be Treated?

The majority of combat wounds are due to fragments from explosives (secondary blast injury). These wounds are grossly contaminated, often carrying clothing and other foreign bodies into the underlying subcutaneous tissues and muscle. Classic war teaching involves debridement, irrigation, and packing all wounds to remain open (2). This treatment involves painful multiple wound packing changes and exposes the depth of the wounds to any environmental contamination (e.g., dust, sand). In currently deployed military hospitals, negative-pressure dressings have been used to treat these wounds. Leininger et al. in a retrospective review of 77 consecutive patients in Iraq with soft tissue wounds treated with negative-pressure dressings revealed an excellent wound infection and wound complication rate (0% and 0%) (26). The wounds were initially debrided and then irrigated. After all gross contamination was removed they placed a negative-pressure dressing (Wound VAC, San Antonio, Texas) at the initial operative debridement with suction set at -125 mmHg. The dressings were changed every two to four days and each patient underwent multiple operating room washouts and redebridements with negative-pressure dressing placement after each washout. The wounds were then closed primarily (delayed primary closure), underwent a split thickness skin graft or tissue flap mobilization after the wound was noted to be clean, with granulation tissue and without signs of infection.

Recommendations: Wound VAC negative-pressure dressings can be used after the initial debridement and irrigation in patients with soft tissue injuries from explosions.

COMBAT BURN CARE

What Are the Advances in Combat Burn Care?

Approximately 5–10% of combat wounded suffer burn injury. Burn patients with significant burn surface area

and depth (>20% total body surface area) must receive intravenous fluid resuscitation to avoid organ failure. Whereas sufficient fluid is a necessity, administering too much fluid is also fraught with complications (27,28). The burn patient in combat operations must go through multiple medical facilities during global evacuation back to the continental United States. This system, which involves multiple physicians and nurses in the initial resuscitation, has led to over-resuscitation of burn patients, especially as the tendency at each level of care is to provide a normal blood pressure until the patient is able to be evacuated to the next level. Over-resuscitation can result in abdominal compartment syndrome and is associated with a high mortality rate.

The implementation of a burn flowsheet that tracks the hourly urine output and hourly intravenous fluid administration rate that holds the physician responsible for the amount of fluid administered has been implemented in combat operations. In a retrospective review, Ennis et al. demonstrated a dramatically lower incidence of over-resuscitation compared to the burn flowsheet preimplementation period (29).

An exciting new area of critical care for combat burn patients is the use of continuous renal replacement therapy (CRRT) in patients with acute kidney injury. Chung et al. performed a retrospective review of combat burn patients with greater than 40% total body surface area burns, acute kidney injury (RIFLE I or RIFLE F criteria), and the need for vasopressors and found that early administration of CRRT was associated with a decrease in mortality when compared to a historically matched control non-CRRT group (30).

Recommendations: Burn patients should be resuscitated with the benefit of a burn resuscitation flowsheet, especially if their care will be undertaken at multiple facilities by multiple physicians to avoid over-resuscitation. During the critical care portion of burn care, CRRT should be considered in the patient with renal failure from sepsis.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Prehospital tourniquets	2008	5,6,7	II	B	Application of prehospital tourniquets is associated with a decrease in combat wounded mortality with very low morbidity.
Imaging for abdominal, flank, and back fragmentation wounds	2008	16	II	C	Use of CT scan in stable patients with fragmentation wounds has allowed nonoperative observation with very low missed injury rate.
Dressings for soft tissue fragmentation wounds	2006	26	II	C	Wound VAC negative-pressure dressing can be used as part of delayed primary closure of fragmentation soft tissue injuries with low infection rate.
Optimal resuscitation of combat wounded undergoing a massive transfusion	2007, 2008	19–21	II	B	Transfusion of FFP to PRBCs in a near 1:1 ratio is associated with a decreased mortality in combat-wounded patients receiving a massive transfusion.
Use of temporary vascular shunts	2006, 2007	23, 24	II	B	Use of vascular shunts in the austere surgical environment can be used effectively as a bridge until more definitive care.
Use of burn patient “flowsheet” in patients undergoing global evacuation	2008	29	II	C	Use of a burn patient flowsheet is associated with a lower rate of over-resuscitation in burn patients treated at multiple facilities undergoing evacuation

Abbreviations: CT, computed tomography; FFP, fresh frozen plasma; PRBCs, packed red blood cells.

REFERENCES

- Owens B, Kragh J, Wenke L, et al. Combat wounds in Operation Iraqi Freedom and Operation Enduring Freedom. *J Trauma* 2008; 64: 295–9.
- Burris D, et al. *Emergency War Surgery*, 3rd edition. Washington D.C.: Borden Institute, 2004.
- Brosch L, Holcomb J, Thompson J, et al. Establishing a human research protection program in a combatant command. *J Trauma* 2008; 64: S9–S13.
- Holcomb J, McMullin N, Pearse L, et al. Causes of death in U.S. special operation forces in the Global War on Terrorism 2001–2004. *Ann Surg* 2007; 245: 986–91.
- Walters T, Wenke J, Kauvar D, et al. Effectiveness of self-applied tourniquets in human volunteers. *Prehosp Emerg Care* 2005; 9: 416–22.
- Beekley A, Sebesta J, Blackburne L, et al. Prehospital tourniquet use in Operation Iraqi Freedom: effect on hemorrhage control and outcomes. *J Trauma* 2008; 64: S28–S37.

7. Kragh J, Walters T, Baer D, et al. Practical use of emergency tourniquets to stop bleeding in major limb trauma. *J Trauma* 2008; 64: S38–S50.
8. Cordts P, Brosch L, Holcomb J. Now and then: combat casualty care policies for Operation Iraqi Freedom and Operation Enduring Freedom compared with those of Vietnam. *J Trauma* 2008; 64: S14–S20.
9. Bickell W, Wall M, Pepe P, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med* 1994; 331: 1105–9.
10. Sondeen JL, Coppes VG, Holcomb JB. Blood pressure at which rebleeding occurs after resuscitation in swine with aortic injury. *J Trauma* 2003 May; 54(5 Suppl): S110–S117.
11. McSwain NE, Frame S, Salome JP, eds. *Pre-hospital Trauma Life Support Manual*, 6th edition. Akron, OH: Mosby, 2005.
12. Pusateri A, McCarthy S, Gregory K, et al. Effect of a chitosan-based hemostatic dressing on blood loss and survival in a model of severe venous hemorrhage and hepatic injury in swine. *J Trauma* 2003; 54: 177–82.
13. Wedmore I, McManus J, Pusateri A, et al. A special report on the chitosan-based hemostatic dressing: experience in current combat operations. *J Trauma* 2006; 60: 655–8.
14. Kelly J, Ritenour A, McLaughlin D, et al. Injury severity and causes of death from Operation Iraqi Freedom and Operation Enduring Freedom: 2003–2004 versus 2006. *J Trauma* 2008; 64: S21–S27.
15. Beekley A, Blackburn LH, Sebesta J, et al. Selective non-operative management of penetrating torso injury from combat fragmentation wounds. *J Trauma* 2008; 64: S108–S117.
16. McLaughlin D, Niles S, Salinas J, et al. A predictive model for massive transfusion in combat casualty patients. *J Trauma* 2008; 64: S57–S63.
17. Schreiber M, Perkins J, Kiraly L, et al. Early predictors of massive transfusion in combat casualties. *J Trauma* 2007; 205: 541–5.
18. Holcomb J, Jenkins D, Rhee P, et al. Damage control resuscitation: directly addressing the early coagulopathy of trauma. *J Trauma* 2007; 62: 307–10.
19. Borgman M, Spinella P, Perkins J, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007; 63: 805–13.
20. Stinger H, Spinella P, Perkins P, et al. The ratio of fibrinogen to red blood cells transfused affects survival of casualties receiving massive transfusions at an army combat support hospital. *J Trauma* 2008; 64: S79–S85.
21. Spinella P, Perkins J, Grathwohl K, et al. Effect of plasma and red blood cell transfusion on survival in patients with combat related traumatic injuries. *J Trauma* 2008; 64: S69–S78.
22. Plotkin A, Wade C, Jenkins D, et al. A reduction in clot formation rate and strength assessed by thrombelastography is indicative of transfusion requirements in patients with penetrating injuries. *J Trauma* 2008; 64: S64–S68.
23. Clouse D, Rasmussen T, Peck M, et al. In-theater management of vascular injury: 2 years of the Balad vascular registry. *J Am Coll Surg* 2007; 204: 625–32.
24. Chambers LW, Green DJ, Sample K, et al. Tactical surgical intervention with temporary shunting of peripheral vascular trauma sustained during Operation Iraqi Freedom: one unit's experience. *J Trauma* 2006; 61: 824–30.
25. Ritenour A, Dorlac W, Fang R, et al. Complications after fasciotomy revision and delayed compartment release in combat patients. *J Trauma* 2008; 64: S153–S162.
26. Leininger B, Rasmussen T, Smith D, et al. Experience with wound vac and delayed primary closure of contaminated soft tissue injuries in Iraq. *J Trauma* 2006; 61: 1207–11.
27. Ivy ME, Atweh N, Palmer J, et al. Intra-abdominal hypertension and abdominal compartment syndrome in burn patients. *J Trauma* 2000; 49: 387–91.
28. Saffle JR. The phenomenon of “fluid creep” in acute burn resuscitation. *J Burn Care Re.* 2007; 28: 382–95.
29. Ennis J, Chung K, Renz E, et al. Joint theater trauma system implementation of burn resuscitation guidelines improves outcome in severely burned military casualties. *J Trauma* 2008; 64: S146–S152.
30. Chung K, Juncos L, Wolf S, et al. Continuous renal replacement therapy improves survival in severely burned military casualties with acute kidney injury. *J Trauma* 2008; 64: S179–S187.

Evidence-Based Surgery: Pediatric Trauma

Gerald Gollin

Question Summary		
Question	Answer	Grade
When is a CT scan of the head indicated in pediatric head trauma?	If one of the referenced decision tools are used. In general, if one of the following are present: GCS < 15, evidence of skull fracture, headache, vomiting, coagulopathy, or seizure.	B
Is there a role for hypertonic saline in pediatric head injury?	There is no evidence to support a reduction in mortality or even severe morbidity with hypertonic saline. There is limited evidence for its role in lowering refractory intracranial hypertension with limited side effects.	C
When is clinical clearance of the cervical spine appropriate in children?	If there is no neck pain, midline tenderness, neurological deficit, or painful distracting injury in a child older than seven. There is not enough evidence in younger patients to support application of clinical clearance except in unusually mature children.	B
How should femur fractures be managed in children?	Excluding patients under five and those with very proximal or distal fractures, significant contamination, or gross comminution, intramedullary rod placement results in shorter recovery time at a cost comparable to other methods.	B
How should blunt pancreatic transection be managed in children?	There is insufficient evidence to support the superiority of early pancreatectomy or nonoperative management of pancreatic transection. The incidence of this injury is likely too low to permit a large, randomized controlled trial.	C
Abbreviations: CT, computed tomography; GCS, Glasgow Coma Score.		

INTRODUCTION

Injuries in children are frequently managed in a similar manner as adults. However, the unique anatomy, physiology, and psychology of children mandate care in the application of evidence obtained from studies of adults to the pediatric population. This chapter focuses on five questions in pediatric trauma that are relevant to the daily practice of those who care for injured children.

WHEN IS A CT SCAN OF THE HEAD INDICATED IN PEDIATRIC HEAD TRAUMA?

There are approximately 435,000 emergency department visits a year in the United States for head injuries in children 14 years old and younger (1). Among these, 37,000 are hospitalized and 2,685 die. Computed tomography (CT) scanning has become an indispensable tool in the identification of significant intracranial injuries in children.

A study of 400 children with a Glasgow Coma Score (GCS) of greater than 12 and a negative CT scan of the

head found that only 4 patients were readmitted with a neurological diagnosis and only 1, who was on warfarin, required craniotomy (2). Based on this and similar findings in adults, most pediatric physicians confidently discharge head-injured children with unremarkable CT scan findings. However, a protocol of CT scanning for all pediatric head injuries is neither cost-effective nor safe, considering that one in a thousand CT scans in children may result in a malignancy (3).

Some had believed that a patient with normal mental status and no history of a loss of consciousness is at such a low risk for intracranial injury that a CT scan need not be performed. Simon et al. cast significant doubt on this in a retrospective review of 429 children with head trauma and GCS of 14 or 15 (4). Among 219 with a GCS of 15 and a reliable history of no loss of consciousness, there were 35 intracranial injuries (16%), of which 4 required operative intervention and 1 needed intubation. Based on these findings, the authors recommended a policy of "liberal" CT scanning.

Subsequent studies have aimed to more precisely define the population at risk for intracranial injury by

expanding the criteria examined beyond mental status and loss of consciousness. Haydel et al. reviewed 175 children between 5 and 17 years of age who had a loss of consciousness but a GCS of 15 and a normal neurological exam (5). If CT scans had been obtained only in children with at least one of these six conditions: headache, vomiting, intoxication, short-term memory loss, seizure, or physical evidence of trauma above the clavicles, intracranial injuries would have been identified with a sensitivity of 100% [95% confidence interval (CI) 73–100%] and the use of CT scanning would have been reduced by 23%. Generalization of these criteria is limited by a very low confidence limit and the exclusion of children under five years of age.

In 2003, a prospective evaluation of 2,043 children with nontrivial head trauma, including 327 under 2 years of age, was published (6). Head CT scans were done in 1,271. Of the 98 who had evidence of brain injury on CT, 96 had at least one of the following: abnormal mental status (GCS < 15), clinical signs of skull fracture, scalp hematoma (when <2 years old), or a history of vomiting. The sensitivity of an algorithm using these variables to identify patients who require CT scanning was 98% (95% CI = 92.8–99.8%). In an effort to derive a decision tool to identify those at risk for the more worrisome occurrence of a head injury that requires an intervention, another set of variables (GCS < 15, signs of skull fracture, vomiting, and headache) was identified for which the presence of at least one identified these more serious injuries with a sensitivity of 100% (95% CI = 97.2–100%). Finally, the finding of a focal neurological deficit, GCS < 15 and/or vomiting, predicted all 29 cases in which a neurosurgical procedure was required, yielding a sensitivity of 100% (95% CI = 90.2–100%).

The National Emergency X-Radiography Utilization Study II (NEXUS II) was a prospective, multicenter study of adults and children with blunt head trauma that sought to derive a decision tool that could be used to identify patients at risk for intracranial injury who should undergo CT scanning (7). An algorithm was developed that identified intracranial injuries with a sensitivity of 98.3% (95% CI = 97.2–99%). Oman et al. evaluated this decision instrument in the subset of 1,666 children in the original study (8). The NEXUS II decision tool for children included seven variables: clinical evidence of skull fracture, altered alertness, neurological deficit, persistent vomiting, scalp hematoma, abnormal behavior, and coagulopathy. The occurrence of one or more of these variables identified 136 of 138 significant injuries for a sensitivity of 98.6% (95% CI = 94.9–99.8%). All of the 25 clinically important injuries in children under 3 years old were identified, although the confidence interval for this subset was large due to the small population.

The importance of using precision in applying the two decision tools described above was highlighted by Sun et al. (9), who assessed a subtle modification of the criteria described by Palchak et al. (6) with the pediatric subset of the NEXUS II database. By substituting the criteria “severe headache” for “headache” and “high-risk vomiting” for “vomiting,” 13 (9%) of patients with clinically important intracranial injuries would not be identified as needing head CT scanning.

In 2008, two other large studies developed decision-making algorithms in children with blunt head trauma. Dunning et al. prospectively evaluated 766 children who

underwent head CT and found that if at least 1 of 13 conditions were present (including loss of consciousness, seizure, and evidence of basilar skull fracture), patients with an intracranial injury could be identified with a sensitivity of 98% (95% CI = 96–100%) (10). The four missed injuries included two depressed skull fractures and one case that required craniotomy.

Atabaki et al. (11) evaluated an eight-component decision tool (including evidence of basilar skull fracture, age under 2, and dizziness) in 1,000 children with GCS >13 (11). The sensitivity of this algorithm was 95.4% (95% CI = 86.2–98.8%). None of the potentially missed injuries required neurosurgical intervention.

Recommendation: A Grade B recommendation can be made for using the decision tools described in the NEXUS II study, by Palchak et al., or by Dunning et al. in determining which children with head trauma require a head CT scan. No protocol of selective CT scanning will identify every intracranial injury. Ultimately, decision making must weigh how many and what missed injuries are justified by the prevention of a radiation-induced malignancy or the saving of several million dollars.

IS THERE A ROLE FOR HYPERTONIC SALINE IN PEDIATRIC HEAD INJURIES?

Head injuries result in direct and indirect costs of \$56 billion (12). Aside from prevention, the devastating impact of childhood injury can only be reduced by advancements in treatment.

Intracranial hypertension accompanies serious brain injury and is contributed to by multiple factors. The initial injury may result in hemorrhage in the subdural, epidural, and/or subarachnoid space, thereby increasing the volume within the rigid cranial vault. The secondary response to injury is characterized by the development of edema due to alterations in cerebral blood flow, ischemia, and ultimately cellular necrosis. The resultant inflammatory response, although beneficial for healing, leads to further edema and a continuing cycle of ischemia, necrosis, and inflammation. If this scenario is not controlled, herniation and global cerebral ischemia ensue.

The cornerstone of management of brain injury in children or adults is the prevention of intracranial hypertension and the maintenance of cerebral perfusion pressure through medical and operative interventions. Depending on the neurological examination and the intracranial pressure (ICP) and cerebral perfusion pressure (CPP), interventions such as elevation of the head of the bed, prevention of hyperthermia, and sedation may progress to mechanical ventilation with mild hyperventilation, chemical paralysis, administration of a hyperosmolar solution, barbiturate coma, and decompressive craniotomy.

The role of hyperosmolar agents in reducing experimental cerebral edema has been known for almost a century (13). In the early 1960s mannitol began to be used in patients with head injury (14), but its efficacy in adults and children remains unclear (15–16). In that context, this section focuses on the question of whether the administration of hypertonic saline is a safe and effective adjunct to other, more traditional means of controlling ICP dynamics in children.

Each of the studies that have been performed assessing hypertonic saline in pediatric head trauma have limited numbers of subjects and unique protocols, and none have directly compared hypertonic saline to mannitol.

In 1992, Fisher performed a double-blind, crossover study in 18 children with traumatic brain injury that assessed the short-term efficacy of 3% saline in reducing ICP as compared to normal (0.9%) saline (NS) (17). Each child received a bolus of each fluid, after which ICP was followed for two hours. On average, after administration of NS, ICP changed minimally from 19.3 mmHg to 20.0 mmHg. In contrast, after a bolus of 3% saline ICP decreased from 19.9 to 15.8 mmHg ($p = 0.003$). After hypertonic saline infusion, there was a reduced requirement for additional interventions to control ICP.

A randomized, controlled trial that compared the efficacy of hypertonic saline to lactated Ringer's solution (LR) was carried out in 35 children with GCS <8 (18). Subjects received either 1.75% saline, with an aim of increasing serum sodium to 145 to 150 mEq/L, or LR for 72 hours. The group treated with hypertonic saline required fewer interventions to maintain an ICP less than 15 mmHg ($p < 0.02$), had shorter intensive care stays ($p = 0.04$), and a lower incidence of acute respiratory distress syndrome (ARDS) ($p = 0.01$) and other complications than the group that received LR.

Khanna et al. reported a prospective trial of 3% saline in 10 children with traumatic brain injury in 2000 (19). In this study, hypertonic saline was continuously infused and titrated to maintain ICP less than 20 mmHg when other measures failed. More patients were not enrolled because standard measures, including mannitol, sedation, and hyperventilation, were usually successful in lowering ICP. The elevation in serum sodium concentration was limited to 15 mEq/L/day. At the start of therapy, the mean ICP of the subjects was 26 mmHg. A statistically significant inverse correlation between serum sodium and ICP was demonstrated. Over 72 hours, the frequency of ICP spikes decreased ($p < 0.01$) and CPP increased ($p < 0.01$). Reversible renal failure developed in two of the subjects. One patient, who presented two days after nonaccidental trauma, died.

A retrospective study of 68 children with intracranial hypertension treated with hypertonic saline was published in 2000 (20). In this series, 3% saline was used as rescue therapy in a similar manner as in Khanna et al.'s study when mannitol, hyperventilation, and other measures failed to maintain ICP less than 20 mmHg. The mean serum sodium in these cases was 160 mEq/L. Mortality was 15% and lower than what would be expected based on injury severity. Two deaths were due to cerebral edema, five were as a consequence of sepsis and multisystem organ failure, and one was from ARDS. Seventy-four percent of patients had complete recovery or only moderate neurological deficits, and 11% had severe deficits. When serum sodium exceeded 180 mEq/L, only one of four patients survived, and that subject had severe neurological deficits. Two theoretical complications of hypertonic saline administration, central pontine myelinolysis and subarachnoid hemorrhage due to rapid brain shrinkage, did not occur in any subjects.

Recommendation: Only a Grade C recommendation can be made for the use of hypertonic saline to reduce

ICP in children. Its efficacy in lowering the incidence of mortality or severe neurological morbidity is even less well supported. Until a large, randomized, controlled trial assesses the use of hypertonic saline in traumatic brain injury in children in a consistent protocol, it will be difficult to use it with confidence that its safety and efficacy exceeds standard treatment modalities.

WHEN IS CLINICAL CLEARANCE OF THE CERVICAL SPINE APPROPRIATE IN CHILDREN?

Cervical spine injuries are diagnosed in about 2% of cases of pediatric trauma (21). As compared to adult trauma patients, the incidence of cervical spine injury in the pediatric trauma population is much lower. In children with pain and tenderness of the cervical spine or neurological deficits it is imperative that imaging studies be obtained and interpreted carefully by a radiologist with pediatric expertise. The unique bony anatomy of the developing spine can lead to overcalling of injuries and ligamentous laxity can result in a spinal cord injury without radiological abnormality (SCIWORA) in which plain films and even CT scans may show no evidence of a dangerous spinal instability. In pediatric trauma victims with no obvious signs or symptoms of injury to the cervical spine, clinicians must balance the risk of a potentially disastrous missed injury against the cost and radiation exposure of universal imaging.

The concept of "clinical clearance" of the cervical spine has evolved over the past 20 years. In an effort to reduce the time and expense of cervical spine imaging in trauma patients, investigators have worked to define the circumstances under which imaging may be omitted without resultant missed injuries. Early studies in adults (22) suggested that as many as 20% of cervical spine injuries would be missed with protocols of selective imaging based on a lack of neck pain and mechanism of injury.

Velmahos et al. (23) refined the selection criteria used to determine eligibility for a clinical clearance protocol in a prospective study of trauma victims without neck pain by eliminating cases in which patients were intoxicated and had otherwise altered levels of consciousness, a subset that accounted for most of the missed injuries in previous reports. They identified 549 cases in which there was no neck tenderness with palpation or active motion. Patients with distracting injuries and head/facial injuries were included. Of these 549 cases, there were no cervical spine injuries identified by imaging studies. However, this cohort included only 18 patients under 10 years of age.

A large, prospective, multicenter study evaluated the efficacy of the NEXUS decision instrument for cervical spine imaging in 31,000 trauma victims without neck pain or neurological deficit (24). A substudy by Vicello et al. (25) focused on 3,065 patients younger than 18 years of age. There were 2,160 patients between 9 and 17, 817 between 2 and 8, and 88 less than 2 years of age. About 20% of the 3,065 cases evaluated were deemed "low risk," based on a lack of pain or midline tenderness, alertness, no neurological deficit, and no "painful distracting injury." In none of these cases was there a cervical spine injury. Thirty patients (0.98%) who did not satisfy low-risk criteria had cervical spine injuries. However, even this large study is

not definitive evidence for the safety of clinical cervical spine clearance in children. This study found no cases of SCIWORA, only four injuries in children under nine years of age, and none in those under two, making interpretation particularly difficult in the younger child. Although the sensitivity of the NEXUS instrument for the identification of cervical spine injury in children was 100%, due to the low incidence of injury in this population, the lower limit of the 95% CI for sensitivity was only 88%. To achieve a confidence interval for sensitivity of only 0.5%, a study of 80,000 children would be required.

Garton et al. (26) retrospectively reviewed the 20-year experience with cervical spine injury in children at a single institution. This study included 190 children with cervical spine injury, many more than in the study of Vicello. The sensitivity of the NEXUS criteria for injury was 100% in those 8 and older, but 2 of the 33 patients under 8 (6 and 18 months old) were found to have cervical spine injuries despite fulfilling "low-risk" NEXUS criteria.

Recommendation: Unless a prospective trial of at least 80,000 childhood trauma victims without neck pain that includes a large number of children under age eight is performed, the available adult and pediatric data will have to be interpreted carefully to avoid missed cervical spine injuries with 100% effectiveness. A Grade B recommendation may be made for clinical clearance of the cervical spine in teens and preteens using the NEXUS criteria, based on the available pediatric studies and more abundant adult data. In all children under age eight who fulfill the NEXUS criteria, due to the infrequency of injury, the relative paucity of data, and the variability in patients' ability to focus during a neck examination, more clinical judgment is necessary, but routine clinical clearance may not be recommended. Whether adults, much less children, with long bone fractures and other potentially distracting injuries are candidates for clinical spine clearance, despite the lack of missed injuries in this population in the Velmahos study, is not clear. Such cases were not included in the NEXUS studies of adults or children, so no recommendation for clinical clearance may be made in this population, although individual patients with other injuries may be judged competent to undergo physical examination of the cervical spine.

HOW SHOULD FEMUR FRACTURES BE MANAGED IN CHILDREN?

Femur fractures occur relatively frequently in the multiply injured pediatric patient (27), and it is in this context most trauma surgeons will encounter this condition. Expedient and effective treatment is imperative for a good long-term outcome. The options for management of femur fractures depend on the age of the patient, the type of fracture or fractures, and the desires of the patient and family.

Most pediatric orthopedic surgeons agree that for the majority of fractures in children under five years of age, the most appropriate management is traction and spica cast placement. For the mature adolescent intramedullary rodding is usually best (28), except in the case of very proximal or distal fractures, extensive soft tissue injury, gross comminution, or significant contamination

(29). The optimal management of children between 5 and 16 is more controversial (30) and is the subject of this section.

Multiple case series have documented successful experience with traction and spica cast application, external fixation, compression plating, and internal fixation with either rigid or flexible intramedullary rods. However, due to a paucity of randomized controlled trials and a tremendous heterogeneity of clinical material in the available studies, a 2001 evidence-based working group of pediatric orthopedic surgeons was unable to reach consensus as to the optimal care for children with femur fracture (30).

Comparative assessment of the management options for femur fracture must address the short and long-term anatomical and psychosocial outcomes as well as the potential complications inherent to specific treatment methods, such as pressure ulceration with spica casting, pin infections with external fixation, and migration of intramedullary rods. Differences in the definitions used by authors to determine adequate initial reduction or malunion can make comparison of results difficult. Interpretation of even the best-powered, randomized studies requires weighing of the significance of these "apples and oranges" of outcomes.

One of the largest reports of a consecutive series of external fixation of femur fractures studied 96 children between 3 and 15 (31). In this population there was an average hospital stay of 8.7 days and fixators were removed at an average of 61 days. There were two refractures (6%).

Hip spica application was compared to external fixation for the treatment of femur fracture in a multicenter, randomized, controlled trial published in 2005 (33). In this study of children between 4 and 10, 60 were randomized to hip spica and 48 to external fixation. The mean duration of initial hospitalization (3.4 versus 5.3 days, $p = 0.01$), total hospitalization (4.1 versus 5.9 days, $p = 0.02$), and overall treatment (58 versus 77 days, $p = 0.01$) for the hip spica group was significantly less than for those treated with external fixation. Malunions, including leg length discrepancies and excessive angulations occurred in 45% of the patients managed with hip spica but in only 16% of the external fixator group ($p = 0.002$). The clinical significance of this difference is unclear because assessment concluded at two years, but permanent gait abnormalities can result from substantial malunions. Pin site infections occurred in 45% of those treated with external fixation. No pressure ulcers or other direct complications of spica casting were reported. Psychosocial assessments were similar in the two groups.

Despite similar rates of patient and child satisfaction with the two treatments, these results suggest a trade-off between a shorter treatment duration with hip spica and a lower rate of malunion with external fixation.

A large, consecutive series of intramedullary rod placements in 52 children between ages 5 and 14 demonstrated excellent outcomes (32). The average hospital stay for those with isolated injuries was 3 days, and full weight bearing was achieved by 30 days. There were good functional results and only minor complications.

A prospective, nonrandomized, cohort study published in 2004 compared traction followed by hip spica application to placement of an elastic, titanium intramedullary rod in children between 6 and 16 with diaphyseal femur fractures

(29). Skeletal traction and spica cast application was used in 35 patients and titanium nails in 49. All fractures healed, and only three (8.5%) of those treated with traction and spica casting had malunions at the time of healing. The group treated with titanium elastic nails had significantly shorter times to discharge (5 versus 24 days, $p < 0.0001$), walking unaided (14 versus 70 days, $p < 0.0001$), and returning to school (48 versus 103 days, $p < 0.0001$). Although operative costs for the traction/spica were lower, they were made up for by the cost of longer hospitalization, yielding similar total costs for the two groups. An outcome questionnaire showed a trend toward better functional outcome at six months in the group managed with the titanium elastic nail and equivalent outcome after a year. Complications among the patients treated with traction and spica casting occurred in 34% and included malunion (3), loss of reduction (2), refracture (2), and pressure ulceration (4). In the titanium nail group, 21% of patients sustained complications, including irritation at the nail entry site (8), refracture after early nail removal (1), and bending of the nail after a fall (1). There were no malunions with titanium nailing.

This study, though limited by a lack of randomization, long-term follow-up, and insufficient functional assessment, demonstrated faster recovery with the use of a titanium elastic nail compared to traction and spica cast application. Costs were comparable and complications, though of a different nature for each technique, were similar in incidence.

A small randomized, controlled trial compared external fixation (10 patients) to elastic titanium nail insertion (9 patients) in children between 5 and 15 (34). This study represented the initial experience with elastic nail placement for the investigators. Children managed with intramedullary rod placement achieved full weight bearing, full range of motion, and return to school more rapidly than the external fixation group; however, there were too few subjects to allow for statistical significance to be reached.

Recommendation: Based on the available evidence, a Grade B recommendation may be made for intramedullary rod placement in most children with femur fractures between 5 and 15 years who lack the exclusion criteria discussed. If performed by an experienced surgeon, this treatment would reduce hospital stay and time to return to school, minimize early complications and psychosocial impact, and optimize long-term anatomical and functional outcome at a cost comparable to other methods.

HOW SHOULD BLUNT PANCREATIC TRANSECTION BE MANAGED IN CHILDREN?

Pancreatic injuries are rare in children, occurring in only 0.3% to 0.7% of trauma admissions (35–36). As with other solid organs, the severity of pancreatic trauma is based on the extent and location of injury (37). Grade I and II injuries are minor and major contusions, respectively. Distal transections and duct injuries are classified as grade III, proximal transections are grade IV, and massive disruptions of the pancreatic head are grade V. It is generally accepted that most grade I and II injuries are initially best managed nonoperatively (35,38–41). Grade V injuries are often devastating due to duodenal and biliary involvement and frequently necessitate laparotomy.

For children with pancreatic transections that do not involve the duodenum or bile duct (grades II and III injuries) there are several initial management strategies that have been advocated and used with success, including (1) expectant management, (2) early endoscopic retrograde cholangiopancreatography (ERCP) and ductal stenting, and (3) distal pancreatectomy. Due to the infrequent occurrence of pancreatic transection, there are no Level I or Level II data on which to base management. Determinations of what constitutes best practice for pediatric pancreatic transection must be made from, at best, consecutive case series.

Snajdauf et al. reviewed 13 operations for pancreatic injury (42). The average length of stay was 20 days, and there was no long-term morbidity or mortality. The importance of early diagnosis was emphasized in this series in which the postoperative stay after delayed diagnosis of injury was 67 days.

Another relatively large series of 11 pancreatic transections included 9 cases in which distal pancreatectomy was accomplished within 72 hours (35). The median length of stay for these early operated patients was 11 days. The only morbidity reported was a pancreatic fistula in one patient.

The largest published series documenting early operative management of pancreatic transections in children (43) reported a median length of stay of 11.5 days when an operation, usually a distal pancreatectomy, was performed with 48 hours of injury in 16 cases. Length of stay was substantially longer after delayed diagnosis or failed nonoperative management. Three of the early operated patients developed adhesive small bowel obstructions that required lysis of adhesions, but no pancreas-related complications were reported.

The largest and most successful consecutive series of nonoperative management of pancreatic injuries have come from the Hospital for Sick Children in Toronto. In 1998, the outcome of 35 children who sustained pancreatic injuries, including 11 cases that presented as a transection, was published (44). Only 5 of these 11 patients with transections developed pseudo-cysts. No operative intervention was required in any, although percutaneous drainage was performed in four. The average length of stay was 25 days and less for those that did not develop a pseudo-cyst. A subsequent study from the same institution focused on 10 cases managed nonoperatively (45). Four of these patients developed pseudo-cysts, and three were percutaneously drained. The median hospital stay was 24 days.

A smaller, consecutive series of nonoperatively managed pancreatic injuries that included five grade III injuries was reported by Kouchi et al. (46). In each case a pseudo-cyst developed. Three cysts that were less than 10 cm in diameter resolved in 27–103 days with expectant management. The other two grew progressively, necessitating cyst-enteric drainage in one and percutaneous drainage of the other. In both cases there was an uncomplicated recovery. No data regarding length of stay were presented.

More recently, an intermediate approach of early, ERCP-guided pancreatic ductal stent placement has been described as a means of reducing the length of stay and morbidity of nonoperative protocols for pancreatic transection in children while avoiding laparotomy. Experience with this technique developed in adults (47) and has been applied in children in some centers with qualified ERCP practitioners.

Initial experiences with ductal stenting in children was in the form of case reports (38,48) in which three cases with good outcomes were presented.

In the largest series of ductal stenting, 12 children with presumed pancreatic transection underwent ERCP (49). In 11 cases, a ductal injury was identified and an attempt was made to place a stent. Stents were technically feasible in nine cases. Three of these stents were advanced beyond the site of injury, and six were placed via the pancreatic duct into a pseudo-cyst. In two cases an endoscopic cyst-gastrostomy was subsequently performed, and in another, percutaneous cyst drainage was required. The remaining stented patients required no further interventions. Average length of stay for the children who received stents was 27 days (3–51 days). If the cases in which a percutaneous or cyst-enteric drainage was not required, length of stay was 18 days.

Recommendation: Because there are no randomized trials or large cohort studies that compare the various treatment modalities for pancreatic transection, any attempt

to draw conclusions regarding best practice from the studies is limited by the potential bias whereby only the most favorable series have been published. Nonetheless, some generalizations may be made: (1) If a distal pancreatectomy is performed in the first 48–72 hours after injury, a length of stay of 11–20 days, on average, could be predicted. (2) When pancreatectomy is undertaken after three days, length of stay and morbidity may be substantially greater. (3) Length of stay with initial non-operative management and selective, percutaneous, or cyst-enteric drainage of resultant pseudo-cysts may result in an average length of stay as low as 24 days, although hospitalizations of many months and total parenteral nutrition (TPN)-related complications will occur in some cases. (4) There is no clear evidence that ERCP and ductal stenting reduce length of stay or the incidence of pseudo-cyst development as compared to purely non-operative management. In addition, specific expertise must be available to make this technique safe and effective.

Summary of Cited Studies

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Palchak	6	2003	IIb	Brain injury on CT scan, no brain injury on CT scan	PCS	NR	Prediction of brain injury by CT decision tool
Oman	8	2006	IIb	Brain injury on CT scan, no brain injury on CT scan	PCS	NR	Prediction of brain injury by CT decision tool
Dunning	10	2006	IIb	Brain injury on CT scan, no brain injury on CT scan	PCS	NR	Prediction of brain injury by CT decision tool
Fisher	17	1992	IIb	3% saline, normal saline	RCT	2 hours	ICP change
Simma	18	1998	IIb	Lactated Ringer's, normal saline	RCT	NR	ICP, CPP, hospital and ICU stay, survival
Khanna	19	2000	IV	3% saline	CS	72 hours	ICP spike frequency, serum sodium, renal failure
Peterson	20	2000	IV	3% saline	CS	NR	ICP, renal failure
Vicello	25	2001	IIb	Low risk for cervical spine injury, high risk for injury	PCS	NR	Cervical spine injury
Garton	26	2008	IIb	Low risk for cervical spine injury, high risk for injury	RCS	NR	Cervical spine injury
Flynn	29	2004	IIb	Traction/hip spica, intramedullary rod	PCS	1 year	Malunion, refracture, pressure ulcer, hospital stay, return to school
Cramer	32	2000	IV	Intramedullary rod	CS	NR	Malunion, rotation, leg length discrepancy, hospital stay, time to weight bearing
Bar-On	34	1997	IIb	External fixation, intramedullary rod	RCT	14 months	Time to weight bearing, full range of motion, return to school
Meier	35	2001	IV	Distal pancreatectomy, observation	CS	NR	Hospital stay, pseudo-cyst development
Keller	41	1997	IV	Early diagnosis and operation, late diagnosis	RCS	12 months–12 years	Hospital stay, pseudo-cyst development
Nadler	43	1999	IV	Early diagnosis and operation, late diagnosis	RCS	NR	Hospital stay, morbidity
Shilyansky	44	1998	IV	Nonoperative management	CS	10 months	Time to enteral feeding, hospital stay, pseudo-cyst development
Wales	45	2001	IV	Nonoperative management	CS	47 months	Time to enteral feeding, hospital stay, pseudo-cyst development, endocrine/exocrine dysfunction
Kouchi	46	1999	IV	Nonoperative management	CS	NR	Pseudo-cyst development, mortality
Houben	49	2007	IV	Pancreatic ductal stenting	CS	2 years	Time to enteral feeding, hospital stay, requirement for cyst-enterostomy

Abbreviations: CPP, cerebral perfusion pressure; CS, case series; CT, computed tomography; GCS, Glasgow Coma Score; ICP, intracranial pressure; ICU, intensive care unit; NR, not reported; PCS, prospective cohort study; RCS, retrospective cohort study; RCT, randomized controlled trial.

REFERENCES

- Langlois JA, Rutland-Brown W, Thomas KE. Traumatic Brain Injury in the United States: emergency Department Visits, Hospitalizations, and Deaths. Atlanta, GA: Centers for Disease Control and Prevention, Nation Center for Injury Prevention and Control, 2006.
- Davis RL, Hughes M, Gubler KD, et al. The use of cranial CT scans in the triage of pediatric patients with mild head injury. *Pediatrics* 1995; 95: 345–9.
- Brenner DJ, Ellison CD, Hall EJ, et al. Estimated risks of radiation induced fatal cancer from pediatric CT. *Am J Roentgenol* 2001; 176: 289–96.
- Simon B, Letorunean P, Vitorino E, et al. Pediatric minor head trauma: indications for computed tomographic scanning revisited. *J Trauma* 2001; 51: 231–8.
- Haydel MJ, Shembekar AD. Prediction of intracranial injury in children aged five years and older with loss of consciousness after minor head injury due to nontrivial mechanisms. *Ann Emerg Med* 2003; 42: 507–14.
- Palchak MJ, Holmes JF, Vance CW, et al. A decision rule for identifying children at low risk for brain injuries after blunt head trauma. *Ann Emerg Med* 2003; 42: 492–506.
- Mower WR, Hoffman JR, Herbert M, et al. for the NEXUS II Investigators. National Emergency X-Radiology Utilization Study. Developing a clinical decision instrument to rule out intracranial injuries in patients with minor head trauma: methodology of the NEXUS II investigation. *Ann Emerg Med* 2002; 40: 505–14.
- Oman JA, Cooper RJ, Holmes JF, et al. for the NEXUS II investigators. Performance of a decision rule to predict need for computed tomography among children with blunt head trauma. *Pediatrics* 2006; 117: e238–e246.
- Sun BC, Hoffman JR, Mower WR. Evaluation of a modified prediction instrument to identify significant pediatric intracranial injury after blunt head trauma. *Ann Emerg Med* 2007; 49: 325–32.
- Dunning J, Daly JP, Lomas J-P, et al. Derivation of the children's head injury algorithm for the prediction of important clinical events decision rule for head injury in children. *Arch Dis Child* 2006; 91: 885–91.
- Atabaki SM, Stiell IG, Bazarian JJ, et al. a clinical decision rule for cranial computed tomography in minor pediatric head trauma. *Arch Pediatr Adolesc Med* 2008; 162: 439–45.
- Thurman D. The epidemiology and economics of head trauma. In: Miller L, Hayes R, eds., *Head Trauma Basic, Preclinical and Clinical Directions*. New York: Wiley, 2001.
- Weed LH, McKibben PS. Pressure changes in the cerebrospinal fluid following intravenous injection of solutions of various concentrations. *Am J Physiol* 1919; 48: 512–30.
- Wise BL, Chater N. Use of hyperosmolar mannitol solutions to lower cerebrospinal fluid pressure and decrease brain bulk in man. *Surg Forum* 1961; 12: 398–9.
- Adelson PD, Bratton SL, Carney NA, et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents. Chapter 11. Use of hyperosmolar therapy in the management of severe pediatric traumatic brain injury. *Pediatr Crit Care Med* 2003; 4(3 suppl): S40–S44.
- Wakai A, Roberts I, Schierhout G. Mannitol for acute traumatic brain injury. *Cochrane Database Syst Rev* 2005; 4: CD001049.
- Fisher B, Thomas D, Peterson B. Hypertonic saline lowers raised intracranial pressure in children after head trauma. *J Neurosurg Anesth* 1992; 4: 4–10.
- Simma B, Burger R, Falk M, et al. A prospective, randomized, and controlled study of fluid management in children with severe head injury: Lactated Ringer's solution versus hypertonic saline. *Crit Care Med* 1998; 26: 1265–70.
- Khanna S, Davis D, Petersoon B, et al. Use of hypertonic saline in the treatment of severe refractory posttraumatic intracranial hypertension in pediatric traumatic brain injury. *Crit Care Med* 2000; 28: 1144–51.
- Peterson B, Khanna S, Fisher B, et al. Prolonged hypernatremia controls elevated intracranial pressure in head-injured pediatric patients. *Crit Care Med* 2000; 28: 1136–43.
- Brown RL, Brunn MA, Garcia VF. Cervical spine injuries in children: a review of 103 patients treated consecutively at a level 1 pediatric trauma center. *J Pediatr Surg* 2001; 36: 1107–14.
- Jacobs LM, Schwartz R. Prospective analysis of acute cervical spine injury: a methodology to predict injury. *Ann Emerg Med* 1986; 15: 44–9.
- Velmahos GC, Theodorou D, Tatevossion R, et al. Radiographic cervical spine evaluation in the alert asymptomatic blunt trauma victim: much ado about nothing? *J Trauma* 1996; 40: 768–74.
- Hoffman JR, Mower WR, Wolfson AB, et al. Validity of a set of clinical criteria to rule out injury to the cervical spine in patients with blunt trauma. National Emergency X-Radiography Utilization Study Group. *N Engl J Med* 2000; 343: 94–9.
- Vicello P, Simon H, Pressman BD, et al. A prospective multicenter study of cervical spine injury in children. *Pediatrics* 2001; 108: e20.
- Garton HJ, Hammer MR. Detection of pediatric cervical spine injury. *Neurosurgery* 2008; 62: 700–8.
- Jawandi AH, Letta M. Injuries associated with fracture of the femur secondary to motor vehicle accidents in children. *Am J Orthop* 2003; 32: 459–62.
- Reeves RB, Ballard RI, Hughes JL. Internal fixation versus traction and casting of adolescent femoral shaft fractures. *J Pediatr Orthop* 1995; 15: 457–60.
- Flynn JM, Luedtke LM, Canley TJ, et al. Comparison of titanium elastic nails with traction and a spica cast to treat femoral fractures in children. *J Bone Joint Surg Am* 2004; 86: 770–7.
- Saunders JO, Browne RH, Mooney JF, et al. Treatment of femoral fractures in children by pediatric orthopedists: results of a 1998 survey. *J Pediatr Orthop* 2001; 21: 436–41.
- Hedin H, Hjorth K, Rehnberg L, et al. External fixation of displaced femoral shaft fractures in children: a consecutive study of 98 fractures. *J Orthoped Trauma* 2003; 17: 250–6.
- Cramer KE, Tornetta P, Spero CR, et al. Ender rod fixation of femoral shaft fractures in children. *Clin Ortho* 2000; 376: 119–23.
- Wright JG, Wang EEL, Owen JL, et al. Treatments for paediatric femoral fractures: a randomized trial. *Lancet* 2005; 365: 1153–8.
- Bar-On E, Sagiv S, Porat S. External fixation or flexible intramedullary nailing for femoral shaft fractures in children. *J Bone Joint Surg* 1997; 79B: 975–8.
- Meier DE, Coln CD, Hicks BA, et al. Early operation in children with pancreas transection. *J Pediatr Surg* 2001; 36: 341–4.
- Jobst MA, Canty TG, Lynch FP. Management of pancreatic injury in pediatric blunt abdominal trauma. *J Pediatr Surg* 1999; 34: 818–23.
- Moore EE, Cogbill TH, Malangoni MA, et al. Organ injury scaling II: pancreas, duodenum, small bowel, colon and rectum. *J Trauma* 1990; 30: 1427–9.
- Canty TG, Weinman D. Treatment of pancreatic duct disruption in children by an endoscopically placed stent. *J Pediatr Surg* 2001; 36: 345–8.
- Rescorla FJ, Plumley DA, Sherman S, et al. The efficacy of early ERCP in pediatric pancreatic trauma. *J Pediatr Surg* 1995; 30: 336–40.

40. Graham CA, O'Tolle SJ, Watson AJ, et al. Pancreatic trauma in Scottish children. *JR Coll Surg Edinb* 2000; 45: 223–6.
41. Keller MS, Stafford PW, Vand DW. Conservative management of pancreatic trauma in children. *J Trauma* 1997; 42: 1097–100.
42. Snajdauf J, Rygl M, Kalousova J, et al. Surgical management of major pancreatic injury in children. *Eur J Pediatr Surg* 2007; 17: 317–21.
43. Nadler EP, Gardner M, Schall LC, et al. Management of blunt pancreatic injury in children. *J Trauma* 1999; 47: 1098–103.
44. Shilyansky J, Sena LM, Kreller M, et al. Nonoperative management of pancreatic injuries in children. *J Pediatr Surg* 1998; 33: 343–9.
45. Wales PW, Shuckett B, Kim PCW. Long-term outcome after nonoperative management of complete traumatic pancreatic transection in children. *J Pediatr Surg* 2001; 36: 823–7.
46. Kouchi K, Tanabe M, Yoshida H, et al. Nonoperative management of blunt pancreatic injury in childhood. *J Pediatr Surg* 1999; 34: 1736–9.
47. Huckfeldt R, Agee C, Nichols W, et al. Endoscopic intrapancreatic stent for traumatic duct injury. *Injury* 1995; 26: 553–4.
48. Cay A, Mustafa I, Bektas O, et al. Nonoperative treatment of traumatic pancreatic duct disruption in children with an endoscopically placed stent. *J Pediatr Surg* 2005; 40: e9–e12.
49. Houben CH, Niyi AA, Patel S, et al. Traumatic pancreatic duct injury in children: Minimally invasive approach to management. *J Pediatr Surg* 2007; 42: 629–35.

An Evidence-Based Approach to Geriatric Trauma

Carl I. Schulman

Question Summary		
Question	Answer	Grade
Are there any patient characteristics or pre-morbid conditions that are known to increase mortality and/or require specialized treatment?	The current evidence points to worse outcomes for geriatric patients with preexisting chronic disease. There are no recommendations, however, for how this information can be used to improve care.	C
What is the impact on treatment and outcome for patients on warfarin?	Geriatric patients with warfarin use, elevated international normalized ratio, and intracranial hemorrhage have worse outcomes. Again, no interventions have been proven beneficial to reduce mortality in this cohort.	C
What is the impact on treatment and outcome for patients on beta-blockers, and when should they be used?	No specific recommendation can be made as to the use or timing of beta-blockers in the geriatric trauma patient. Further research is definitely needed.	C
What are the optimal triage guidelines for the geriatric trauma patient?	There is insufficient evidence to make any evidence-based conclusions on the optimal triage guidelines for the geriatric trauma patient. The current recommendations from the American College of Surgeons Committee on Trauma are similarly based and will remain the standard until better studies are performed.	D
What are the optimal strategies for resuscitation and monitoring of the geriatric trauma patient?	It appears that aggressive therapy and monitoring improves outcomes in a very select subset of geriatric trauma patients. Identifying these patients and the exact intervention remains in need of further high-quality studies.	B
Are there any injury-prevention programs that have been shown to work for geriatric patients?	Regular strength and balance exercises are effective at preventing falls and injuries in elderly people. Hip protectors can be considered in high-risk groups.	A
Are there any circumstances where withholding/withdrawing care is appropriate?	Current recommendations cannot be made at this time. The existing data, however, can be used to aide physicians in their conversations with patients and families about end-of-life decisions.	C

INTRODUCTION

Geriatric trauma care will become an increasingly important part of the spectrum of trauma care. The Baby Boomers will start to reach age 65 beginning in 2011. This means the elderly will comprise a larger proportion of trauma victims and are the fastest-growing segment of the population. As of 2005, trauma is the fifth leading cause of death in all age groups and the ninth leading cause for those 65 years and older (1). The rate per 100,000, however, is 38.0 for all groups and 96.5 for those >65 (1). Perhaps even more important is the added influence of comorbid conditions in this age group. In the population 65 and older, 42% reported some type of long-lasting condition or a disability. In those aged 65 to 74, 32% reported at least one disability, in contrast with 72% of people 85 and over (2,3).

The definition of "geriatric" is the subject of much controversy. The absolute age of the patient may not be the most important factor is defining the population of older adults who require specialized care. It may be a mix of chronological age, physiological age, the presence of preexisting conditions, or a combination of these factors. It is important to be able to identify those at increased risk and understand that the data we use to make such decisions are based on studies with myriad age ranges and definitions of the geriatric trauma patient.

The most commonly used age cut-off for elderly or geriatric patients is 65 years old. There are, however, some data to suggest that those even as young as 45 may have poorer outcomes than their younger counterparts, and that those greater than 75 years may be at especially high risk (4,5).

ARE THERE ANY PATIENT CHARACTERISTICS OR PREMORBID CONDITIONS THAT ARE KNOWN TO INCREASE MORTALITY AND/OR REQUIRE SPECIALIZED TREATMENT?

There is a preponderance of evidence to suggest that elderly trauma patients have a higher level of injury related mortality than their younger counterparts. The presence of preexisting conditions (PECs) contributes to much of this increased risk of death and is greatest in patients with the least severe injuries, with a lesser effect on those with moderate injuries (6,7). In addition, this increased risk of death varies according to the type and number of PECs.

The concept of physiologic age is often used as a surrogate for the presence of PECs. Examination of hospital discharge data for trauma patients in the state of California found that PECs were important predictive factors of mortality, independent of age (5,7). A similar study of 8,000 trauma patients demonstrated a threefold increase in mortality in patients with PECs, compared to those without PECs (8).

A review of a state trauma database with over 30,000 records over a 13-year period showed an overall mortality of 7.6% with an increase of 6.8% for each year over age 65. The presence of PECs was still found to have an independent effect on mortality after controlling for initial vital signs, Glasgow Coma Score (GCS), and Injury Severity Score (ISS). The strongest effects were seen for hepatic disease (odds ratio 5.1), renal disease (odds ratio 3.1), and cancer (odds ratio 1.8), yet in this study warfarin therapy was not an independent predictor of mortality (9).

Effect of PECs on Outcome in Geriatric Trauma Patients

- Level of evidence: III
- Strength of recommendation: C

Summary: The current evidence, although all retrospective, points to worse outcomes for geriatric patients with preexisting chronic disease. There are no recommendations, however, for how this information can be used to improve care.

WHAT IS THE IMPACT ON TREATMENT AND OUTCOME FOR PATIENTS ON WARFARIN?

Pieracci found that in patients with a therapeutic international normalized ratio (INR) (≥ 2), there were increased odds of intracranial hemorrhage (ICH) [odds ratio (OR) = 2.59, 95% confidence interval (CI) 0.92–7.32, $p = 0.07$] and overall mortality (OR = 4.48, 95% CI 1.60–12.50, $p = 0.004$) (10). Warfarin use in the absence of a therapeutic INR was not associated with adverse outcomes. In an attempt to improve treatment of trauma patients with preinjury warfarin anticoagulation, Ivascu and colleagues evaluated the implementation of a “Coumadin protocol” compared to historical controls. They found no difference in time until warfarin reversal and no improvement in survival in head-injured patients on preinjury warfarin (11).

Another retrospective review confirmed increased mortality in those >70 years old if on oral anticoagulants and that both mortality and ICH were increased with increasing INR (INR over 4.0 had mortality 50%, risk of ICH 75%) (12). A very small study of orthopedic trauma patients on warfarin found increased delay to surgery, hospital length of stay, transfusion requirements, and discharge disposition, but not on mortality (13). Another small series found those >55 and warfarin use had more severe injuries and a higher mortality (14). A prospective study of 159 patients with a mean age of 75 ± 13 years compared to age-matched historical controls demonstrated no increased risk for fatal hemorrhagic complications in the absence of head trauma, but if intracranial injury is present, those taking warfarin have a statistically higher mortality rate (15). This is contrasted by two older retrospective reviews of large registries suggesting no adverse impact on mortality or length of stay (16,17).

Impact on Treatment and Outcome for Geriatric Trauma Patients on Warfarin

- Level of evidence: III
- Strength of recommendation: C

Summary: Geriatric patients with warfarin use, elevated INR, and ICH have worse outcomes. Again, no interventions have been proven beneficial to reduce mortality in this cohort.

WHAT IS THE IMPACT ON TREATMENT AND OUTCOME FOR PATIENTS ON BETA-BLOCKERS, AND WHEN SHOULD THEY BE USED?

This issue is certainly not limited to the geriatric trauma patient, but surprisingly there has been only one study on beta-blocker use in trauma patients. It was a retrospective review that concluded the OR for fatal outcome was 0.3 ($p < 0.001$) for the cohort using beta-blockers compared to controls and was more pronounced in patients with a significant head injury. They concluded beta-blocker therapy is safe and may be beneficial in selected trauma patients with or without head injury (18).

Impact on Treatment and Outcome for Patients on Beta-blockers

- Level of evidence: III
- Strength of recommendation: C

Summary: No specific recommendation can be made as to the use or timing of beta-blockers in the geriatric trauma patient. Further research is needed.

WHAT ARE THE OPTIMAL TRIAGE GUIDELINES FOR THE GERIATRIC TRAUMA PATIENT?

Triage is the process of sorting patients based on their need for immediate medical treatment as compared to their chance of benefiting from such care. Triage attempts to maximize patient benefit based on available resources. “Resources for Optimal Care of the Injured Patient—2006”

from the American College of Surgeons Committee on Trauma recommends patients greater than 55 years old should be considered for transport to a trauma center (19). The reality, however, is that elderly trauma patients are less likely to be triaged to a trauma center. Several studies have documented that undertriage is much more common in patients over the ages of 55 and even worse for those over 65 (20–23). Only with better recognition of the importance of identifying severe injury in elderly patients can triage be improved by prehospital and hospital providers.

The most common scoring systems (Revised Trauma Score, GCS, APACHE, etc.), along with more basic measures such as initial blood pressure, respiratory rate, and base deficit, have been shown to correlate with outcome in the geriatric population. The Trauma Score (TS) may be the most useful in the prehospital and early hospital setting as a triage tool. It varies from 0 to 16 and contains blood pressure, respiratory rate, respiratory effort, GCS, and capillary refill. Several studies have documented the correlation between the TS (or Revised Trauma Score) on mortality in the geriatric population. A case-matched review of 100 elderly patients showed that no patient hospitalized with severe injuries survived with a TS < 9 and no elderly patients with a TS < 7 even survived to reach the hospital (24). Another study confirmed this 100% mortality with a TS < 7 (25). The predictive ability of the trauma score has also been applied to elderly patients admitted to the intensive care unit. These population-based studies may provide some guidance when counseling families about the expected outcomes and making end-of-life decisions, but they cannot be directly translated to individual patients.

The ISS is a good predictor of survival in most trauma populations, including the elderly population. However, the delay in obtaining the data required to calculate the score makes it not useful as a triage tool. The basic physiologic variables contained in the TS are the only available alternatives. Unfortunately, none of these markers are specific enough to make decisions on definitive care, although they may provide some guidance and help direct future research efforts in this area.

Optimal Triage Guidelines for the Geriatric Trauma Patient

- Level of evidence: III/IV
- Strength of recommendation: D

Summary: There is insufficient evidence to make any evidence-based conclusions on the optimal triage guidelines for the geriatric trauma patient. The current recommendations from the American College of Surgeons Committee on Trauma are similarly based and will remain the standard until better studies are performed.

WHAT ARE THE OPTIMAL STRATEGIES FOR RESUSCITATION AND MONITORING OF THE GERIATRIC TRAUMA PATIENT?

Geriatric trauma patients are more likely to present in shock than younger patients matched for trauma and ISS (26). It is unclear, however, which geriatric patients will benefit from more aggressive resuscitation and invasive monitoring.

This decision may be more difficult due to the coexistence of underlying disease in the geriatric population.

A prospective study of elderly patients (>65 years of age) who presented with predefined criteria attempted to answer these questions. The criteria were a pedestrian-motor vehicle mechanism, initial blood pressure less than 150 mmHg, acidosis, multiple fractures, and head injuries. Patients meeting these criteria were treated with invasive hemodynamic monitoring, including a pulmonary artery catheter, and moved to the intensive care unit as soon as possible to optimize hemodynamic parameters, including cardiac index and oxygen consumption. The ability to optimize cardiac output and systemic vascular resistance was greater in survivors compared to nonsurvivors. Occult shock was found in 13 of 30 (43%) patients, despite being hemodynamically stable on initial presentation. Mortality was high in these patients, and 54% died (27). This underscores the fact that geriatric trauma patients with significant underlying physiologic abnormalities may be difficult to identify early in the course of treatment and may be at greater risk for mortality.

A prospective study compared the responses of old (≥ 65 years) and young (<65 years) trauma patients resuscitated using a standardized protocol to attain and maintain an oxygen delivery index of 600 ml/min/m² or greater ($\text{DO}_2\text{I} \geq 600$) for the first 24 hours in the intensive care unit. Inclusion criteria were designed to select patients at high risk of postinjury multiple organ failure and included major organ or vascular injury and/or skeletal fractures, initial base deficit of 6 mEq/L or greater, need for 6 units or more of packed red blood cells in the first 12 hours, or age of 65 years or older with any two previous criteria. The clinical endpoint was a $\text{DO}_2\text{I} \geq 600$ using a pulmonary artery catheter, infusion of crystalloid solutions, transfusion of packed red blood cells, and moderate inotropic support as needed in that sequence. A total of 12 old patients and 54 young patients were resuscitated according to the protocol. For old patients, 9 (75%) attained $\text{DO}_2\text{I} \geq 600$, and 11 (92%) survived seven or more days and five (42%) 30 or more days. For young patients, 45 (83%) attained the DO_2I goal, and 48 (89%) survived 30 or more days. Outcomes were worse for the elderly cohort, but the authors concluded resuscitation is not futile (28). This study is limited by the lack of a control group of elderly patients who were not resuscitated with the study protocol.

The only randomized trial of resuscitation in geriatric trauma patients was in hip fracture patients. They compared monitoring with the use of a pulmonary artery catheter to a standard central venous catheter. A significant increase in mortality was noted in the nonmonitored group (29% versus 2.9%) (29). Unfortunately, the study did not include the multiply injured trauma patient, and the exact protocol by which patients were optimized with the use of the pulmonary artery catheter is not clear. Additionally, this study was performed in 1995, before the current era of more modern critical care, with less reliance on invasive monitoring and the more recent literature showing no benefit to the use of a pulmonary artery catheter in most situations.

Which patients are in need of aggressive resuscitation and monitoring has yet to be determined. A trauma score <15, a base deficit of ≥ 6 or worse, or the presence of shock (systolic blood pressure <90) have all been associated with worse outcomes and may help identify

patients who would benefit from aggressive resuscitation (25,30–32). The geriatric trauma patient may exhibit subtle or no signs of shock so that a heightened level of suspicion is required at all times while assessing and treating the geriatric trauma patient.

Optimal Strategies for Resuscitation and Monitoring of the Geriatric Trauma Patient

- Level of evidence: II
- Strength of recommendation: B

Summary: It appears that aggressive therapy and monitoring improves outcomes in a very select subset of geriatric trauma patients. Identifying these patients and the exact intervention remains in need of further high-quality studies.

ARE THERE ANY INJURY PREVENTION PROGRAMS THAT HAVE BEEN SHOWN TO WORK FOR GERIATRIC PATIENTS?

The ultimate ability to influence outcome lies in the reduction of injuries. Injury prevention has proven to be successful for a wide variety of traumatic injuries. Because the majority of elderly injuries result from falls, this has been the most studied area. Many methods and programs already exist and have been proven effective in elderly populations. Some examples include regular exercise, supplementation of vitamin D and calcium, withdrawal of psychotropic medication, cataract surgery, professional assessment and modification of environmental hazards, hip protectors, and multifactorial prevention programs (33). It is worthwhile for the trauma surgeon to be aware of such programs and serve as a source of information, referral, and perhaps even program implementation in high-need, underserved areas.

Although there are many studies that have shown a decrease in the rate of falls, few have focused on the actual decrease of fractures. A prospective study with a 10-year follow-up showed that a program of back-strengthening exercises for 2 years reduced the risk of spine fractures by more than 60% (34). A larger randomized trial showed that impact exercise in 72–74-year-old women reduced fracture risk by over 60% (35). This is coupled with numerous other population-based studies confirming these effects (33).

An interesting approach worth mention is the use of hip protectors. Many studies of their use, including a recent review of randomized trials, suggested a benefit and a cost savings for those at high risk, such as nursing home or institutionalized patients (36).

Injury-prevention Programs that Have Been Shown to Work for Geriatric Patients

- Level of evidence: I
- Strength of recommendation: A

Summary: Based on an overwhelming amount of population-based data (not all presented here) regular strength and balance exercises are effective at preventing falls and injuries in elderly people. Hip protectors can be considered in high-risk groups.

ARE THERE ANY CIRCUMSTANCES WHERE WITHHOLDING/WITHDRAWING CARE IS APPROPRIATE?

The combination of age, injury severity, and underlying disease makes even the most advanced modern medical care futile for certain patients. This, however, is a very individualized decision. Some patients and families might consider a 1% chance of any type of survival (i.e., even a poor functional outcome) acceptable and desire all possible medical efforts. Patients who cannot reasonably be expected to maintain their quality of life as the result of severe injuries may not wish to continue with possible life-saving treatment. Although no prospective trial will ever be done to definitively identify the criteria by which care should be withheld, there are several studies that attempt to provide some insight.

Arterial base deficit has been correlated with mortality in the geriatric population and provides some clues as to prognosis. In a study of elderly (>55) trauma patients those with a severe base deficit (−10 or worse) had an 80% mortality; those with a moderate (−6 to −9) base deficit had a 60% mortality; and those with a mild base deficit (−3 to −5) had a 23% mortality. Highlighting the difficulty in identifying severe injuries in this population, even those with a normal base deficit (2 to −2) had a 18% mortality (30).

A review of the National Trauma Data Bank attempts to provide criteria for the futility of care in elderly trauma patients. They stratified the patients into “young” old (65–74 years) and “old” old (75–84 years). A multiple regression analysis of over 76,000 records was performed to identify predictors of a 95% probability of death. This cut-off to determine a futile effort is subject to controversy and individual interpretation. Injuries to the brain, chest, and abdomen were the strongest anatomic injury predictors of mortality ($p < 0.001$ for all), whereas worsening base deficit and systolic blood pressure less than 90 were the strongest physiologic predictors of mortality. In the 65–74-year-old age group, only hypotensive patients admitted with a severe thoracic and/or abdominal injury who also had severe injuries to the brain [Abbreviated Injury Score (AIS) ≥ 4] or profound shock (base deficit ≤ -12) had a less than 5% chance of survival. For those aged 75 to 84, even moderate injury to the brain (AIS ≤ 3) and moderate shock (base deficit ≤ -6) were associated with a less than 5% chance of survival. Finally, for those age 85 or older, profound shock or the combination of moderate shock and moderate injury to the head was associated with a less than 5% chance of survival (37).

Unfortunately, none of these criteria are specific enough to make decisions on withdrawal of care for any individual patient, but they may, once again, aid in decisions at the end of life.

Circumstances Where Withholding/Withdrawing Care Is Appropriate

- Level of evidence: III
- Strength of recommendation: C

Summary: Based on poor-quality trials and the inability to apply population-based data to individual patients, current recommendations cannot be made at this time. The existing data, however, can be used to aide physicians in their conversations with patients and families about end-of-life decisions.

CONCLUSION

Geriatric trauma remains a significant cause of morbidity and mortality. Practitioners need to be aware of the anatomic, physiologic, and mechanistic differences encountered in this population. The effects of preexisting medical conditions

place elderly patients at increased risk and make it difficult for them to compensate in the face of injury. In addition, geriatric trauma patients may have atypical presentations. A heightened level of suspicion, starting with appropriate triage to a trauma center and continuing throughout the spectrum of care, is the only way to avoid poor outcomes.

High-quality trials are sparse relating to the care of the elderly trauma patient, but the prevention literature is clear, and strength and balance programs are effective at reducing injury. The ultimate decision to withhold or withdraw care is also a difficult question that remains to be answered and may never reach the level of evidence required for any firm recommendation.

Literature Supporting Evidence-Based Recommendations for Geriatric Trauma

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
McGwin	6	2004	IIIb	50–65 and >65	RCS	N/A	In-hospital mortality
Morris	7	1990	IIIb	Age-matched adult trauma patients	RCS/CC	N/A	In-hospital mortality
Morris	5	1990	IIIb	All California trauma admissions 1986	RCS	N/A	Mortality stratified by injury severity
Milzman	8	1992	IIIb	8,000 adult trauma patients 1986–90	RCS	N/A	Mortality
Grossman	9	2002	IIIb	>65 statewide trauma database	RCS	N/A	30 day in-hospital mortality
Pieracci	10	2007	IIIb	>65 suspected head injury single Level I center	RCS	N/A	ICH and mortality
Ivascu	11	2006	IIb	Anticoagulated trauma patients	PCS	Hospital discharge	Progression of ICH and mortality
Franko	12	2006	IIIb	Adult TBI patients, young versus >70	RCS	N/A	ICH and mortality
Kirsch	13	2004	IIIb	Patients on warfarin with orthopedic fractures	RCS	N/A	Delay to surgery, LOS, transfusion, discharge disposition.
Lavoie	14	2004	IIIb	>55 with TBI and warfarin use	RCS	N/A	Severity of injury and mortality
Mina	15	2003	IIb	All trauma patients taking warfarin	PCS	Hospital discharge	Hemorrhagic complications and mortality
Wojcik	17	2001	IIIb	All trauma patients taking warfarin	RCS	N/A	LOS and mortality
Kennedy	16	2000	IIIb	All trauma patients taking warfarin	RCS	N/A	Mortality
Arbabi	18	2007	IIIb	All trauma patients receiving beta-blockers	RCS	N/A	Mortality
ACS-COT	19	2006	IV		NR		
Ma	20	1999	IIIb	1995 Maryland statewide prehospital data	RCS	N/A	Transfer to trauma center
Phillips	21	1996	IIIb	Florida triage records	RCS	N/A	Appropriate triage
Zimmer-Gembeck	22	1995	IIIb	All trauma admissions	RCS	N/A	Over and undertriage
Osler	24	1998	IIIb	Geriatric trauma patients	RCS	N/A	Mortality
Knudson	25	1994	IIIb	>65 blunt trauma, three registries	RCS	N/A	Mortality
Davis	30	1998	IIIb	>55 yo trauma registry Level 1 center	RCS	N/A	ISS and mortality
Scheetz	23	2003	IIIb	Patient discharge data adult Level 1 centers	RCS	N/A	Undertriage and overtriage
Scalea	27	1990	IIb	>65 PHBC, BP <150, acidosis, fx, and TBI	PCS	Hospital discharge	Hemodynamic parameters and mortality
McKinley	28	2000	IIb	> and <65 yo, high risk, BD –6, >6 U PRBC	PCS	Hospital discharge	LOS and mortality
Schultz	29	1985	IIb	Elderly hip fractures	PCS	Hospital discharge	Mortality

(Continued)

Literature Supporting Evidence-Based Recommendations for Geriatric Trauma (Continued)

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Pellicane	31	1992	IIIb	>65 trauma patients	RCS	N/A	Trauma score, complications, and mortality
Van Aalst	32	1991	IIb	>65 years, blunt trauma, ISS >16	PCS	2.8 years	20 measures of functional ability
Nirula	37	2004	IIIb	>65, National Trauma Board Databank 1994–2001	RCS	N/A	Mortality
Sinaki	34	2002	I	Postmenopausal women	RCT	10 years	Vertebral fracture
Korpelainen	35	2006	I	>70 yo women	RCT	30 months	Fall-related fractures
Parker	36	2004	I	Multiple trials	RCT	Variable	Hip fracture

Abbreviations: BD, base deficit; BP, blood pressure; ICH, intracranial hemorrhage; ISS, Injury Severity Score; LOS, length of stay; NR, not reported; PCS, prospective cohort study; PHBC, pedestrian hit by car; PRBC, packed red blood cells; RCS, retrospective cohort study; RCT, randomized controlled trial; TBI, traumatic brain injury.

REFERENCES

1. CDC. National vital statistics reports: deaths, leading causes for 2004. 2007; 56.
2. Gist Y, Hetzel L. We the people: aging in the United States. U.S. Census Bureau 2004.
3. Hetzel L, Smith A. The 65 years and over population: 2000. U.S. Census Bureau 2001.
4. Champion HR, Copes WS, Buyer D, et al. Major trauma in geriatric patients. *Am J Public Health* 1989; 79: 1278–82.
5. Morris JA Jr, MacKenzie EJ, Damiano AM, et al. Mortality in trauma patients: the interaction between host factors and severity. *J Trauma* 1990; 30: 1476–82.
6. McGwin G Jr., MacLennan PA, Fife JB, et al. Preexisting conditions and mortality in older trauma patients. *J Trauma* 2004; 56: 1291–6.
7. Morris JA Jr, MacKenzie EJ, Edelstein SL. The effect of preexisting conditions on mortality in trauma patients. *JAMA* 1990; 263: 1942–6.
8. Milzman DP, Boulanger BR, Rodriguez A, et al. Pre-existing disease in trauma patients: a predictor of fate independent of age and injury severity score. *J Trauma* 1992; 32: 236–43; discussion 243–4.
9. Grossman MD, Miller D, Scaff DW, et al. When is an elder old? Effect of preexisting conditions on mortality in geriatric trauma. *J Trauma* 2002; 52: 242–6.
10. Pieracci FM, Eachempati SR, Shou J, et al. Degree of anticoagulation, but not warfarin use itself, predicts adverse outcomes after traumatic brain injury in elderly trauma patients. *J Trauma* 2007; 63: 525–30.
11. Ivascu FA, Janczyk RJ, Junn FS, et al. Treatment of trauma patients with intracranial hemorrhage on preinjury warfarin. *J Trauma* 2006; 61: 318–21.
12. Franko J, Kish KJ, O'Connell BG, et al. Advanced age and preinjury warfarin anticoagulation increase the risk of mortality after head trauma. *J Trauma* 2006; 61: 107–10.
13. Kirsch MJ, Vrabec GA, Marley RA, et al. Preinjury warfarin and geriatric orthopedic trauma patients: a case-matched study. *J Trauma* 2004; 57: 1230–3.
14. Lavoie A, Ratte S, Clas D, et al. Preinjury warfarin use among elderly patients with closed head injuries in a trauma center. *J Trauma* 2004; 56: 802–7.
15. Mina AA, Bair HA, Howells GA, et al. Complications of preinjury warfarin use in the trauma patient. *J Trauma* 2003; 54: 842–7.
16. Kennedy DM, Cipolle MD, Pasquale MD, et al. Impact of preinjury warfarin use in elderly trauma patients. *J Trauma* 2000; 48: 451–3.
17. Wojcik R, Cipolle MD, Seislove E, et al. Preinjury warfarin does not impact outcome in trauma patients. *J Trauma* 2001; 51: 1147–51; discussion 1151–2.
18. Arbabi S, Champion EM, Hemmila MR, et al. Beta-blocker use is associated with improved outcomes in adult trauma patients. *J Trauma* 2007; 62: 56–61; discussion 61–2.
19. Committee on Trauma ACS. Resources for the Optimal Care of the Injured Patient, vol. 14. Chicago: American College of Surgeons, 2006.
20. Ma MH, MacKenzie EJ, Alcora R, et al. Compliance with prehospital triage protocols for major trauma patients. *J Trauma* 1999; 46: 168–75.
21. Phillips S, Rond PC III, Kelly SM, et al. The failure of triage criteria to identify geriatric patients with trauma: results from the Florida Trauma Triage Study. *J Trauma* 1996; 40: 278–83.
22. Zimmer-Gembeck MJ, Southard PA, Hedges JR, et al. Triage in an established trauma system. *J Trauma* 1995; 39: 922–8.
23. Scheetz LJ. Effectiveness of prehospital trauma triage guidelines for the identification of major trauma in elderly motor vehicle crash victims. *J Emerg Nurs* 2003; 29: 109–15.
24. Osler T, Hales K, Baack B, et al. Trauma in the elderly. *Am J Surg* 1988; 156: 537–43.
25. Knudson MM, Lieberman J, Morris JA Jr., et al. Mortality factors in geriatric blunt trauma patients. *Arch Surg* 1994; 129: 448–53.
26. Clancy TV, Ramshaw DG, Maxwell JG, et al. Management outcomes in splenic injury: a statewide trauma center review. *Ann Surg* 1997; 226: 17–24.
27. Scalea TM, Simon HM, Duncan AO, et al. Geriatric blunt multiple trauma: improved survival with early invasive monitoring. *J Trauma* 1990; 30: 129–34; discussion 134–6.
28. McKinley BA, Marvin RG, Cocanour CS, et al. Blunt trauma resuscitation: the old can respond. *Arch Surg* 2000; 135: 688–93; discussion 694–5.
29. Schultz RJ, Whitfield GF, LaMura JJ, et al. The role of physiologic monitoring in patients with fractures of the hip. *J Trauma* 1985; 25: 309–16.
30. Davis JW, Kaups KL. Base deficit in the elderly: a marker of severe injury and death. *J Trauma* 1998; 45: 873–7.

31. Pellicane JV, Byrne K, DeMaria EJ. Preventable complications and death from multiple organ failure among geriatric trauma victims. *J Trauma* 1992; 33: 440–4.
32. van Aalst JA, Morris JA Jr, Yates HK, et al. Severely injured geriatric patients return to independent living: a study of factors influencing function and independence. *J Trauma* 1991; 31: 1096–101; discussion 1101–2.
33. Kannus P, Sievanen H, Palvanen M, et al. Prevention of falls and consequent injuries in elderly people. *Lancet* 2005; 366: 1885–93.
34. Sinaki M, Itoi E, Wahner HW, et al. Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone* 2002; 30: 836–41.
35. Korpelainen R, Keinänen-Kiukaanniemi S, Heikkinen J, et al. Effect of impact exercise on bone mineral density in elderly women with low BMD: a population-based randomized controlled 30-month intervention. *Osteoporos Int* 2006; 17: 109–18.
36. Parker MJ, Gillespie LD, Gillespie WJ. Hip protectors for preventing hip fractures in the elderly. *Cochrane Database Syst Rev* 2004; CD001255.
37. Nirula R, Gentilello LM. Futility of resuscitation criteria for the “young” old and the “old” old trauma patient: a national trauma data bank analysis. *J Trauma* 2004; 57: 37–41.

Rural Trauma

Burke Thompson

Rural Trauma Question Summary		
Question	Answer	Grade of support
Does mode of transportation impact mortality?	Unclear	D
Are mortality rates higher for patients injured in rural areas?	Yes	C; there is inconsistency
What are the roles of rural physicians?	Assess, resuscitate, perform initial stabilizing procedures	B
Has rural trauma system development impacted care?	Yes	B

INTRODUCTION

Trauma system development has evolved over the past 30 years. Prior to this time, the delivery of trauma care by physicians was quite inconsistent (1). The implementation of Advanced Trauma Life Support (ATLS) both revolutionized and helped standardize the care of injured patients. What has yet to be standardized is the best system to get the injured to a location where the teachings of ATLS can be applied.

The care of patients injured in a rural setting has not been studied extensively. The literature that exists often shows that patients injured in a rural setting do not do as well as those injured in urban areas. The improvement in rural trauma patient outcomes is an important avenue of current research. Active projects are under way by Dr. Michael Rotondo and others at Eastern Carolina University to further this cause. We await upcoming publications.

In this chapter, we review the available literature, addressing several important clinical questions regarding rural trauma and discuss the varied levels of evidence presented.

DOES THE MODE OF TRANSPORTATION OF RURAL TRAUMA PATIENTS IMPACT MORTALITY?

Patients who are injured in rural or remote areas are usually transported by emergency helicopter or ground transportation. Much of the literature that exists compares these modes. Often, cost analysis is the goal, but outcome analysis has been measured (2–4). Mann and colleagues found an increase in mortality following the loss of an air medical program. Nicholl et al. compared cost and performance of air versus ground transport of injured patients in the rural setting.

To investigate this further, Mitchell et al. devised a study to compare the mortality of blunt trauma patients transported by air versus ground in a rural trauma system in Nova Scotia (5). Their trauma center serves a predominately rural province. Communications and dispatch are centralized. This study used the trauma registry and included all trauma activations over a four-year period from March 27, 1998, to March 28, 2002. Penetrating trauma was not included. Seven hundred ninety-one patients were evaluated using the Trauma and Injury Severity Score (TRISS) to determine whether there was a difference in outcomes between patients transported by air and those transported by ground ambulance. This included transportation both from the scene and from small regional hospitals.

The air transport patients fared better, with 6.4 more survivors than expected per 100 patients. The ground transport cohort showed outcomes that were worse than expected. There were 2.4 unexpected deaths per 100 patients taken by ground. There was a 25% reduction in mortality with the use of air medical services. This difference was statistically significant.

Air transport systems are costly. There is a lack of Level I evidence to support universal application of these systems. The data that exist do not suggest a common pattern. Geographical limitations do come into play in different regions and this must be considered. Further investigation is warranted. Grade of recommendation: D.

ARE MORTALITY RATES HIGHER FOR TRAUMA PATIENTS INJURED IN RURAL AREAS?

National Center for Health Statistics (NCHS) data have shown that death rates for unintentional injury in 2001 were higher in rural counties compared with large metropolitan counties (6). This is also reflected in Centers for Disease

Control and Prevention (CDC) data for 2004 (7). The leading cause of unintentional injury death in the United States is motor vehicle crash (MVC) (8). There has been a disparity noted comparing rural to urban death rates after MVC (9,10). The mortality is inversely proportional to population density. This disparity may be increasing.

Muelleman et al. designed a study to investigate this concept further (11). The purpose was to analyze whether there is a regional variation in the risk of death after MVC controlling for injury severity. All fatal and injury-related crashes in Nebraska from 1996 through 1999 were evaluated using the Crash Outcome Data Evaluation System data set. Injury Severity Scores (ISSs) were calculated. The odds ratio for death was calculated for three rural county groupings compared with urban locations. This study included a large volume of patients. About one half of patient records had adequate information to calculate ISS, and this amounted to 28,859 patients. Adjusting for ISS, the odds of death were 1.98 times higher in small rural counties compared with urban counties. When speed limit (higher in rural areas), age, and alcohol use were controlled for, odds of death in rural crashes were still significantly higher. The authors postulated that variations in medical care might account for some of this difference.

Another outcomes study was done by McCowan et al. at the University of Utah (12). This was a retrospective review of all adult helicopter emergency transports in 2001, and it compared rural versus urban trauma patients. It included the registry data for three Level I trauma centers. This study examined in-hospital mortality, length of stay, and discharge status of victims of blunt trauma. Included were 271 urban and 141 rural transports. After controlling for age, gender, and ISS, there were no significant mortality differences between the two groups, despite longer transport times.

Although there are federal statistics supporting the existence of a higher mortality rate associated with rural versus urban trauma, there are no Level I data. The data that do exist in the literature are inconsistent. Grade of recommendation: C.

WHAT ARE THE ROLES OF RURAL PHYSICIANS?

In studies showing a disparity in outcomes between rural and urban trauma patients, the inexperience of rural physicians is often listed as a possible cause. A rural trauma course is being piloted in North Carolina to address this issue. Results have not been published yet. Investigation into the role of rural physicians in trauma management has been undertaken in Australia due to its particular population distribution.

Lopez et al. investigated early trauma management skills in Australian general practitioners (13). A course is taught in Australia called the Early Management of Severe Trauma (EMST). This is similar to ATLS. Lopez et al. sought to evaluate the skill and comfort levels of general practitioners in managing trauma patients. All general practitioners who completed the EMST course between 1989 and 2004 and resided in rural western Australia were surveyed. Background and open-ended questions were included. Results showed the physicians were confident with IV access and fluid resuscitation. They felt least comfortable doing procedures such as diagnostic peritoneal lavage and

surgical airway insertion. Low confidence was also seen in interpretation of cervical spine radiographs and in the management of penetrating torso injuries and severe head injuries. Most felt able to intubate and insert chest tubes. Those with more recent trauma experience were more confident of their abilities.

The surveyed physicians also listed ways to improve the EMST course. Popular suggestions were making refresher courses more accessible, increasing procedure instruction, and teaching from a rural perspective.

Cheffins and colleagues looked specifically at rural general practitioner management of vehicle-related trauma patients (14). Australian data have shown morbidity and mortality resulting from rural MVCs to be twice that resulting from urban crashes (15). The study by Cheffins et al. looked specifically at management challenges facing rural physicians via an interview process. The physicians were selected from areas having high road crash numbers. Still, about half of those surveyed reported treating vehicle-related injury less than monthly. Less than 6% reported weekly experience. Lack of frequent exposure limited comfort level with severely injured patients. The physicians also often saw patients with delayed presentation of injuries, such as soft tissue injuries, whiplash, and chronic pain syndromes. Access to specialty services was a big concern. The specialties felt to be most in need were orthopedics, acute care surgery, and rehabilitation. Chronic pain and mental health services were also felt to be lacking. Whether or not the patients had private insurance was often seen to determine the level of care. In general, there was also a perceived need for better injury prevention efforts in the rural setting.

The lack of high-volume experience for rural physicians in managing injured patients may impact the care they provide. Structured educational programs that focus on initial stabilization followed by transfer to a definitive care center are critical to address this worldwide problem. Grade of recommendation: B.

HAS RURAL TRAUMA SYSTEM DEVELOPMENT IMPACTED CARE?

A wealth of literature exists regarding the benefits of trauma center care. Most publications, though, describe urban trauma centers with large patient volumes. Much less is known about the performance of rural trauma centers and how they perform as part of a larger trauma system.

A retrospective study by Helling at the University of Missouri investigated the performance of rural trauma centers and how the experience of their trauma surgeons might shape future educational efforts to optimize rural trauma care (16). Missouri has three levels of trauma centers. Level I centers are large, urban, tertiary referral facilities with full subspecialty support. Level III centers are rural and do not require orthopedic or neurosurgical coverage. The state trauma registry was reviewed over a two-year period from 2002 and 2003. Admissions to Level III centers were examined for acuity, severity, and type of injury. Experiences with chest, abdominal, and neurologic trauma were examined in detail. Helling found acuity and severity of injuries to be greater at Level I and Level II centers. Mortality at Level III centers was significantly lower than at the other centers, but the rate of death within 24 hours

of admission was no different. Only 1% of patients admitted to Level III centers needed emergent chest or abdominal surgery. The Level III centers were seen to perform as expected as part of the integrated state trauma system. The relative paucity of severe head, chest, and abdominal injuries seen at such centers presents a challenge to the rural trauma surgeon to maintain the skills required in caring for these patients.

System development and improvement is the key to successful rural trauma management. McDermott et al. in Victoria, Australia, looked specifically at MVC mortality before and after implementing a new trauma care system (17). This system included a division of rural trauma services. Prior to the new system, patients injured in a rural setting were usually transported to the nearest public hospital and treated by junior emergency department staff. A few severely injured patients were flown to the single Level I trauma center from the scene. Many errors and potentially preventable deaths were noted. Despite reporting these, outcomes did not improve. A new system was then devised (18).

The new system was based on a tiered designation of trauma centers. Rural locations were served by "regional trauma services" and "urgent care services." Triage criteria determined the destination of patients transported from the scene. Later transfer to a higher level of care was done as appropriate. A trauma registry was started to allow evaluation of results. The study compared patients treated from 1997 to 1998 with those from 2002 to 2004. Demographics and ISSs were not significantly different. The mean time from crash to hospital increased in the later group. The rural ambulance service also had longer on-scene times. TRISS analysis showed the two patient populations to be similar. The preventable death rate dropped from 5% to 3% after the new system was implemented. Combined preventable and potentially preventable death rates decreased significantly as well. Management deficiencies were also reduced. Some of these improvements were attributed to quicker triage and transfer of severely injured patients to a Level I trauma center. All in all, this was seen as a successful system.

Shafi et al. in the United States hypothesized that statewide trauma systems independently reduce injury mortality (19). This was a nationwide cross-sectional study that used data from the CDC, the National Highway Traffic Safety Administration, the U.S. Department of Transportation, and the U.S. Census Bureau. Motor vehicle death rates per 100,000 population were compared between states with and without trauma systems. Management of rural population distribution was analyzed. Death rates have declined over time as new statewide trauma systems came on line. Rural population distribution, however, remained an independent predictor of mortality. The explanation of this was felt to be multifactorial.

Tiesman et al. investigated the effects of a rural trauma system on traumatic brain injuries (20). Timely arrival at definitive care is especially important in traumatic brain injury (TBI). The Iowa System Trauma Registry data set was analyzed before (1997–1998) and after (2002–2003) implementation of a rural trauma system. There was a significant reduction in 72-hour mortality for TBI after system implementation. More severely injured patients were triaged or transported to a higher level of care. In-hospital mortality was reduced.

The literature that is available suggests that rural trauma care is significantly improved if it is part of a regional trauma system. Grade of recommendation: B.

REFERENCES

1. American College of Surgeons, Advanced Trauma Life Support for Doctors, 6th edition. Chicago: American College of Surgeons, 1997, 11.
2. Mann NC, Pinkney KA, Price DD, et al. Injury mortality following the loss of air medical support for rural interhospital transport. *Acad Emerg Med* 2002; 9: 694–8.
3. Cummings G, O'Keefe G. Scene disposition and mode of transport following rural trauma: a prospective cohort study comparing patient costs. *J Emerg Med* 2000; 18: 349–54.
4. Nicholl JP, Beeby NR, Brazier JE. A comparison of the costs and performance of an emergency helicopter and land ambulances in a rural area. *Injury* 1994; 25: 145–53.
5. Mitchell AD, Tallon JM, Sealy B. Air versus ground transport of major trauma patients to a tertiary trauma centre: a province-wide comparison using TRISS analysis. *Can J Surg* 2007; 50: 129–33.
6. Eberhardt MS, Ingram DD, Makuc DM et al. Urban and Rural Chartbook, Health United States 2001. National Center for Health Statistics, 2001.
7. National Center for Health Statistics, Centers for Disease Control and Prevention. NCHS data on injuries, 2004. <http://cdc.gov/nchs/data/factsheets/injury.pdf> (accessed February 13, 2007).
8. Vyrostek SB, Annett JL, Ryan GW. Surveillance for fatal and non-fatal injuries—United States 2001. *MMWR* 2004; 53: 1–57.
9. Baker SP, Whitfield RA, O'Neill B. Geographic variations in mortality from motor vehicle crashes. *N Engl J Med* 1987; 316: 1384–7.
10. Muelleman RL, Mueller K. Fatal motor vehicle crashes: variations of crash characteristics within rural regions of different population densities. *J Trauma* 1996; 11: 316–20.
11. Muelleman RL, Wadman MC, Tran TP, et al. Rural motor vehicle crash risk of death is higher after controlling for injury severity. *J Trauma* 2007; 62: 221–6.
12. McCowan CL, Swanson ER, Thomas F, et al. Outcomes of blunt trauma victims transported by HEMS from rural and urban scenes. *Prehosp Emerg Care* 2007; 11: 383–8.
13. Lopez DG, Hamdorf JM, et al. Early trauma management skills in Australian general practitioners. *ANZ J Surg* 2006; 76: 894–7.
14. Cheffins TE, Blackman R, Veitch C. Rural GPs' management of vehicle related trauma. *Aust Fam Phys* 2007; 36: 782–4.
15. Strong K, Trickett P, Titulaer I, et al. Health in Rural and Remote Australia. Australian Institute of Health and Welfare, 1998.
16. Helling TS. Trauma care at rural level III trauma centers in a state trauma system. *J Trauma* 2007; 62: 498–503.
17. McDermott FT, Cordner SM, Cooper DJ, et al. Management deficiencies and death preventability of road traffic fatalities before and after a new trauma care system in Victoria, Australia. *J Trauma* 2007; 63: 331–8.
18. Review of Trauma and Emergency Services—Victoria: final Report of the Ministerial Task Force on Trauma and Emergency Services and the Department Working Party on Emergency and Trauma Services. Victoria, Australia: Human Services, 1999.
19. Shafi S, Nathens AB, Elliott AC, et al. Effect of trauma systems on motor vehicle occupant mortality: a comparison between states with and without a formal system. *J Trauma* 2006; 61: 1374–9.
20. Tiesman H, Young T, Torner JC, et al. Effects of a rural trauma system on traumatic brain injuries. *J Neurotrauma* 2007; 24: 1189–97.

Reducing Patient Errors in Trauma Care

Kenneth D. Stahl and Susan E. Brien

Recently significant attention has been focused on patient safety, defined as the risks patients face, not from their injuries or their disease processes but from the health care system itself. Although the exact magnitude of patient errors remains to be specifically defined, the fact that errors in patient care occur and that some patients are seriously and sometimes fatally harmed is no longer in dispute (1). Trauma centers are studying errors in the management of injured patients, and these events are better understood. Preventable deaths due to human and system errors account for up to 10% (2–4) of fatalities in patients with otherwise survivable injuries cared for at Level I trauma centers. These unintended deaths equate to as many as 15,000 lost lives per year in the United States or 2 lives lost/hour, 24 hours/day, 365 days/year (5) (calculation based on 161,269 deaths in the United States as the result of injuries). This rate of death due to error in trauma patients is two to four times higher than deaths due to errors reported in the general hospital patient population (6) (calculation based on an estimate of 44–98,000 deaths due to medical error in a population of 2,391,399 deaths in 1999).

The three highest risk areas for commission of errors have been identified in the places trauma surgeons work and trauma care is delivered: in the operating room (7), the emergency department (8,9), and intensive care units (10). Furthermore, the situations that are most conducive to producing errors are the very environments in which trauma victims present—unstable patients, fatigued operators, incomplete histories, time-critical decisions, concurrent tasks, involvement of many disciplines, complex teams, transportation of unstable patients, and multiple hand-offs of patient management. As such, Gruen et al. (3) point out that trauma care creates a “perfect storm for medical errors.”

High-risk, error-intolerant organizations, such as commercial aviation, nuclear power operators, and the military, where circumstances closely mirror the environment of trauma surgery, have devised evidence-based solutions to reducing adverse outcomes with excellent results (11). Because all of these environments are so similar, trauma care represents, to paraphrase William Stewart Halstead, “a laboratory of the highest order” (12) to study these events in the light of information gleaned in other endeavors. Trauma provides us with the opportunity to understand errors in emergency patient care and build on lessons learned in other high-risk environments to develop an evidence-based model that reduces the risks our patients face from our attempts to repair their injuries.

WHERE AND HOW DO ERRORS OCCUR IN THE CARE OF TRAUMA PATIENTS?

To understand the complexity of errors in trauma care, it is important to establish the phase of management that the event occurred and the nature of the event. The three phases of trauma care for this purpose are: (1) resuscitation phase, (2) operative phase, and (3) critical care phase. In a historic but informative retrospective observational study of errors causing morbidity and mortality, Davis et al. (13) report on 1,295 trauma deaths at their Level I center, in which they documented 1,032 significant patient errors that were judged avoidable by two independent reviewers. These errors contributed to 76 preventable or potentially preventable deaths (5.6% of fatalities over the study period). Of these fatal errors, 36% occurred in the resuscitative phase, 14% to the operative phase, and 50% to the critical care phase. Gruen et al. (3) studied avoidable deaths and identified 64 (2.5%) of 2,594 deaths due to error at their Level I trauma center. These were also analyzed by phase of trauma management showing a similar distribution of fatal patient errors. They document 34% of errors occurred in the emergency department (ED) (20% during initial assessment and resuscitation, 14% during the secondary survey and initial diagnostic tests), 8% during stabilization and interhospital transport, 11% during initial interventions (surgery and/or angiography), and 37% during the intensive care phase.

Data confirming the error risk during the intensive care unit (ICU) phase of management come from an observational study by Donchin et al. (10). The authors documented 554 patient errors during the four-month study with a rate of 1.7 errors per patient per day. Rothschild et al. (14) carried out a similar study of 391 ICU patients. One hundred twenty adverse events occurred in 79 (20.2%) patients, including 54 (45%) preventable adverse events (AEs) as well as 223 potentially fatal errors. The rates per 1,000 patient-days for all AEs, preventable AEs, and serious errors were 80.5, 36.2, and 149.7, respectively. Among AEs, 13% (16/120) were life-threatening or fatal, and among errors judged to be serious, 11% (24/223) were potentially life-threatening. Most serious medical errors occurred during the ordering or execution of treatments, especially medications (61%; 170/277). Further confirmatory results were reported by Orgeas et al. (15) who studied 3,611 ICU patients. Their study documented that 39.2% of patients suffered at least one AE and 22.7% of patients two or more AEs (mean 2.8 AEs/patient) with median time to first

AE = 4 ICU days. The presence of at least one AE increased the odds ratio of mortality as much as 17-fold over matched controls without AEs.

The nature of these errors can best be characterized utilizing the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standard nomenclature for the taxonomy of adverse outcomes adopted from Chang et al. (16) that categorizes errors into five complementary root nodes.

1. **Impact:** the outcome or effects of medical error and systems failure, commonly referred to as the degree of harm to the patient with greatest degree of harm being patient death.
2. **Type:** the implied or visible processes that were faulty or failed. (These types of errors include errors in diagnosis, operative or procedure management and treatment, prophylaxis, equipment failures, communication breakdowns, and errors in patient transfer).
3. **Domain:** the characteristics of the setting in which an incident occurred and the type of individuals involved. (The setting includes initial assessment and resuscitation, secondary survey and testing areas, interhospital transfers; initial interventions such as angiography and computed tomography scanning, ICU, general inpatient ward, and rehabilitation).
4. **Cause:** the factors and agents that led to an incident usually attributed to what the person who erred understood or thought at the time of the occurrence. Cause errors can be subdivided into the following types. (a) Input error: the input data are incorrectly perceived; therefore, an incorrect intention is formed and the wrong action is performed. (b) Intention error: the input data are correctly perceived, but an incorrect intention is formed, and the wrong action is performed. (c) Execution error: the input data are correctly perceived and the correct intention is formed, but the wrong action is performed; that is, the action is not what was intended.
5. **Prevention and mitigation:** the measures taken or proposed to reduce incidence and effects of adverse occurrences.

The most common error types (node 2) and domain (node 3) contributing to avoidable deaths in trauma fall into three major categories: (1) diagnosis, (2) treatment, and (3) prevention. In Gruen et al.'s (3) analysis, 61% of fatal errors were errors of treatment, 20% were errors in prophylaxis and prevention, 13% were errors in diagnosis, 5% errors in transport and transfer, and 1% were associated with equipment failures. Failures in airway management, missed injuries, and inadequate recognition or control of hemorrhage account for the majority of errors in the treatment node. These authors identified 16% of preventable deaths were due to failure of airway management and 28% failure to identify or control hemorrhage. Ivatury and colleagues (2) document a similar distribution of event types in their study of fatal errors: 16% failure of airway management, 14.5% errors in diagnosis, 11.8% missed diagnosis, and 42.1% errors in critical care management. Houshian et al. (17) identified 8.1% of patients in a Level I trauma center that had suffered an injury that was missed during the primary and secondary survey.

The causes of these errors (node 4) are more difficult to specify. Traditional safety and error literature distributes errors between system and human causes with human errors much more prevalent and comprising 60–80% of the cause of adverse outcomes (18). Similarly, errors in trauma management fall largely into the category of human error. Ivatury et al.'s (2) review identified human error as the cause of 74/76 fatal errors. Human error is classically divided into rule-based, skill-based, and knowledge-based errors. Rule-based errors are considered failures of retrieval of stored sets of instructions or procedures that cause failures to perform familiar tasks. Skill-based errors refer to the failure of smooth execution of highly practiced, largely physical actions in which there is little conscious monitoring. Knowledge-based errors are the most common as well as the most complex errors dealing with failure to perceive and input data correctly, formulate a correct plan, and therefore perform the correct action. There are two corollaries to this type of knowledge error. The first is called intention error where information is correctly perceived but the wrong intention is formed; the second is called execution error, where the data and intent are correct but an error in carrying out the plan is made.

The demands on trauma surgeons who must carry out complex intellectual and dexterous tasks in time-compressed, life-and-death situations make it clear that these types of errors are prone to occur (19). The majority of fatal errors in trauma care have been attributed to a combination of input and intention knowledge errors. Examples include failure to recognize occult sites of bleeding, failure to recognize the severity of injuries and triaging unstable patients to diagnostic rather than operative management (2,3,14,17,20).

With this background information the remainder of this chapter is devoted to discussions of the fifth mode—prevention and mitigation of errors.

Answer: Preventable deaths account for up to 10% of fatalities among patients in Level II trauma centers with otherwise survivable injuries. Level II and III observational studies attribute most of these errors to knowledge-based human error. These errors occur in all three phases of trauma care but most often in the ICU setting.

THERE ARE KNOWN CONDITIONS THAT PREDISPOSE TO ERROR IN OTHER HIGH-RISK ENDEAVORS. DO THESE SAME CONDITIONS EXIST IN TRAUMA MANAGEMENT?

Care of trauma victims is characterized by the need to maintain mental acuity in the face of fatigue, make time-critical decisions, and carry out intricate procedures with life or death consequences. This care also requires control of potentially chaotic environments and rapid processing of complex and often incomplete information. These conditions not only define the circumstances under which trauma care is delivered but also offer insight into the “worst-care scenarios” from which adverse events can result. In everyday life, there are common sets of circumstances that produce a likely outcome. The inevitable result of such sets of conditions are apparent, for example, in motor vehicle accident victims who have been driving while intoxicated, speeding, or not using seat belts. Such sets of circumstances are known as “error-producing conditions” (EPCs) in the aviation

safety literature. These are combinations of conditions that form a common thread of contributing factors to major accidents and incidents. Mathematical modeling of probabilities that a given set of circumstances will result in an error is based on work by Williams (21). Further advances in this field have been developed for the analysis of aviation accidents by Hendy (22). Croskerry and Chisholm have described the impact of sets of similar conditions in emergency medicine (23).

These sets of known EPCs can be used to develop an understanding of the multiple factors that contribute to adverse outcomes in trauma. Hollnagel (24) has emphasized that to prevent errors and accidents, it is necessary to be able to predict them, and these sets of circumstances allow trauma surgeons to make those predictions. EPCs link traditional systems approaches to error with advanced human factors analysis of individual performance. The 10 top EPCs described in aviation accident investigation are as shown in the table below (21).

Rank order	Error-producing condition	Incremental risk of human error*
1	Fatigue/physiological degradation	50×
2	High-risk/low-frequency event	17×
3	Time pressure	11×
4	Low signal to noise ratio	9×
5	Normalization of deviance	8×
6	One-way decision gates	8×
7	Information overload	6×
8	Poor information transfer	5×
9	Faulty risk perception	4×
10	Inadequate standardization	4×

*The interested reader can find incremental risk calculations for each EPC based on mathematical analysis and assumptions found in the referenced text (21).

Just as general error theory divides events into human and system failures, EPCs can be divided into the same groupings with those that affect the individual (fatigue, time pressure, one-way decision gates, and faulty risk perception) separated from system levels factors (high-risk/low-frequency events, low signal to noise ratio, normalization of deviance, information overload, poor information transfer, and inadequate standards). The application of this theory to the field of trauma care gives trauma surgeons the ability to anticipate when patients are at increased risk for unintended outcomes and maintain an especially high degree of vigilance during those time periods.

Data presented in the introductory section of this chapter support the fact that most errors in trauma are related to individual performance, therefore this aspect of the EPC theory is further elaborated. Fatigue (EPC #1) exerts the greatest incremental risk for error and also represents the most common circumstance for trauma surgeons. The literature on fatigue and human error is long and rich and documents the negative impact of fatigue on every aspect of human performance (25,26). Numerous studies are found in the literature specific to physician performance during periods of fatigue (27). The daytime mortality rate of a cohort of 20,547 children admitted to 15 pediatric ICUs compared to nighttime admission revealed

that night admission carries an incremental risk of death from 1.1 to 4.5 (28). The associated physiological degradation of skills and judgment that accompanies fatigue requires no further emphasis than to extrapolate Dawson's often cited laboratory study to the fatigued trauma surgeon who performs with the same aptitude as a person who is legally drunk (29). It is not possible to take fatigue out of trauma management, but it is possible to stress that an individual needs to maintain a high degree of vigilance on his or her actions during these times and rely on team interactions and support to ensure correct perceptions and decisions. Fatigue countermeasures and sleep physiology are also well described and deserve careful review by all trauma team personnel (30). Often accompanying fatigue is time pressure (EPC #3), which acts as a force multiplier on both individuals and teams, exaggerating small missteps, making it much more difficult to catch misperceptions, and fostering errors in communications and information exchange (31).

Faulty risk perception (EPC #9) is another heavily weighted factor in aviation accident studies. The equivalence in trauma is failure to understand the risks a patient faces from the mechanism and/or severity of an injury with potential for incorrect triage and mismanagement. Failure to correctly assess the nature or extent of an injury leads to several well-documented errors in trauma, such as missing a source of hemorrhage in an unstable patient, triaging a patient to angiography, or obtaining a CT scan instead of taking the patient to the operating room. These types of errors are the most frequent causes of death in patients with otherwise survivable injuries (2-4,13,15).

The last individual EPC (#6) is called "one-way decision gates" and has been extensively studied by the National Aeronautics and Space Administration (NASA) because failure to recognize this type of decision bias has claimed the lives of many pilots, their crews, and passengers (32). Also known as "plan continuation bias," this represents the unconscious human bias to pursue a course of action, a treatment plan, or procedure in spite of changing conditions. Surgeons and pilots are goal-directed and oriented toward completing a course of action; the inability to recognize when modifications and/or changes in direction are needed leads to adverse events. This type of task fixation can be exacerbated by stress, fatigue, and time compression (33). In trauma, the results of this type of error are catastrophic and reflected in such tendencies as to keep a patient in the operating room too long in spite of increasing bleeding and coagulopathy, failing to search another body cavity for sources of bleeding, and failing to seek different sources of clinical deterioration after an initial decision has been reached (2-4,13,15).

The other group of EPCs is system related. It is interesting to note that many of these EPCs are alluded to in the trauma literature without the authors directly referencing aviation safety research. They include rarity of occurrence (EPC #2), inadequate supervision or inexperience (EPC #5), effects of information overload (EPC #7), and failure to establish and follow standard protocols (EPC #10) (21). Another condition, loss of continuity of care and poor communication (EPC #8), has been studied in trauma care specifically by Petersen et al. (34), who found that the odds of adverse events could decrease from OR 5.2 to OR 1.5 with standardization of communication and hand-offs.

In summary, EPCs apply to error management in all fields, especially trauma, where the inter-relationship between human and system factors are so crucial. For trauma systems to attain high-reliability organization (HRO)—caliber error management, it is important to understand sets of conditions that make error more likely and with this information understand the nature and extent of error. The next step is using this information to change the conditions that induce error, determine behaviors that prevent or mitigate error, and train personnel in use of error avoidance tools (19).

Answer: The same sets of error producing conditions exist in high-risk organizations as in trauma. The impact of EPCs on human error is substantiated by Level III data. Evidence that these conditions directly contribute to adverse outcomes in trauma remains to be proven.

THERE ARE SAFETY MODELS KNOWN TO REDUCE ERRORS IN OTHER HIGH-RISK ENDEAVORS. ARE THESE METHODS CAPABLE OF REDUCING ERRORS IN THE CARE OF TRAUMA VICTIMS?

HROs are characterized as high-risk, error-intolerant systems that are capable of repetitively carrying out potentially dangerous tasks with virtually no occurrence of adverse outcomes. Commercial aviation serves as the primary example of the HRO safety model as evidenced by a decade of annual Federal Aviation Administration (FAA) statistics indicating that the risk of a major commercial carrier accident ranges from 0.00 to 0.218/1,000,000 flight hours (35). An individual must fly 24 hours/day every day for 570 years before standing a 1% chance of being involved in a fatal commercial aviation accident. This safety record is based on a thorough comprehension of the mechanisms of errors gleaned from collecting incident and error reports. In aviation, as in other HROs, reporting and avoiding error has become a compulsion and a cultural norm.

Detailed analysis of pertinent adverse events and near-miss case studies have generated a body of knowledge known as *high-reliability theory* that defines a number of organizational features likely to reduce the risk of “organizational accidents” and other hazards (36). Those who are attempting to adopt these organizational safety models for use in trauma safety have attempted to pinpoint specific practices to embrace from complex, high-risk industries that manage to operate at consistently high levels of reliability (37). Designers of care systems can increase safety by focusing on three tasks: designing a system to prevent errors, designing procedures to make errors visible when they do occur so that they may be intercepted, and designing methods for minimizing the impact of adverse events when they are not detected and intercepted (38).

HROs manage risks by being completely consumed with understanding and anticipating all possible chances for errors and thereby trapping small missteps before major adverse events have a chance of taking place. The critical importance of this concept of error trapping and recovery from minor adverse events has been demonstrated in numerous HRO safety models (39). HRO reliability can be viewed as a “dynamic nonevent.” It is dynamic because safety is assured by timely system and

individual adjustments. It is a nonevent because successful outcomes rarely call attention to themselves. But an important difference between health care and HROs is that HRO systems are engineered with the expectation that individuals can and will make mistakes and that the system itself, unless properly configured, can fail to catch these mistakes. Physicians and nurses have been granted a loftier status. We are expected *not* to make mistakes despite operating under stressful conditions in a system that is not attuned to catching small missteps. John Nance, an aviation safety expert and founding board member of the National Patient Safety Foundation, has highlighted this paradox. “Safety in aviation has been achieved by recognition of the eternal fallibility of human beings, and the breakthrough realizations of how and why human mistakes occur and how systems can be designed to anticipate and safely absorb such errors” (40). Earlier in this chapter we examined the circumstances of errors in trauma care, and it is crucial for all trauma surgeons to constantly remind themselves and their teams that these circumstances occur with every patient encounter. Trauma surgeons and teams must accept the fact that there are some patients we cannot help, but none we cannot harm, and they must be always vigilant to avoid errors. Sustaining awareness of the potential for failure in daily trauma care and then managing those risks well, continually detecting and intervening in small errors before they induce tragedy, is essential for the safety of injured patients (39).

HRO safety principle 1: Based on this concept, the first and perhaps the most important safety lesson that trauma surgeons and trauma systems can adopt from HROs is a collective preoccupation with the *possibility* of error with every patient contact and the collective preoccupation to guard against this possibility.

Thus HRO system safety is engineered with the expectation that individuals can and will make errors and HROs train their workforce to recognize and recover from them. They continually rehearse familiar scenarios of error and strive to imagine novel ones. Instead of isolating failures, they generalize them and instead of making local repairs, they look for system reforms. This profound understanding of error threats is derived from HRO systemwide use of critical incident reporting (CIR) programs that collect and objectively analyze errors, incidents, and near misses. The largest critical incident data base is maintained by NASA for the FAA known as the Aviation Safety Reporting System (ASRS), and it receives over 30,000 reports annually containing almost 800,000 voluntary, anonymous near misses, incidents, safety violations, and aviation safety risks (41). CIR systems allow the identification of risks for adverse events and patterns of risky actions before they propagate through the system and become realized tragedies. It is impossible to know what has *not* occurred because proactive steps are routinely taken based on incident reporting to avoid adverse events. It is well documented that major changes in HRO systems and laws have come as a result of these reports. The FAA alone has generated over 4,000 aviation safety emergency alerts and airworthiness directives based on ASRS incident reports that have changed unsafe practices, which, without question, have avoided accidents (42). The value of CIR in lowering adverse outcomes has been demonstrated in every HRO system (43).

Especially in health care, there are obvious barriers to reporting errors, and untoward outcomes and many factors contribute to this reluctance (44). One method that has improved reporting is by broadening the targets of incident reporting to include no-harm events and near misses and eased the disincentive to reporting actual adverse outcomes. This has been shown to increase reporting by 3–300-fold (45). Inclusion of these types of minor incidents and near incidents offers other advantages, such as increasing the databases to allow more accurate quantitative analysis, lowering the reporting barrier, allowing recovery strategies to be included and used to generate proactive avoidance schemes, and reducing hindsight bias (46). To successfully collect critical incident information, the data must be used to “generate light not heat,” requiring the system to be totally anonymous and nonpunitive (47). Other important characteristics of suitable reporting systems are that they provide an incentive to report and ensure objective, fair reporting without assigning blame (43). Health care lags significantly behind in the collecting and analyzing critical of incident data because health care incident reporting systems collect only 1.5–10% of actual adverse events (44). Studies to date on CIR systems in health care have concentrated on the identification of root causes of errors and the viability of error reporting, rather than the impact of error reporting on morbidity and mortality statistics. Even so, the use of CIR systems is gaining momentum in several specialties, such as anesthesia (48), emergency medicine (49), and critical care (50). Further progress has been made by the National Patient Safety Foundation that has commissioned the development and implementation of an Internet-based CIR system for use in critical care environments (51). The ultimate aims of incident reporting in trauma are many. It can be used to guide focused enhancements in training, organization, and management, as well as examining past practices to understand how things might be improved and done differently (43).

HRO safety principle 2: Anonymous and nonpunitive CIR with objective event analysis has allowed HROs to understand adverse outcomes at all levels and institute systemwide changes that have avoided further occurrences. Trauma systems need to adopt the same methods as a safety tool in the reduction of errors.

Simulation has been recognized by HROs as one of the critical safety tools to rehearse and train for error recognition and recovery as well as to enhance and practice safety skills. For decades simulators have been used in the aviation industry and by the military and nuclear power plant operators for training and assessment of performance with excellent results (52). Similarly, simulation and role-playing allow trauma teams to replicate the task environments and stresses of patient resuscitation with no risk of adverse outcomes. Errors can be allowed to occur and their outcomes studied by replaying video recordings of the simulation, which are used so participants can see the consequences of their decisions. Presentations of uncommon but critical scenarios that require immediate recognition and attention can be programmed into the simulator and practiced for both pattern recognition and technical management skills (53). Much of the guidance for simulation scenarios is based on CIR data (54), the value of which is described in the previous section.

Anesthesiologists have pioneered the use of simulation and demonstrated the value of simulation in team

training and decision making. Simulation is being used in many centers to train in cognitive and technical skills and team functions to avoid errors (55). Simulation as a method of training in specific trauma skills has been adopted for use in the Advanced Trauma Life Support (American College of Surgeons) and Advanced Trauma Operative Management (56) courses. Simulation has been shown to improve technical surgical skills in other specialties in randomized control studies (57). With regard to trauma team training, a prospective observational study of three-person military resuscitation teams by Holcomb et al. demonstrated significant improvement in scored and timed trauma resuscitation outcomes after simulation practice sessions for multiple injured models with ISS = 41 ($p \leq 0.05$) (58). Falcone et al. (59) have studied the value of team building and team skills training with the use of simulation in pediatric trauma resuscitation and have found a similar significant improvement ($p \leq 0.05$) in multidisciplinary team function and successful injury recognition and resuscitation of injured children. Nationwide studies by the Israeli trauma management system has lead Berkenstadt et al. (60) to advocate broad use of simulation-based medical education in training trauma surgeons and their teams.

HRO safety principle 3: The wide use of simulation for technical skills and cognitive and trauma team training is the next safety lesson that trauma surgeons can adopt from the HRO safety armamentarium (60).

HROs have pioneered safety through both simulation and didactic training in nontechnical skills (NTSs) as well. NTSs are defined as the cognitive, social, and personal resource skills that complement and enhance technical skills and as such contribute to safe and efficient task performance (60). NTSs focus as much on individual interpersonal skills as on team dynamics because the individual is the basic building block from which teams and larger organizational groupings are formed (61). Reader et al. (62) have studied NTSs from analysis of ICU critical incident reports looking for nontechnical contributing factors to error as they apply to anesthesia and ICU teams. They developed a taxonomy of categories labeled “anesthesiologists” NTSs, which was used to retrospectively analyze studies of 2,677 critical incident reports. They documented 5,610 total contributory factors; 50% could be attributed to some form of NTS deficit. Their taxonomy of NTSs closely matches those that have become the foundation of HRO safety:

1. Situational awareness (SA)
2. Crew resource management (CRM)
3. Information processing and decision making under stress and task management
4. Communication skills and team workmanship
5. Leadership and supervision
6. Human factors

These skills are inter-related and revolve on the central axis of teamwork and communication. Training in these skills acknowledges that trauma team composition is rarely fixed due to shift and rotations patterns and other organizational constraints. The flux of team composition mandates that each team member carries with him or her skills that apply regardless of the team make-up at any given period.

1. SA is simply the big picture; it is “the *accurate* perception of what is going on with you, your patient, your team members and the surrounding environment 5 minutes ago, now and 5 minutes from now” (63). Building SA requires developing and maintaining an overall dynamic and temporal awareness of the clinical entirety based on perceiving all elements in the environment, understanding their inter-relationship and implications of each, and using this understanding to think ahead, predict, and anticipate the most likely eventualities. Forming the composite picture of SA also requires the soft skill of perception, derived from the clinical experience that comes with repetition, and develops into astute clinical judgment (64). Prioritizing information and actions are important aspects of situational awareness, as well as making quality and timely decisions and projecting the current situation into the future to make educated guesses as to what lies ahead so that changes in the clinical “big picture” do not come as unmanageable surprises. Although building and maintaining SA is largely an individual skill, it requires team participation in that team members must combine all of their perceptions and experiences to form a correct “big clinical picture.” This must be shared through accurate and timely communication with the team, allowing all team members to modify and reassess their clinical impressions as moment-to-moment situations change. HROs teach and diligently drill SA skills with simulation, repetition, team role-playing, and supervision and have demonstrated effectiveness of this training (65).

2. CRM is an educational program that has evolved over three decades of HRO safety studies. It has evolved from a program focused on individual attitude and awareness to a broad curriculum of behavioral skills and team work attitudes integrated with technical competencies. CRM programs evolved steadily, in part because they were informed by data that validated the importance of human factors. CRM training results in positive reactions to teamwork concepts, increased knowledge of teamwork principles, and improved teamwork performance (66). CRM encompasses skills such as clearly defining team roles and duties, managing distractions, prioritizing tasks, and avoiding task overload, all of which are integral components of a well-functioning trauma team. HRO and aviation-based CRM is defined as maximizing procedural effectiveness by using all available resources, including hardware, software, people, information, and environment. CRM was rapidly adopted by airlines and is required not only for United States-based carriers but also in the 185 countries operating under the UN *International Civil Aviation Organization* mandate.

The by-products of CRM skills are individual and team situational awareness, judgment, safety, resource preservation, and competitive advantage. This important set of skills has been emphasized in the medical literature also to optimize and manage workload and task assignments, clinical task planning, and review and critique strategies (67). Skills such as preprocedure briefs and “time-outs” and postprocedure debriefs are critical safety skills to plan procedures and capture lessons. CRM skills are an indispensable element of communication in the operating room, and Level II data support the conclusion that these skills enhance the performance of the operating team and patient outcomes (68,69).

3. *Decision-making skills* are central to all human intellectual activity and among the most important NTSs health care trainees need to master. It is not excessive to suggest

that decision making is nearly synonymous with thinking (70). Understanding how we process information and arrive at critical decisions, especially under time constraints, fatigue, and stress, is crucial to making the right decisions when there is no room for error (71). Aviation and HROs have developed numerous training methods to sharpen decision-making skills based on decades of data that indicated 47–80% of accidents are based on faulty decision-making capabilities (18). Teaching decision-making skills with simulations, repetitive task rehearsals, and didactic lessons have been shown to enhance outcomes in the emergency room (72) and anesthetic care in the operating room (73).

4. *Effective communication and team skills* are an essential pair of skills in trauma management. HROs view communication as the glue that holds teams together, understanding that team function is a central component of HROs and aviation safety. The Joint Commission (2003) statistics have identified that 67% of the root cause of sentinel events are the result of errors in communication between team members (74). Poor teamwork and communication lapses among members of health care teams have emerged as key factors in the occurrence of errors. In health care, understanding team dynamics and practicing functional team skills is an important aspect of avoiding errors in the management of the trauma patient. Medical teams in general and surgical teams specifically have been studied in depth by many authors (75). Failure to communicate critical information in the operating room occurs in approximately 30% of team exchanges (68). Such failures lead to inefficiency, emotional tension, delay, workarounds, resource waste, patient inconvenience, and procedural error, all of which can portend poor patient outcomes.

HRO models of team training stresses that teams are made up of many people, but teamwork itself is an individual skill (63). HROs further stress that teams are groups of people with similar objectives but differing levels of expertise and different skills; therefore, communication improvement strategies are best seen as the framework for supporting improved team function (76). High-performing teams exhibit a sense of collective efficacy, recognize that they are dependent on each other, and believe that by working together, they can solve complex problems. As defined in HRO safety models, effective teams are dynamic, optimize their resources, engage in self-correction, compensate for each other by providing back-up behaviors, and reallocate functions as necessary. Effective teams can respond efficiently in high-stress, time-restricted environments. Effective teams recognize potential problems or dangerous circumstances and adjust their strategies accordingly (77). Good teamwork establishes and maintains group and individual situational awareness and provides mutual support. Key benefits of good teamwork include added knowledge and expertise available to confront situations and synergy of ideas and skills so that the combined expertise of the group is greater than any individual. This synthesis of ideas and skills makes new options available. Good teams create the big picture of situational awareness together and share information, perceptions, and ideas to keep everyone ahead of the evolving clinical condition.

In all aspects of health care, team care has been shown to be more effective than nonteam care (78,79). Bollomo et al. (79) have documented impressive reductions in mortality, morbidity, and length of stay in patients after major

operations after institution of a formally trained emergency team. Their prospective cohort study shows a reduction in relative risk of 57.8% ($p < 0.0001$) for major complication, reduction in relative risk of postoperative death by 36.6% ($p < 0.0178$), and reduction of postoperative length of stay by four days ($p < 0.0092$). Observational studies in the operating room have consistently demonstrated that training clinicians in nontechnical and teamwork skills provides important safety nets (80). Level II data support the conclusion that team training improves trauma and ICU team performance and recognition of life-threatening injuries with reduction in death, adverse outcomes, and lengths of stay (58,59,79).

5. *Effective leadership and supervision* are crucial parts of team dynamics that have been repeatedly emphasized in HRO and aviation safety (81). Trauma unit leaders perform three key functions: they provide strategic direction, monitor the performance of the team, and teach team members by providing instruction—all tasks that match those that researchers identified in the functional team leadership literature (82). The characteristics of leadership in trauma teams has been studied by Yun et al. in a Level I trauma center (83). They stress the importance of leadership adaptability because team leaders and their teams work in an uncertain and time-constrained environment. Trauma leaders cannot anticipate when critical patients will arrive or how many and what type of injuries they will face. They often do not know with accuracy such essential information as a patient's medical history, and leadership adaptability

becomes more important in uncertain and urgent situations. The ability to get the best performance from all team members and encourage each person to share information and knowledge are traits of good leaders and supervisors that have been stressed in both the HRO literature as well as in reviews by the American College of Surgeons (84).

6. *Human factors* is the science of understanding and analyzing human physiology and how these factors impact performance. This has been dealt with in the section on EPCs. The most important of these factors is fatigue and awareness of the impact of fatigue and sleep debt on performance of critical tasks. Sleep and nap physiology, work attitude, caffeine use, interpersonal relationships, focus, and work environment are all involved in the study and management of human factors. These factors have been emphasized in both the HRO safety literature and medical literature (85).

HRO safety principle 4: The science of HRO safety encompasses a defined set of personal and organizational skills that trauma teams should emulate and adapt for use in trauma care environment.

Answer: Basic HRO safety tools adapted for trauma, play a strong role in capturing and preventing errors. Level II evidence shows that care delivered by teams is more effective than nonteam care. Level II evidence attributes effective communication to be an important mitigator of adverse events.

Table of Evidence, Error in Trauma Care

Trial (Ref no.)	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Median follow-up	Major end point	Interpretations/Comments
2	2007	III	Retrospective cohort study	Peer review complications and deaths to identify patient management errors	Injury to discharge or death	Death	9.9% deaths due to avoidable error in trauma management. Vast majority of errors were human, knowledge based.
3	2006	III	Retrospective cohort study	Study of patterns of error contributing to death	Hospitalization	Death	2.5% deaths preventable. Errors occurred during all phases of trauma care and were primarily human errors leading to failures of correct intentions to treat.
14	2008	II	Prospective observational cohort study	Consecutive ICU patients were monitored for adverse events and matched to cohorts of patients with no adverse events	≥ 2 days in ICU until death or ICU discharge	Death or ICU discharge	Adverse events in the ICU are common and often occurred in combination in individual patients. Several adverse events independently contributed to death odds ratio up to 17 over matched controls.
17	2001	III	Retrospective nonrandomized observational study	Examination of all records of hospitalized trauma patients for missed injuries	Variable—until hospital discharge or death	Missed injury identified	Missed injuries occur at all phases of trauma management and occur in 8.1% of cases.
19	2003	III	Retrospective cohort study	Investigate complications leading to adverse outcomes and death	Prehospital to discharge from rehabilitation	Adverse outcomes and complication leading to death	Identified missed injuries, errors in judgment, and failure to establish adequate airway as leading causes of complication and death.

Abbreviation: ICU, intensive care unit.

Table of Evidence: Error-Producing Conditions

Trial (Ref no.)	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Median follow-up	Major end point	Interpretations/Comments
2	2007	III	Retrospective cohort study	Peer review complications and deaths to identify patient management errors	Injury to discharge or death	Death	9.9% deaths due to avoidable error in trauma management. Vast majority of errors were human, knowledge based.
3	2006	III	Retrospective cohort study	Study of patterns of error contributing to death	Hospitalization	Death	2.5% deaths preventable. Errors occurred during all phases of trauma care and were primarily human errors leading to failures of correct intentions to treat.
28	2004	III	Retrospective cohort study	20,547 emergency PICU admissions	48 hours	Death	Children admitted to PICU experienced increased risk of death (1.6–4.1×) when admitted during evening hours
34	1998	III	Retrospective cohort study	Computerized sign-out checklist to prevent errors in communication with hand-offs of care	4 months	Avoidable adverse event due to cross-coverage lapses judged by three board certified physicians	Odds ratio of preventable adverse events decreased from 5.2 to 1.5 with intervention.

Abbreviation: PICU, pediatric intensive care unit.

Table of Evidence: HRO Safety Skills in Trauma Care

Trial (Ref no.)	Year	Level of evidence	Randomized groups (n)	Intervention/Design	Median follow-up	Major end point	Interpretations/Comments
58	2002	II	Prospective cohort study	Comparison of pre- and postsimulation training on three-person military resuscitation teams	28 days	Successful initial assessment and treatment of critical injuries in simulation	Simulation improved scores and times to successful resuscitation in simulated models of severely injured (ISS = 41) patients.
59	2008	II	Prospective cohort study	160 members of pediatric resuscitation teams participated in expanded trauma education, including monthly trauma simulation sessions using high-fidelity simulators	1 year	Successful team effort at resuscitation of injured children in simulator	Multidisciplinary teams function in the care of pediatric trauma patients can be enhanced and evaluated through the use of high-fidelity simulation.
62	2006	II	Systematic review	Taxonomy and impact of nontechnical skills on errors in ICU patient care	Review	Three reviewers categorized critical incident report errors attributable to nontechnical skills	50% critical incidents had at least one group of nontechnical skills failures as their cause.
68	2004	II	Qualitative, comparative analysis of 421 events		NA		Communications failed in 30% of team exchanges, jeopardizing the safety of one-third of the patients.
79	2004	II	Prospective controlled before-and-after study	Introduction of intensive care-based team on adverse outcomes	4 months	Impact of team management of mortality, LOS, and morbidity after major surgery	Relative risk reduction of 57.8% ($p < 0.0001$) of major complication and relative risk reduction of post operative deaths by 36.6% ($p < 0.0178$) reduction of postoperative LOS 4 days ($p < 0.0092$).
80	2006	Ila	Systematic review	Systematic review	NA		Team care in health care is more effective than nonteam care.

Abbreviations: ICU, intensive care unit; ISS, injury severity score; LOS, length of stay; NA, not applicable.

REFERENCES

- Weingart SN, Wison RM, Gibberd RW, et al. Epidemiology of medical error. *Br Med J* 2000; 320: 774-7.
- Ivatury RR, Guilford K, Malhotra AK, et al. Patient safety in trauma: maximal impact management errors at a Level I trauma center. *J Trauma* 2008; 64: 265-72.
- Gruen RL, Jurkovich GJ, McIntyre LK, et al. Patterns of errors contributing to trauma mortality: lessons learned from 2594 deaths. *Ann Surg* 2006; 244: 371-80.
- Teixeira PG, Inaba K, Hadjizacharia P, et al. Preventable or potentially preventable mortality at a mature trauma center. *J Trauma* 2007; 63: 1338-47.
- Miniño AM, Anderson RN, Fingerhut LA, et al. National vital statistics reports. 2006; 54: 1.
- Institute of Medicine. *To Err Is Human: Building a Safer Health System*. Washington, DC: National Academy Press, 2000.
- Healey MA, Shackford SR, Osler TM, et al. Complications in surgical patients. *Arch Surg* 2002; 137: 611-18.
- Croskerry P, Wears RL. Safety errors in emergency medicine. In: Markovchick VJ, Pons PT, eds., *Emergency Medicine Secrets*, 3rd edition. Philadelphia: Hanley and Belfus, 2002, 29-37.
- Famularo G, Salvini P, Terranova A, et al. Clinical errors in emergency medicine: experience at the emergency department of an Italian teaching hospital. *Acad Emerg Med* 2000; 7: 1278-81.
- Donchin Y, Gopher D, Olin M, et al. A look into the nature and causes of human errors in the intensive care unit. *Crit Care Med* 1995; 23: 294-300.
- Helmreich R. On error management: lessons from aviation. *Br Med J* 2000; 320: 781-5.
- MacCallum WG. National Academy of Sciences of the United States of America biographical memoirs. Vol. 17, seventh memoir, 1935.
- Davis JW, Hoyt DB, McArdle MS, et al. An analysis of errors causing morbidity and mortality in a trauma system: a guide for quality improvement. *J Trauma* 1992; 32: 660-6.
- Rothschild JM, Landrigan CP, Cronin JW, et al. The critical care safety study: the incidence and nature of adverse events and serious medical errors in intensive care. *Crit Care Med* 2005; 33: 1694-700.
- Orgeas MG, Timsit JF, Soufir L, et al. Impact of adverse events on outcomes in intensive care unit patients. *Crit Care Med* 2008; 36: 2041-7.
- Chang A, Schyve PM, Croteau RJ, et al. The JCAHO patient safety event taxonomy: a standardized terminology and classification schema for near misses and adverse events. *Int J Qual Health Care* 2005; 17: 95-105.
- Houshian S, Larsen MS, Holm C. Missed injuries in a Level I trauma center. *J Trauma* 2002; 52: 715-19.
- Shappell S, Detwiler C, Holcomb K, et al. Human error and commercial aviation accidents: an analysis using the human factors analysis and classification system. *Hum Factors* 2007; 49: 227-42.
- Hoyt DB, Coimbra R, Potenza B, et al. A twelve-year analysis of disease and provider complications on an organized Level I trauma service: as good as it gets? *J Trauma* 2003; 54: 26-37.
- Clarke DL, Gouveia J, Thomson SR, et al. Applying modern error theory to the problem of missed injuries in trauma. *World J Surg* 2008; 32: 1176-82.
- Williams JC. A data-based method for assessing and reducing human error to improve operational performance. 4th IEEE conference on Human Factors in Nuclear Power Plants, Monterey, CA, June 1988, 436-50.
- Hendy K. Defense R&D Canada. Toronto Technical Report DRDC, TR 2002-057, March 2003.
- Croskerry P, Chisholm C. What does human factors ergonomics need to know about front-line medicine. In: Tartaglia R, Bagnara S, Bellandi T, et al., eds., *Healthcare Systems Ergonomics and Patient Safety: Proceedings on the International Conference on Healthcare Systems Ergonomics and Patient Safety*. London, UK: Taylor & Francis Group PLC, 2005; 81-5.
- Hollnagel E. *Barriers and Accident Prevention*. Hampshire: Ashgate Publishing, 2004.
- Dinges DF, Rogers NL, Baynard MD. Chronic sleep deprivation. In: Kryger MH, Roth T, Dement WC, eds., *Principles and Practice of Sleep Medicine*. Philadelphia: Elsevier Saunders, 2005.
- Doghramji K. Waking up to sleep deprivation. *Medscape Neurology & Neurosurgery* 2005; 7.
- Weinger MD, Ancoli-Israel S. Sleep deprivation and clinical performance. *JAMA* 2002; 287: 955-7.
- Arias Y, Taylor DS, Marcin JP. Association between evening admissions and higher mortality rates in the pediatric intensive care unit. *Pediatrics* 2004; 113: 530-4.
- Dawson D, Reid K. Fatigue, alcohol and performance impairment. *Nature*. 1997; 388: 235.
- Rosekind MR, Gander PH, Gregory KB, et al. Managing fatigue in operational settings 1: physiological considerations and counter-measures. *Hosp Top* 1997; 75: 23-30.
- Helmreich RL, Merritt AC. *Culture at Work: National, Organizational and Professional Influences*. Aldershot: Ashgate, 1998.
- Dismukes K, Berman BA, Loukopoulos LD. *The Limits of Expertise: Rethinking Pilot Error and Causes of Airline Accidents*. Aldershot: Ashgate, 2007.
- Durden R. Going below minimums. *Av Safety* 2008; 28: 4-7.
- Petersen LA, Orav FA, Teich JM, et al. Using a computerized sign-out program to improve continuity of inpatient care and prevent adverse events. *JT COMM J Qual Improv* 1998; 24: 77-87.
- <http://www.nts.gov/aviation/Stats.htm>
- Shojania KG, Duncan BW, McDonald KM, et al. eds. *Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Evidence Report/Technology Assessment no. 43 (Prepared by the University of California at San Francisco-Stanford Evidence-based Practice Center under Contract No. 290-97-0013), AHRQ Publication No. 01-E058. Rockville, MD: Agency for Healthcare Research and Quality, 2001.
- Reason J. Human error: models and management. *Br Med J* 2000; 320: 768-70.
- Nolan TW. System changes to improve patient safety. *Br Med J* 2000; 320: 771-3.
- Sundt TM, Brown JP, Uhlig PN, STS Workforce on Patient Advocacy, Communications, and Safety. Focus on patient safety: good news for the practicing surgeon. *Ann Thorac Surg* 2005; 79: 11-15.
- Nance J. Personal communication, 2007.
- <http://asrs.arc.nasa.gov>
- http://asrs.arc.nasa.gov/docs/rs/60_Case_for_Confidential_Incident_Reporting.pdf NASA ASRS (Pub. 60).
- Barach P, Small S. Reporting and preventing medial mishaps: Lessons from non-medical near miss reporting systems. *Br Med J* 2000; 320: 759-63.
- Pietro DA, Shyavitz LJ, Smith RA, et al. Detecting and reporting medical errors; why the dilemma? *Br Med j* 2000; 320: 794-8.
- Battles J, Kaplan H, Van der Schaaf T, et al. The attributes of medical event reporting systems. *Arch Pathol Lab Med* 1998; 122: 231-8.
- Wald H, Shojania KG. Incident Reporting. In: Shojania KG, Duncan BW, McDonald KM, et al., eds., *Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Evidence Report/Technology Assessment No. 43 (Prepared by the University of California at San Francisco-Stanford Evidence-based Practice Center under Contract No. 290-97-0013), AHRQ

- Publication No. 01-E058. Rockville, MD: Agency for Healthcare Research and Quality, 2001.
47. Geiduschek JM. Registry offers insight on preventing cardiac arrests in children. *ASA Newsl* 1998; 62: 6:16–18.
 48. Choy CY. Critical incident monitoring in anaesthesia. *Curr Opin Anaesthesiol* 2008; 21: 183–6.
 49. Kram R. Critical incident reporting system in emergency medicine. *Curr Opin Anaesthesiol* 2008; 21: 240–4.
 50. Pronovost PJ, Thompson DA, Holzmueller CG, et al. Toward learning from patient safety reporting systems. *J Crit Care* 2006; 21: 305–15.
 51. Wu AW, Holzmueller CG, Lubomski LH, et al. Development of the ICU safety reporting system. *J Patient Saf* 2005; 1: 23–32.
 52. Klinect JR, Wilhelm JA, Helmreich RL. Threat and error management: data from line operations safety audits. In: *Proceedings of the Tenth International Symposium on Aviation Psychology*. Columbus: Ohio State University, 1999, 683–8.
 53. Gaba DM. Anesthesiology as a model for patient safety in healthcare. *Br Med J* 2000; 320: 785–8.
 54. Beckmann U, Gillies DM. Factors associated with reintubation in intensive care. *Chest* 2001; 120: 538–42.
 55. Gaba DM, Howard SK, Glanagana B, et al. Assessment of clinical performance during simulated crisis using both technical and behavioral ratings. *Anesthesiology* 1998; 89: 8–18.
 56. Jacobs LM, Gross RI, Luk SS. Advanced trauma operative management: surgical strategies for penetrating trauma. *Arch Surg* 2006; 141: 1265–6.
 57. Peugnet F, Dubois P, Rouland JF. Virtual reality versus conventional training in retinal photocoagulation: a first clinical assessment. *Comp Aided Surg* 1998; 3: 20–6.
 58. Holcomb JB, Dumire RD, Cormmett JW, et al. Evaluation of trauma team performance using an advanced human patient simulator for resuscitation training. *J Trauma* 2002; 52: 1078–86.
 59. Falcone RA Jr, Daugherty M, Schweer L, et al. Multidisciplinary pediatric trauma team training using high-fidelity trauma simulation. *J Pediatr Surg* 2008; 43: 1065–71.
 60. Berkenstadt H, Erez D, Munz Y, et al. Training and assessment of trauma management: the role of simulation-based medical education. *Anesthesiol Clin* 2007; 25: 65–74.
 61. Flin R, O'Connor P, Crichton M. *Safety at the Sharp End: A Guide to Non-Technical Skills*. Aldershot: Ashgate Publishing, 2008.
 62. Reader T, Flin R, Lauch K, et al. Non-technical skills in the intensive care unit. *Br J Anaesth* 2006; 96: 552–9.
 63. Kern T. *Redefining Airmanship*. New York: McGraw-Hill, 1997.
 64. Endsley M. Expertise and situation awareness. In: Ericsson KA, et al. eds., *Cambridge Handbook of Expertise and Expert Performance*. New York: Cambridge University Press, 2006.
 65. Banbury S, Dufield H, Hormann J, et al. FASA: development and validation of a novel measure to assess the effectiveness of commercial airline pilot situation awareness training. *Int J Aviat Psych* 2007; 17: 131–52.
 66. Salas E, Burke SC, Bowers CA, et al. Team training in the skies: does crew resource management (CRM) training work? *Hum Factors* 2001; 43: 641–74.
 67. Risser DT, Rice MM, Salisbury ML, et al. The potential for improved teamwork to reduce medical errors in the emergency department. The MedTeams Research Consortium. *Ann Emerg Med* 1999; 34: 373–83.
 68. Awad SS, Fagan SP, Bellows C, et al. Bridging the communication gap in the operating room with medical team training. *Am J Surg* 2005; 190: 770–4.
 69. Lingard L, Epsin S, Whyte S, et al. Communication failures in the operating room: an observational classification of recurrent types and effects. *Qual Saf Health Care* 2004; 13: 330–4.
 70. Patel VL, Kaufman DR, Arocha JF. Emerging paradigms of cognition in medical decision-making. *J Biomed Inform* 2002; 35: 52–75.
 71. Croskerry P. The cognitive imperative: thinking about how we think. *Acad Emerg Med* 2000; 7: 1223–31.
 72. Small SD, Wuerz RC, Simon R, et al. Demonstration of high-fidelity simulation team training for emergency medicine. *Acad Emerg Med* 1999; 6: 312–23.
 73. Gaba DM, Howard SK, Fish KJ, et al. Simulation-based training in anesthesia crisis resource management (ACRM): a decade of experience. *Sim Gaming* 2001; 32: 175–93.
 74. <http://www.jcaho.org/accredited+organizations.htm>
 75. Salas E, Cannon-Bowers J, Weaver J. Command and control teams; principles for training and assessment. In: Flin R, Arbutnot K, eds., *Incident Command: Tales from the Hot Seat*. Aldershot: Ashgate, 2002.
 76. Hackman JR. Learning more by crossing levels: evidence from airplanes, hospitals and orchestras. *J Org Behav* 2003; 24: 905–22.
 77. Baker DP, Salas E, Barach P. Medical teamwork and patient safety: the evidence-based relation. Final Report 2003. Center for Quality Improvement and Patient Safety and AHRQ and the Department of Defense.
 78. Jeffcott SA, MacKenzie CF. Measuring team performance in healthcare: review of research and implications for patient safety. *J Crit Care* 2008; 23: 188–96.
 79. Bellomo R, Goldsmith S, Uchino J, et al. Prospective controlled trial of effect of medical emergency team on postoperative morbidity and mortality rates. *Crit Care Med* 2004; 32: 916–21.
 80. Healey AN, Undre S, Vincent CA. Defining the technical skills of teamwork in surgery. *Qual Saf Health Care* 2006; 15: 231–4.
 81. Day DV, Halpin SM. Leadership development: a review of industry best practices. Technical Report 111, Alexandria VA: U.S. Army Research Institute for the Behavioral and Social Sciences, 2001.
 82. Klein KJ. Teamwork in a Shock Trauma Unit: New Lessons in Leadership: 2006; Knowledge@Wharton, <http://knowledge.wharton.upenn.edu/article.cfm?articleid=1048>.
 83. Yun S, Faraj S, Sims HP. Contingent leadership and effectiveness of trauma resuscitation teams. *J Appl Psychol* 2005; 90: 1288–96.
 84. Healy GB, Barker J, Madonna G. The surgeon as a leader. *Bull Am Col Surg* 2006; 91: 26–9.
 85. Jha AK, Duncan BW, Bates DW. Fatigue, sleepiness and medical errors. In: Shojania KG, Duncan BW, McDonald KM, et al., eds., *Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Evidence Report/Technology Assessment No. 43 (Prepared by the University of California at San Francisco–Stanford Evidence-based Practice Center under Contract No. 290-97-0013), AHRQ Publication No. 01-E058. Rockville, MD: Agency for Healthcare Research and Quality, 2001.

Small Bowel Surgery

Erik J. Teicher, John J. Hong, Michael M. Badellino, and Michael D. Pasquale

Clinical Questions		
Question	Answer	Grade
Are there other agents and/or techniques that can be used to improve the duration of POI?	Minimally invasive surgical techniques, local epidural anesthetics, avoidance of NGT, and early enteric feedings.	A
Does chewing gum shorten the duration of POI?	Yes, chewing gum has been shown to decrease length of POI and LOS.	A
Does the use of selective opiate receptor inhibitors decrease duration of POI?	Yes, it has an impact of both the duration of POI, tolerance of solid diet, and LOS, but unclear on cost/benefit ratio.	A
Are there any techniques/agents that have been shown to decrease intra-abdominal adhesion formation following laparotomy?	Sharp dissection, minimizing tissue trauma, decreasing foreign bodies in surgical field, barrier devices.	A
What does the use of water-soluble contrast do?	Causes an osmosis of water into the bowel lumen and decreases edema of the bowel wall, which promotes proximal bowel distention and increases the pressure gradient across an obstructing region.	
Is the early use of water soluble contrast indicated in the diagnosis/management of SBO?	The use of water-soluble contrast has shown to predict the success of conservative management, but has not been shown to decrease the need for operation.	A
Can CT predict the need for operation in patients with incomplete SBO?	CT scan can diagnose SBO and SBO causing ischemia and the requirement for surgical intervention.	A
Is there any difference between stapled or hand sewn techniques for bowel anastomosis?	There has been no difference shown between the two, however, stapled anastomoses have a higher rate of stricture.	A
Abbreviations: CT, computed tomography; LOS, length of stay; NGT, nasogastric tube; POI, postoperative ileus; SBO, small bowel obstruction.		

POSTOPERATIVE ILEUS

Ileus has been historically defined as the functional inhibition of propulsive bowel activity irrespective of pathogenic mechanism. Postoperative ileus (POI) is the uncomplicated ileus occurring following surgery, generally resolving spontaneously in about 2 to 3 days, whereas paralytic POI is that form that lasts longer than 3 days (1). POI contributes to postoperative patient discomfort, delays enteral feeding, hinders patient mobility, and increases hospital length of stay (LOS) (2).

Artinyan and colleagues examined the extent and duration of POI in 88 patients who underwent elective abdominal surgery. The duration of POI was 10 days or less in 96.6% of patients, and the median duration was 5 days. The mean number of days to initiation of unrestricted clear liquids was 1.6, and 22.7% of patients were tolerating a solid diet by postoperative day (POD) 6. Variables within the patient population such as age, body mass index, anesthesia time, surgery time, estimated blood loss (EBL), and total opioid dose were examined to determine whether correlation exists to duration of POI. Statistically, only the EBL and total opioid dose were independently and significantly associated with duration of POI (3).

POI is characterized by impairment of gastrointestinal motility after abdominal or other surgical procedures, accumulation of gas and fluids in the bowel, and the delayed passage of flatus and defecation (4). The clinical findings are variable, with some patients remaining essentially asymptomatic and others with abdominal pain and distention, diet intolerance, nausea and vomiting, and absent bowel sounds. POI affects all portions of the gastrointestinal (GI) tract and the recovery of each occurs at different rates. The function of the small intestine returns first, within 4–24 hours after surgery, followed by the stomach in 24–48 hours, and large intestine function returns last within 48–72 hours (5).

GI motility is controlled by several physiologic mechanisms, including the autonomic nervous system, GI hormones, inflammation, and various metabolic disturbances such as electrolyte imbalances and acid/base status. Surgery and anesthetic agents, including opioid medications, can alter these factors and effect bowel motility (6).

There is no diagnostic test that can exclude or confirm the diagnosis of POI. Radiographs of the abdomen may show nonspecific dilated loops of small and large bowel. Upper GI series and abdominal computerized axial tomography scans may be used when it is required to differentiate an ileus from bowel obstruction. The recognition of

POI is based on the usual signs and symptoms in the proper postoperative setting.

The resolution of POI is marked with the passage of flatus or defecation as colonic motility is the last portion of the GI tract to recover from an ileus. Other criteria that can demonstrate the resolution of POI include the return of bowel sounds, a decrease in nasogastric tube (NGT) drainage, a change in the consistency of NGT drainage with decreasing amounts of bile, and the tolerance of oral intake.

MANAGEMENT OF POI

Are There Other Agents and/or Techniques That Can Be Used to Improve the Duration of POI?

There are a variety of management approaches that can be used to reduce the prevalence of POI. Minimally invasive surgical techniques, such as laparoscopy, have advantages over traditional open procedures, including diminished pain, faster recovery, improved cosmesis, fewer complications related to surgery such as adhesions or hernias, shorter LOS, and faster resolution of POI. Controlled studies have demonstrated a reduced duration of POI and an associated reduction in LOS. Lacy et al. examined patients with colon cancer that were randomized to either laparoscopic assisted colectomy or open colectomy. It was shown that those patients randomized to the laparoscopic group had a mean time of 36 hours until recovery of POI, compared to 55 hours in the open group. Mean LOS was 5.2 versus 7.9 days for the laparoscopic group and open groups, respectively. The laparoscopic group had a decreased time to oral intake and lower requirement for NGT insertion as well (7). A retrospective review of all consecutive patients who underwent either laparoscopic assisted colectomy or open colectomy was examined by Salimath and colleagues. They found in 247 patients that first passage of flatus took 2.9 days and 3.6 days, first bowel movement took 3.7 days and 4.4 days, and LOS lasted 4.4 days and 8 days in the laparoscopic and open groups, respectively (8).

It has been well established that opioid analgesia has a profound impact on GI motility and the length of POI (9). These effects are observed with systemic opioid administration with intravenous patient-controlled analgesia, intramuscular opioid injection, or epidural opioid administration (10). A literature review showed multiple studies demonstrating the improved effect of epidural local anesthetics on the duration of POI (11). A recent review concluded that epidural local anesthetics reduced the time of POI by 36 hours when compared to systemic opioids and 24 hours when compared with epidural opioids (12). There was no statistical difference comparing local epidural anesthetic to combination epidural local and opioid administration. Based on the information that opioids inhibit GI motility and prolong POI, various methods have been introduced to decrease opioid usage in providing analgesia. The most established technique of opioid-sparing analgesia is to provide pain relief with nonsteroidal anti-inflammatory (NSAID) medications. In experimental and clinical studies, administration of NSAIDs has resulted in less postoperative nausea and vomiting and improvement in GI motility and shortening of POI (13,14).

The NGT may potentially exacerbate POI despite popular belief that they encouraged their resolution (15).

The routine removal of the NGT after surgery is now recommended to help avoid other complications resulting from their prolonged usage. Rhinitis, maxillary sinusitis, and pharyngitis are potential consequences of their use (16). McAlister et al. demonstrated that the postoperative use of an NGT was a major risk factor for pulmonary complications, including pneumonia, atelectasis, or respiratory failure requiring mechanical ventilation in a study with 1,055 patients who underwent nonthoracic surgery (17). The perioperative use of an NGT had an odds ratio of 7.7 in causing pulmonary complications. A recent meta-analysis by Nelson and colleagues showed that in abdominal operations of any type, the use of an NGT delayed the return of bowel function (18). This review of 28 studies was conducted that fulfilled the eligibility criteria of patients having abdominal operations of any type, emergency or elective, who were randomized before completion of the operation to receive an NGT and have it remain in place until intestinal function had returned or to selective use of a tube with early removal. The data showed that those postsurgical patients not having an NGT routinely inserted experienced an earlier return of bowel function.

Han-Geurts and colleagues showed that early enteral feedings have now been shown to be safe and beneficial for the patient, allowing earlier tolerance of a solid diet and return of bowel function (19). A randomized prospective study investigated 128 patients undergoing open abdominal colorectal or vascular procedures who were assigned to either a conventional return to regular diet group or a group that allowed resumption of diet as soon as tolerated. A normal diet was tolerated after a median of 2 days in the as tolerated group compared with 5 days in the conventional group, and thus had a shortened LOS. In another prospective randomized study, Stewart et al. determined that there was an earlier passage of flatus and bowel movement of approximately 1 day sooner, a toleration of regular diet 3 days earlier, and hospital discharge 2 days before controls in a group that started clear liquids 4 hours after elective colorectal surgery (20).

Recommendation: Based on the available data, it has been shown that minimally invasive surgical techniques, when appropriate, as well as the use of local epidural anesthetic anesthesia, avoidance of NGT usage, and early enteral feedings contribute to earlier resolution of POI and decreased hospital LOS and should be utilized in patients after surgery.

Does Chewing Gum Shorten the Duration of Postoperative Ileus?

Based on the evidence that early enteral feedings lessened the extent of POI, Asao and colleagues (21) examined the effect of gum chewing as an alternative approach to stimulate bowel function in the postoperative period. Gum is postulated to increase vagal tone, usually provided by food, and to increase the release of GI hormones associated with bowel motility. Their data showed an earlier return of bowel function in a small series of 19 patients who underwent laparoscopic colon resection for cancer who were prospectively randomized to either a gum chewing or a control group. The first passage of flatus was about 24 hours sooner, and the first defecation was approximately 2.7 days sooner in the gum chewing group than

controls (21). Another prospective study, published by Schuster and colleagues, randomized 34 patients scheduled for elective open sigmoidectomy for diverticular disease or cancer into a gum chewing or control group. The first passage of flatus occurred on postoperative hour 65.4 in the gum chewing group versus 80.2 in the control group. The first bowel movement occurred on postoperative hour 63.2 and 89.4 in the gum chewing and control groups, respectively (22). Furthermore, a systemic review of the literature and meta-analysis conducted by Chan and Law in 2006 showed that when combined with usual postoperative care, surgical patients randomized to gum chewing passed flatus 24.3% earlier, had bowel movements 32.7% sooner, and were discharged from the hospital 17.6% faster than those with standard postoperative care alone (23).

Recommendation: According to prospective studies, gum chewing has shortened the duration of POI and hospital LOS and should be employed in postoperative patients.

Does the Use of Selective Opiate Receptor Inhibitors Decrease Duration of POI?

A novel approach for the management of POI recently has been the development of a selective opioid receptor antagonist. There are three opioid receptor subtypes, μ , κ , and δ , involved in regulation of GI tract function (24). The μ receptor is the important subtype involved in GI motility, transit time, and central pain management (25). Alvimopan (trade name Entereg) is a synthetic, peripherally acting μ opioid antagonist that has limited GI absorption and does not cross the blood-brain barrier (26). Clinical trials have supported the use of alvimopan in the management of POI by accelerating GI recovery. In the first published study of 78 patients undergoing partial colectomy of total abdominal hysterectomy, 6mg alvimopan shortened the POI, measured by the median time to first flatus which decreased from 70 to 49 hours; median time to first bowel movement, which decreased from 111 to 70 hours; and median time until readiness to hospital discharge, which decreased from 91 to 68 hours compared to placebo (27). Wolff and colleagues (28) prospectively randomized 500 patients undergoing bowel resection or radical hysterectomy to receive either alvimopan or placebo and demonstrated the time to GI recovery was improved by 15–20 hours following doses of 6mg and 22–28 hours following doses of 12mg alvimopan. The mean time to hospital discharge was 13 and 20 hours sooner for patients treated with the 6 or 12mg doses, respectively (28). Delaney examined effects of alvimopan in approximately 400 patients undergoing bowel resection, simple hysterectomy, or radical hysterectomy. In this study, the mean return of GI function for all patients was improved by 14.1 hours after doses of 6mg and by 7.5 hours after doses of 12mg alvimopan. Alvimopan 6mg dose accelerated the time to hospital discharge compared to placebo by a mean difference of approximately 14 hours in this study (29). Viscusi et al. investigated the effects of alvimopan in approximately 600 patients who underwent open laparotomy for bowel resection, simple hysterectomy, or radical hysterectomy and found GI recovery, as measured by tolerance of solid diet, passage of flatus, and defecation, accelerated by 7.5 hours for the 6mg dose and 9.9 hours for the 12mg dose. The mean time to discharge

order was reduced by 14.2 hours for the 6mg dose and 15.2 hours for the 12mg dose (30). These trials observed no differences between placebo and alvimopan treated patients for postoperative opioid consumption and POI related morbidity as shown by a lower postoperative NGT insertion, increased LOS, or readmission. Using pooled data from alvimopan trials, Wolff and colleagues (31) showed that overall POI morbidity in the placebo groups ranged from 14.1% to 19.7%, whereas those groups treated with alvimopan ranged from 6.6% to 11.2%. Approximately 7% of patients in the placebo groups experienced complications of POI resulting in increased LOS, compared to 2% of patients in the alvimopan groups. Last, patients treated with alvimopan were less likely to undergo readmission (4.9% alvimopan, 8.3% placebo) for POI complications at 10 days, whereas those readmitted at 7 days were comparable between groups (31).

Recommendation: Alvimopan has improved the duration of POI and hospital LOS in prospective randomized studies. It should be noted, however, that these prospective randomized trials were sponsored by the drug manufacturer.

INTRA-ABDOMINAL ADHESIONS

Intra-abdominal adhesions are now the most frequent complication of abdominal surgery, subsequently developing in over 93% of patients undergoing laparotomy (32). The peritoneal cavity is the space between the visceral and parietal peritoneum, making up a closed sac in the male and an open sac in the female through the gynecological tract. The peritoneum consists of a connective tissue layer covered by a mesothelium. Under normal conditions, the peritoneal cavity contains approximately 10cc of serous fluid. This fluid circulates within the abdominal cavity through well-defined routes and is in continuity with the vascular system via lymphatics.

Intra-abdominal adhesions are caused by peritoneal trauma and inflammation that results in a decrease of blood flow and local angiogenesis (33). This corresponds to an increase in the vascular permeability and release of inflammatory cells. Inactive fibrinogen at the site of peritoneal injury then becomes activated to a fibrin gel that connects the two damaged layers of peritoneum. There is a fibrinolytic process that attempts to control fibrin formation by hydrolyzing this to fibrin split products, which is initiated by plasmin, an active protease formed by the action of plasminogen activators on its precursor, plasminogen. The theory of adhesion formation is characterized by a decrease in the plasminogen activator activity, largely mediated through tissue plasminogen activator, resulting in a pathologic alteration in fibrinolysis (34). The nondegraded fibrin matrix remains, and the regeneration process leads to its organization and resulting in adhesion development between two damaged peritoneal surfaces in apposition (35). Adhesions contain inflammatory cells that include fibroblasts, macrophages, mast cells, eosinophils, red blood cells, and tissue debris. The amounts of cells decrease and the adhesions mature into fibrous bands composed of collagens and covered by mesothelium.

The most frequently encountered clinical manifestation of abdominal adhesions is small bowel obstruction

(SBO), with 74% of cases being related to previous surgery (36). Reviews of hospital admissions for adhesional SBO have identified a mortality rate of almost 10% (37), increasing to approximately 15% in patients undergoing small bowel resection (38). Adhesional SBO requiring surgical treatment has a 33% risk of inadvertent enterotomy and the presence of adhesions have a 19% risk of inadvertent enterotomy during a reoperative laparotomy (39). One study that examined effects of previous surgery on operative times showed that adhesions from previous surgery significantly increase operative time with a median time of 18 minutes (40). There is a 20–50% mortality rate in those patients who have an undetected bowel injury when undergoing operation for adhesional SBO (41). Adhesiolysis remains the treatment for adhesions, although adhesions reform in approximately 85% of patients (42).

Are There Any Techniques/Agents That Have Been Shown to Decrease Intra-Abdominal Adhesion Formation Following Laparotomy?

There are a variety of technical methods that have been employed to attempt to minimize the formation of postoperative abdominal adhesions. Studies have shown that sharp mechanical transection of tissues was followed by the least amount of tissue reaction and necrosis compared to other means of transection (43). The presence of foreign material that arise from gauze, sponges, starch powder, suture, debris from surgical drapes, gowns, masks, and many other items can elicit a peritoneal inflammation and be found in postoperative adhesions, allowing a causal relationship between the presence of foreign material and formation of adhesions (44). Closure of the peritoneum does not offer benefit in reducing postoperative adhesion formation, as seen in a prospective study by Tulandi and colleagues. They analyzed patients undergoing laparotomy for gynecological procedures and compared separate closure of the peritoneum and fascia to closure of the fascia only; they found the incidence of adhesion formation was not statistically different between the group with peritoneal closure (22.2%) and the group without peritoneal closure (15.8%) (45). Another prospective study randomizing patients to closure of the peritoneum as a separate layer compared to single layer closure of the fascia showed no difference in wound complications such as infection, dehiscence, or subsequent incisional hernia development between the two groups (46). Nonclosure of the peritoneum is safer, allowing the underlying viscera to remain under direct visualization during closure, and reduces operative time.

Studies evaluating laparoscopic to open surgery have revealed a lower rate of postoperative adhesions. Polymeneas et al. found a 44% rate of loose, easily separable adhesions between the gallbladder liver bed and the omentum or the duodenum after laparoscopic cholecystectomy, whereas after open cholecystectomy all patients (100%) had thick and extensive adhesions to the operative site (47). Audebert et al. compared 125 patients with different prior laparoscopic procedures to 131 patients with previous horizontal suprapubic laparotomy and to 89 patients with previous midline laparotomy. The rates of umbilical adhesions were 1.6% after laparoscopy compared with 19.8% in those with a horizontal suprapubic laparotomy and 51.7%

in those with a midline laparotomy (48). These studies have shown that laparoscopy is associated with fewer adhesions at the operative site, to the incision site, and research has demonstrated a lower rate of reformation of adhesions after laparoscopic adhesiolysis (49). Milingos et al. assessed adhesion reformation as a secondary endpoint in his clinical study regarding pregnancy rates after open microsurgical and laparoscopic adhesiolysis by calculating initial adhesion scores in a small group of patients who afterward underwent open adhesiolysis through laparotomy or laparoscopic adhesiolysis for periadnexal adhesions as the only cause of their infertility. The scores were similar before adhesiolysis, but three to six months after the operation, at a second-look laparoscopy, there was a greater reduction of the scores in the laparoscopic group than in group that underwent laparotomy (50).

There has been substantial investigation targeting a variety of mechanisms involved in adhesion formation. NSAIDs have been examined for their ability of reducing postoperative adhesions and their use has showed benefit in animal models (51–53). Corticosteroids have also been examined with similar outcomes (54,55). Other studies have examined agents that may interfere with the pathways of deposition and degradation of fibrin. The anticoagulants heparin and low molecular weight heparin have demonstrated a decrease in adhesion formation in animal studies (56,57). Agents that cause fibrinolysis, such as recombinant tissue plasminogen activator, also showed promise in animal models in reduction of postoperative adhesions (58–60). The majority of these investigations that have reported success in using these various agents to prevent postoperative adhesions are limited to animal studies; similar results in humans is lacking.

Barrier devices have been used to separate the layers of the peritoneum and provide protection from adhesion formation. Ideally, a barrier device should be easy to apply by laparoscopic and open surgical methods, provide unrestricted coverage of the affected peritoneum, and remain effective throughout the healing process (61). Barriers have been developed in various forms, including polymer solutions and solid membranes of polysaccharides, such as hyaluronic acid, cellulose, dextran, or chitosan. Solutions are applied at the end of the procedure and may form viscous gels. Membranes are placed directly on potential sites of adhesions. Various barriers currently FDA-approved include regenerated cellulose (Interceed), expanded polytetrafluoroethylene (Preclude), hyaluronic acid-carboxymethylcellulose (Seprafilm), polylactide membrane (Surgiwrap), and icodextrin solution (Adept). Seprafilm is a nontoxic, nonimmunogenic, biocompatible material that was designed to reduce postoperative abdominal adhesion formation. It turns into a hydrophilic gel approximately 24 hours after placement and provides a protective coating around traumatized tissues for up to 7 days during remesothelialization. A recent meta-analysis studying the efficacy of Seprafilm in eight randomized controlled trials with the outcomes of 4,203 patients evaluated. Adhesions were classified as grade 0; no adhesions, grade 1; least severe and filmy, avascular, and translucent, grade 2; moderately severe and medium thickness and limited vascularity; grade 3, very severe and dense and highly vascularized. The incidence of grade 0 adhesions was significantly higher than observed

among control group patients. The incidence of grade 1 adhesions was statistically insignificant between Seprafilm and control groups. The severity of grade 2 and 3 for adhesions among Seprafilm-treated patients was significantly less than observed for control group patients. The meta-analysis showed that Seprafilm decreases abdominal adhesions following surgery (62). There are studies that show the overall incidence of postoperative SBO was unchanged between patients treated with Seprafilm and controls (63). The frequency of abdominal abscesses was slightly higher, although nonsignificant, whereas the incidence of fistulas, sepsis, and peritonitis occurred more frequently than controls (2 versus <1%) and when wrapped around a fresh anastomosis had a higher frequency of anastomotic leaks (4 versus 2%) (64).

Recommendation: There are a variety of methods that can be used to decrease the formation of postoperative abdominal adhesions, such as using sharp dissection and minimizing tissue trauma, reducing the amount of foreign body contamination within the surgical field, and employing minimally invasive surgical techniques if indicated. The use of barriers between the peritoneal layers seems logical; however, the improvement in postoperative adhesion formation observed has shown no impact on the rate of postoperative SBO.

ADHESIONAL SBO

Adhesional SBO may require immediate operative intervention to minimize risk of necrotic bowel and perforation when clinical evidence of strangulation exists (65). In those patients who do not show this clinical picture, a trial of nonoperative management is acceptable (66). The conventional approach has been to allow 48 hours of nonoperative management as the majority of adhesional SBO resolve by this time (67).

DIAGNOSIS OF SBO

What Does the Use of Water-Soluble Contrast Do?

The role of water-soluble contrast medium in adhesive SBO in predicting the need for surgery after conservative management fails has been evaluated recently. Meglumine amidotrizoate (trade name Gastrografin) is the most commonly used water-soluble contrast agent and is a mixture of sodium diatrizoate and meglumine diatrizoate with an osmolality of 1,900 mOsm/L. Gastrografin acts by causing an osmosis of water into the bowel lumen, decreasing the edema of the bowel wall, which contributes to proximal bowel distention, increasable the pressure gradient across an obstructing region (68).

Is the Early Use of Water-Soluble Contrast Indicated in the Diagnosis/Management of SBO?

The use of Gastrografin has been studied for its use in the prediction of successful nonoperative management of SBO and whether it has a therapeutic function in the resolution of SBO; this was evaluated in a meta-analysis by Abbas and colleagues (69). There were six prospective randomized controlled studies investigating the diagnostic use of Gastrografin in determining the successful conservative

management of SBO. Patients that present with SBO without indications for immediate surgery were evaluated with 100 cc Gastrografin, orally or by NGT, followed by abdominal imaging in 4–24 hours. The presence of contrast in the colon indicates a partial SBO and increases the probability of its resolution with conservative management. However, contrast does not reach the colon, then the SBO is considered complete and is unlikely to resolve without a surgical intervention. There were six prospective randomized studies that addressed whether Gastrografin has a therapeutic role in the treatment of SBO. These showed no observed difference in resolution of SBO between Gastrografin and placebo in those patients what would require surgery. Therefore, Gastrografin is useful in the prediction of successful conservative management of SBO, however, it has no benefit in the treatment of SBO based on the meta-analysis.

Recommendation: Water-soluble contrast agents such as Gastrografin have been shown to predict successful conservative management in patients who present without clinical findings suggesting the need for operation. However, Gastrografin has not been shown to reduce the need for surgical intervention in patients with postoperative SBO.

Can CT Predict the Need for Operation in Patients with Incomplete SBO?

Plain abdominal radiographs have proven to be diagnostic of SBO in only 67–80% of patients (70). Abdominal radiographs can be entirely normal in patients with complete, closed-loop obstruction or strangulation associated with obstruction (71). The computed tomography (CT) scan has a well-established role in the diagnosis of SBO since the first large published series showing its utility and efficacy (72). CT findings of SBO include distended bowel loops proximal to collapsed loops, air-fluid levels, and a possible transition point. Studies have since proved the value of CT in confirming the diagnosis and revealing the cause of SBO, with a sensitivity of 94–100% and an accuracy of 90–95% (73). Further reviews have shown that CT is highly accurate for diagnosing ischemic bowel with a sensitivity of 83%, specificity of 92%, positive predictive value of 79%, and a negative predictive value of 93% (74). CT findings of slight thickening of the bowel wall, the “target sign,” engorgement of the mesenteric vasculature, and mesenteric edema are all potential signs of early or reversible small bowel strangulation; bowel infarction on gangrene may be demonstrated by CT findings of high attenuation of the bowel wall, pneumatosis, hemorrhagic changes in the mesentery, gas in the portal vein, and poor or no enhancement of the bowel wall. Investigators, using a combination of five highly specific findings, including poor enhancement of the bowel wall, a serrated beak, diffuse engorgement of mesenteric vasculature or mesenteric haziness, an unusual course of mesenteric vasculature, and a large amount of ascites, correctly identified 85% of patients with a strangulated SBO (75).

Recommendation: CT scan of the abdomen has the ability to identify SBO by specific findings and can use other specific findings to diagnose bowel ischemia and allow for surgical intervention. Following obstructive series, patients presenting with SBO should be evaluated with CT scan of the abdomen if clinically warranted.

Is There Any Difference Between Stapled or Hand-sewn Techniques for Bowel Anastomosis?

A meta-analysis was conducted to compare hand-sewn to stapled anastomosis which combined data from 13 randomized controlled trials in colon and rectal surgery. Overall, there were no significant differences between hand-sewn and stapled anastomoses for mortality; total, radiological, and clinical anastomotic leak rates; cancer recurrence rate; or wound infection rate. However, a significant difference existed favoring hand-sewn anastomoses for strictures and intraoperative technical problems (76). The possibility of an overactive inflammatory response and higher collagen levels may be responsible for the increased stricture rate with stapled anastomoses (77).

Recommendation: Prospective randomized trials have shown no differences between hand-sewn and stapled anastomoses; however, the rate of postoperative stricture formation may be higher with stapled anastomoses. Surgeon preference and comfort should dictate the type of anastomosis that is performed.

REFERENCES

- Livingston EH, Passaro EP. Postoperative ileus. *Dig Dis Sci* 1990; 35: 121–31.
- Kehlet H, Holte K. Review of postoperative ileus. *Am J Surg* 2001; 182(Suppl): 3–10.
- Artinyan A, Nunoo-Mensah JW, Balasubramaniam S, et al. Prolonged postoperative ileus—definition, risk factors, and predictors after surgery. *World J Surg* 2008; 32: 1495–500.
- Holte K, Kehlet H. Postoperative ileus: a preventable event. *Br J Surg* 2000; 87: 1480–93.
- Clevers GJ, Smout AJ. The natural course of postoperative ileus following abdominal surgery. *Neth J Surg* 1989; 41: 97–9.
- Mattei P, Rombeau JL. Review of the pathophysiology and management of postoperative ileus. *World J Surg* 2006; 30: 1382–91.
- Lacy AM, Garcia-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomized trial. *Lancet* 2002; 359: 2224–9.
- Salimath J, Jones MW, Hunt DL, et al. Comparison of return of bowel function and length of stay in patients undergoing laparoscopic versus open colectomy. *JSLs* 2007; 11: 72–5.
- DeWinter BY, Boeckstaens GE, DeMan JG, et al. Effects of mu- and kappa-opioid receptors on postoperative ileus in rats. *Eur J Pharmacol* 1997; 339: 63–7.
- Petros JG, Realica R, Ahmad S, et al. Patient-controlled analgesia and prolonged ileus after uncomplicated colectomy. *Am J Surg* 1995; 170: 371–4.
- Fotiadis RJ, Badvie S, Weston MD, et al. Epidural analgesia in gastrointestinal surgery. *Br J Surg* 2004; 91: 828–41.
- Jorgensen H, Wetterslev J, Moiniche S, et al. Epidural local anesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV, and pain after abdominal surgery. *Cochrane Database Syst Rev*. 2001; 1: CD001893.
- Kelley MC, Hocking MP, Marchand SD, et al. Ketorolac prevents postoperative small intestine ileus in rats. *Am J Surg* 1993; 171: 85–8.
- Ferraz AA, Cowles VE, Condon RE, et al. Nonopioid analgesics shorten the duration of postoperative ileus. *Am Surg* 1995; 61: 1079–83.
- Cheatham ML, Chapman WC, Key SP, et al. A meta-analysis of selective versus routine nasogastric decompression after elective laparotomy. *Ann Surg* 1995; 221: 469–76.
- Desmond P, Raman R, Idikula J. Effect of nasogastric tubes on the nose and maxillary sinus. *Crit Care Med* 1991; 19: 509–11.
- McAlister FA, Bertsch K, Man J, et al. Incidence of and risk factors for pulmonary complications after nonthoracic surgery. *Am J Respir Crit Care Med* 2005; 171: 514–17.
- Nelson R, Tse B, Edwards S. Systematic review of prophylactic nasogastric decompression after abdominal operations. *Br J Surg* 2005; 92: 673–80.
- Han-Geurts IJ, Hop WC, Kok NF, et al. Randomized clinical trial of the impact of early enteral feeding on postoperative ileus and recovery. *Br J Surg* 2007; 94: 555–61.
- Stewart BT, Woods RJ, Collopy BT, et al. Early feeding after elective open colorectal resections: a prospective randomized trial. *Aust NZ J Surg* 1998; 68: 125–8.
- Asao T, Kuwano H, Nakamura J, et al. Gum chewing enhances early recovery from postoperative ileus after laparoscopic colectomy. *J Am Coll Surg* 2002; 195: 30–2.
- Schuster R, Grewal N, Greaney GC, et al. Gum chewing reduces ileus after elective open sigmoid colectomy. *Arch Surg* 2006; 141: 174–6.
- Chan MK, Law WL. Use of chewing gum in reducing postoperative ileus after elective colorectal resection: a systematic review. *Dis Colon Rectum* 2007; 50: 2149–57.
- Sternini C, Patierno S, Selmer IS, et al. The opioid system in the gastrointestinal tract. *Neurogastroenterol Motil* 2004; 16(Suppl): 3–16.
- Schmidt WK. Alvimopan (ADL 8-2698) is a novel peripheral opioid antagonist. *Am J Surg* 2001; 182(Suppl): 27–38.
- Leslie JB. Alvimopan for the management of postoperative ileus. *Ann Pharmacother* 2005; 39: 1502–10.
- Taguchi AT, Sharma N, Saleem RM, et al. Selective postoperative inhibition of gastrointestinal opioid receptors. *N Engl J Med* 2001; 345: 935–40.
- Wolff BG, Michelassi F, Gerkin TM, et al. Alvimopan, a novel, peripherally acting μ opioid antagonist. Results of a multicenter, randomized, double-blind, placebo-controlled, phase III trial or major abdominal surgery and postoperative ileus. *Ann Surg* 2004; 240: 728–35.
- Delaney CP, Weese JL, Hyman NH, et al. Phase III trial of alvimopan, a novel, peripherally acting, μ opioid antagonist, for postoperative ileus after major abdominal surgery. *Dis Colon Rectum* 2005; 48: 1114–25.
- Viscusi ER, Goldstein S, Witkowski T, et al. Alvimopan, a peripherally acting μ -opioid receptor antagonist, compared with placebo in postoperative ileus after major abdominal surgery. *Surg Endosc* 2006; 20: 64–70.
- Wolff BG, Weese JL, Ludwig KA, et al. Postoperative ileus-related morbidity profile in patients treated with alvimopan after bowel resection. *J Am Coll Surg* 2007; 204: 609–16.
- Menzies D, Ellis H. Intestinal obstruction from adhesions—how big is the problem? *Ann R Coll Surg Engl* 1990; 72: 60–3.
- Cheong YC, Laird SM, Li TC, et al. Peritoneal healing and adhesion formation/reformation. *Hum Reprod Update* 2001; 7: 556–66.
- Holmdahl L. The role of fibrinolysis in adhesion formation. *Eur J Surg* 1997; 163(Suppl): 24–31.
- Holmdahl L, Eriksson E, Eriksson BI, et al. Depression of peritoneal fibrinolysis during operation is a local response to trauma. *Surgery* 1998; 123: 539–44.
- Menzies D. Postoperative adhesion: their treatment and relevance in clinical practice. *Ann R Coll Surg Engl* 1993; 75: 147–53.
- Menzies D, Parker M, Hoare R, et al. Small bowel obstruction due to postoperative adhesions: treatment patterns and

- associated costs in 110 hospital admissions. *Ann R Coll Surg Engl* 2001; 83: 40–6.
38. Wysocki A, Pozniczek M, Kulawik J, et al. Peritoneal adhesions as a cause of small bowel obstruction. *Przegl Lek* 2003; 60: 32–5.
 39. Van der Krabben AA, Dijkstra FR, Nieuwenhuijzen M, et al. Morbidity and mortality of inadvertent enterotomy during adhesiotomy. *Br J Surg* 2000; 87: 467–71.
 40. Coleman MG, McLain AD, Moran BJ. Impact of previous surgery on time taken for incision and division of adhesions during laparotomy. *Dis Colon Rectum* 2000; 43: 1297–9.
 41. Van Goor H. Consequences and complications of peritoneal adhesions. *Colorectal Dis* 2007; 9(Suppl): 25–34.
 42. Diamond MP, Freeman ML. Clinical implications of post-surgical adhesions. *Hum Reprod Update* 2001; 7: 567–76.
 43. Elkins TE, Stovall TG, Warren J, et al. A histologic evaluation of peritoneal injury and repair: implications for adhesion formation. *Obstet Gynecol* 1987; 70: 225–8.
 44. Saxen L, Myllarniemi H. Foreign material and postoperative adhesions. *N Engl J Med* 1968; 279: 200–2.
 45. Tulandi T, Hum HS, Gelfand MM. Closure of laparotomy incisions with or without peritoneal suturing and second-look laparoscopy. *Am J Obstet Gynecol* 1988; 158: 536–7.
 46. Hugh TB, Nankivell C, Meagher AP, et al. Is closure of the peritoneal layer necessary in the repair of midline surgical abdominal wounds? *World J Surg* 1990; 14: 231–4.
 47. Polymeneas G, Theodosopoulos T, Stamatiadis A, et al. A comparative study of postoperative adhesion formation after laparoscopic vs open cholecystectomy. *Surg Endosc* 2001; 15: 41–3.
 48. Audebert AJ, Gomel V. Role of microlaparoscopy in the diagnosis of peritoneal and visceral adhesions and in the prevention of bowel injury associated with blind trocar insertion. *Fertil Steril* 2000; 73: 631–5.
 49. Gutt CN, Oniu T, Schemmer P, et al. Fewer adhesions induced by laparoscopic surgery? *Surg Endosc* 2004; 18: 898–906.
 50. Milingos S, Kallipolitis G, Loutradis D, et al. Adhesions: laparoscopic surgery versus laparotomy. *Ann NY Acad Sci* 2000; 900: 272–85.
 51. De Leon FD, Toledo AA, Sanfilippo JS, et al. The prevention of adhesion formation by nonsteroidal antiinflammatory drugs: an animal study comparing ibuprofen and indomethacin. *Fertil Steril* 1984; 41: 639–42.
 52. Guvenal T, Cetin A, Ozdemir H, et al. Prevention of postoperative adhesion formation in rat uterine horn model by nimesulide: a selective COX-2 inhibitor. *Hum Reprod* 2001; 16: 1932–5.
 53. Nishimura K, Nakamura RM, DiZerega GS. Ibuprofen inhibition of postsurgical adhesion formation: a time and dose response biochemical evaluation in rabbits. *J Surg Res* 1984; 36: 115–24.
 54. Maurer JH, Bonaventura LM. The effect of aqueous progesterone on operative adhesion formation. *Fertil Steril* 1983; 39: 485–9.
 55. Höckel M, Ott S, Siemann U, et al. Prevention of peritoneal adhesions in the rat with sustained intraperitoneal dexamethasone delivered by a novel therapeutic system. *Ann Chir Gynaecol* 1987; 76: 306–13.
 56. Kutlay J, Ozer Y, Isik B, et al. Comparative effectiveness of several agents for preventing postoperative adhesions. *World J Surg* 2004; 28: 662–5.
 57. Bahadir I, Oncel M, Kement M, et al. Intra-abdominal use of taurolidine or heparin as alternative products to an antiadhesive barrier (Seprafilm) in adhesion prevention: an experimental study on mice. *Dis Colon Rectum* 2007; 50: 2209–14.
 58. Doody KJ, Dunn RC, Buttram VC. Recombinant tissue plasminogen activator reduces adhesion formation in a rabbit uterine horn model. *Fertil Steril* 1989; 51: 509–12.
 59. Orita H, Fukasawa M, Girgis W, et al. Inhibition of postsurgical adhesions in a standardized rabbit model: intraperitoneal treatment with tissue plasminogen activator. *Int J Fertil* 1991; 36: 172–7.
 60. Menzies D, Ellis H. The role of plasminogen activator in adhesion prevention. *Surg Gynecol Obstet* 1991; 172: 362–6.
 61. Yeo Y, Kohane DS. Polymers in the prevention of peritoneal adhesions. *Eur J Pharm Biopharm* 2008; 68: 57–66.
 62. Zeng Q, Yu Z, You J, et al. Efficacy and safety of Seprafilm for preventing postoperative abdominal adhesions: systematic review and meta-analysis. *World J Surg* 2007; 31: 2125–31.
 63. Fazio VW, Cohen Z, Fleshman JW, et al. Reduction in adhesive small-bowel obstruction by Seprafilm® adhesion barrier after intestinal resection. *Dis Colon Rectum* 2005; 49: 1–11.
 64. Beck DE, Cohen Z, Fleshman JW, et al. A prospective, randomized, multicenter, controlled study of the safety of Seprafilm® adhesion barrier in abdominopelvic surgery of the intestine. *Dis Colon Rectum* 2003; 46: 1310–19.
 65. Playforth RH, Holloway JB, Griffin WO. Mechanical small bowel obstruction: A plea for early surgical intervention. *Ann Surg* 1970; 171: 783–8.
 66. Seror D, Feigin E, Szold A, et al. How conservatively can postoperative small bowel obstruction be treated? *Am J Surg* 1993; 165: 121–5.
 67. Cox MR, Gunn IF, Eastman MC, et al. The safety and duration of non-operative treatment for adhesive small bowel obstruction. *Aust NZ J Surg* 1993; 63: 367–71.
 68. Laerum F, Stordahl A, Aase S. Water-soluble contrast media compared with barium in enteric follow-through. Local effects and radiographic efficacy in rats with simple obstruction of the small bowel. *Acta Radiol* 1988; 29: 603–10.
 69. Abbas SM, Bissett IP, Parry BR. Meta-analysis of oral water-soluble contrast agent in the management of adhesive small bowel obstruction. *Br J Surg* 2007; 94: 404–11.
 70. Maglinte DD, Balthazar EJ, Kelvin FM, et al. The role of radiology in the diagnosis of small bowel obstruction. *Am J Radiol* 1997; 168: 1171–80.
 71. Gough IR. Strangulating adhesive small bowel obstruction with normal radiographs. *Br J Surg* 1978; 65: 431–4.
 72. Megibow AJ, Balthazar EJ, Cho KC, et al. Bowel obstruction: evaluation with CT. *Radiology* 1991; 180: 313–18.
 73. Maglinte DD, Gage SN, Harmon BH, et al. Obstruction of the small intestine: Accuracy and role of CT in diagnosis. *Radiology* 1993; 188: 61–4.
 74. Mallo RD, Salem L, Lalani T, et al. Computed tomography of ischemia and complete obstruction in small bowel obstruction: a systematic review. *J Gastrointest Surg* 2005; 9: 690–4.
 75. Ha HK, Kim JS, Lee MS, et al. Differentiation of simple and strangulated small-bowel obstructions: usefulness of known CT criteria. *Radiology* 1997; 204: 507–12.
 76. MacRae HM, McLeod RS. Handsewn vs. stapled anastomoses in colon and rectal surgery: a meta-analysis. *Dis Colon Rectum* 1998; 41: 180–9.
 77. Dziki AJ, Duncan MD, Harmon JW, et al. Advantages of handsewn over stapled bowel anastomosis. *Dis Colon Rectum* 1991; 34: 625–7.

An Evidence-Based Approach to Upper GI Bleed Management

John G. Schneider and Bruce A. Crookes

UGI Bleeds: Question Summary		
Question	Answer	Grade
What is the role of medical therapy in prevention of UGI bleeds?	PPI should be used as stress ulcer prophylaxis in critically ill patients.	A
	Risk of ulcer formation is significantly reduced with maintenance PPI or H2RA for patients who take NSAIDs regularly.	A
	Beta-blockers can be used safely for primary prophylaxis of variceal bleeding.	B
What is the role of medical therapy in treating active UGI bleeds?	PPI should be preferentially used over H2RAs to reduce bleeding episodes after successful endoscopy.	A
	Octreotide should be used to slow the rate of variceal bleeding until definitive endoscopy is performed.	B
	Endoscopy should be used as first-line treatment for actively bleeding ulcers as it provides additional prevention of rebleeding compared to medical therapy.	A
What is the role of endoscopy for treating or preventing UGI bleeds?	Endoscopic banding ligation is the treatment of choice for acute variceal bleeding and should be undertaken as soon as possible.	A
	Banding ligation is effective for preventing variceal bleeding and should be used when medical prophylaxis cannot be tolerated.	A
	Angiography is safe and should be used in patients with massive UGI bleeding who are too ill to undergo an operation.	B
What is the role for interventional radiology in treating UGI bleeds?		C
Abbreviations: H2RA, histamine-2 receptor antagonist; NSAIDs, nonsteroidal anti-inflammatory drugs; PPI, proton pump inhibitor; UGI, upper gastrointestinal.		

INTRODUCTION

Upper gastrointestinal (UGI) bleeding is a common cause for admission to the intensive care unit and accounts for over 300,000 admissions in the United States alone (1,2). Optimal outcomes depend on rapid identification of the etiology and implementation of appropriate pharmacologic and procedural therapies.

Ulcer disease accounts for the majority of these cases. Other etiologies include varices, Mallory-Weiss syndrome, vascular lesions, and inflammatory states of the UGI tract. Despite advances in pharmacology and endoscopic therapies over the past several decades, all-cause mortality has remained constant, ranging from 6–10% (1–3) and up to 50% for variceal bleeding (4). Medical comorbidities and use of anticoagulants complicates treatment. Fortunately, over 80% of UGI bleeds stop spontaneously. When bleeding continues for high-risk patients, prompt decisive management is required. Lastly, best practices should be used to prevent further episodes.

The initial guidelines for management of UGI bleeding were published almost 20 years ago. Over this period, significant advancements in treatment have been developed. This chapter reviews the current evidence, including recent practice guidelines for the prevention and management of UGI bleeding.

WHAT IS THE ROLE OF MEDICAL THERAPY IN THE PREVENTION OF UGI BLEEDS, AND HOW SUCCESSFUL IS IT?

The use of medical prophylaxis is highly dependent on the potential etiology of the bleeding. In some cases, this is primary prevention, whereas in others secondary prevention is the goal. Because ulcer disease is the primary cause of many UGI bleeds, providers must identify the reason for ulceration. There are three principle causes: stress-related mucosal damage, nonsteroidal anti-inflammatory drug (NSAID) use, and *Helicobacter pylori* infection.

Patients who are critically ill have a number of causes for ulcer formation, including decreased mucous secretion, altered GI motility, and mucosal ischemia (5). These factors are especially prevalent in patients with large burns, head injury, coagulopathy, or those who require mechanical ventilation. Traditionally, antacids, sucralfate, or histamine-2 receptor antagonists (H2RA) have been used (5). All are able to reduce bleeding episodes; none, however, have been shown to be superior. Cook et al. (6) found that ranitidine had lower bleeding rates than sucralfate. Several other studies showed decreased mortality and pneumonia rates with sucralfate (5,7,8). More recently, proton pump inhibitors (PPIs) have been studied for stress ulcer prophylaxis.

These agents are able to keep gastric pH > 4 by suppressing acid secretion (5). Conrad et al. (9), in a randomized double-blind study, found omeprazole to be more effective than cimetidine in preventing GI bleeding in critically ill patients. This drug was able to reduce the rate of bleeding from 6.8% to 4.5%. Unfortunately, neither pneumonia nor mortality rates were improved.

Similarly, pharmacotherapy is beneficial for preventing bleeding related to NSAIDs used for pain relief or cardiovascular disease. Some have suggested changing from aspirin to clopidogrel for cardio- or cerebrovascular disease. Chan et al. (10) found in a randomized placebo-controlled study that patients with a history of bleeding ulcers have less frequent bleeding when esomeprazole was added to aspirin, as opposed to changing to clopidogrel, by a rate of 0.7% as compared to 8.6%. Alternative drugs, such as COX-2 inhibitors also can be used when NSAIDs are used for pain control in arthritis. In another study by Chan et al. (11) found that in patients who were *H. pylori*-negative and taking nonaspirin NSAIDs, there was additional reduction in UGI bleeding from 8.8% to 0% when esomeprazole was added after they were changed to celecoxib. Lai et al. (13) studied patients who were taking aspirin and were *H. pylori*-positive. After eradication therapy, patients were randomized to lansoprazole or placebo, while continuing aspirin. The PPI group had an ulcer complication rate of 1.6% compared to 14.8% with placebo. Udd et al. (12) found that regular and high-dose omeprazole are equally effective for preventing peptic ulcer bleeding.

Though acid suppression is the cornerstone of preventative therapy for ulcer-related bleeding, reduction of portal venous pressure is most effective for preventing esophageal bleeding. Beta-blockers are the main class of drugs to be employed to accomplish this goal. They were first used in this role in the 1980s, after introduction by Lebrec (15) and others. This group found that patients with large varices were significantly less likely to bleed when nadolol was compared with placebo (16). Kiire similarly found that propranolol significantly reduced bleeding compared to placebo in secondary prevention (17). Other drugs, such as isosorbide mononitrate (IM), have also been investigated to prevent variceal bleeding. Angelico et al. (18) found that propranolol and IM provided similar protection against variceal bleeding. However, long-term use of nitrates has been linked to increased mortality. A recent review by Talwalkar and Kamath showed that beta-blockers provide a 9% absolute risk reduction for primary prophylaxis and 21% reduction for secondary prevention. They also note that no individual trial has linked beta-blocker prophylaxis to improved survival, but this has been demonstrated in meta-analysis (19). Some authors have investigated a combination of beta-blockers and nitrates. Merkel et al. (20) demonstrated a decreased bleeding risk, from 29% to 12%, with a combination treatment. However, some studies have shown an increased rate of adverse events with combination treatments (19). Other authors have investigated the use of beta-blockers to prevent the formation and growth of varices. Merkel and colleagues (21) found that the risk of variceal growth was decreased from 21% to 7% and 51% to 20%, at one- and five-year follow-up, respectively. However, Groszmann et al. (22) studied patients with cirrhosis and portal hypertension and were unable to show that

beta-blockers prevented variceal formation. Additionally, recent studies have compared beta-blockers and endoscopic ligation as primary prophylaxis.

Recommendations

1. PPI should be used as stress ulcer prophylaxis in critically ill patients to prevent GI bleeding.
2. The risk of ulcer formation for patients taking NSAIDs is significantly reduced with PPI or H2RA prophylaxis.
3. Beta-blockers can be used safely for primary prophylaxis from variceal bleeding and may slow the growth of small varices.

Strength of recommendations: 1, A; 2, A; 3, B.

WHAT IS THE ROLE OF MEDICAL THERAPY IN TREATING UGI BLEEDS, AND HOW EFFECTIVE IS IT?

As mentioned, most UGI bleeds stop spontaneously. However, clinicians should optimize patient outcomes through both pharmacologic and procedural interventions. UGI bleeds caused by ulcer disease are treated with acid suppression, just as in prevention. Initially, H2Ras were the main pharmacologic option. In the mid-1980s, Collins and Langman (23) found that these drugs decreased rates of surgery and death in certain populations. Over the next decade, however, PPIs were introduced. Lanis et al. (24) found that omeprazole was superior to ranitidine in decreasing rebleeding episodes, but no differences were found in mortality or units of blood transfused. Khuroo and colleagues (25) found that PPIs reduced ongoing bleeding from 36.4% to 10.9%, and reduced the need for surgery as compared to placebo. Lau et al. (26) also found that PPI treatment was superior in preventing rebleeding after endoscopic treatment of ulcer bleeding. Daneshmand et al. (27), however, did not find that omeprazole reduced mortality, rebleeding, or transfusion requirements, but they were able to demonstrate a decrease in the endoscopic signs of bleeding with PPI treatment. Regional differences in patient populations may account for these differences, as one study was conducted in Europe and the other in Asia. Another study by Lau et al. (28) similarly found a decrease in the signs of recent bleeding with PPI treatment, and demonstrated a decreased need for endoscopic therapy.

In addition to acid suppression, treating ulcer etiology is imperative. This includes managing critical illness, limiting NSAID use, and treating *H. pylori* when appropriate. Riemann et al. (29) demonstrated that curative triple therapy with PPI was superior to maintenance therapy with H2RAs. However, Sung et al. (30) showed that medical therapy should not stand alone. Their study found that patients treated with both endoscopy and PPI were much less likely to rebleed than PPI treatment alone (1.1% compared to 11.6%).

Medical treatment of variceal bleeding differs from ulcer bleeding in that therapeutic agents are different than those used for prophylaxis. The mainstays of active variceal bleeding pharmacologic treatment are vasoconstrictive and vasoactive drugs. Vasopressin and terlipressin are

vasoconstrictive agents that have been shown to decrease active variceal bleeding. However, these drugs can have significant side effects, including headache, pulmonary edema, and coronary vasoconstriction (33). Octreotide is the main vasoactive drug used to treat variceal bleeding. It is a hormone analog of somatostatin that alters GI hormone signaling, decreases gastric and pancreatic secretions, and alters splanchnic blood flow. Multiple studies have demonstrated the superior efficacy of octreotide over vasopressin (32–34) for stopping active bleeding and preventing rebleeds. Despite this, no mortality benefit is gained. The recent meta-analysis by Gross et al. (31) found that vasoconstrictive therapy was only 68.7% successful compared to vasoactive therapy, which was 75.9% successful. Banding ligation, however, is the most effective therapy and should be the primary intervention for stopping variceal bleeding (31).

Recommendations

1. PPIs should be preferentially used over H2RAs to reduce rebleeding episodes after successful endoscopic therapy.
2. Octreotide should be used to slow the rate of variceal bleeding, until definitive endoscopic therapy can be implemented.

Strength of recommendations: 1, A; 2, B.

WHAT IS THE ROLE OF ENDOSCOPY IN TREATING OR FOR PROPHYLAXIS UGI BLEEDS, AND HOW SUCCESSFUL IS IT?

Endoscopy is beneficial in UGI bleeds because it can be simultaneously diagnostic and therapeutic, particularly in patients with no prior history of bleeding. Ulcer bleeding can be stopped or reduced with medical treatment, as discussed previously. However, multiple studies have shown that endoscopy confers further prevention of rebleeding (30,35). Endoscopic findings of active bleeding or a visible vessel require treatment due to high rates of rebleeding. Ulcers with an adherent clot are more controversial. Bini and Cohen (35) directly compared endoscopy with medical treatment in patients with adherent clot. They found that recurrent bleeding, mean hospital stay, transfusion requirements, and repeat endoscopy were significantly reduced with endoscopy. Several methods are available to achieve endoscopic hemostasis, including adrenaline injections, lasers, and heater probes. However, no significant differences have been found among individual injection or thermal coagulation therapies (2). Similarly, Chung et al. (36) found that initial hemostasis was achieved equally by injection and heater probe. For ulcers with spurting vessels, however combination treatment with injection and heater probe reduced the rate of surgery from 29.6% to 6.5%. Still, patients sometimes fail endoscopic treatment. Lau et al. (37) studied patients who had undergone successful initial endoscopic treatment and randomized them to surgery or repeat endoscopy if they rebleed. Over one-quarter of patients who were randomized to have repeat endoscopy still required salvage surgery (37).

Whereas endoscopy is used solely for treatment of ulcer disease, this intervention can be used for both treatment of active bleeding and prophylaxis for patients with varices. Options for endoscopic management of varices include injection sclerotherapy and banding ligation. Both techniques have been used for the control of acute hemorrhage. Multiple studies, however, have found that ligation is superior to sclerotherapy (4,40,41). Banding has a lower rebleeding rate and reduced complications. Steigmann et al. (39) also showed a higher mortality rate in patients that had sclerotherapy used for the control of hemorrhage. Additionally, the recent meta-analysis by Gross et al. (31) demonstrated the superiority of endoscopic banding ligation over medical therapy in the treatment of acute variceal bleeding. The combination of banding and sclerotherapy has been evaluated as well. Neither Laine et al. (42) nor Saeed et al. (43) were able to demonstrate additional benefit to combination therapy, with the later study showing an increased complication rate with dual treatment.

Although endoscopic banding is superior for treating acute bleeding, the role of endoscopy and the type of treatment for prophylaxis is discordant more divisive. Van Buuren et al. (38) found that there was no difference in the number of episodes of bleeding when sclerotherapy was compared with no treatment. Villanueva et al. (45) found that combination medical therapy was more successful in preventing bleeding. Additionally, other trials have shown increased mortality rates with sclerotherapy, and this practice is not recommended (4). Endoscopic banding has been widely studied for prophylaxis of variceal bleeding. This technique is often compared with medical prophylaxis to beta-blockers alone or in combination with IM. A recent study by Wang et al. (48) found that combined medical (beta-blocker plus IM) and procedural therapies were equally effective for primary prophylaxis. Conversely, Sarin et al. (44) showed that banding reduced initial bleeding risk from 43% to 15% compared to beta-blocker alone. Villanueva et al. (46) showed that combined medical therapy was superior for secondary prophylaxis without an all-cause mortality benefit. Lo et al. (49) recently published that banding was better for secondary prevention, but combined medical therapy improved overall survival. Meta-analysis by Gluud et al. (47) showed that banding ligation reduced bleeding episodes as compared to beta-blockers without any difference in mortality.

Recommendations

1. Endoscopic treatment should be used to stop active hemorrhage from ulcer disease and confers additional prevention of rebleeding episodes.
2. Endoscopic banding ligation is the treatment of choice for acute variceal hemorrhage and should be undertaken as soon as possible.
3. Banding ligation is an effective means of preventing variceal bleeding and can be used when medical prophylaxis cannot be tolerated.

Strength of evidence: 1, A; 2, A; 3, B.

WHAT IS THE ROLE OF INTERVENTIONAL RADIOLOGY IN TREATING UGI BLEEDS?

Angiography has been established as the primary therapy for many lower GI bleeds. However, its role in UGI bleeding is not as well defined. There are many case reports for more obscure sources, such as small bowel diverticula or mesenteric aneurysms. Angiography has been used since the 1970s for control of GI hemorrhage for both diagnosis and therapy (50). Defreyn et al. (51) published a series of patients with GI bleeding treated with angioembolization that showed patients with an UGI source had higher rates of rebleeding and lower success rate than compared to lower GI sources. However, Careira et al. (52) showed that embolization was successful 90% of the time in a study with predominately UGI bleeds. Other studies have found similar success rates (53,54). Poultides et al. (55) recently published a series of patients with gastroduodenal hemorrhage that underwent embolization with a 94% technical and 51% clinical success rate. Most of these studies indicate that embolization should be used in patients with massive ongoing hemorrhage who cannot tolerate surgery due to medical comorbidities.

Recommendation

Angiography should be used in patients with massive hemorrhage who are too ill to undergo an operation. Strength of Recommendation: C.

REFERENCES

- Conrad SA. Acute upper gastrointestinal bleeding in critically ill patients: causes and treatment modalities. *Crit Care Med* 2002; 30: S365-S368.
- Barkun A, Bardou M, Marshall JK. Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding. *Ann Int Med* 2003; 139: 843-57.
- Eisen GM, Dominitz JA, Faigel DO, et al. An annotated algorithmic approach to upper gastrointestinal bleeding. *Gastrointest Endosc* 2001; 53: 859-63.
- Qureshi W, Adler DG, Davila R, et al. ASGE guideline: the role of endoscopy in the management of variceal hemorrhage, updated 2005. *Gastrointest Endosc* 2005; 62: 651-5.
- Jung R, MacLaren R. Proton-pump inhibitors for stress ulcer prophylaxis in critically ill patients. *Ann Pharmacother* 2002; 36: 1929-37.
- Cook DJ, Guyatt G, Marshall J, et al. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. *N Engl J Med* 1998; 338: 791-7.
- Cook DJ, Reeve BK, Scholes LC. Histamine-2-receptor antagonists and antacids in the critically ill population: stress ulceration versus nosocomial pneumonia. *Infect Control Hosp Epidemiol* 1994; 15: 437-42.
- Cook DJ, Reeve BK, Guyatt GH, et al. Stress ulcer prophylaxis in critically ill patients. Resolving discordant meta-analyses. *JAMA* 1996; 275: 308-14.
- Conrad SA, Gabrielli A, Margolis B, et al. Randomized, double-blind comparison of immediate-release omeprazole oral suspension versus intravenous cimetidine for the prevention of upper gastrointestinal bleed in critically ill patients. *Crit Care Med* 2005; 33: 760-5.
- Chan FK, Ching JY, Hung LC, et al. Clopidogrel versus aspirin and esomeprazole to prevent recurrent ulcer bleeding. *N Engl J Med* 2005; 352: 238-44.
- Chan FK, Wong VW, Suen BY, et al. Combination of a cyclooxygenase-2 inhibitor and a proton-pump inhibitor for prevention of recurrent ulcer bleeding in patients at very high risk: a double-blind, randomised trial. *Lancet* 2007; 369: 1621-6.
- Udd M, Miettinen P, Palmu M, et al. Regular-dose versus high-dose omeprazole in peptic ulcer bleeding. *Scand J Gastroenterol* 2001; 36: 1332-8.
- Lai KC, Lam SK, Chu KM, et al. Lansoprazole for the prevention of recurrences of ulcer complications from long-term low-dose aspirin use. *N Engl J Med* 2002; 346: 2033-8.
- Leontiadis GI, Sreedharan A, Dorward S, et al. Systematic reviews of the clinical effectiveness and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding. *Health Technol Assess* 2007; 11: 1-164.
- Lebrech D, Bernuau J, Rueff B, et al. Propranolol in prevention of recurrent gastrointestinal bleeding in cirrhotic patients. *Lancet* 1981; 317: 920-1.
- Lebrech D, Poynard T, Capron JP, et al. Nadolol for prophylaxis of gastrointestinal bleeding in patients with cirrhosis: a randomized trial. *J Hepatol* 1988; 118-25.
- Kiire CF. Controlled trial of propranolol to prevent recurrent variceal bleeding in patients with non-cirrhotic portal fibrosis. *Br Med J* 1989; 298: 1363-5.
- Angelico M, Carli L, Piat C, et al. Isosorbide-5-mononitrate versus propranolol in the prevention of first bleeding in cirrhosis. *Gastroenterology* 1993; 104: 1460-5.
- Talwalker JA, Kamath PS. An evidence-based medicine approach to beta-blocker therapy in patients with cirrhosis. *Am J Med* 2004; 116: 759-66.
- Merkel C, Marin R, Sacerdoti D, et al. Long-term results of a clinical trial of nadolol with or without isosorbide mononitrate for primary prophylaxis of variceal bleeding in cirrhosis. *Hepatology* 2000; 32: 1175-6.
- Merkel C, Marin R, Angeli P, et al. A placebo-controlled clinical trial of nadolol in the prophylaxis of first of small esophageal varices in cirrhosis. *Gastroenterology* 2004; 127: 476-84.
- Groszmann RJ, Garcia-Tsao G, Bosch J, et al. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. *N Engl J Med* 2005; 353: 2254-61.
- Collins R, Langman M. Treatment with histamine H2 antagonists in acute upper gastrointestinal hemorrhage: implications of randomized trials. *N Engl J Med* 1985; 313: 660-6.
- Lanas A, Artal A, Blás JM, et al. Effect of parenteral omeprazole and ranitidine on the gastric pH and the outcome of bleeding peptic ulcer. *J Clin Gastroenterol* 1995; 21: 103-6.
- Khuroo MS, Yattoo GN, Javid G, et al. A comparison of omeprazole and placebo for bleeding peptic ulcer. *N Engl J Med* 1997; 336: 1054-8.
- Lau JYW, Sung JY, Lee KKC, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. *N Engl J Med* 2000; 343: 310-16.
- Daneshmand TK, Hawkey CJ, Langman MJS, et al. Omeprazole versus placebo for acute upper gastrointestinal bleeding: randomised double blind controlled trial. *Br Med J* 1992; 304: 143-7.
- Lau JY, Leung WK, Wu JCY, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. *N Engl J Med* 2007; 356: 1631-40.
- Riemann JF, Schilling D, Schauwecker P, et al. Cure with omeprazole plus amoxicillin versus long-term ranitidine therapy in *Helicobacter pylori*-associated peptic ulcer bleeding. *Gastrointest Endosc* 1997; 46: 299-304.
- Sung JY, Chang FKL, Lau JYW, et al. The effect of endoscopic therapy in patients receiving omeprazole for bleeding ulcers with nonbleeding visible vessels or adherent clots. *Ann Intern Med* 2003; 139: 237-43.

31. Gross M, Schiemann U, Mühlhöfer A, et al. Meta-analysis: efficacy of therapeutic regimens in ongoing variceal bleeding. *Endoscopy* 2001; 33: 737–46.
32. Hwang SJ, Lin HC, Chang CF, et al. A randomized controlled trial comparing octreotide and vasopressin in the control of acute esophageal variceal bleeding. *J Hepatol* 1992; 16: 320–5.
33. Jenkins SA, Baxter JN, Corbett W, et al. A prospective randomised controlled clinical trial comparing somatostatin and vasopressin in controlling acute variceal haemorrhage. *Br Med J* 1985; 290: 275–8.
34. Corley DA, Cello JP, Adkisson W, et al. Octreotide for acute esophageal variceal bleeding: a meta-analysis. *Gastroenterology* 2001; 120: 946–54.
35. Bini EJ, Cohen J. Endoscopic treatment compared with medical therapy for the prevention of recurrent ulcer hemorrhage in patients with adherent clots. *Gastrointest Endosc* 2003; 58: 707–14.
36. Chung SSC, Lau JYW, Sung JY, et al. Randomised comparison between adrenaline injection alone and adrenaline injection plus heat probe treatment for actively bleeding ulcers. *Br Med J* 1997; 314: 1307–11.
37. Lau JYW, Sung JY, Lam Y, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. *N Engl J Med* 1999; 340: 751–6.
38. Van Buuren HR, Rasch MC, Batenburg PL, et al. Endoscopic sclerotherapy compared with no specific treatment for the primary prevention of bleeding from esophageal varices. A randomized controlled multicentre trial. *BMC Gastroenterol* 2003; 3: 22.
39. Stiegmann GV, Goff JS, Michaletz-Onody PA, et al. Endoscopic sclerotherapy as compared with endoscopic ligation for bleeding esophageal varices. *N Engl J Med* 1992; 326: 1527–32.
40. Gimson AES, Ramage JK, Panos MZ, et al. Randomised trial of variceal banding ligation versus injection sclerotherapy for bleeding oesophageal varices. *Lancet* 1993; 342: 391–4.
41. Laine L, El-Newihi HM, Migikovsky B, et al. Endoscopic ligation compared with sclerotherapy for the treatment of bleeding esophageal varices. *Ann Intern Med* 1993; 119: 1–7.
42. Laine L, Stein C, Sharma V. Randomized comparison of ligation versus ligation plus sclerotherapy in patients with bleeding esophageal varices. *Gastroenterology* 1996; 110: 529–33.
43. Saeed ZA, Stiegmann GV, Ramirex FC, et al. Endoscopic variceal ligation is superior to combined ligation and sclerotherapy for esophageal varices: a multicenter prospective randomized trial. *Hepatology* 1997; 25: 71–4.
44. Sarin SK, Lamba GS, Kumar M, et al. Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. *N Engl J Med* 1999; 340: 988–93.
45. Villanueva C, Balanzó J, Novella MT, et al. Nadolol plus isosorbide mononitrate compared with sclerotherapy for the prevention of variceal rebleeding. *N Engl J Med* 1996; 334: 1624–9.
46. Villanueva C, Miñana J, Ortiz J, et al. Endoscopic ligation compared with combined treatment with nadolol and isosorbide mononitrate to prevent recurrent variceal bleeding. *N Engl J Med* 2001; 345: 647–55.
47. Gluud LL, Klingenberg S, Nikolova D, et al. Banding ligation versus beta-blockers as primary prophylaxis in esophageal varices: systematic review of randomized trials. *Am J Gastroenterol* 2007; 102: 2842–8.
48. Wang HM, Lo GH, Chen WC, et al. Comparison of endoscopic variceal ligation and nadolol plus isosorbide-5-mononitrate in the prevention of first variceal bleeding in cirrhotic patients. *J Chin Med Assoc* 2006; 69: 453–60.
49. Lo GH, Chen WC, Lin CK, et al. Improved survival in patients receiving medical therapy as compared with banding ligation for the prevention of esophageal variceal rebleeding. *Hepatology* 2008; 48: 580–7.
50. Rahn NH III, Tishler JM, Han SY, et al. Diagnostic and Interventional angiography in acute gastrointestinal hemorrhage. *Radiology* 1982; 143: 361–6.
51. Defreyne L, Vanlangenhove P, De Vos M, et al. Embolization as a first approach with endoscopically unmanageable acute nonvariceal gastrointestinal hemorrhage. *Radiology* 2001; 218: 739–48.
52. Careira JM, Reyes R, Pulido-Duque JM, et al. Diagnosis and percutaneous treatment of gastrointestinal hemorrhage. *Rev Esp Enferm Dig* 1999; 91: 684–92.
53. Toyoda H, Nakano S, Takeda I, et al. Transcatheter arterial embolization for massive bleeding duodenal ulcers not controlled by endoscopic hemostasis. *Endoscopy* 1995; 27: 304–7.
54. Park MH, Park GS, Park SW, et al. Clinical effectiveness of transcatheter arterial embolization for acute upper and lower non-variceal gastrointestinal bleeding. *Kor J Gastroenterol* 2005; 46: 262–8.
55. Poultsides GA, Kim CJ, Orlando R III, et al. Angiographic embolization for gastroduodenal hemorrhage. *Arch Surg* 2008; 143: 457–61.

Peptic Ulcer Disease

Wayne H. Schwesinger

Clinical Questions		
Questions	Answers	Grade
How has the surgery of PUD changed over time?	The number of operations performed for PUD has declined by >80% over the past two decades. The most common indications are perforation and bleeding. Operations for intractability are rare. Patients are generally older, sicker, and more often female.	B
What are the major risk factors for PUD?	In Western countries, PUD is primarily caused by <i>Helicobacter pylori</i> infection and NSAID use. Idiopathic causes include ZES, G-cell hyperplasia, Crohn's disease, cocaine abuse, and systemic mastocytosis.	A
What is the appropriate therapy for <i>Helicobacter pylori</i> -positive PUD?	First-line therapy combines PPI + clarithromycin + amoxicillin or metronidazole and has a successful eradication rate of 78–90%. Rescue therapies are available for nonresponders.	A
How can the risk of PUD be minimized in patients requiring regular NSAID therapy?	If found, <i>H. pylori</i> should be eradicated before NSAID therapy is initiated. Misoprostol, PPI therapy, and double-dose H2RA therapy are all effective in reducing the risk of NSAID-induced GI complications.	A
In a patient suspected of having a bleeding peptic ulcer, what should the initial approach be?	A rapid and accurate diagnosis and aggressive resuscitation should proceed simultaneously in patients thought to be bleeding from an UGI source.	A
In patients with bleeding ulcers, what is the current role of endoscopy?	Endoscopy is the definitive diagnostic and prognostic study. It is also an effective therapeutic tool with initial hemostasis rates of 85–100%.	A
What is the role of pharmacotherapy in the management of a bleeding peptic ulcer?	When used as an adjunct to endoscopic therapy, PPIs reduce the risk of further bleeding and the need for surgery.	A
Under what circumstances is an operation indicated for a bleeding peptic ulcer?	Surgery is indicated for peptic ulcer hemorrhage that is not controlled by endoscopic therapy or recurs following apparently successful endoscopic therapy (5–20%).	A
What surgical techniques are associated with the lowest rate of UGI rebleeding?	When used for peptic ulcer bleeding, combined partial gastric resection and vagotomy is associated with the lowest recurrence rate. However, this approach also has a higher rate of short-term and long-term postoperative complications. Vagotomy with oversewing of the ulcer is effective when combined with anti- <i>H. pylori</i> therapy in <i>H. pylori</i> + patients.	A
What approach is preferred for the management of perforated PUD?	Nonoperative therapy can be used in selected patients who are found to have a sealed perforation on contrast study. Patch closure is indicated in most patients. <i>H. pylori</i> should be eradicated when infection is present. The laparoscopic approach is being used with increased frequency.	B
Abbreviations: GI, gastrointestinal; H2RA, histamine-2 receptor antagonist; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; PUD, peptic ulcer disease; UGI, upper gastrointestinal.		

HOW HAS THE SURGERY OF PEPTIC ULCER DISEASE CHANGED OVER TIME?

Few diseases in Western society have been so dramatically transformed over time as peptic ulcer disease (PUD). Although rarely described in the early medical literature, its incidence reached epidemic proportions by the mid-1900s, then slowly began to decline (1,2). From the beginning, operative therapy served as an important cornerstone

in the management of PUD because the available medical measures were often ineffective. Landmark investigations by Beaumont, Pavlov, Dragsted, and Edkins, among others, served as the pathophysiological foundation on which many new surgical strategies for the management of PUD were developed (3). Though these operations appeared to be very effective at controlling both intractable and complicated PUD, they could be associated with significant short-term and long-term consequences (4).

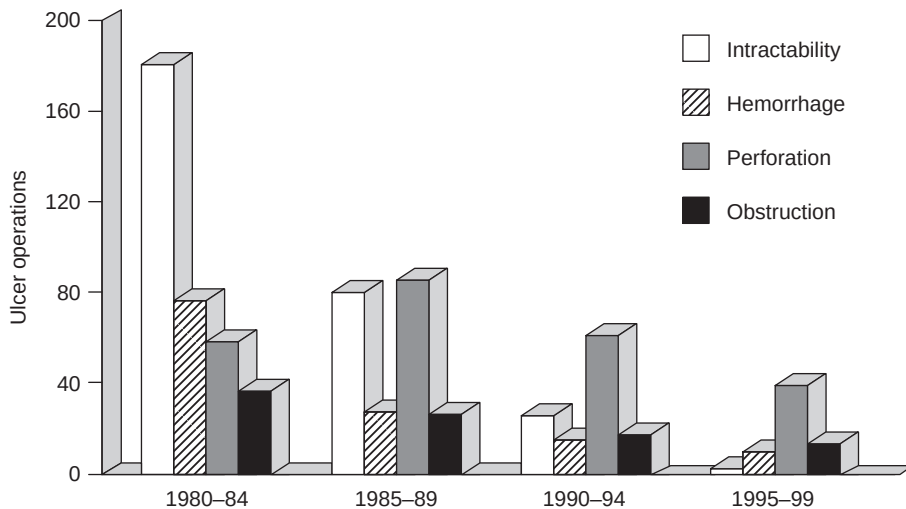


Figure 46.1 Time trends of operations for peptic ulcer disease by indications. Source: Adapted from 9.

Simultaneously, major progress was also being made with two different nonoperative approaches to the management of PUD: pharmacotherapy and flexible endoscopy. Antisecretory therapy, introduced in 1977, largely replaced both the Sippy diet and antacid therapy and a decade later was itself superseded by the introduction of the first proton pump inhibitor (PPI). In 1983, a specific infectious etiology for PUD was suggested by Warren and Marshall; within a decade more than 1,500 scientific articles were being published on the topic annually (5). The possibility of a medical cure with antibiotic therapy was quickly established.

As a result of these pharmacological advances and evolving endoscopic techniques, the profile of surgery for PUD has dramatically changed. Since 1960, multiple investigators have noted a significant reduction in total operative volume (6–8).

A personal survey of a 20-year experience in two major teaching hospitals demonstrated an 80% decrease in the overall number of operations for PUD (9) (Fig. 46.1). Currently, the most common indications for surgery are perforation and bleeding, whereas intractability has become nearly obsolete.

Other studies have demonstrated that patient demographics are also continuing to change. Patients hospitalized with PUD are now older, more frequently female, and more likely to have major comorbid conditions (10,11). Such individuals are also more likely to require an emergency operation (12).

Recommendation: The number of operations performed for PUD has declined by >80% over the past two decades. The most common indications are perforation and bleeding. Operations for intractability are rare. Patients are generally older, sicker, and more often female (Recommendation grade: B).

WHAT ARE THE MAJOR RISK FACTORS FOR PUD?

By the mid-twentieth century, it was generally agreed that gastric hyperacidity was the cause of PUD. Thus, the commonly quoted aphorism: “no acid, no ulcer” (13). Early

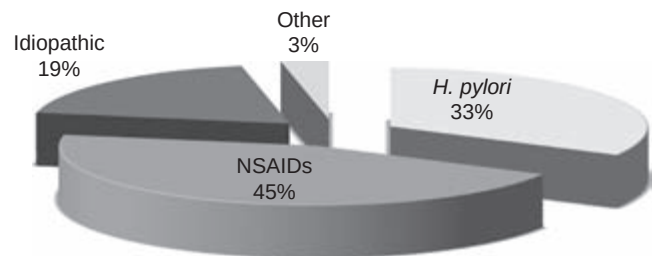


Figure 46.2 Etiologic distribution of peptic ulcer disease. Source: Adapted from 102.

speculations on the specific pathogenetic factors causing hyperacidity focused on the relative contributions of stress, smoking, familial predisposition, hormonal changes, aspirin intake, and dietary indiscretions.

A paradigm shift occurred when it was recognized that either *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug (NSAID) use could be implicated in most cases of peptic ulceration, albeit through entirely different mechanisms (14–16) (Fig. 46.2). With *H. pylori* infection, a complex interaction occurs between bacterial virulence factors (cagA, cagPAI, vacA), host factors (interleukins, tumor necrosis factor- α , chemokines), and environmental factors (smoking, high salt intake) (17,18). The result is a persistent chronic gastritis. The location of the infection in the stomach helps determine the clinical course. Antral-dominant infections result in reduced somatostatin levels, hypergastrinemia, and gastric acid hypersecretion and can produce duodenal ulcers. Body-dominant infections are associated with mucosal atrophy and hypochlorhydria; this pattern may result in benign gastric ulcers or malignancy.

The gastric mucosal injury caused by NSAIDs (including aspirin) results mostly from inhibition of the constitutive enzyme cyclo-oxygenase-1 (COX-1) a major product of arachidonic acid metabolism in the gastric mucosa. COX-1 is responsible for the release of prostacyclin a potent

cytoprotectant and, when inhibited, allows gastric acid and other irritants to damage the mucosa. Another isoform, COX-2, is induced by inflammatory stimuli and has significant anti-inflammatory activity but few gastric side effects (19).

Importantly, a synergism can develop between the two major risk factors. In a meta-analysis of 25 related studies, *H. pylori* infection was found to increase the risk of PUD 3.5-fold in NSAID users compared with noninfected patients (20).

The category of idiopathic, non-NSAID, and non-*H. pylori* PUD can be accounted for by inaccurate *H. pylori* testing, covert NSAID use, or otherwise altered gastric physiology. Non-NSAID and non-*H. pylori* ulcers tend to occur in older and sicker patients and are associated with a higher recurrence rate (21). Other causes of ulceration include the Zollinger-Ellison syndrome, G-cell hyperplasia, Crohn's disease, cocaine abuse, and systemic mastocytosis (22).

Recommendation: In Western countries, PUD is primarily caused by *H. pylori* infection and NSAID use. Idiopathic causes include Zollinger-Ellison syndrome, G-cell hyperplasia, Crohn's disease, cocaine abuse, and systemic mastocytosis (Recommendation Grade: A)

WHAT IS THE APPROPRIATE THERAPY FOR *H. PYLORI*-POSITIVE PUD?

In patients with PUD who are *H. pylori*-positive, eradication of the organism is indicated. In a Cochrane analysis of over 3,900 patients in 34 trials, the ulcer healing rate after therapy was 75–85% and the recurrence rate was 12–14% (23). First-line therapy as recommended in the Maastricht Consensus Report 2-2000 combines a PPI with clarithromycin and amoxicillin or metronidazole twice daily for one to two weeks (24). Successful eradication can be achieved with initial treatment in 78–90% of patients (25). Second-line rescue treatment with quadruple therapy typically combines a PPI with bismuth, metronidazole, and tetracycline. Eradication should always be confirmed with either a urea breath test or a stool antigen. Antimicrobial resistance is the usual cause of repeated treatment failures, and cultures with sensitivities may be necessary to tailor treatment protocols in selected patients. The Helicobacter Antimicrobial Resistance Monitoring Program studied 347 clinical isolates and found that the highest rate of resistant strains occurred with metronidazole (25.1%) and clarithromycin (12.9%) (26). Amoxicillin resistance was uncommon (0.9%).

Recommendation: First-line therapy combines PPI + clarithromycin + amoxicillin or metronidazole and has a successful eradication rate of 78–90%. Rescue therapies are available for nonresponders (Recommendation grade: A).

HOW CAN THE RISK OF PUD BE MINIMIZED IN PATIENTS REQUIRING REGULAR NSAID THERAPY?

Several options are available for reducing the risk of peptic ulcers in patients receiving NSAIDs. In NSAID-naïve patients who are infected with *H. pylori*, eradication of the organism before beginning NSAID therapy is associated with a significant reduction in the risk of ulcer (27). However, chronic NSAID users do not appear to be protected by the eradication of *H. pylori* (28). PPIs, the prostaglandin

analog misoprostol, and double-dose histamine-2-receptor antagonists (H2RA) are all effective in preventing NSAID-induced ulcers (29,30). Misoprostol usage is limited by its frequent association with diarrhea.

Recommendation: If found, *H. pylori* should be eradicated before NSAID therapy is initiated. Misoprostol, PPI therapy, and double-dose H2RA therapy are all effective in reducing the risk of NSAID-induced GI complications (Recommendation grade: A).

IN A PATIENT SUSPECTED OF HAVING A BLEEDING PEPTIC ULCER, WHAT SHOULD THE INITIAL APPROACH BE?

Optimal management depends on a timely and accurate diagnosis and an adequate resuscitation, processes that should proceed concurrently. The initial clinical approach is determined in large part by the patient's presentation. A history of red blood or dark "coffee ground" emesis nearly always indicates an upper gastrointestinal source. The rectal passage of black, digested blood (melanic stool) is also indicative of a lesion proximal to the ligament of Trietz (31). The passage of bright red blood per rectum usually suggests a primary colorectal source, but it also occurs in patients with upper tract lesions when the rate of bleeding is rapid and the transit time is brief.

A rapid assessment of the patient's hemodynamic and physical status can guide early therapy and appropriate triage. The presence of hemorrhagic shock, either compensated or decompensated, mandates aggressive fluid management with blood products and/or crystalloid. In addition, preexisting comorbidities such as cardiac disease or hepatic or renal dysfunction must be addressed to avoid deterioration. Specific coagulation abnormalities must also be rapidly corrected. Endpoints for resuscitation include (1) normalization of blood pressure, (2) restoration of hemoglobin concentration, (3) correction of coagulopathies, and (4) correction of end-organ dysfunction (32). Such an aggressive and multifaceted approach is supported in the controlled study of Baradarian et al., in which intensive monitoring and early hemodynamic stabilization were provided by a specialized resuscitation group (33). This resulted in a significant reduction in the associated mortality when compared with routine floor management.

During resuscitation, nasogastric tube placement is used to sample the contents of the stomach. In patients who present with a history of hematemesis, nasogastric aspiration of fresh, red blood indicates the presence of ongoing bleeding and is an independent predictor of poor clinical outcome when compared with aspiration of either clear or "coffee ground" material (34). In bleeding patients who present with melena without hematemesis, a bloody nasogastric aspirate provides strong evidence for a lesion in the upper gastrointestinal tract (specificity = 91–95%) (35,36). However, a negative aspirate is less reliable because it may fail to detect duodenal lesions (sensitivity = 42–73%).

Nasogastric tubes can also be used for gastric lavage prior to endoscopy, but success is limited by the size of the tube and the presence of clots. Alternatively, prokinetic agents are able to effectively clear the stomach. Several randomized, controlled clinical trials have documented that a preendoscopic bolus or infusion of erythromycin improves

the quality of the subsequent endoscopic examination and reduces the need for repeat endoscopic procedures (37,38). This approach appears to be cost-effective (39).

Recommendation: A rapid and accurate diagnosis and aggressive resuscitation should proceed simultaneously in patients thought to be bleeding from an upper gastrointestinal source. (Recommendation Grade: A).

IN PATIENTS WITH BLEEDING ULCERS, WHAT IS THE CURRENT ROLE OF ENDOSCOPY?

Endoscopy is the definitive diagnostic study for upper gastrointestinal (UGI) bleeding. In a multicenter study of 11,160 patients with nonvariceal UGI bleeding, endoscopy identified the bleeding site in 83% of cases. The most common finding was peptic ulcers (32%) with gastric ulcers more common than duodenal ulcers (54% versus 37%) (40).

Risk stratification is another important function of endoscopy because it guides early management (Table 46.1) (41). Patients with a clean-based ulcer or a nonprotruding pigmented spot are at low risk of rebleeding and generally require no further endoscopic interventions. Conversely, high-risk stigmata, such as an actively bleeding ulcer or an ulcer with a visible vessel, forecast a poor outcome and indicate the need for aggressive endoscopic therapy. Another subset of patients who have an ulcer with an adherent clot also appears to be at high risk for rebleeding and benefits from removal of the clot and directed endoscopic therapy (42).

The optimal timing for endoscopy continues to be debated. It is generally agreed that patients who are actively bleeding or who are unstable require urgent endoscopy to prevent further deterioration. In the remaining patients, the recommended timing ranges from urgent to elective. Recent data appear to support the use of early endoscopy to identify low-risk patients who will require only brief or no hospitalization (43). It has been argued that such an approach improves resource utilization. However, two randomized trials addressing this issue differ in their conclusions, with only one showing significant cost savings (44,45). Presumably, this disparity results from differences in practice patterns.

Ulcer bleeding stops spontaneously in the majority of patients (80–85%) (46). In the remainder, endoscopic therapy has proven efficacious and cost-effective (43,47). By 1992, a meta-analysis of 30 randomized clinical trials was reported in which a variety of endoscopic hemostatic techniques was compared to medical therapy alone (48). The endoscopically treated group demonstrated significant reductions in further bleeding [odds ratio (OR), 0.38; 95% confidence interval (CI), 0.32–0.45], need for surgery (OR, 0.36; 95%

CI, 0.28–0.45), and mortality (OR, 0.55; 95% CI, 0.40–0.76). Serious complications directly related to endoscopy were infrequent and included induced rebleeding (0.4%) and perforation (0–0.9%).

Numerous studies have been conducted comparing the wide variety of available hemostatic techniques: injection, thermal, and mechanical. Overall, initial hemostasis rates range from 85% to 100% for all methods (49). However, injection therapy alone, whether with dilute epinephrine, thrombin, polidocanol, or cyanoacrylate, is associated with a higher rebleeding rate and a more frequent need for surgery than when combined with any other therapy (50). A recent Cochrane systematic review of 17 randomized studies has confirmed that dual therapy with epinephrine injection and any other technique reduces the further bleeding rate from 18.8% to 10.4%, emergency surgeries from 10.8% to 7.1%, and mortality from 5% to 2.5% without increasing the complication rate (51). Interestingly, evidence is emerging that monotherapy with thermal or mechanical methods may be as effective as epinephrine-based combination therapy except in those patients with profound bleeding (52,53).

Recommendation: Endoscopy is the definitive diagnostic and prognostic study. It is also an effective therapeutic tool with initial hemostasis rates of 85–100% (Recommendation grade: A).

WHAT IS THE ROLE OF PHARMACOTHERAPY IN THE MANAGEMENT OF A BLEEDING PEPTIC ULCER?

Pharmacotherapy in patients with bleeding PUD significantly impacts outcome. PPI infusion when used as an adjunct to endoscopic therapy reduces the risk of further bleeding (0.49 OR, 95% CI, 0.37–0.65) and decreases the need for surgery (OR, 0.61, 95% CI 0.48–0.78) (54). Such therapy should be initiated as early as possible. In a recent randomized study, preendoscopic PPI was found to facilitate clot formation at the bleeding site and reduce the need for endoscopic therapy (55). As noted in another preendoscopic study, other clinical outcomes (rebleeding, surgery, mortality) were not significantly affected (56).

All patients who are found to be infected with *H. pylori* should receive oral eradication therapy as soon as practicable because the continued long-term presence of *H. pylori* predicts rebleeding (57). Thus, in a meta-analysis of seven studies, successful eradication therapy was found to reduce rebleeding rates to 2.9% compared with 20% in the noneradicated group (OR, 0.17, 95% CI, 0.10–0.32) (58). Furthermore, eradication therapy has been shown to be the most cost-effective approach to the bleeding patient (59).

In the absence of *H. pylori* infection, NSAID usage is commonly found to be a contributing cause of ulcer bleeding and may actually have more severe consequences. A single case-control study of this issue has demonstrated that NSAID-related bleeding when compared to matched *H. pylori*-positive cases is associated with an increased risk of rebleeding (32.4% versus 13.3%, $p = 0.001$), an increased need for surgical therapy (15.2% versus 4.8%, $p = 0.01$), and an increased mortality (15.2% versus 3.8%, $p = 0.005$) (60).

Recommendation: When used as an adjunct to endoscopic therapy, PPIs reduce the risk of further bleeding and the need for surgery (Recommendation grade: A).

Table 46.1 Stratification of Risks in Patients with Bleeding Ulcers Based on Endoscopic Findings

	Continued/Recurrent bleeding	Mortality
Active bleeding	55%	11%
Visible vessel	43%	11%
Adherent clot	22%	7%
Flat spot	10%	3%
Clean base	5%	2%

Source: Adapted from Ref. 41.

UNDER WHAT CIRCUMSTANCES IS AN OPERATION INDICATED FOR A BLEEDING PEPTIC ULCER?

WHAT TECHNIQUES ARE ASSOCIATED WITH THE LOWEST RATE OF REBLEEDING?

Surgical therapy is indicated in patients whose bleeding is not controlled by nonoperative measures (61, 62). The presence of exsanguinating hemorrhage or the lack of endoscopic support are self-evident indications for emergency operation. Recurrent bleeding after endoscopy is a more common (albeit less precise) indication. In 5–20% of patients who undergo endoscopic hemostasis, bleeding continues or recurs, a finding that is associated with an increase in mortality of 5- to 16-fold over controls (63). Risk factors identified by two separate logistic regression analyses as independent predictors of rebleeding or mortality include advanced age, shock, comorbidities, size of ulcer, and presence of major stigmata of hemorrhage (64,65).

Most patients with rebleeding can benefit from second-look endoscopy performed to provide additional hemostatic therapy if necessary. In a randomized trial comparing endoscopic retreatment with surgery, control of bleeding was achieved endoscopically in 35 of 48 patients (72.9%) with fewer complications experienced than in the surgery alone group (7 versus 16) (66). Another randomized trial compared a scheduled second therapeutic endoscopy within 16–24 hours after the initial endoscopy with a control group without a routine second endoscopy. The rate of recurrent bleeding was significantly lower in the second-look group (5% versus 13.8%, $p = 0.03$) and a trend toward fewer operations for rebleeding was identified (67). Further controlled studies are clearly necessary, but both selective and routine second-look endoscopy appear to favorably influence the outcome of peptic ulcer bleeding.

Unsuccessful endoscopic retreatment manifest as persistent or recurrent bleeding should be addressed by operation. However, as noted in the comprehensive review by Ohmann et al., an informed choice concerning the most appropriate procedure is difficult because timely, relevant, and high-grade surgical evidence is rare (68). As a result, widely divergent opinions prevail (69). Only two controlled, randomized trials comparing various operative approaches have been published since 1990, one from France and a second from England (60,70) (Table 46.2). A small, retrospective, multicenter study from Scotland and a large audit from the Department of Veterans Affairs National Surgical Quality Improvement Program (NSQIP) database have also been

reported (71,72). The studies by Poxon et al. and Kubba et al. compare conservative operations (ulcer oversewing or excision) with more advanced procedures (vagotomy plus pyloroplasty or resection). Millat et al. and de la Fuente et al. compare two different advanced therapies (vagotomy, pyloroplasty, and ulcer oversewing versus vagotomy and resection).

Notably, all operative techniques described in these studies resulted in a similar, relatively high mortality rate. In two of the four studies, the least aggressive forms of therapy were associated with a significantly higher rate of rebleeding. Taken together, such sparse data provides little guidance for the surgeon faced with treating a patient who presents with hemorrhage refractory to nonoperative therapies. Based on the available literature and personal experience, the author prefers to oversee the bleeding vessel in duodenal ulcers with the addition of a truncal vagotomy and pyloroplasty. Bleeding gastric ulcers are managed with partial gastric resection but without vagotomy. In each situation, the patient should be tested for *H. pylori* infection and treated, if positive. Eradication of the organism must be confirmed.

Recommendations: Surgery is indicated for peptic ulcer hemorrhage that is not controlled by endoscopic therapy or recurs following apparently successful endoscopic therapy (5–20%) (Recommendation grade: A).

When used for peptic ulcer bleeding, combined partial gastric resection and vagotomy is associated with the lowest recurrence rate. However, this approach also has a higher rate of short-term and long-term postoperative complications. Vagotomy with oversewing of the ulcer is effective when combined with anti-*H. pylori* therapy in *H. pylori*-positive patients (Recommendation grade: A).

WHAT APPROACH IS PREFERRED FOR THE MANAGEMENT OF PERFORATED PUD?

Perforation is a potentially catastrophic complication of PUD that is usually heralded by the abrupt and dramatic onset of severe, midepigastic or generalized abdominal pain. Because the large majority of perforations occur on the anterior aspect of the stomach or duodenum, pneumoperitoneum is present in 80–90% of cases and is readily detectable on plain abdominal films or computed tomography scan (73). Posterior perforations are rare (2%) and have a more insidious presentation and a worse outcome (74).

Table 46.2 Selected Trials of Surgical Management of Bleeding Peptic Ulcer

Author (Ref.)	Study type	n	Operation	Re-bleeding (%)	Mortality (%)
Poxon (70)	CRT	62	Oversewing/excision	7 (11.3)*	16 (26)
		67	TV/P or TV/A	4 (5.0)*	13 (19)
Milatt (69)	CRT	58	Oversewing/TV/P	10 (17)	13 (22.4)
		60	Resection	2 (3)	14 (23.3)
Kubba (71)	NRT	31	Oversewing	7 (23)*	7 (23)
		36	TV/P or TV/A	1 (2.7)*	5 (14)
de la Fuente (72)	NSQIP audit	518	TV and drainage	57 (11.0)	93 (18.0)
		389	TV and resection	46 (11.8)	70 (17.22)

Abbreviations: A, antrectomy; CRT, controlled randomized trial; NRT, nonrandomized trial; NSQIP, national surgical quality improvement program; P, pyloroplasty; TV, truncal vagotomy.

* $p < 0.05$.

The therapy of ulcer perforation should address three separate but related issues: the perforation itself, its underlying cause, and the resultant peritonitis and sepsis. In the latter regard, it is generally agreed that initial management should include rapid fluid resuscitation, nasogastric tube drainage, and systemic antibiotic administration. There is less unanimity about the respective roles of operative and nonoperative therapies for the actual perforation and its associated pathogenetic factors.

Peptic ulcer perforation remains a highly morbid condition with a related mortality of 8–30% (75,76). Based on a number of multifactorial analyses, several predictors of postoperative complications and death have been consistently identified including: treatment delay, circulatory shock, and major concurrent illness (77–79). Moreover, it has been suggested that these predictors can be used to stratify patients and to plan initial therapy. Using such an approach, Rahman et al. identified 84 high-risk patients in a cohort of 626 patients with perforated ulcer and managed them nonoperatively with peritoneal tube drainage (80). They found a significant decrease in overall mortality compared with historical controls who had undergone conventional operative treatment (9.5% versus 3.9%; $p < 0.0001$).

The use of nonoperative therapy for ulcer perforation remains controversial but appears to be gaining wider acceptance. As early as 1961, contrast studies documented that more than 40% of perforations were sealed by the time of clinical presentation (81). Subsequently, multiple non-randomized studies have indicated that nonoperative treatment of sealed perforations can result in a lower morbidity and mortality than with conventional surgical therapy (82–85) (Table 46.3). However, nonoperative treatment fails

in 16–32% of perforated patients, necessitating emergency operation. In the only controlled, randomized trial published to date, Crofts et al. compared initial nonoperative therapy with early operation in 83 patients with perforation (86). No difference was noted in mortality (4.7% versus 5.0%), but the hospital stay was 35% longer in the nonoperative group, and patients over 70 years of age were significantly less likely to respond to conservative measures. The mixed results with nonoperative therapy suggest that such an approach cannot be universally applied; however, its selective use especially in high-risk patients may be appropriate if a strict protocol and close follow-up can be ensured (87).

Specific operative strategies for the management of ulcer perforation have continued to evolve. Prior to recognition of the pathogenic roles of *H. pylori* and NSAIDs, numerous studies comparing simple closure with definitive operations (vagotomy with or without resection) appeared to demonstrate a lower recurrence rate following the more aggressive approach (88–90) (Table 46.4). Subsequently, excellent long-term results were observed in 107 carefully selected patients followed for 2–20 years after patch closure and parietal cell vagotomy (91). The authors reported an operative mortality of 0.9% and a recurrence rate of 7.4%. However, a more recent controlled randomized study comparing simple closure with vagotomy and pyloroplasty in over 200 patients failed to demonstrate an advantage in mortality or recurrence following the more definitive procedure (92).

In the current *Helicobacter* era, pharmacotherapy has largely replaced definitive surgery in the management of ulcer perforation (93). Worldwide, the prevalence of *H. pylori* infection in patients with perforated peptic ulcer is reported to range from 47% to 100% (94). Persistence of the infection

Table 46.3 Selected Trials of Nonoperative Management of Perforated Peptic Ulcer

Author (Ref.)	Study type	n	Treatment	Recurrent, %	Mortality, %
Marshall (85)	NRT	49	nonoperative	16.3	6.1
		21	operative	0	14.3
Crofts (86)	CRT	40	nonoperative	27.5	5.0
		43	operative	0	4.7
Berne (83)	NRT	35	nonoperative	0	3.0
		294	operative	NA	6.2

Abbreviations: CRT, controlled randomized trial; NRT, nonrandomized trial.

* $p < 0.05$.

Table 46.4 Selected Trials of Surgical Management of Perforated Peptic Ulcer

Author (Ref.)	Study type	n	Treatment	Recurrent, %	Mortality, %
Boey (88)	CRT	41	Closure	36.6*	0
		37	Closure/PCV	10.6	0
Tsugawa (89)	NRT	15	Closure	63.6*	26.7*
		24	Closure/TV	38.1	12.5
Jordan (90)	NRT	306	Closure	35.9	10.4
		208	Antrectomy/TV	24.4	2.5
Gutierrez de La Pena (92)	CRT	117	Closure	7.1	4.3
		90	V/P	4.4	4.4

Abbreviations: CRT, controlled randomized trial; NRT, nonrandomized trial; PCV, parietal cell vagotomy; TV, truncal vagotomy.

* $p < 0.05$.

after perforation predicts recurrence of the ulcer, whereas successful eradication of the organism results in a significant reduction in ulcer recurrence rates (95,96). In a related study of patients followed for 18 months, ulcer recurrence was noted in 70% of patients with persistent infection but in only 19% of those in whom *H. pylori* was eradicated (97). In a controlled, randomized trial comparing PPI therapy with anti-*Helicobacter* therapy following simple closure of the ulcer, the relapse rate was found to be significantly reduced in the anti-*Helicobacter* group after one year (4.8% versus 38.1%; $p < 0.001$) (98).

These data suggest that the majority of patients with perforated peptic ulcers can be treated with simple closure of the ulcer when the procedure is combined with appropriate medical measures such as anti-*Helicobacter* therapy, PPI administration, or NSAID modulation. More definitive surgical approaches may be reserved for patients with recurrent ulcer disease or for perforations that are associated with hemorrhage or obstruction.

Successful closure of perforations can be achieved with either open or laparoscopic techniques. A recent meta-analysis of 1,113 patients from 15 selected studies found that the laparoscopic approach required longer operating times but was associated with less postoperative analgesic use, a shorter hospital stay, and fewer wound infections (99). Two randomized studies confirm that laparoscopic and open repairs are equally safe and effective (100,101). However, the global conversion rate, laparoscopic to open, was 16.2%. A Cochrane review of these studies concluded that more randomized studies were needed and noted that no cost-benefit assessment has been attempted. In a recently described variant of the purely laparoscopic approach, intraoperative endoscopy is performed concurrent with laparoscopy and an endoscopic grasper used to pull omentum into the perforation (102). Similar improvements in pain control and hospital stay are reported when compared to standard open procedures.

Recommendations: Nonoperative therapy can be used in selected patients who are found to have a sealed perforation on contrast study. Patch closure is indicated in most patients. *H. pylori* should be eradicated when infection is present. The laparoscopic approach is being used with increased frequency (Recommendation grade: B).

REFERENCES

- Baron J, Sonnenberg A. Hospital admission for peptic ulcer and indigestion in London and New York in the 19th and early 20th centuries. *Gut* 2001; 568–70.
- Post P, Kuipers E, Meijer G, et al. Declining incidence of peptic ulcer but not of a nation-wide in The Netherlands. *Aliment Pharmacol Ther* 2006; 23: 1587–93.
- Modlin I. From Prout to the proton pump. A history of the science of gastric acid secretion and the surgery of peptic ulcer. *Surg Gynecol Obstet* 1990; 170: 81–95.
- Grob G. The rise of peptic ulcer 1900–1950. *Perspectives Biol Med* 2003; 46: 550–66.
- Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis (letter). *Lancet* 1983; 1: 1273–5.
- Gustavsson S, Kelly K, Melton L III, et al. Trends in peptic ulcer surgery. A population-based study in Rochester, Minnesota. 1956–1985. *Gastroenterology* 1988; 94: 688–94.
- Larson G, Davidson P. The decline in surgery for peptic ulcer disease. *J Ky Med Assoc* 1986; 84: 233–6.
- Smith B, Stabile B. Emerging trends in peptic ulcer disease and damage control surgery in the *H. pylori* era. *Am Surg* 2005; 71: 797–801.
- Schwesinger W, Page C, Sirinek K, et al. Operations for peptic ulcer disease: paradigm lost. *J Gastrointest Surg* 2001; 5: 438–43.
- Ohmann C, Imhof M, Ruppert C, et al. Time-trends in the epidemiology of peptic ulcer bleeding. *Scand J Gastroenterol* 2005; 40: 914–20.
- Rockall T, Logan R, Devlin H, et al. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. *Br Med J* 1995; 311: 222–6.
- Fowler S, Khoubian J, Mathiasen R, et al. Peptic ulcers in the elderly is a surgical disease. *Am J Surg* 2001; 182: 733–7.
- Schwarz K. Über penetrierende magen und jejunalgeschwür. *Beitr Klin Surg* 1919; 67: 96.
- Schwesinger W. Is *Helicobacter pylori* a myth or the missing link? *Am J Surg* 1996; 172: 411–17.
- Garcia Rodriguez L, Barreales Tolosa L. Risk of upper gastrointestinal complications among users of traditional NSAIDs and COXIBs in the general population. *Gastroenterology* 2007; 132: 498–506.
- Bliss D, Stabile B. The impact of ulcerogenic drugs on surgery for the treatment of peptic ulcer disease. *Arch Surg* 1991; 126: 609–12.
- Dixon M. Pathophysiology of *Helicobacter pylori* infection. *Scand J Gastroenterol* 1994; 29: 7–10.
- Das J, Paul N. Epidemiology and pathophysiology of *Helicobacter pylori* infection in children. *Ind J Ped* 2007; 74: 287–90.
- Vane J, Botting R. Mechanism of action of nonsteroidal anti-inflammatory drugs. *Am J Med* 1998; 104: 2S–8S.
- Huang JQ, Sridhar S, Hunt R, et al. Role of *Helicobacter pylori* infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. *Lancet* 2002; 359: 14–22.
- Peura D. The problem of *Helicobacter pylori*-negative idiopathic ulcer disease. *Baillière's Clin Gastroenterol* 2000; 14: 109–17.
- Yuan Y, Hunt R. Treatment of non-NSAID and non-*H. Pylori* gastroduodenal ulcers and hypersecretory states. In: Wolfe M, ed., *Therapy of Digestive Disorders*, 2nd edition. Philadelphia: Saunders Elsevier, 2006, 315–36.
- Ford A, Delaney B, Forman D, et al. Eradication therapy for peptic ulcer disease in *Helicobacter pylori* positive patients. *Cochrane Database of Systematic Reviews* 2006; 1: CD003840.
- Malfetheriner P, Mégraud F, O'Morain C, et al. Current concepts in the management of *Helicobacter pylori* infection—The Maastricht 2-2000 Consensus Report. *Aliment Pharmacol Ther* 2002; 16: 167–80.
- Laine L, Suchower L, Frantz J, et al. Twice-daily, 10-day triple therapy with omeprazole, amoxicillin, and clarithromycin for *Helicobacter pylori* eradication in duodenal ulcer disease: result of three multicenter, double-blind, United States trials. *Am J Gastroenterol* 1998; 93: 2106–12.
- Duck W, Sobel J, Pruckler J, et al. Antimicrobial resistance among *Helicobacter pylori*-infected persons, United States. *Emerging Infect Dis* 2004; 10: 1088–110.
- Chan F, Graham D. Prevention of non-steroidal anti-inflammatory drug gastrointestinal complications—review and recommendations based on risk assessment. *Aliment Pharmacol Ther* 2004; 19: 1051–61.
- Hawkey C, Tulassay Z, Szczepanski L, et al. Randomised controlled trial of *Helicobacter pylori* eradication in patients on non-steroidal anti-inflammatory drugs: HELP NSAIDs study. *Lancet* 1998; 352: 1016–21.
- Rostom A, Dube C, Wells G, et al. Prevention of NSAID-induced gastroduodenal ulcers. *Cochrane Database of Systematic Reviews* 2002; 4: CD002296.
- Vonkeman H, Fernandes R, van der Palen J, et al. Proton-pump inhibitors are associated with a reduced risk

- for bleeding and perforated gastroduodenal ulcers attributable to non-steroidal anti-inflammatory drugs: a nested case-control study. *Arth Res Ther* 2007; 9: R52.
31. Blecker E, Heller J, Schmitz V, et al. Diagnosis and management of upper gastrointestinal bleeding. *Dtsch Arztebl Int* 2008; 105: 85–94.
32. Matlock J, Freeman M. Non-variceal upper GI hemorrhage: doorway to diagnosis. *Gastrointest Endosc* 2005; 7: 112–17.
33. Baradarian R, Ramdhaney S, Chapalamadugu R, et al. Early intensive resuscitation of patients with upper gastrointestinal bleeding decreases mortality. *Am J Gastroenterol* 2004; 99: 619–22.
34. Aljebreen A, Fallone C, Barkun A. Nasogastric aspirate predicts high-risk endoscopic lesions in patients with acute upper-GI bleeding. *Gastrointest Endosc* 2004; 59: 172–8.
35. Witting M, Magder L, Heins A, et al. Usefulness and validity of diagnostic nasogastric aspiration in patients without hematemesis. *Ann Emerg Med* 2004; 43: 525–32.
36. Adamopoulos A, Baibas N, Efstathiou S, et al. Differentiation between patients with acute upper gastrointestinal bleeding who need early urgent upper gastrointestinal endoscopy and those who do not. A prospective study. *Eur J Gastroenterol Hepatology* 2003; 15: 381–7.
37. Frossard J, Spahr L, Queneau P, et al. Erythromycin intravenous bolus infusion in acute upper gastrointestinal bleeding: a randomized, controlled, double-blind trial. *Gastroenterology* 2002; 123: 17–23.
38. Carbone N, Pauwels A, Serfaty L, et al. Erythromycin infusion prior to endoscopy for acute upper gastrointestinal bleeding: a randomized, controlled, double-blind trial. *Am J Gastroenterol* 2006; 101: 1211–15.
39. Winstead N, Wilcox C. Erythromycin prior to endoscopy for acute upper gastrointestinal haemorrhage: a cost-effectiveness analysis. *Aliment Pharmacol Ther* 2007; 26: 1371–7.
40. Enestvedt B, Gralnek I, Mattek N, et al. An evaluation of endoscopic indications and findings related to nonvariceal upper-GI hemorrhage in a large multicenter consortium. *Gastrointest Endosc* 2008; 67: 422–9.
41. Laine L, Peterson W. Bleeding peptic ulcer. *N Eng J Med* 1994; 331: 717–27.
42. Kahi C, Jensen D, Sung J, et al. Endoscopic therapy versus medical therapy for bleeding peptic ulcer with adherent clot: a meta-analysis. *Gastroenterology* 2005; 129: 855–62.
43. Gralnek I, Jensen D, Kovacs T, et al. An economic analysis of patients with active arterial peptic ulcer hemorrhage treated with endoscopic heater probe, injection sclerosis, or surgery in a prospective, randomized trial. *Gastrointest Endosc* 1997; 46: 105–12.
44. Lee J, Turnipseed S, Romano S, et al. Endoscopy-based triage significantly reduces hospitalization rates and costs of treating upper GI bleeding: a randomized controlled trial. *Gastrointest Endosc* 1999; 50: 755–61.
45. Bjorkman DJ, Zaman A, Fennerty B, et al. Urgent vs. elective endoscopy for acute non-variceal upper-GI bleeding: an effectiveness study. *Gastrointest Endosc* 2004; 60: 1–8.
46. Sung J. Current management of peptic ulcer bleeding. *Nat Clin Pract Gastroenterol Hepatol* 2006; 3: 24–32.
47. Sacks H, Chalmers T, Blum A, et al. Endoscopic hemostasis an effective therapy for bleeding peptic ulcers. *JAMA* 1990; 264: 494–9.
48. Cook D, Guyatt G, Salens B, et al. Endoscopic therapy for acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. *Gastroenterology* 1992; 102: 139–48.
49. Park C, Lee S, Park J, et al. Optimal injection volume of epinephrine for endoscopic prevention of recurrent peptic ulcer bleeding. *Gastrointest Endosc* 2004; 60: 875–80.
50. Marmo R, Rotondano G, Piscopo R, et al. Dual therapy versus monotherapy in the endoscopic treatment of high-risk bleeding ulcers: a meta-analysis of controlled trials. *Am J Gastroenterol* 2007; 102: 279–89.
51. Vergara M, Calvet X, Gisbert J. Epinephrine injection versus epinephrine injection and a second endoscopic method in high risk bleeding ulcers. *Cochrane Database of Systematic Reviews* 2007; 2: CD005584.
52. Sung J, Tsoi K, Lai L, et al. Endoscopic clipping versus infection and thermo-coagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis. *Gut* 2007; 56: 1364–72.
53. Saltzman J, Strate L, Di Sena V, et al. Prospective trial of endoscopic clips versus combination therapy in upper GI bleeding (Protect-UGI Bleeding). *Am J Gastroenterol* 2005; 100: 1–6.
54. Leontiadis G, Sharma V, Howden C. Proton pump inhibitor therapy for peptic ulcer bleeding: cochrane collaboration meta-analysis of randomized controlled trials. *Mayo Clin Proc* 2007; 82: 286–96.
55. Lau J, Sung J, Lee K, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. *N Eng J Med* 2000; 343: 310–16.
56. Dorward S, Sreedharan A, Leontiadis G, et al. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. *Cochrane Database of Systematic Reviews* 2006; 4: CD005415.
57. Lai K, Hui W, Wong W, et al. Treatment of *Helicobacter pylori* in patients with duodenal ulcer hemorrhage—a long-term randomized, controlled study. *Am J Gastroenterol* 2000; 95: 2225–32.
58. Gisbert J, Pajares J. *Helicobacter pylori* infection and perforated peptic ulcer prevalence of the infection and role of antimicrobial treatment. *Helicobacter* 2003; 8: 159–67.
59. Sharma V, Sahai A, Corder F, et al. *Helicobacter pylori* eradication is superior to ulcer healing with or without maintenance therapy to prevent further ulcer haemorrhage. *Aliment Pharmacol Ther* 2001; 15: 1939–47.
60. Adamopoulos A, Efstathiou S, Tsioulos D, et al. Bleeding duodenal ulcer: comparison between *Helicobacter pylori* positive and *Helicobacter pylori* negative bleeders. *Dig Liver Dis* 2004; 36: 13–20.
61. Lau J, Chung S. Surgery in the acute management of bleeding peptic ulcer. *Bailliere's Clin Gastroenterol* 2000; 14: 505–18.
62. Cowles R, Mulholland M. Surgical management of peptic ulcer disease the *Helicobacter* era—management of bleeding peptic ulcer. *Surg Laparosc Endosc Percutan Tech* 2001; 11: 2–8.
63. Rockall T, Logan R, Devlin H, et al. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. *Br Med J* 1995; 311: 222–6.
64. Rockall T, Logan R, Devlin H, et al. Risk assessment after acute upper gastrointestinal haemorrhage. *Gut* 1996; 38: 316–21.
65. Branicki F, Coleman S, Fok P, et al. Bleeding peptic ulcer: a prospective evaluation of risk factors for rebleeding and mortality. *World J Surg* 1990; 14: 262–70.
66. Lau J, Sung J, Lam Y, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. *N Eng J Med* 1999; 340: 751–6.
67. Chiu P, Lam C, Lee S, et al. Effect of scheduled second therapeutic endoscopy on peptic ulcer rebleeding: a prospective randomized trial. *Gut* 2003; 52: 1403–7.
68. Ohmann C, Imhof M, Ruppert C, et al. Time-trends in the epidemiology of peptic ulcer bleeding. *Scand J Gastroenterol* 2005; 40: 914–20.
69. Millat B, Hay J, Valleur P, et al. Emergency surgical treatment for bleeding duodenal ulcer: oversewing plus vagotomy versus gastric resection, a controlled randomized trial. *World J Surg* 1993; 17: 568–74.

70. Poxon V, Keighley M, Dykes PW, et al. Comparison of minimal and conventional surgery in patients with bleeding peptic ulcer: a multicentre trial. *Br J Surg* 1991; 78: 1344–5.
71. Kubba A, Choudari C, Rajgopal C, et al. The outcome of urgent surgery for major peptic ulcer haemorrhage following failed endoscopic therapy. *Euro J Gastroenterol Hepatol* 1996; 8: 1175–8.
72. De la Fuente S, Khuri S, Schiffner T, et al. Comparative analysis of vagotomy and drainage versus vagotomy and resection procedures for bleeding peptic ulcer disease: results of 907 patients from the Department of Veterans Affairs National Surgical Quality Improvement Program Database. *J Am Coll Surg* 2006; 202: 78–86.
73. Chen C, Huang H, Yang C, et al. The features of perforated peptic ulcers in conventional computed tomography. *Hepato-gastroenterology* 2001; 48: 1393–6.
74. Wong C, Chow P, Ong H, et al. Posterior perforation of peptic ulcers: presentation and outcome of an uncommon surgical emergency. *Surgery* 2004; 135: 321–5.
75. Svanes C, Salvesen H, Stangeland L, et al. Perforated peptic ulcer over 56 years. Time trends in patients and disease characteristics. *Gut* 1993; 34: 1666–71.
76. Bucher P, Oulbaci W, Morel P, et al. Results of conservative treatment for perforated gastroduodenal ulcer in patients not eligible for surgical repair. *Swiss Med Wkly* 2007; 137: 337–40.
77. Millat B, Hay J, Valleur P, et al. Emergency surgical treatment for bleeding duodenal ulcer: oversewing plus vagotomy versus gastric resection, a controlled randomized trial. *World J Surg* 1993; 17: 568–74.
78. Testini M, Portincasa P, Piccinni G, et al. Significant factors associated with fatal outcome in emergency open surgery for perforated peptic ulcer. *World J Gastroenterol* 2003; 9: 2338–40.
79. Sharma SS, Mamtani MR, Sharma MS, et al. A prospective cohort study of postoperative complications in the management of perforated peptic ulcer. *BMC Surgery* 2006; 6: 8.
80. Rahman M, Islam M, Flora S, et al. Mortality in perforated peptic ulcer patients after selective management of stratified poor risk cases. *World J Surg* 2007; 31: 2341–4.
81. Jacobson G, Berne C, Meyers H, et al. The examination of patients with suspected perforated ulcer using a water-soluble contrast medium. *Am J Roentgenol Radium Therap Nucl Med* 1961; 86: 37–49.
82. Donovan A, Vinson T, Maulsby G, et al. Selective treatment of duodenal ulcer with perforation. *Ann Surg* 1979; 189: 627–36.
83. Berne T, Donovan A. Nonoperative treatment of perforated duodenal ulcer. *Arch Surg* 1989; 124: 830–2.
84. Cocks J, Kernutt R, Singlair W, et al. Perforated peptic ulcer: a deliberative approach. *Aust NZ J Surg* 1989; 59: 379–85.
85. Marshall C, Ramaswamy P, Bergin F, et al. Evaluation of a protocol for the non-operative management of perforated peptic ulcer. *Br J Surg* 1999; 86: 131–4.
86. Crofts T, Park K, Steele R, et al. A randomized trial of nonoperative treatment for perforated peptic ulcer. *N Eng J Med* 1989; 320: 970–3.
87. Donovan AJ, Berne V, Donovan JA. Perforated duodenal ulcer: an alternative therapeutic plan. *Arch Surg* 1998; 133: 1166–71.
88. Boey J, Branicki F, Alagaratnam T, et al. Proximal gastric vagotomy. The preferred operation for perforations in acute duodenal ulcer. *Ann Surg* 1988; 208: 169–74.
89. Tsugawa K, Koyanagi N, Hashizume M, et al. The therapeutic strategies in performing emergency surgery for gastroduodenal ulcer perforation in 130 patients over 70 years of age. *Hepatol-Gastroenterol* 2001; 48: 156–62.
90. Jordan G, DeBakey M, Duncan J, et al. Surgical management of perforated peptic ulcer. *Ann Surg* 1974; 179: 628–33.
91. Jordan PH, Thornby J. Perforated pyloroduodenal ulcers long-term results with omental patch closure and parietal cell vagotomy. *Ann Surg* 1995; 221: 479–88.
92. Gutierrez de la Pena C, Marquez, Fakih F. Simple closure or vagotomy and pyloroplasty for the treatment of a perforated duodenal ulcer: comparison of results. *Dig Surg* 2000; 17: 225–8.
93. Gilliam AD, Speake WJ, Lobo M, et al. Current practice of emergency vagotomy and *Helicobacter pylori* eradication for complicated peptic ulcer in the United Kingdom. *Brit J Surg* 2003; 90: 88–90.
94. Gisbert J, Pajares J. *Helicobacter pylori* infection and perforated peptic ulcer. Prevalence of the infection and role of antimicrobial treatment. *Helicobacter* 2003; 8: 159–67.
95. Sebastian M, Prem Chandran V, Elashaal Y, et al. *Helicobacter pylori* infection in perforated peptic ulcer disease. *Br J Surg* 1995; 82: 360–2.
96. Kate V, Ananthakrishnan N, Badrinath S, et al. Effect of *Helicobacter pylori* eradication on the ulcer recurrence rate after simple closure of perforated duodenal ulcer: retrospective and prospective randomized controlled studies. *Br J Surg* 2001; 88: 1054–8.
97. Bose AC, Kate V, Ananthakrishnan N, et al. *Helicobacter pylori* eradication prevents recurrence after simple closure of perforated duodenal ulcer. *J Gastroenterol Hepatol* 2007; 22: 345–8.
98. Ng E, Lam Y, Sung J, et al. Eradication of *Helicobacter pylori* prevents recurrence of ulcer after simple closure of duodenal ulcer perforation. *Ann Surg* 2000; 231: 153–8.
99. Lunevicius R, Morkevicius M. Comparison of laparoscopic vs open repair for perforated duodenal ulcers. *Surg Endosc* 2005; 19: 1565–71.
100. Siu W, Leong H, Law B, et al. Laparoscopic repair for perforated peptic ulcer: a randomized controlled trial. *Ann Surg* 2002; 235: 313–19.
101. Lau WY, Leung KL, Kwong KH, et al. A randomized study comparing laparoscopic versus open repair of perforated peptic ulcer using suture or sutureless technique. *Ann Surg* 1996; 224: 131–8.
102. Malkov I, Zaynutdinov A, Veliyev N, et al. Laparoscopic and endoscopic management of perforated duodenal ulcer. *J Am Coll Surg* 2004; 198: 352–5.

Enterocutaneous Fistula

Peter A. Learn

Clinical Questions and Grades		
Question	Answer	Grade of recommendation
What factors predict mortality in ECF?	A model incorporating APACHE II scoring and serum albumin is highly accurate in predicting mortality.	A
Do VTACs increase the risk of fistula formation?	In trauma patients, probably not. In patients with abdominal sepsis, caution is advised until better studies are obtained.	C
What is the optimal nutritional strategy in ECF?	TPN not only can provide complete nutritional support to patients but may also increase rates of closure.	C
What is the role of somatostatin or octreotide in the management of ECF?	Enteral nutrition should be considered on a selective basis.	C
	Somatostatin and octreotide do not significantly increase the frequency of spontaneous ECF closure.	B
What is the optimal timing for elective surgical intervention for ECF?	Somatostatin may decrease both fistula output and time to spontaneous closure.	B
	Octreotide is inconsistently demonstrated to decrease fistula output.	D
What is the optimal timing for elective surgical intervention for ECF?	Avoid elective surgery until at least six weeks, preferably several months, after diagnosis, and only after stabilization of nutritional status and resolution of sepsis.	D
Is surgical closure of the fistula best accomplished by resectional or nonresectional approaches?	Resection of the involved segment of bowel is preferred when possible.	C
Abbreviations: ECF, enterocutaneous fistula; TPN, total parenteral nutrition; VTAC, vacuum-based temporary abdominal closure.		

Enterocutaneous fistula (ECF) remains one of the most challenging surgical problems in alimentary tract surgery, with significant rates of associated morbidity and mortality. The difficulty of fistula management can be compounded by the interplay of the underlying pathology, ongoing sepsis, and the physiologic derangements caused by the fistula itself. The heterogeneity of the etiology, location, and behavior of ECF further complicates the study of therapeutic interventions. The treatment of patients with ECF remains largely guided by fundamental principles of resuscitation, control of sepsis, aggressive wound care, control of effluent, nutritional support, and appropriately timed surgical intervention. Although many of these principles of modern management still rely heavily on historical experience and expert opinion, adequate data exist on some aspects to provide an evidence-based framework for ECF management. This chapter specifically covers the management of external intestinal fistulas. Studies limited

exclusively to pancreatic, anorectal, or inflammatory bowel disease fistulas are excluded.

WHAT FACTORS PREDICT MORTALITY IN ECF?

Although most studies on ECF report mortality figures, almost none have established models to predict mortality. One exception is a study by Altomare et al. (1) in which a predictive model was derived from logistic regression analysis on a retrospective cohort of 70 consecutive patients from 1981 to 1986. The model, incorporating only the APACHE II score and serum albumin at time of diagnosis, was then prospectively evaluated in a subsequent 17 patients and demonstrated an accuracy of 94% in predicting mortality (Level Ib).

Answer: An accurate estimation of mortality can be calculated using a model incorporating APACHE II score

and serum albumin, although the model would benefit from further validation in other cohorts (Level Ib evidence, Grade B recommendation).

DO VACUUM-BASED TEMPORARY ABDOMINAL CLOSURES IN OPEN ABDOMEN MANAGEMENT INCREASE THE RISK OF FISTULA FORMATION?

Open abdomen management and temporary abdominal closures are frequently employed in cases of damage control procedures, to facilitate planned reoperations, and in the treatment or prevention of abdominal compartment syndrome. ECF remains a source of significant morbidity in open abdomen management. Based on several retrospective studies and one prospective study reported since 2000, this complication occurs in 6–17% of patients managed for open abdomens due to trauma or abdominal sepsis. Mortality in patients with both open abdomens and ECF is reported to be as high as 60%, although the underlying pathology leading to open abdomen management clearly plays a role in increasing mortality. Vacuum-based temporary abdominal closures (VTACs) have been popularized for the management of the open abdomen wound, but some concern has been expressed about the fistulogenic potential of these strategies.

Despite numerous studies published on the management of the open abdomen, many cataloging the use of VTAC, few have specifically addressed the risk for fistula formation. Several studies have reported results on the use of VTACs in trauma, the largest of which was a retrospective study reporting a seven-year experience in 112 consecutive trauma patients (2). The investigators observed an incidence of ECF of only 4.5%, a finding consistent with several smaller studies (Level IV evidence). In contrast, Rao et al. observed very different results in a retrospective study evaluating their experience in the use of a proprietary vacuum-assisted closure system in 29 consecutive non-trauma patients (3). In this population, two-thirds of which were treated for abdominal sepsis, 20% developed fistulas (Level IV evidence).

Answer: Avoiding the use of VTAC due to concern about fistula formation in trauma is unsupported by currently available data (Level IV evidence, Grade C recommendation). However, patients being treated with open abdomen management for intra-abdominal sepsis may have a different degree of risk for fistula formation, and judicious use may be appropriate in this population until the true risk can be determined in controlled studies (Level IV evidence, Grade C recommendation).

WHAT IS THE OPTIMAL NUTRITIONAL STRATEGY IN ECF?

The significant nutritional demands of ECF are well recognized and result from the interplay of several factors, including premorbid malnutrition, intestinal failure resulting from fistula diversion, fistula-related sepsis, and persisting underlying pathology. Ensuring adequate nutritional support is a fundamental principal in fistula management, and both enteral and parenteral approaches have been evaluated to varying degrees.

Total parenteral nutrition (TPN) reached widespread availability in the 1970s and was quickly applied to the nutritional support of patients with ECF. The best data available supporting its use are obtained from prospective cohort studies using historical controls (Level IV evidence). In these early studies, patients receiving TPN had approximately twice the ECF closure rate and at least half to one-quarter the mortality (4,5). Though significant methodological flaws make the exact degree of improvement attributable strictly to TPN difficult to ascertain, its clear benefits in modern management preclude the ability to subject the intervention to placebo-controlled study.

Enteral nutrition has also been advocated as a viable means of supporting patients with ECF, and published case series reports (6,7) have demonstrated the ability to meet nutritional requirements with various forms of enteral nutrition in select populations (Level IV evidence). Additionally, recognized benefits of enteral nutrition include protection of mucosal integrity and lower costs than TPN. However, the use of TPN or enteral nutrition exclusively or in combination has never been adequately evaluated in a controlled study.

Answer: TPN can be used to provide complete nutritional support to patients with ECF and potentially increase rates of fistula closure (Level IV evidence, Grade C recommendation). Enteral nutrition is attractive for its potential benefits over long-term TPN and deserves further evaluation against TPN in controlled studies. Because enteral nutrition has been observed to meet the nutrition needs of some patients, it can be considered for use on a selective basis, in the setting of a clinical study, or as an adjunct to TPN, although it is not clear if rates of fistula closure or time to closure are positively affected relative to TPN alone (Level IV evidence, Grade C recommendation).

WHAT IS THE ROLE OF SOMATOSTATIN OR SOMATOSTATIN ANALOGS IN THE MANAGEMENT OF ECF?

Early case series reporting the use of somatostatin and its analogs in the treatment of ECF fostered optimism about the potential for this therapy and ultimately led to the reporting of several clinical trials, making this question the most rigorously studied aspect of ECF management. The ability to combine the results of the trials, however, is limited by their usage of different analogs and doses for different lengths of time in heterogeneous populations.

Sancho et al. (8) reported the most well-designed of these studies, a randomized, double-blind, placebo-controlled trial of octreotide therapy in the early treatment of postoperative ECF (Level Ib evidence). The study population included patients with gastric, intestinal, and a small number of pancreatic fistulae diagnosed within eight days of enrollment, stratified into two groups by daily volume of output and regardless of presence of ongoing sepsis. Patients with underlying radiation injury or malignancy were excluded. Patients received standardized support therapy, including TPN, and the trial treatment: either subcutaneous octreotide 100 µg three times a day (14 patients)

or saline placebo administered identically (17 patients). The trial treatment was administered either for 20 days of continuous treatment or until fistula closure. Randomization scheme and postrandomization exclusion events were reported, and the trial was powered to detect a decrease of fistula output of 50% or greater. In this trial, administration of octreotide failed to reduce fistula output better than placebo did. Spontaneous closure events occurred in each arm, but neither the incidence nor the mean time to closure reached statistical significance, although the study was not powered to study these endpoints.

Interestingly, these results contrasted somewhat with the same group's prior results published in 1987 (9). In this randomized, placebo-controlled, double-blind, crossover study (Level Ib evidence), 14 patients with postoperative small bowel ECF underwent standardized treatment with TPN for seven days. The patients then received either octreotide (225–300 µg daily divided in three doses) or saline placebo for two days. After two days, the groups were crossed over to the other treatment. After the four days of the crossover portion of the trial, all patients were treated indefinitely with octreotide to the point of fistula closure or surgical intervention. Although a power analysis and other important information were not reported as in the later trial, octreotide in this study clearly reduced fistula output volume by at least half with a rebound in output following interruption of octreotide therapy by placebo. The differences in the results of these two studies by the same group are attributed by the authors to a possible effect of the timing of octreotide administration after stabilization of the ECF.

Two further randomized controlled trials have been published on this topic. In 1992, Torres et al. (10) published the results of a multicenter, randomized (scheme unreported), single-blind, placebo-controlled trial of continuous intravenous somatostatin infusion (Level IIb evidence). The study results demonstrated no difference in the frequency of fistula closure, although it appeared that fistula output and time to closure was decreased in the somatostatin group. However, absence of information on the age of the fistulas, crossover of three patients from the placebo arm to the somatostatin arm, and intergroup differences in pretreatment fistula output complicates the interpretation of the results. In addition, the evaluation of time to closure would have benefited from a more sophisticated event analysis technique (i.e., Kaplan-Meier analysis). In 1993, Scott et al. (11) published results of their randomized, double-blind, placebo-controlled trial of octreotide (Level IIb evidence). Though they did not observe significant reductions in fistula losses or increased rates of spontaneous closure, a high dropout rate and small sample size impair the interpretation of the results.

Answer: No evidence from controlled trials supports the use of somatostatin or octreotide to increase the frequency of spontaneous ECF closure (Level Ib evidence, Grade A recommendation). One study using somatostatin demonstrated a significant decrease in fistula output and time to closure but would benefit from further well-designed confirmatory studies (extrapolation from Level Ib and IIb studies, grade B recommendation). Octreotide has not been consistently demonstrated to decrease fistula output or time to closure and support for its use must be

considered limited (conflicting results from Level Ib and IIb studies, grade D recommendation).

WHEN IS THE OPTIMAL TIMING FOR ELECTIVE SURGICAL INTERVENTION FOR ECF?

The subject of optimal timing for elective surgical intervention has not been rigorously, prospectively evaluated. It is commonly recommended to avoid operation if possible until at least six weeks, with many experts recommending waiting four to six months. Suggested clinical criteria to achieve the lowest rates of recurrence and mortality include resolution of obliterative peritonitis suggested by the return of a pliable abdomen and prolapse of the fistulous bowel, absence of sepsis and stabilization of other comorbid conditions, and restoration of adequate nutritional status, often using the serum albumin as a rough surrogate. Unfortunately, although some of these criteria have been suggested in multivariate analyses of retrospective case series, none have been tested in a prospective fashion and are based on Level IV and V evidence.

Answer: If possible, surgery to address the ECF specifically should be avoided for at least six weeks, preferably taking place several months after fistula diagnosis and assuming stabilization of nutritional status and resolution of sepsis (Level IV and V evidence, Grade D recommendation).

IS SURGICAL CLOSURE OF THE FISTULA BEST ACCOMPLISHED BY RESECTIONAL OR NONRESECTIONAL APPROACHES?

The choice between resectional (i.e., small bowel resection) and nonresectional (i.e., oversewing or wedge repair) techniques to address the bowel of origin has not been studied prospectively. However, in a retrospective study of 205 patients undergoing surgery for ECF (12), fistula recurrence occurred in 32.7% of patients treated with nonresectional techniques compared with 18.4% of patients undergoing segmental resection of the fistulous origin. The association of nonresectional techniques with recurrence of the fistula was confirmed on multivariate analysis (Level IV evidence).

Answer: Resection of the segment of bowel from which the fistula originates should be used preferably over nonresectional techniques when possible (Level IV evidence, Grade C recommendation).

REFERENCES

1. Altomare DF, Serio G, Pannarale OC, et al. Prediction of mortality by logistic regression analysis in patients with postoperative enterocutaneous fistulae. *Br J Surg* 1990; 77: 450.
2. Barker D, Kaufman H, Smith L, et al. Vacuum pack technique of temporary abdominal closure: a 7-year experience with 112 patients. *J Trauma Inj Infect Crit Care* 2000; 48: 201.
3. Rao M, Burke D, Finan PJ, et al. The use of vacuum-assisted closure of abdominal wounds: a word of caution. *Colo Dis* 2007; 9: 266.
4. Deitel M. Nutritional management of external gastrointestinal fistulas. *Can J Surg* 1976; 19: 505.

5. Thomas RJ. The response of patients with fistulas of the gastrointestinal tract to parenteral nutrition. *Surg Gynecol Obstet* 1981; 153: 77.
6. Levy E, Frileux P, Cugnenc PH, et al. High-output external fistulae of the small bowel: management with continuous enteral nutrition. *Br J Surg* 1989; 76: 676.
7. Teubner A, Morrison K, Ravishankar HR, et al. Fistuloclysis can successfully replace parenteral feeding in the nutritional support of patients with enterocutaneous fistula. *Br J Surg* 2004; 91: 625.
8. Sancho JJ, di Costanzo J, Nubiola P, et al. Randomized double-blind placebo-controlled trial of early octreotide in patients with postoperative enterocutaneous fistula. *Br J Surg* 1995; 82: 638.
9. Nubiola C, Nubiola-Calonge P, Badia JM, et al. Blind evaluation of the effect of octreotide (SMS 201-995), a somatostatin analogue, on small-bowel fistula output. *Lancet* 1987; 2: 672.
10. Torres AJ, Landa JI, Moreno-Azcoita M, et al. Somatostatin in the management of gastrointestinal fistulas. A multicenter trial. *Arch Surg* 1992; 127: 97.
11. Scott NA, Finnegan S, Irving MH. Octreotide and postoperative enterocutaneous fistulae: a controlled prospective study. *Acta Gastroenterol Belg* 1993; 56: 266.
12. Lynch AC, Delaney CP, Senagore AJ, et al. Clinical outcome and factors predictive of recurrence after enterocutaneous fistula surgery. *Ann Surg* 2004; 240: 825.

Paraesophageal Hernia Repair

Omid Noormohammadi, Alicia Logue and Kent R. Van Sickle

Clinical Questions		
Question	Answer	Grade of recommendation
Should all PEHs be repaired?	Yes	B and C
Surgical repair of asymptomatic PEH in high-risk or elderly patient?	Yes	B and C
What is the natural history of PEHs?	No	B
What is the recurrence rate of surgically repaired PEH?	—	—
Is laparoscopic repair indicated in all PEH patients?	0–42%	A, B, C
	Yes	B and C
Abbreviation: PEH, paraesophageal hernia.		

WHAT IS THE DEFINITION OF A PARAESOPHAGEAL HERNIA?

The term paraesophageal hernia (PEH) was first described by Akerlund in 1926 and is descriptive of hiatal hernias where the fundus of the stomach lies cephalad to the gastroesophageal junction but the gastroesophageal junction remains in a normal or nearly normal anatomic location below the diaphragm. These are classified as Type II hiatal hernias (see following discussion), and they are an uncommon form of hiatal hernias, estimated to represent only 5% of all hiatal hernias. Despite their relatively low incidence, several controversies exist over the optimal management and long-term consequences of PEHs.

WHAT ARE THE CLASSIFICATIONS OF PEHS?

Hiatal hernias can be classified into three main types:

- Type I: Classic sliding hiatal hernia; in which the gastroesophageal junction migrates cephalad through the esophageal hiatus.
- Type II: True paraesophageal or rolling hernia, in which the fundus herniates into the mediastinum relative to a normally positioned gastroesophageal junction.
- Type III: Combined or mixed hiatal hernia, in which both the gastroesophageal junction and the fundus herniate into the thorax.

A Type IV hernia is also often described where all of the stomach and/or other viscera (i.e., colon, spleen, pancreas) herniate into the chest, although this is technically a form of the Type III hernia.

SHOULD ALL PEHS BE REPAIRED?

There has been extensive controversy regarding the necessity to repair all PEHs, particularly in asymptomatic or high-risk patients. Traditionally, operative intervention has been the favored management of asymptomatic hernias secondary to the concern regarding strangulation reported in by Skinner and Hill (1,2). More recent studies show that the occurrence of such complications, such as incarceration and strangulation, are actually much lower than previously reported. A review of the Mayo Clinic followed 23 patients who followed with expectant management noted that after a six-year follow-up, none of the patients developed severe complications, such as strangulation (3). In another study, Stylopoulos et al. used a Markov Monte Carlo decision model and reported that there was only a 1.1% per year risk for a 65-year-old patient to develop a life-threatening complication associated with PEH (4). The mortality rate reported for elective PEH repair was 1.4% compared to a mortality rate of 5.4% in emergency PEH repair. This should be taken into consideration because the majority of patients presenting with PEH tend to be elderly with other substantial comorbidities. Wolf et al. published a review that detailed the use of laparoscopic repair of PEH and indicated that elderly asymptomatic patients with multiple comorbidities should be treated expectantly. However, young, low-risk patients are more likely to benefit surgical repair to avoid future acute or chronic symptoms resulting from an unrepaired PEH (5).

Answer: The majority of published reports suggest that all PEHs in good-risk surgical patients should be repaired to prevent the development of potentially life threatening complications (Grade B and C recommendations).

WHAT IS THE EVIDENCE FOR/AGAINST SURGICAL REPAIR OF AN ASYMPTOMATIC PEH IN AN ELDERLY OR HIGH-RISK PATIENT?

Complications from PEHs and the risk of repair are more considerable among the elderly. However, a prospective study examined 171 patients >65 years of age that underwent laparoscopic PEH repair over a span of 10 years suggested that repair resulted in few major complications

and achieved a good symptomatic outcome. Although patients over 75 years of age had an overall higher complication rate than younger individuals, serious (Grade ≥ 2) complications occurred relatively infrequently in this elderly age group (6). Another prospective study collected data on 35 elderly patients (>70 years of age) who had a laparoscopic repair of a symptomatic PEH over a 4-year period and assessed their health through a Quality of Life in Reflux and Dyspepsia questionnaire. Questionnaires were obtained in 30 of 35 patients and showed significant improvement in quality of life (7).

Although there have been multiple studies that assess the risk of surgical repair of symptomatic PEHs in the elderly, there are very few that involve patients showing asymptomatic conditions. The concept of elective surgery being beneficial in an asymptomatic hernia to prevent the risk of future emergent complications is controversial. In the review article by Stylopoulos et al. (4), a Markov Monte Carlo decision analytic model was developed to track a hypothetical cohort of patients with asymptomatic PEHs associated with two different treatment strategies. These included elective laparoscopic hernia repair (ELHR) or watchful waiting. When ELHR was used for patients 65 years of age or older, it resulted in a reduction of 0.13 quality-adjusted life-years. The probability of developing acute symptoms requiring emergency surgery was estimated from a pooled analysis of five studies (3,8–11). In these studies, the authors reported the exact interval for which the hernia had been known to be present before the surgical repair. The highest rate was 7/100 patients per year, reported by Hallissey et al. (10) (approximately 58 patient-years follow-up). Allen et al. (3) reported the longest follow-up in the literature (735 patient-years) and found an incidence rate of 7/1,000 patients per year, 10 times lower than the rate reported by Hallissey et al. Based on these five studies, the pooled annual probability of developing acute symptoms requiring emergency surgery was estimated to be 1.16% per year, ranging from 0.69% to 1.93%. The lifetime risk of developing acute symptoms is 18% for a 65-year-old patient and decreases exponentially as the patient's age increases. The model assumed that watchful waiting was the optimal treatment strategy in 83% of patients, and thus ideal for initial management of patients with asymptomatic or minimally symptomatic PEHs (4).

Answer: Patients in good health with a reasonable life expectancy benefit from repair of asymptomatic PEHs, whereas expectant management is justified in those with considerable morbidities (Grade B and C recommendations).

WHAT IS THE NATURAL HISTORY OF PEHS?

The 2002 article by Stylopoulos et al. (4) reviewed the literature, noting five studies regarding the course of asymptomatic PEHs. They noted that the annual probability of a patient developing symptoms that would require acute operative intervention to be $\sim 1.16\%$ per year. In addition, they also noted that the lifetime risk for a 65-year-old patient to develop symptoms was $\sim 18\%$, with the incidence decreasing with age. Therefore, watchful waiting is an acceptable form of management in the asymptomatic

elderly patient, particularly those with significant comorbidities.

Answer: The likelihood of patients with PEHs developing significant symptoms is only 1.16% per year, and the lifetime risk for a 65-year-old patient developing symptoms is 18% and the incidence decreases with age (Grade B recommendation).

WHAT ARE THE RECURRENCE RATES FOR LAPAROSCOPICALLY REPAIRED PEH?

Depending on the type of procedure used to repair the PEH, recurrence rates can vary from 12% to 42% (12–14). In a study conducted by Hashemi et al., three different surgical approaches to PEH repair were studied. Of the 54 patients who underwent repair, laparotomy was chosen in 13, thoracotomy in 14, and laparoscopy in 27. The results reported that the laparoscopic approach had the highest recurrence rate (42%) of the three surgical approaches, but the majority of the recurrences were asymptomatic (13). In a literature review involving 20 studies relevant to laparoscopic PEH repair, data were collected on 1,415 patients with a mean age of 65.7 years. Results showed that of those undergoing contrast swallow, 26.9% had evidence of recurrence. The study concluded that although laparoscopic repair had distinct advantages over open surgery (fewer complications and shorter hospital stay), it did also prove to have higher recurrence rates (15).

Recently, many surgeons have started applying the use of synthetic mesh with tension-free closures to repair PEH, in hope of reducing recurrence rates. One such trial involved a multicenter, prospective, randomized study of the value of a biologic prosthesis, small intestinal submucosa (SIS), in laparoscopic PEH repair. It was noted that at the six-month follow-up, only 9% of the patients in the SIS group developed a recurrent hernia, compared to 24% of the primary group. Both groups also showed an improved quality of life (SF-36) as well as a significant reduction in all associated symptoms. Therefore, it was concluded that biologic prosthesis reinforcement during laparoscopic PEH repair will lower the recurrence rate, without increasing the rate of any associated side effects or complications (16). In a single-institution, prospective, randomized trial, the use of polytetrafluoroethylene (PTFE) mesh was used to compare recurrence rates of primary repair to mesh reinforcement for hiatal defect closure. There were eight hernia recurrences (22%) in the primary group and none in the PTFE group. Therefore, this study concluded that the use of prosthetic reinforcement may lower recurrence rates for large hiatal hernias (17).

Answer: The recurrence rates for laparoscopically repaired PEHs range from 0% to 42% and are highly dependent on technique of repair and/or the use of prosthetic mesh. Recurrence rates are significantly reduced when either synthetic or biologic mesh is used to reinforce hiatal closure (Grades A, B, and C recommendations).

IS LAPAROSCOPIC REPAIR INDICATED IN ALL PATIENTS WITH PEH?

There has been much debate over the choice between laparoscopic and open repair of PEHs. A number of studies

have been conducted comparing the two, resulting in contrasting conclusions. Hashemi et al. concluded that both groups have very similar symptomatic outcomes, but the recurrence rate of the laparoscopic group was significantly higher than that of the open group (42% versus 15%) (13). In another study by Schauer et al., the data reported a lower recurrence rate of reflux symptoms in the laparoscopic group compared to the open group (6% versus 16%). It went further to report a reduction in blood loss, hospital stay, and overall morbidity when the laparoscopic approach was performed (18).

In a more recent study from McGill University, data were collected on 60 primary PEH patients at one institution over a 12-year span. The open group (n = 25) and laparoscopic group (n = 35) were then compared for overall outcomes on the basis of quality of life questionnaires and radiographs. Results indicated that laparoscopic repair lead to lower blood loss, fewer complications, and shorter hospital stay. Although the quality of life was similar between the two groups, radiographic results indicated that recurrence rates were higher for the open group (44% versus 23%) (19).

A retrospective multi-institutional review of PEH repair was conducted at the Calgary Health Region to compare the outcomes between laparoscopic (n = 46) and open (n = 47) repair. Though the recurrence rates were similar between the two (9%), the laparoscopic approach resulted in a shorter hospital stay (5 days versus 10 days) and fewer postoperative complications (22% versus 53%). It was noted though that these results were based off short-term follow-ups (16–18 months), and long-term follow ups would be necessary to determine the procedure of choice (20). In retrospective review, Mattar and colleagues looked at short- and long-term complications of laparoscopic PEH repair in a total of 83 patients with a mean follow-up of 40 months (14). The overall morbidity

and mortality in this series was 10% and 2%, respectively, and although 33% of patients studied with a barium swallow > one year postoperatively demonstrated “anatomic recurrence,” only 8% reported symptoms and 4% required reoperation.

Answer: Laparoscopic repair is associated with improved short-term outcomes and either equivalent or improved long-term recurrence rates (Grade B and C recommendations).

ARE THERE ANY NONSURGICAL OR ENDOSCOPIC MANAGEMENT OPTIONS FOR HIGH-RISK PATIENTS WITH PEH?

A study conducted by Kercher et al. took a look at a new minimally invasive technique to treat symptomatic high-risk PEH patients—laparoscopic-assisted endoscopic reduction and fixation of the stomach. The study included eleven elderly patients (mean age of 78.3 years) that all presented with a symptomatic PEH and three other serious comorbidities. Management of the PEH was achieved with flexible endoscopy and double percutaneous endoscopic gastrostomy tube insertion with or without laparoscopic assistance. Over a mean follow-up of 4.1 months, it was noted that all patients had achieved weight gain and reduced many other symptoms associated with PEH. It was also concluded that this technique may eliminate the risks of gastric volvulus and strangulation, both of which are major complications of PEH in high-risk patients (21).

Answer: A new endoscopic option using a double percutaneous endoscopic gastrostomy technique has been described, but the series is too small and follow-up is too short to offer any recommendations (Grade C/D recommendation).

Levels of Evidence

Study design	Year	Ref.	Level of evidence	Major endpoint	Median follow-up	Strength of recommendation	Findings
RCT	2006	16	Ib	Recurrence	6 months	A	Biologic prosthesis reinforcement + 1° closure reduce recurrence rate
Case series	2002	14	IV	Symptoms (HB, regurg, etc.)	40 months	C	Improvement of symptoms w/ elective repair; 2% mortality
Case-control study	1998	18	IV	PEH-related symptoms	13 month	C	Improvement in symptoms 84% open PEH versus 94% lap PEH
RCT	2002	17	Iib	Recurrences (mesh versus 1° repair)	2.5 years	B	Recurrence rate 22% w/ primary repair vs. 0% w/ PTFE mesh rep

Abbreviations: HB, heartburn; PEH, paraesophageal hernia; PTFE, polytetrafluoroethylene; RCT, randomized controlled trial.

REFERENCES

1. Skinner DB, Belsey RH. Surgical management of esophageal reflux and hiatus hernia. Long-term results with 1,030 patients. *J Thor Cardiovasc Surg* 1967; 53: 33–54.
2. Hill LD. Incarcerated paraesophageal hernia. A surgical emergency. *Am J Surgery* 1973; 126: 286–91.
3. Allen MS. Intrathoracic stomach. Presentation and results of operation. *J Thor Cardiovasc Surg* 1993; 105: 253–8; discussion 258–9.
4. Stylopoulos N, Gazelle GS, Rattner DW. Paraesophageal hernias: operation or observation? *Ann Surg* 2002; 236: 492–500.
5. Wolf PS, Oelschlager BK. Laparoscopic paraesophageal hernia repair. *Adv Surg* 2007; 41: 199–210.

6. Gangopadhyay N. Outcomes of laparoscopic paraesophageal hernia repair in elderly and high-risk patients. *Surgery* 2006; 140: 491–8; discussion 498–9.
7. Hazebroek EJ. Laparoscopic paraesophageal hernia repair: quality of life outcomes in the elderly. *Dis Esophagus* 2008.
8. Pitcher DE. Successful laparoscopic repair of paraesophageal hernia. *Arch Surg* 1995; 130: 590–6.
9. Gantert WA. Laparoscopic repair of paraesophageal hiatal hernias. *Jo Am Coll Surgeons* 1998; 186: 428–32; discussion 432–23.
10. Hallissey MT. Paraesophageal hiatus hernia: surgery for all ages. *Ann R Coll Surg Eng* 1992; 74: 23–5.
11. Carlson MA. Management of intrathoracic stomach with polypropylene mesh prosthesis reinforced transabdominal hiatus hernia repair. *J Am Coll Surgeons* 1998; 187: 227–30.
12. Horgan S. Repair of paraesophageal hernias. *Am J Surg* 1999; 177: 354–8.
13. Hashemi M. Laparoscopic repair of large type III hiatal hernia: objective followup reveals high recurrence rate. *J Am Coll Surgeons* 2000; 190: 553–60; discussion 560–1.
14. Mattar SG. Long-term outcome of laparoscopic repair of paraesophageal hernia. *Surg Endosc* 2002; 16: 745–9.
15. Mehta S. Review of outcome after laparoscopic paraesophageal hiatal hernia repair. *Surg Lapar Endosc Perc Tech* 2006; 16: 301–6.
16. Oelschlager BK. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. *Ann Surg* 2006; 244: 481–90.
17. Frantzides CT, Madan AK, Carlson MA, et al. A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. *Arch Surg* 2002; 137: 649–52.
18. Schauer PR. Comparison of laparoscopic versus open repair of paraesophageal hernia. *Am J Surg* 1998; 176: 659–65.
19. Ferri LE. Should laparoscopic paraesophageal hernia repair be abandoned in favor of the open approach? *Surg Endosc* 2005; 19: 4–8.
20. Karmali S. Primary laparoscopic and open repair of paraesophageal hernias: a comparison of short-term outcomes. *Dis Esophagus* 2008; 21: 63–8.
21. Kercher KW. Minimally invasive management of paraesophageal herniation in the high-risk surgical patient. *Am J Surg* 2001; 182: 510–14.

Appendicitis

Peter P. Lopez and Amy De Rosa

Clinical Questions		
Question	Answer	Grade of recommendation
What are the most reliable clinical findings on history and physical examination to rule in or out appendicitis?	Abdominal pain often localized to the epigastrium or periumbilical area followed by anorexia and nausea are the most reliable diagnostic findings on history and physical exam.	C
What is the best laboratory test to make the diagnosis of appendicitis?	Overall laboratory markers of acute inflammation in acute appendicitis remain highly sensitive but relatively nonspecific when it comes to making the diagnosis of appendicitis. No one test has been found to be both highly sensitive and specific for acute appendicitis.	B
Does giving a patient with suspected appendicitis pain medicine decrease the ability to make the diagnosis of appendicitis?	Giving pain medicine to adults and children suspected of acute appendicitis prior to surgical evaluation does not seem to affect diagnostic accuracy or outcomes.	B
What operation is better for treating acute appendicitis?	Data support the use of performing laparoscopic appendectomy for patients with acute appendicitis if the surgical expertise and equipment are available.	B
Does giving prophylactic antibiotics to patients with appendicitis who undergo appendectomy decrease infectious complications?	Antibiotic prophylaxis is effective in preventing postoperative wound infections and intra-abdominal abscesses. The type of antibiotic and preferred time and duration of antibiotic administration needs to be evaluated.	B
What is the best diagnostic imaging modality to diagnose acute appendicitis?	The most accurate imaging modality for making the diagnosis of appendicitis is computed tomography. The routine use of performing CT on all patients suspected to have appendicitis cannot be recommended at this time.	B
Is interval appendectomy necessary?	The routine performance of interval appendectomy after nonoperative treatment of complicated acute appendicitis is not supported. Routine interval appendectomy is not a cost-effective intervention.	C
Should antibiotic treatment alone replace appendectomy for acute appendicitis?	Antibiotics should not be used routinely as the primary treatment of acute appendicitis. Surgery continues to remain the primary option for the treatment of acute appendicitis.	B
Abbreviation: CT, computed tomography.		

Acute appendicitis remains the most common surgical emergency of the abdomen in the United States, occurring in about 250,000 patients each year. The lifetime risk of developing appendicitis is 7%; however, the lifetime rate of an appendectomy is 12% for men and 25% for women. Appendicitis is most frequently seen in patients in their second and fourth decade of life, with a mean age of 31.3 and a median age of 22 years (1).

Early reports of a potentially lethal inflammatory disease process of the right lower quadrant were known as perityphlitis. Reginald Fitz (2) in 1886 first described this inflammatory disease process of the right lower quadrant as appendicitis, including the clinical sequelae of abscess

formation and perforation. The diagnosis of acute appendicitis remains a challenging clinical entity, especially for women of childbearing age and those patients who are at the extremes of age. The timely and accurate recognition of patients with appendicitis requiring urgent surgical and nonsurgical management continues to be the overriding principle in the workup and treatment of patients with suspected appendicitis. Delays in the diagnosis and treatment of acute appendicitis can result in an increased morbidity and mortality.

Important questions to consider in the care of a patient with appendicitis include how to make the diagnosis of appendicitis, whether one treat appendicitis medically

or surgically, and whether one perform an open or laparoscopic appendectomy. Patients with suspected appendicitis are prone to the development of complications, including intra-abdominal abscess formation, wound infection, an increased length of hospital stay, negative appendectomy rate, bleeding, bowel injury, infertility, delayed return to full activity, and mortality.

WHAT ARE THE MOST RELIABLE CLINICAL FINDINGS ON HISTORY AND PHYSICAL EXAMINATION TO RULE IN OR OUT APPENDICITIS?

The clinical diagnosis of appendicitis relies mainly on a detailed history and physical exam (3). By performing a thorough history and physical exam, an experienced clinician can accurately diagnose acute appendicitis in the majority of cases (4). A typical patient will present with vague abdominal pain (usually epigastric region) followed by anorexia and nausea, with or without vomiting. The pain then shifts to the right lower quadrant as the inflammation of the appendix progresses and involves the overlying peritoneum. The common symptoms of appendicitis include abdominal pain—approximately 100%, anorexia—approximately 100%, nausea—90%, and pain migration, typically from the periumbilical area to the right lower quadrant—approximately 50% (5). Occasionally, patients complain of urinary symptoms, diarrhea, or constipation from inflammation adjacent to the ureter, bladder, rectum, or colon. As clinicians have found out, these clinical features are not entirely reliable. The history and physical exam remain the most reliable predictor for the diagnosis of appendicitis. Most patients with appendicitis, except the very young, very old, and those who are neurologically impaired, have some degree of tenderness on palpation of the abdomen. The sequence of symptom appearance in more than 95% of patients with acute appendicitis, is anoxia first, followed by abdominal pain, and vomiting if it occurs. In 1996, a meta-analysis performed by Wagner et al. (6) reported the sensitivity, specificity, and positive likelihood ratio with a 95% confidence interval for findings on the clinical examination characteristic of appendicitis. They reported sensitivity, specificity, and positive likelihood ratio for right lower quadrant pain (0.81, 0.53, 7.31–8.46), fever (0.67, 0.79, 1.94), and anorexia (0.68, 0.36, 1.27).

Physical exam findings are determined by the anatomic position of the inflamed appendix and whether the appendix has ruptured. Vital signs are usually normal in uncomplicated appendicitis with a slight elevation in temperature (by 1°C or 1.8°F) with or without a slight elevation in heart rate. Patients with appendicitis prefer to lie still because motion can increase their pain. If the appendix lies in the classic anterior position, tenderness will be maximal at McBurney's point (7). Rebound tenderness is usually elucidated on palpation of the right lower quadrant. Rovsing's sign is found in some patients with appendicitis when pain is elucidated in the right lower quadrant when palpating the left lower quadrant.

Deviation from these commonly associated physical findings usually are related to the anatomic position of the inflamed appendix. The anatomic location of the appendix

is conveniently describes as paracolic (the appendix lies in the right paracolic gutter lateral to the cecum), retrocecal (the appendix lies posterior to the cecum and may be partially or totally extraperitoneal), preileal (the appendix is anterior to the terminal ileum), postileal (the appendix is posterior to the ileum), promontoric (the tip of the appendix lies in the vicinity of the sacral promontory), pelvic (the tip of the appendix lies in or toward the pelvis), and subcecal (the appendix lies inferior to the cecum) (8). Wakeley (9) performed a postmortem analysis of 10,000 cases and described the frequency of the location of the appendix as follows: retrocecal, 65.3%; pelvic, 31%; subcecal, 2.3%; preileal, 1%; and right paracolic and postileal, 0.4%. A retrocecal appendix can cause fewer anterior abdominal findings and may have pain located in the flank. If the inflamed appendix is located in the pelvis, no abdominal tenderness may be found on abdominal palpation. When the appendix occupies an unusual location, making the diagnosis of appendicitis can be more difficult and may contribute to delays in presentation and treatment.

Answer: Abdominal pain often localized to the epigastrium or periumbilical area followed by anorexia and nausea are the most reliable diagnostic findings on history and physical exam (Grade C recommendation).

WHAT IS THE BEST LABORATORY TEST TO HELP MAKE THE DIAGNOSIS OF APPENDICITIS?

The use of laboratory values in diagnosing appendicitis has been disappointing as no one test has been found to be highly sensitive and specific. The white blood cell (WBC) count was found to be of limited value for making the diagnoses of appendicitis in one study (10), whereas in another study an elevated WBC count was found to more diagnostic of advanced appendicitis than all acute appendicitis (11). The sensitivity of an elevated WBC count above 10,000/ μ l in acute appendicitis is 70–90%, but the specificity is very low (12). A high WBC count ($>18,000$ cells/ μ l) suggests complicated appendicitis with either gangrene or perforation. The diagnostic value of C-reactive protein and erythrocyte sedimentation rate in diagnosing appendicitis have been disappointing (13). In a recent publication by Beltran and colleagues (14), his group found that the use of WBC and C-reactive protein individually or together had a high sensitivity to differentiate patients with and without appendicitis. Still other studies have shown that cytokines and acute-phase reaction proteins, such as interleukin-6 (IL-6), tumor necrosis factor (TNF- α), lipopolysaccharide-binding protein, α 1-glycoprotein (α 1GP), and endotoxin, are elevated in acute appendicitis. The result of many of these studies is that these inflammatory markers are elevated in appendicitis (a high sensitivity), but many are not specific enough to reliably make the diagnosis of acute appendicitis (15–17).

Answer: Overall laboratory markers of acute inflammation in acute appendicitis remain highly sensitive but relatively nonspecific when it comes to making the diagnosis of acute appendicitis. No one test has been found to be both sensitive and specific for the diagnosis of acute appendicitis (Grade B recommendation).

DOES GIVING A PATIENT WITH SUSPECTED APPENDICITIS PAIN MEDICINE DECREASE THE ABILITY TO MAKE THE DIAGNOSIS OF APPENDICITIS?

It has been taught that patients with abdominal pain should not receive narcotics for fear of masking a surgical condition, such as appendicitis in patients who present with acute abdominal pain. In a retrospective study by Aydelotte et al. (18), 75 patients who were diagnosed with acute appendicitis that was confirmed intraoperatively had their charts reviewed. A total of 10 men and 14 women received narcotics prior to surgical evaluation, and 28 men and 14 women were not given narcotics prior to surgical evaluation. In this study there were no statistically significant differences between the groups of patients in regard to length of hospital stay, time to operation, complication rate, perforation rate, and negative appendectomy rate. The authors concluded that the administration of narcotics before evaluation of the patient by a surgeon for acute appendicitis had no effect on patient outcomes in their retrospective study (Level III evidence). In a prospective randomized double-blind study of parenteral tramadol analgesic use versus placebo in 68 emergency department (ED) patients with right lower quadrant pain resulted in significant levels of pain control without concurrent normalization of abdominal pain (19). In another prospective, double-blind study in ED patients with undifferentiated abdominal pain, patients were randomized to receive placebo or morphine sulfate (MS) (20). Diagnostic accuracy did not differ between MS and control groups (64.2% versus 66.7%). Results of this study support the practice of early provision of analgesia to patients with undifferentiated abdominal pain. In a study by Wolfe and associates (21), a prospective double-blind crossover study was performed to determine if giving patients with suspected appendicitis morphine had an impact on their physical exam. The authors concluded from their study that patients with signs of appendicitis who received morphine had significant improvement in their pain without changes in their physical exam. A prospective randomized study was performed in children with a presumptive diagnosis of appendicitis who were randomized to receive parenteral MS or placebo (22). The authors found no difference in the time to surgical decision and no decrease in pain at 30 minutes between MS at a dose of 0.1 mg/kg and placebo. In another randomized study in children with acute abdominal pain, morphine was found to effectively reduce the intensity of pain and did not seem to impede the diagnosis of appendicitis (23).

Answer: Giving pain medicine to adults and children suspected of acute appendicitis prior to surgical evaluation does not seem to affect diagnostic accuracy or outcomes (Grade B recommendation).

WHAT OPERATION IS BETTER FOR TREATING ACUTE APPENDICITIS: LAPAROSCOPIC OR OPEN APPENDECTOMY?

The treatment for acute appendicitis has been to perform an appendectomy through a right lower quadrant incision since its introduction by McBurney (24) in 1894. The first laparoscopic appendectomy was described by Semm (25)

in 1983. This new surgical technique was slow to be accepted because the standard open technique provided excellent therapeutic efficacy combined with low morbidity and mortality rates. The use of laparoscopic appendectomy varies considerable. It seems that the most important determinate of whether a patient will have an open or laparoscopic appendectomy is the preference or experience of treating surgeon, which may very significantly even within an institution (26). During the traditional open appendectomy technique performed through a muscle-splitting incision in the right lower quadrant, the appendix is usually ligated with an absorbable suture. Inversion of the appendiceal stump has been advocated to prevent leakage and fistulization, but studies have shown no difference in complication rates between inversion and simple ligation (27). The peritoneal cavity is usually irrigated after an appendectomy. The skin incision is normally closed without sequelae, although if the wound is grossly contaminated, one may consider delayed primary closure or simply allow the wound to heal by secondary intention (28). Leaving an intraperitoneal drain has not been shown to be useful even in cases of perforated appendix (29).

Is laparoscopic appendectomy better than open appendectomy? The answer to this question depends on the outcomes being measured. Studies have looked at various outcome measures, such as duration of operation, cost of operation, cost of hospitalization, length of hospital stay, the time to return to work, and postoperative pain. Although many of the randomized controlled trials comparing laparoscopic and open appendectomy are plagued by several biases, they represent the best evidence available.

The Cochrane Library published a systemic review of randomized clinical trials comparing open with laparoscopic appendectomy in October 2004 (30). This review included randomized clinical trials comparing laparoscopic appendectomy (LA) versus open appendectomy (OA) in adults and children. The authors included 54 studies, of which 45 compared LA (with or without diagnostic laparoscopy) versus OA in adults. The authors reported that wound infections were less likely after LA than after OA [odds ratio (OR) 0.45; 95% confidence interval (CI) 0.35 to 0.58], but the incidence of intra-abdominal abscesses was increased after LA (OR 2.48; CI 1.45 to 4.21). The duration of LA was 12 minutes (CI 7 to 16) longer to perform than OA. Pain on postop day 1 was reduced by 9 mm (CI 5 to 13 mm) on a 100 mm visual analog scale after LA compared to OA. Hospital stay was shortened by 1.1 day (CI 0.6 to 1.5) after LA. Return to normal activity, work, and sport occurred earlier after LA than after OA. Though the operation costs of LA were significantly higher, the costs outside the hospital were reduced. Five randomized studies on children found similar results to those found in adults. The authors concluded that in clinical settings where surgical expertise and equipment are available and affordable, LA seems to have various advantages over OA. They recommend LA be done for patients with suspected appendicitis especially in young, female, obese, and employed patients (Grade B recommendation).

Answer: The data support the use of performing laparoscopic appendectomy for patients with acute appendicitis if the surgical expertise and equipment are available (Grade B recommendation).

DOES GIVING PROPHYLACTIC ANTIBIOTICS TO PATIENTS WITH APPENDICITIS WHO UNDERGO APPENDECTOMY DECREASE INFECTIOUS COMPLICATIONS?

Appendicitis, once diagnosed, is usually followed by an appendectomy. Two major postoperative complications following appendectomy are wound infections and intra-abdominal abscesses. Prior to the use of antibiotics, there was a 10–40% rate of wound infections and intra-abdominal abscesses after appendectomy (31,32). The use of antibiotics to reduce postoperative morbidity following appendectomy has been studied. In a recent meta-analysis of these studies, the results confirm an overall effect of antibiotics given along with an appendectomy, regardless if administered as either prophylactic (single-dose administration) for “normal removed appendix” or “simple appendicitis” (phlegmonous) or as repetitive treatment in the case of “complicated appendicitis” (gangrenous or perforated) (33).

Acute appendicitis is a polymicrobial infection. In 1938, William Altemeier isolated at least four different organisms per specimen in patients with perforated appendicitis (34). More recent reports demonstrate on average up to 12 organisms per specimen from patients with gangrenous or perforated appendicitis (35). Few bacteria are cultured from peritoneal fluid of patients with acute appendicitis only, however, bacteria are recovered from peritoneal fluid in over 80% patients with gangrenous or perforated appendicitis. *Bacteroides fragilis* and *Escherichia coli* are the two most common organisms, with both present in over 70% of cases (36). In patients with gangrenous and perforated appendicitis, cultures are often positive, and the same organisms are cultured from the wound, peritoneal fluid, and appendiceal wall.

Andersen and colleagues performed a meta-analysis of randomized or controlled clinical trials investigating the use of antibiotics versus placebo for patients with suspected appendicitis who underwent an appendectomy (33). The authors evaluated 45 studies with 9,576 patients; their outcome measures were wound infection, intra-abdominal abscess, hospital length of stay, and mortality. They concluded that the use of antibiotics is superior to placebo in preventing wound infection and intra-abdominal abscesses in patients with acute, gangrenous, and perforated appendicitis. They were unable to determine from their analysis the optimal duration of antibiotic treatment for complicated appendicitis. The authors found that from their data, a single dose of antibiotics may have the same impact as multiple doses, although it is best to administer the first dose preoperatively. The choice of which antibiotics to use should be based on the bacteriology of appendicitis and provide coverage for Gram-negative and anaerobic organisms.

Answer: Antibiotic prophylaxis is effective in preventing postoperative wound infections and intra-abdominal abscesses. The type of antibiotic and preferred time and duration of administration of antibiotic needs to be evaluated (Grade B recommendation).

WHAT IS THE BEST DIAGNOSTIC IMAGING MODALITY TO DIAGNOSE ACUTE APPENDICITIS?

Many different radiologic modalities have been used to diagnose acute appendicitis. The optimal radiologic technique

for acute appendicitis should be accurate, quick, safe, readily available, cost-efficient, and should provide little risk or discomfort to the patient. The use of abdominal ultrasound and computed tomography (CT) has proven extremely useful in diagnosing appendicitis in equivocal cases of appendicitis. However, routine use of these modalities in all patients with suspected appendicitis is not well established (37). Despite the recent increase in the use of these diagnostic tests, such as abdominal ultrasonography and CT, these tests have not increased the diagnostic accuracy of making the diagnosis of acute appendicitis.

The use of plain radiography for diagnosing acute gastrointestinal diseases has been around since the early 1900s. The appearance of an opaque fecalith in the right lower quadrant is often quoted as being the hallmark radiographic finding in acute appendicitis, but less than 5–8% of patients present with this finding (38). Other common but nonspecific findings for acute appendicitis on plain films include localized paralytic ileus, loss of the cecal shadow, blurring of the right psoas muscle, and rightward scoliosis of the lumbar spine (39). In a recent study of 821 consecutive patients hospitalized for suspected appendicitis, no individual radiographic finding was highly sensitive or specific in making the diagnosis of appendicitis (40). Plain abdominal radiographs may be indicated when other acute abdominal conditions, such as gastric or duodenal perforation, intestinal obstruction, or ureteral calculus, may be the cause of right lower quadrant abdominal pain (41). Overall, plain abdominal radiographs are not cost-effective and lack both sensitivity and specificity in the diagnosis of appendicitis (Grade B and C recommendations).

Ultrasound has been used to diagnose appendicitis since Deutsch and Leopold (42) first visualized the inflamed appendix in 1981. Ultrasound has not been used frequently to diagnose appendicitis because of the interference of the ultrasound image by overlying bowel gas, the slow development of a transducer with enough spatial resolution to pick up small structures such as the appendix, and the fact that these images and their interpretation are highly dependent on operator technical skills (8). The inflamed appendix as seen by ultrasound includes the following findings: an appendix of 7 mm or more in anteroposterior diameter; an immobile, thick-walled, noncompressible luminal structure seen in cross-section referred to as a target lesion; or the presence of an appendicolith, a blind-ending structure consisting of anechoic lumen surrounded by mucosa and a hypoechoic thickened wall adjacent to the cecum (43). Despite these well-described ultrasound findings, there is no evidence-based standard of findings by which an individual radiologist will use to make the diagnosis of appendicitis. In a prospective study by Rettenbacher et al. (44) using ultrasound to diagnose appendicitis, the authors used six different ultrasound findings to diagnose appendicitis; unfortunately, they did not state whether all six of the findings were necessary to make the diagnosis of appendicitis or if they could have used just one or two to make the diagnosis. In a recent systemic review of the use of ultrasound to diagnosis acute appendicitis in adults and adolescent patients, the diagnostic accuracy of using graded compression ultrasound (US) was reported to have an overall sensitivity of 0.86 (CI 0.83–0.88) and a specificity of 0.81 (CI 0.78–0.84) with a positive likelihood ratio of 5.8 (CI 3.5–9.5) (45) (Level IIb evidence).

CT has been used as a diagnostic modality for acute abdominal pain since it became available in the late 1970s. Findings strongly suggestive of acute appendicitis on standard abdominal CT scan include (1) a thick wall ($>2\text{mm}$), often with "targeting" (concentric thickening of the inflamed appendix wall); (2) increased diameter of the appendix ($>7\text{mm}$); (3) an appendicolith; (4) a phlegmon or abscess; or (5) free fluid (46). Stranding of the adjacent fatty tissues in the right lower quadrant is also commonly associated with acute appendicitis. The top four CT findings suggestive of appendicitis are an enlarged appendix, appendiceal wall thickening, appendiceal wall enhancement, and periappendiceal fat stranding (47,48). However, if air is seen in the appendix or if the appendiceal lumen is filled with contrast and there are no other abnormalities seen on CT, these findings virtually eliminate appendicitis as a diagnosis. Appendicitis cannot be excluded by CT if the appendix is not visualized on the scan. CT is also useful in diagnosing an appendiceal abscess and can be used to guide percutaneous drainage of the abscess. CT can be helpful in diagnosing other causes of acute abdominal pain in patients suspected of acute appendicitis.

The performance of CT scans to evaluate right lower quadrant pain has increased considerably since Rao and colleagues (49) reported an accuracy rate of 98% using CT with rectal contrast in diagnosing acute appendicitis. Rao et al. also reported that the use of CT at their institution decreased the rate of removal of a normal appendix from 20% before the introduction of CT scanning to 7% after (50). Other authors have not found CT to be so accurate. Perez et al. (51) found the accuracy of CT to diagnosis appendicitis to be 80%. Morris et al. (52) reported a diagnostic accuracy of CT of 90% at their institution. In a study performed by Holloway and associates (53), using a well-defined CT imaging protocol as an adjunct to the clinical diagnosis of acute appendicitis, they found the accuracy of CT to be 97.8% with a negative appendectomy rate of 3%. The authors also reported on 104 patients who underwent appendectomy without the CT protocol who had a negative appendectomy rate of 12.5%. In a retrospective review of CT use in children suspected of appendicitis, a normal appendix was removed in 7% of children who underwent CT prior to appendectomy, 11% of children who underwent US prior to appendectomy, and 8% of children with no preoperative radiologic study (54).

Many studies have found CT to be accurate in diagnosing acute appendicitis, but there is still controversy regarding the optimal CT technique for patients with suspected appendicitis. Three more common CT techniques used to diagnose appendicitis include unenhanced CT of the abdomen and pelvis, the use of either oral and/or intravenous contrast CT of the abdomen and pelvis, and focused appendiceal CT using rectally administered contrast. Every institution has their own preference to which CT technique they use to diagnose appendicitis, all of which seem to be accurate.

In a systemic review performed by van Redan et al. (55) comparing graded compression US to CT in the diagnosis of appendicitis, the authors found the respective mean sensitivities for CT and graded compression US were 91% (95% CI 84–95%) and 78% (95% CI 67–86%) ($p < 0.017$); the respective mean specificities for CT and graded compression US were 90% (95% CI 85–94%) and 83% (95% CI

76–88%) ($p < 0.037$). Calculated positive likelihood ratios for CT and graded compression US were 9.29 (95% CI 6.86–12.58) and 4.5 (95% CI 3.03–6.68), respectively ($p = 0.011$). The authors concluded from their meta-analysis of head-to-head comparison studies in patient populations with a high prevalence of appendicitis that CT was found to have a better test performance than did graded compression US in the diagnosis of acute appendicitis. The authors recommend the use of CT in patients suspected of acute appendicitis (Level IIb evidence).

Should CT be used routinely in the diagnostic evaluation of patients suspected of appendicitis? Because of the increasing reports of excellent accuracy rates of CT diagnosing appendicitis, some have called for its routine use for all patients with possible appendicitis (51,56–58). Others have questioned the need for routine use of CT for all patients especially those with classic clinical presentations. McCay and Shepherd (59) recommend only ordering CT for patients presenting to the emergency room suspected of having appendicitis if their Alvarado score (60) is between 4 and 6. The authors do not recommend a CT if the Alvarado score is lower than 3, and they recommend a surgical consult for patients with an Alvarado score of 7 or more. In a prospective randomized study of patients presenting to the emergency room for possible appendicitis comparing clinical assessment versus CT, the reported diagnostic accuracy was 90% for clinical assessment and 92% for CT (61). The authors concluded that clinical assessment unaided by CT reliably identifies patients with acute appendicitis who need an operation. They do not advocate the routine use of CT for diagnosis of suspected appendicitis.

In a prospective randomized study subsequently performed in women of childbearing age who presented to the emergency room with the suspected diagnosis of appendicitis, women were randomized to the clinical assessment-only arm or the CT arm (62). In this study, the reported accuracy for the diagnosis of appendicitis was 93% for both clinical assessment and CT. The authors concluded from the data that a CT scan reliably identifies women of childbearing age who need an appendectomy, and CT seems to be as good as clinical assessment alone. In a recent retrospective study, the negative appendectomy rate for patients who had a CT scan prior to appendectomy was 6%, and it was also 6% for patients who underwent an appendectomy based on clinical exam alone (63). The study also found that preoperative CT scans increased the appendectomy rate only in patients with a low clinical suspicion of appendicitis. In a retrospective study in children reported by Martin and associates (64), the liberal use of CT scans did not decrease the negative appendectomy rate. Thus, selective use of CT scans seems more appropriate than the routine use of CT in diagnosing suspected appendicitis, the CT scan should be obtained in clinical settings in which other sources of pathology other than appendicitis may cause pain or the clinical history is not helpful in making the diagnosis of appendicitis.

Answer: The most accurate imaging modality for making the diagnosis of appendicitis is CT. The routine use of performing CT on all patients suspected of appendicitis cannot be recommended at this time (Grade B recommendation).

IS INTERVAL APPENDECTOMY NECESSARY?

Patients presenting with a periappendiceal mass or abscess diagnosed preoperatively by physical examination or imaging studies can be treated with antibiotics and then possibly have their periappendiceal abscess drained by image-guided percutaneous catheter (65). With the increased use of CT in the work-up of acute appendicitis, the ability to identify complicated appendicitis preoperatively has allowed for the utilization of initial nonoperative therapy (66). Generally, antibiotics for 7–14 day with or without catheter drainage has been necessary to treat patients with complicated appendicitis. An interval appendectomy has been advocated after the abscess and surrounding inflammation have resolved usually six to eight weeks after initial nonoperative treatment to prevent recurrent appendicitis and treat other tumor pathology of the cecum and appendix (67). Alternative treatment options of complicated appendicitis have included early aggressive resection (68), or initial conservative treatment with interval appendectomy only if symptoms recur (69,70). Immediate appendectomy may be technically demanding because of the distorted anatomy and the challenges faced when closing an inflamed/necrotic appendiceal stump. Many times the immediate exploration ends up in an ileocecal resection or a right-sided hemicolectomy due to inflammation distorting the tissue planes or a suspicion of malignancy. Following successful nonsurgical treatment of a periappendiceal mass, the need for interval appendectomy has recently been questioned as the risk of recurrence is relatively small, 0.2–7% (8,71,72).

In a two other recent retrospective studies, it was found that children presenting with complicated appendicitis could be successfully treated with conservative treatment followed by appendectomy (73,74). Roach et al. (73) concluded from their data that children who presented with prolonged symptoms and a discrete appendiceal abscess or phlegmon, drainage and performance of a delayed appendectomy should be the treatment of choice. In another study done on children with complicated appendicitis, the benefits of laparoscopic interval appendectomy included that the surgery could be safely be performed in children and that it was associated with a shorter hospital stay and minimal morbidity, analgesia, and scarring. These authors recommended that interval laparoscopic appendectomy be routinely performed because it eliminates the risk of recurrent appendicitis and serves to excise undiagnosed carcinoid tumors (75).

In a large retrospective study performed by Kaminski et al. (76), 32,938 patients were hospitalized with acute appendicitis. Emergency appendectomy was performed in 31,926 (97%) patients. Nonoperative treatment was used initially in 1,012 patients (3%). Of these, 148 (15%) had an interval appendectomy, and the remaining 864 (85%) did not. In their study, only 39 patients (5%) had recurrence of appendicitis after a median follow-up of four years. Males were more likely to have recurrence of their symptoms than females. Median length of hospital stay was four days for the admission for recurrent appendicitis compared with six days for the interval appendectomy admission. The authors concluded that because most patients with acute appendicitis undergo appendectomy initially, and those who are treated nonoperatively have a low recurrence rate

of appendicitis; they could not justify the practice of routine interval appendectomy after initial successful nonoperative treatment of appendicitis. In a similar retrospective study in children reported by Paupong et al. (77), there were 6,439 patients, of which 6,367 (99%) underwent initial appendectomy for acute appendicitis. Seventy-two (1%) patients were initially managed nonoperatively, and 11 patients had interval appendectomy. Of the remaining 61 patients without interval appendectomy, 5 (8%) developed recurrent appendicitis. The authors concluded that because recurrent appendicitis is rare in children after successful nonoperative treatment of perforated appendicitis, performance of routine interval appendectomy is not necessarily indicated.

Stevens and de Vries (78) reported on their experience of performing an interval appendectomy only after symptoms developed rather routinely in their patients with complicated appendicitis. They concluded that the rate of appendectomies performed dropped by 63% and the total length of hospital stay also decreased by four days. A group from China reported that performing an interval appendectomy only after symptoms develop was more cost-effective than performing routine interval appendectomy (79). In their study the authors showed that performance of routine interval appendectomy would increase the cost per patient by 38% compared with follow-up and appendectomy after recurrence of symptoms.

In a systemic review of the nonsurgical treatment of appendiceal abscess or phlegmon, the need for an interval appendectomy was evaluated (80). Findings from the meta-analysis: nonsurgical treatment fails in 7.2% of cases (CI 4.0–10.5%), the risk of recurrent symptoms is 7.4% (CI 3.7–11.1%), the risk of finding malignant disease is 1.2% (CI 0.6–1.7%), and the risk of finding an important benign disease is 0.7% (CI 0.2–11.9%) during follow-up. From the meta-analysis (mainly from retrospective studies), the authors support the practice of nonsurgical treatment without interval appendectomy in patients with appendiceal abscess or phlegmon.

Answer: The routine performance of interval appendectomy after nonoperative treatment of complicated acute appendicitis is not supported. Routine interval appendectomy is not a cost-effective intervention (Grade B recommendation).

SHOULD ANTIBIOTIC TREATMENT REPLACE APPENDECTOMY FOR ACUTE APPENDICITIS?

Nonoperative treatment of acute appendicitis with antibiotics alone has been reported to be successful (81,82). Andersson writes that an increasing amount of circumstantial evidence suggests that not all patients with appendicitis will progress to perforation and that resolution may be a common event (83,84). Other evidence of resolving appendicitis are reports of a history of recurrent appendicitis, obviously a consequence of spontaneous resolution, which can be found in up to 6.5% of patients operated on for appendicitis (85). In the past, appendectomy has been associated with higher morbidity and mortality, especially in older patients, those with perforation and sepsis, and those who have a normal appendix at the time of appendectomy. To date, unfavorably high rates of recurrent

symptoms of appendicitis (up to 70% at one year) have been reported in patients who have received antibiotic treatment (86,87).

In 1995, Eriksson and Granstrom (88) reported a randomized controlled trial of appendectomy versus antibiotics alone in 40 patients suspected to have appendicitis who presented with abdominal pain for less than 72 hours. Twenty patients underwent surgery, and 20 patients received intravenous antibiotics for two days, followed by an eight-day course of oral antibiotics. The authors concluded that antibiotic treatment in patients with acute appendicitis was as effective as surgery. However, they reported a 15% negative appendectomy rate for the surgery group and a 40% recurrence rate of appendicitis in the antibiotic-treated group, which led to an appendectomy within one year of treatment. A recent multicenter trial randomly allocated 252 male patients (age 18–50) to either antibiotic treatment (intravenous cefotaxime and tinidazole for 2 days followed by oral ofloxacin and tinidazole for 10 days) or appendectomy for acute uncomplicated appendicitis; the authors concluded that antibiotic treatment could serve as an alternative to appendectomy (89). The complication rate among the surgery group was 14%

(17/124), mainly wound infections. Of the 128 patients enrolled in the antibiotic group, 15 (12%) were operated on within the first 24 hours due to lack of improvement in symptoms and apparent local peritonitis. The operation showed that seven patients (5%) had perforation. A total of 113 patients were successfully treated with antibiotics and were sent home for oral antibiotic therapy for 10 days. The recurrence rate within one year was 15% (16 patients) in the group treated with antibiotics. Overall the success rate of conservative management of acute appendicitis with antibiotics is ~70% at best for male patients with unequivocal clinical and laboratory signs of uncomplicated appendicitis. These conclusions have, however, been made on the basis of only one year of follow-up data, and the continued lifetime risk for and associated morbidity and mortality of appendicitis remain to be investigated. The recommendation of antibiotic treatment as an alternative to surgery for patients with acute appendicitis can not be made at this time (90).

Answer: Antibiotics should not be used routinely as the primary treatment of acute appendicitis. Surgery continues to remain the primary treatment option for the treatment of acute appendicitis (Grade B recommendation).

Levels of Evidence

Subject	Years	Ref.	Level of evidence	Strength of recommendation	Findings
Physical findings	1996–2003	3–6	IIC	C	Abdominal pain localized to the right lower quadrant
Laboratory tests	1989–2006	10–17	IIb	B	WBC is best, but no test is both sensitive and specific
Pain medicine	2000–2007	18–23	IIb	B	Pain meds are okay to give
Best operation	1894–2004	24–26, 30	IIb	B	Laparoscopic appendectomy
Antibiotic use in appendicitis	1995–2005	32, 33, 35, 36	IIb	B	Antibiotics decrease infectious complications
Imaging modality	1988–2008	8, 37–64	IIb	B	CT scan most accurate
Interval appendectomy	1993–2007	8, 67–84	IIb	B	Interval appendectomy not recommended
Treatment antibiotics only	1995–2007	85–90	IIb	B	Surgery still treatment of choice

Abbreviations: CT, computed tomography; WBC, white blood cell count.

REFERENCES

- Addiss DG, Schaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990; 132: 910–25.
- Fitz RH. Perforating inflammation of the vermiform appendix: with special reference to its early diagnosis and treatment. *Trans Assoc Am Phys* 1886; 1: 107.
- Bergeron E, Richer B, Gharib R, et al. Appendicitis is a place for clinical judgement. *Am J Surg* 1999; 177: 460–2.
- Silen W. Cope's Early Diagnosis of the Acute Abdomen, 19th edition. New York: Oxford University Press, 1996.
- Shelton T, McKinlay R, Schwartz RW. Acute appendicitis: current diagnosis and treatment. *Curr Surg* 2003; 60: 502–5.
- Wagner J, McKinney WP, Carpenter JL. Does this patient have appendicitis? *JAMA* 1996; 276: 1589–94.
- McBurney C. Experience with early operative interference in cases of disease of the vermiform appendix. *NY State Med J* 1889; 50: 676.
- Prystowsky JP, Pugh CM, Nagle AP. Appendicitis. *Curr Prob Surg* 2005; 42: 685–742.
- Wakeley CP. The position of the vermiform appendix as ascertained by an analysis of 10,000 cases. *J Anat* 1933; 67: 277–83.
- Vermeulen B, Morabia A, Unger PF. Influence of white blood cell count on surgical decision making in patients with abdominal pain in the right lower quadrant. *Eur J Surg* 1995; 161: 483–6.
- Andersson RE, Hugander AP, Ghazi SH, et al. Diagnostic value of disease history, clinical presentation, and inflammatory parameters of appendicitis. *World J Surg* 1999; 23: 133–40.
- Hoffmann J, Raussen O. Aids in the diagnosis of acute appendicitis. *Br J Surg* 1989; 76: 774–6.
- Jaye DL, Waites KB. Clinical applications of C-reactive protein in pediatrics. *J Pediatr Infect Dis J* 1997; 16: 735–46.
- Beltran MA, Almonacid J, Vicencio A, et al. Predictive value of white blood cell count and C-reactive protein in children with appendicitis. *J Pediatr Surg* 2007; 42: 1208–14.
- Sack U, Biederer B, et al. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surg* 2006; 6: 15.

16. Paaanen H, Mansikka A, Laato M, et al. Novel serum inflammatory markers in acute appendicitis. *Scand J Clin Lab Invest* 2002; 62: 579-84.
17. Yildirim O, Solak C, Kocer B, et al. The role of serum inflammatory markers in acute appendicitis and their success in preventing negative laparotomy. *J Invest Surg* 2006; 19: 345-52.
18. Aydelotte JD, Collen JF, Martin R. Analgesic administration prior to surgical evaluation for acute appendicitis. *Curr Surg* 2004; 61: 373-5.
19. Manadevan M, Graff L. Prospective randomized double blind study of analgesic use for ED patients with right lower quadrant abdominal pain. *Am J Emerg Med* 2000; 18: 753-6.
20. Thomas SH, Silen W, Cheema F, et al. Effects of morphine analgesia on diagnostic accuracy in emergency department patients with abdominal pain: a prospective, randomized trial. *J Am Coll Surg* 2003; 196: 18-31.
21. Wolfe JM, Smithline HA, Phippen S, et al. Does morphine change the physical examination in patients with acute appendicitis? *Am J Emerg Med* 2004; 22: 280-5.
22. Bailey B, Bergeron S, Gravel J, et al. Efficacy and impact of intravenous morphine before surgical consultation in children with right lower quadrant pain suggestive of appendicitis: a randomized controlled trial. *Ann Emerg Med* 2007; 50: 371-8.
23. Green R, Bulloch B, Kabani A, et al. Early analgesia for children with acute abdominal pain. *Pediatrics* 2005; 116: 978-83.
24. McBurney C. The incision made in the abdominal wall in cases of appendicitis, with description of a new method of operating. *Ann Surg* 1894; 20: 38-43.
25. Semm K. Endoscopic appendectomy. *Endoscopy* 1983; 15: 59-64.
26. Cervini P, Smith LC, Urbach DR. The surgeon on call is a strong factor determining the use of a laparoscopic approach for appendectomy. *Surg Endosc* 2002; 16: 1774-7.
27. Street D, Bodai BI, Owens LJ, et al. Simple ligation vs. stump ligation in appendectomy. *Arch Surg* 1988; 123: 689.
28. Cohn SM, Giannotti G, Ong AW, et al. Prospective randomized trial of two wound management strategies for dirty abdominal wounds. *Ann Surg* 2001; 233: 409-13.
29. Greenall MJ, Evans M, Pollack AV. Should you drain a perforated appendix? *Br J Surg* 1978; 65: 880.
30. Sauerland S, Lefering R, Neugebauer EAM. Laparoscopic versus open laparoscopic surgery for suspected appendicitis. *Cochrane Database of Systemic Reviews* 2004; 4.
31. Fischer AC. Acute appendicitis. In: Cameron JL, ed., *Current Surgical Therapy*, 7th edition. St Louis, MO: Mosby, 2001: 267-72.
32. Almqvist P, Leandroer L, Tornqvist A. Timing of antibiotic treatment in non-perforated gangrenous appendicitis. *Eur J Surg* 1995; 161: 431-3.
33. Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendectomy. *Cochrane Database of Systemic Review* 2005; 3.
34. Altmeier WA. The bacterial flora of acute perforated appendicitis with peritonitis. A bacteriological study based upon a hundred cases. *Ann Surg* 1938; 107: 517-28.
35. Bennion RS, Thompson JE Jr, Baron EJ, et al. Gangrenous and perforated appendicitis with peritonitis: treatment and bacteriology. *Clin Ther* 1990; 12(Suppl C): 31-44.
36. Bennion RS, Thompson JE. Appendicitis. In: Fry DE, ed., *Surgical Infections*. Boston: Little, Brown, 1995: 241-50.
37. Old JL, Dusing RW, Yap W, et al. Imaging for suspected appendicitis. *Am Fam Phys* 2005; 71: 71-8.
38. Berry J Jr, Malt RA. Appendicitis near its centenary. *Ann Surg* 1984; 200: 567-75.
39. Graffeo CS, Counselman FL. Appendicitis. *Emerg Med Clin North Am* 1996; 14: 653-71.
40. Rao PM, Rhea JT, Rao JA, et al. Plain abdominal radiography in clinically suspected appendicitis: diagnostic yield, resource use, and comparison with CT. *Am J Emerg Med* 1999; 17: 325-8.
41. Boleslawski E, Panis Y, Benoist S, et al. Plain abdominal radiography as a routine procedure for acute abdominal pain of the right lower quadrant: prospective evaluation. *World J Surg* 1999; 23: 262-4.
42. Deutsch A, Leopold GR. Ultrasonic demonstration of the inflamed appendix: case report. *Radiology* 1981; 140: 163-4.
43. Adams DH, Fine C, Brooks DC. High-resolution real-time ultrasonography. A new tool in the diagnosis of acute appendicitis. *Am J Surg* 1988; 155: 93-7.
44. Rettenbacher T, Hollerweger A, Macheiner P, et al. Presence or absence of gas in the appendix: additional criteria to rule out or confirm acute appendicitis-evaluation with US. *Radiology* 2000; 214: 183-7.
45. Terasawa T, Blackmore CC, Bent S. Systemic review: computed tomography and ultrasonography to detect acute appendicitis in adults and adolescents. *Ann Intern Med* 2004; 141: 537-46.
46. Melton GB, Duncan MD. Acute appendicitis. In: Cameron JL, ed., *Current Surgical Therapy*, 9th edition. St Louis, MO: Mosby, 2008; 257-61.
47. Choi D, Park H, Lee YR, et al. The most useful findings for diagnosing acute appendicitis in contrast enhanced helical CT. *Acta Radiol* 2003; 44: 574-82.
48. Hansen AJ, Young SW, De Petris G, et al. Histologic severity of appendicitis can be predicted by computed tomography. *Arch Surg* 2004; 139: 1304-8.
49. Rao PM, Rhea JT, Novelline RA, et al. Effect of computed tomography of the appendix on treatment of patients and use of hospital resources. *N Engl J Med* 1998; 338: 141-6.
50. Rao PM, Rhea JT, Rattner DW, et al. Introduction of appendiceal CT: impact on negative appendectomy and appendiceal perforation rates. *Ann Surg* 1999; 229: 344-9.
51. Perez J, Barone JE, Wilbanks TO, et al. Liberal use of computed tomography scanning does not improve the diagnostic accuracy in appendicitis. *Am J Surg* 2003; 185: 194-7.
52. Morris KT, Kavanagh M, Hansen P, et al. The rational use of computed tomography scans in the diagnosis of appendicitis. *Am J Surg* 2002; 183: 547-50.
53. Holloway JA, Westerbuhr LM, Chain J, et al. Is appendiceal computed tomography in a community hospital helpful? *Am J Surg* 2003; 186: 682-4.
54. Patrick DA, Janik JE, Janik JS, et al. Increased CT scan utilization does not improve the diagnostic accuracy of appendicitis in children. *J Pediatr Surg* 2003; 38: 659-62.
55. Van Randen A, Bipat S, Zwindermann AH, et al. Acute Appendicitis: Meta-analysis of diagnostic performance of CT and graded compression US related to prevalence of disease. *Radiology* 2008.
56. Peck J, Peck A, Peck C. The clinical role of noncontrast helical computed tomography in the diagnosis of appendicitis. *Am J Surg* 2000; 180: 133-6.
57. Rhea JT, Rao PM, Novelline RA, et al. A focused appendiceal CT technique to reduce the cost of caring for patients with clinically suspected appendicitis. *Am J Roentgenol* 1997; 169: 113-18.
58. Pena BM, Taylor GA, Lund DP, et al. Effect of computed tomography on patient management and costs in children with suspected appendicitis. *Pediatrics* 2001; 107: 1231.
59. McKay R, Shepherd J. The use of the clinical scoring system by Alvarado in the decision to perform computed tomography for acute appendicitis in the ED. *Am J Emerg Med* 2007; 25: 489-93.
60. Alvarado A. A practical score for early diagnosis of acute appendicitis. *Ann Emerg Med* 1986; 15: 557-65.

61. Hong JJ, Cohn SM, Ekeh AP, et al. A prospective randomized study of clinical assessment versus computed tomography for the diagnosis of acute appendicitis. *Surg Infect (Larchmt)* 2003; 3: 231–9.
62. Lopez PP, Cohn SM, Popkin CA, et al. The use of computed tomography scan to rule out appendicitis in women of child-bearing age is as accurate as clinical exam: a prospective randomized trial. *Am Surg* 2007; 73: 1232–6.
63. Petrosyan M, Estrada J, Chan S, Somers S, et al. CT scan in patients with suspected appendicitis: clinical implications for the acute care surgeon. *Eur Surg Res* 2008; 40: 211–19.
64. Martin AE, Vollman D, Adler B, et al. CT scans may not reduce the negative appendectomy rate in children. *J Pediatr Surg* 2004; 39: 886–90.
65. Von Sonnenberg E, Wittich GR, Casola G, et al. Periappendiceal abscesses: percutaneous drainage. *Radiology* 1987; 163: 23–6.
66. Frei SP, Bond WF, Bazuro RK, et al. Appendicitis outcomes with increased computed tomographic scanning. *Am J Emerg Med* 2008; 26: 39.
67. Nitecki S, Assalia A, Schein M. Contemporary management of appendiceal mass. *Br J Surg* 1993; 30: 18.
68. Thompson JE Jr, Bennion RS, Schmit PJ, et al. Cecetomy for complicated appendicitis. *J Am Coll Surg* 1994; 179: 135.
69. Adalla SA. Appendiceal mass: interval appendectomy should not be the rule. *Br J Clin Pract* 1996; 50: 168.
70. Ein SH, Shandling B. Is interval appendectomy necessary after rupture of an appendiceal mass? *J Pediatr Surg* 1996; 31: 849.
71. Nguyen DB, Silen W, Hodin RA. Interval appendectomy in the laparoscopic era. *J Gastrointest Surg* 1999; 3: 189–93.
72. Andersson RE, Petzhold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. *Ann Surg* 2007; 246: 741–8.
73. Roach JP, Patrick DA, Bruny JL, et al. Complicated appendicitis in children: a clear role for drainage and delayed appendectomy. *Am J Surg* 2007; 194: 769–72.
74. Bufo AJ, Shah RS, Li MH, et al. Interval appendectomy for perforated appendicitis in children. *J Laparoendosc Adv Surg Tech A* 1998; 8: 209–14.
75. Owen A, Moore O, Marven S, et al. Interval laparoscopic appendectomy in children. *J Laparoendosc Adv Surg Tech A* 2006; 16: 308–11.
76. Kaminski A, Liu IL, Appelbaum H, et al. Routine interval appendectomy is not justified after initial nonoperative treatment of acute appendicitis. *Arch Surg* 2005; 140: 897–901.
77. Paupong D, Lee SL, Haigh PI, et al. Routine interval appendectomy in children is not indicated. *J Pediatr Surg* 2007; 42: 1500–3.
78. Stevens CT, de Vries JE. Interval appendectomy as indicated rather than as routine therapy: fewer operations and shorter hospital stays. *Ned Tijdschr Geneesk* 2007; 31: 151: 759–63.
79. Lai HW, Loong CC, Wu CW, et al. Watchful waiting versus interval appendectomy for patients who recovered from acute appendicitis with tumor formation: a cost-effectiveness analysis. *J Chin Med Assoc* 2005; 68: 431–4.
80. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. *Ann Surg* 2007; 246: 741–8.
81. Groetsch SM, Shaughnessy JM. Medical management of acute appendicitis: a case report. *J Am Board Fam Prac* 2001; 14: 225–6.
82. Salim AS, Ahmed TM. Antibiotic treatment of acute appendicitis—initial observations. *Saudi Med J* 2001; 22: 643–4.
83. Migraine S, Atri M, Bret PM, et al. Spontaneously resolving acute appendicitis: clinical and sonographic documentation. *Radiology* 1997; 205: 55–8.
84. Andersson RE. The natural history and traditional management of appendicitis revisited: spontaneous resolution and predominance of prehospital perforations imply that a correct diagnosis is more important than an early diagnosis. *World J Surg* 2007; 31: 86–92.
85. Barber MD, McLaren J, Rainey JB. Recurrent appendicitis. *Br J Surg* 1997; 84: 110–12.
86. Humes DJ, Simpson J. Acute appendicitis. *Br Med J* 2006; 333: 530–4.
87. Cobben LP, de Van Otterloo AM, Puylaert JB. Spontaneously resolving appendicitis: frequency and natural history in 60 patients. *Radiology* 2000; 215: 349–52.
88. Eriksson S, Granstrom L. Randomized controlled trial of appendectomy versus antibiotic therapy for acute appendicitis. *Br J Surg* 1995; 82: 166–9.
89. Styruud J, Eriksson S, Nilsson I, et al. Appendectomy versus antibiotic treatment in acute appendicitis: a prospective multicenter randomized controlled trial. *World J Surg* 2006; 30: 1033–7.
90. Soreide K. Should antibiotic treatment replace appendectomy for acute appendicitis? *Nat Clin Pract Gastroenterol Hepatol* 2007; 4: 584–5.

Lower Gastrointestinal Bleeding

Steven D. Schwartzberg

Key Issues in the Management of Lower Gastrointestinal Bleeding		
Question	Answer	Grade of recommendation
What is the diagnostics accuracy of Tc-99 sulfur colloid injection versus Tc-99-tagged red cells?	Tc-99-labeled RBCs appears superior to Tc-99 sulfur colloid injection.	B
	For all comers, about half of the scans will be positive. Angiography is not indicated when scintigraphy is negative. Positive scans should be followed up with further localization studies to improve anatomic accuracy.	C
What is the diagnostic accuracy of colonoscopy, radionuclide scanning, and angiography in the setting of LGIB?	Colonoscopy when available is the most accurate method of diagnosing LGIB and is the gold standard against which other studies are measured offering control of some lesions as well. Scintigraphy may offer valuable information for angiographic screening but is insufficient for operative planning alone. MDCT is emerging as a valuable noninvasive modality but has not been sufficiently studied to determine whether it can be used as a sole modality for operative planning.	C
		C
		C
What is the ideal order of diagnostic test in the setting of LGIB?	Colonoscopy is the ideal single test in the face of LGIB. In the event this is not available and an intervention is required, scintigraphy or MDCT should be performed to rule out proximal sources in the small bowel prior to angiographic embolization/vasopressin or surgical resection.	C
		C
What is the clinical effectiveness intra-arterial vasopressin infusion versus transcatheter embolization?	The major drawbacks of vasopressin therapy are coronary ischemia and rebleeding after cessation of therapy. Cessation of bleeding occurs in up to 90% of patients. Some studies have shown significant rebleeding after therapy is stopped. On the other hand, embolic therapy shows a similar rate of initial hemorrhage control with less early rebleeding, however, there is at about a 10% risk of significant colon ischemia. Super-selective embolism has not eliminated ischemia as a risk. The late rebleeding risk is 10–15% with either techniques.	No recommendations
What are the criteria for surgical intervention in LGIB and what operation should be done?	Patients who bleed 2 or more units of blood should receive an evaluation to localize the source of bleeding expeditiously.	C
	Clinical stability and available testing options will determine to what extent localization studies can be performed so that excessive transfusion is avoided (>10 units).	C
	Persistent bleeding with true anatomic localization may allow for segmental resection otherwise subtotal colectomy with ileorectostomy should be performed.	C
Abbreviations: LGIB, lower gastrointestinal bleeding; MDCT, multidetector computed tomography; RBCs, red blood cells.		

INTRODUCTION

The diagnosis of lower gastrointestinal bleeding (LGIB) begins with two basic principles. First, the surgeon must have a clear picture of the nature of the blood loss, differentiating bright red blood per rectum from maroon stool and these from true melena. This gives the physician a first-order approximation as to the site of bleeding, leading to the second principle, which is to rule out an upper gastrointestinal sources very early in the work-up. There are classic challenges for selecting the best therapeutic option for a given patient that require surgeons to make thoughtful

choices based on the available data in the context of the status of individual patients. The other realization that must be confronted is that each hospital is different in terms of resource availability. Nuclear medicine or angiographic expertise may be limited to weekday daylight or not available at all in some settings. These realities force surgeons to have intimate familiarity of the effectiveness of all the diagnostic and therapeutic options required in the diagnosis and management of LGIB. This is particularly challenging because the nature of the clinical problem does not lend itself easily to randomized controlled trials. Review of the available literature reveals few prospective studies as well.

WHAT IS THE DIAGNOSTICS ACCURACY OF TC-99 SULFUR COLLOID INJECTION VERSUS TC-99-TAGGED RED CELLS?

In 1982, Alavi reported on the utility of intravenous administration of 99m-technetium sulfur colloid (1) (level IV evidence). His group cited potential hemorrhage detection at bleeding rates as low as 0.05cc/min allowing for detection even in patients with negative arteriography. In 1983 Winn retrospectively reviewed 63 patients studied with this technique (2) (level IV evidence). He found that the likelihood of a positive arteriogram was 15% when 99m-technetium sulfur colloid was negative. Miskowak demonstrated 85% sensitivity and 100% specificity when Tc-labeled red cells were used to diagnose LGIB (3) (level IV evidence). Markisk found similar accuracy (91%) and no occurrence of positive angiography when scintigraphy was negative (4) (level IV evidence). There is little comparative literature except that of Siddiqui who performed a comparison of Tc-99m sulfur colloid and Tc-99m-tagged red blood cells (RBCs) scintigraphy in 27 patients prospectively (5) (level Ib evidence). They found far greater sensitivity in the tagged RBC group, with 70% of the studies destined to be positive diagnostic in the first hour, although animals studies demonstrated similar sensitivity for both techniques (6). Other retrospective studies have shown similar findings when using Tc-99m-labeled RBCs, suggesting high sensitivity, somewhat lesser specificity, and good utility as a screen for angiography because contrast studies are rarely positive in scintigraphy negative patients (7–17) (level IV evidence). It is pointed out in nearly all of these studies that the anatomic accuracy of Tc-99-labeled positive scan is in the 70–85% range. Rapid transit of tagged hemorrhaged red cells within the lumen of the colon is cited for this discrepancy. Because of this and the fact that many scans are negative, Levy pointed out that the resection site utility of Tc-99-labeled RBCs is a small percentage of all scans performed (18) (level IV evidence). Ng suggests that the angiographic yield could be further refined by selecting only patients who scintigraphy is positive early after injection (19) (level IV evidence).

Answer: Tc-99-labeled RBCs appears superior to Tc-99 sulfur colloid injection (Grade B recommendation). For all comers, about half of the scans will be positive. Angiography is not indicated when scintigraphy is negative. Positive scans should be followed up with further localization studies to improve anatomic accuracy (Grade C recommendation).

WHAT IS THE DIAGNOSTIC ACCURACY OF COLONOSCOPY, RADIONUCLIDE SCANNING, AND ANGIOGRAPHY IN THE SETTING OF LGIB?

Neither scintigraphy nor angiography alone are a sufficient guide for surgical resection. Hunter pointed that as many as 42% of patients could have an undesirable result if a limited surgical procedure was planned on the basis of Tc-99-labeled RBCs alone (20) (level IV evidence). Whitaker demonstrated that angiography alone is also of limited sensitivity and specificity (21) (level IV evidence). As noted, the yield can be improved with preangiography scintigraphy. Furthermore, surgical site resection utility of angiography was noted to be low in a retrospective study by Cohn in 1998 (22) (level IV evidence), where only 12% of the

angiograms were useful in selecting the site of colon resection, noting an 11% complication rates from angiography. Computed tomography (CT) has been used to evaluate LGIB. Several authors have studied computed tomographic angiography (CTA) and found this method to be 70–80% sensitive and 100% specific for evaluating colonic angiodysplasia and other GI sources (23, 24, 25) (level IV evidence). Jaeckle evaluated the accuracy of multidetector row helical CT (MDCT) for detection and localization hemorrhage. They found MDCT to be 92% accurate with ongoing bleeding frequently demonstrated (26) (level IV evidence). In a prospective study of 26 patients for massive GI bleeding, Yoon demonstrated that arterial phase MDCT was about 90% sensitive and 99% specific with an overall accuracy rate of 88%. The negative predictive value was 98%, suggesting formal angiography would not be indicated in MDCT-negative studies (27) (level IIIB evidence). This test was found to be readily available and sufficiently sensitive for Duchesne to suggest MDCT as the initial screen for LGIB (28) (level V evidence).

Angiography and panendoscopy were first compared in 55 patients in 1976 with comparable accuracy (29) (level IIIB evidence). Chaudhry and colleagues studied 85 patients where unprepped colonoscopy was performed as the initial evaluation in cases of suspected LGIB. They concluded that this method was 95% sensitive and allowed for concomitant therapeutic control in 63% of the patients with active bleeding. In addition, they were able to diagnose that the source of bleeding was proximal to the ileocecal valve in 10% of the total patients studied (30) (level IV evidence). Early colonoscopy is associated with shorter hospitalizations (31) (level IV evidence). Haykir evaluated the diagnostic accuracy of magnetic resonance (MR) colonography and CT colonography with conventional colonoscopy. MR was slightly more accurate than CT and close to conventional colonoscopy in sensitivity with discovery of the lesion 96% of the time (32) (level IIIB evidence).

Answer: Colonoscopy when available is the most accurate method of diagnosing LGIB and is the gold standard against which other studies are measured offering control of bleeding from some lesions as well (Grade C recommendation). Scintigraphy may offer valuable information for angiographic screening but is insufficient for operative planning alone (Grade C recommendation). MDCT is emerging as a valuable noninvasive modality but has not been sufficiently studied to determine whether it can be used as a sole modality for operative planning (Grade C recommendation).

WHAT IS THE IDEAL ORDER OF DIAGNOSTIC TEST IN THE SETTING OF LGIB?

The critical purpose for performing diagnostic testing in LGIB is to rule out the presence of bleeding above the ileocecal valve, which has been noted to be as high as 9% of patients presenting for evaluation (18,30). There are no prospective randomized trials addressing this point. Chaudhry and Green suggest that colonoscopy is an accurate single stage evaluation for LGIB (30,33) (level IV evidence). Because this is an invasive procedure, it may not always be readily available. It has been demonstrated that the yield from angiography for all comers is low (21,34) (level IV evidence). Furthermore, in this potentially volume depleted population, the incidence of complications from

contrast angiography has been underappreciated (22) (level IV evidence). The positive predictive value of either scintigraphy or MDCT is sufficient to utilize either of these test prior to angiography (14–16,27,28) (level IV evidence).

Answer: Colonoscopy is the ideal single test in the face of LGIB. In the event this is not available and an intervention is required, scintigraphy or MDCT should be performed to rule out proximal sources in the small bowel prior to angiographic embolization/vasopressin or surgical resection (Grade C recommendation).

WHAT IS THE CLINICAL EFFECTIVENESS OF INTRA-ARTERIAL VASOPRESSIN INFUSION VERSUS TRANSCATHETER EMBOLIZATION?

Athanasoulis reported successful cessation of bleeding in 22 of 24 patients (92%) with hemorrhage from colonic diverticulosis using selective intra-arterial vasopressin (35) (level IV evidence). Fourteen of the 24 patients underwent surgical resection (58%) for persistent hemorrhage, early rebleeding, late rebleeding, or planned resection. Similar control has been reported by others (36) (level IV evidence). In a three-year review of medically compromised patients using intra-arterial vasopressin, a 63% success rate in controlling colonic hemorrhage was demonstrated. Rebleeding occurred in 16% of these patients with high morbidity and mortality (37) (level IV evidence). Browder found similar results with 90% of patients controlled with intra-arterial vasopressin but a 50% rebleed rate on cessation of therapy (38) (level IV evidence). Other authors have reported lower success rates in the 35% range with this technique (34) (level IV evidence). Similarly there are numerous series reporting of control of LGIB with intra-arterial embolization with similar or better success compared to vasopressin; however, nearly all of these reported a higher incidence of complication of the therapy (i.e., the embolus versus the pharmacologic agent) with embolization, most notably colonic necrosis (36,39–42) (level IV evidence). Gomes compared these techniques in a single-hospital retrospective review and found similar rates of hemorrhage control but a higher rate of rebleeding in the vasopressin group (43) (level IV evidence).

Patel and Nawawi have recently advocated super-selective embolization to minimize colonic ischemia with good hemorrhage control in a small series (41,44,45) (level IV evidence). Preclinical data in a porcine model supports the theory that being “super” selective may enhance the safety of this technique (46). Burgess and Kickuth, however, reported colonic necrosis even with this technique (45,47) (level IV evidence).

Answer: The major drawbacks of vasopressin therapy are coronary ischemia and rebleeding after cessation of

therapy. Cessation of bleeding occurs in up to 90% of patients. Some studies have shown significant rebleeding after therapy is stopped. On the other hand, embolic therapy shows a similar rate of initial hemorrhage control with less early rebleeding; however, there is at about a 10% risk of significant colon ischemia. Super-selective embolism has not eliminated ischemia as a risk. The late rebleeding risk is 10–15% with either technique (no recommendations).

WHAT ARE THE CRITERIA FOR SURGICAL INTERVENTION IN LGIB, AND WHAT OPERATION SHOULD BE DONE?

Extensive preoperative testing in patients with emergent surgical conditions results in a delay in care with often difficult-to-document benefit (48) (level IV evidence). In the case of LGIB, it is warranted to avoid colonic resection for sources proximal to the ileocecal valve (48). Localization of massive LGIB lowers perioperative mortality when compared to blind resection, but still is in the 8–18% range (34,38,49) (level IV evidence). Ideally, surgical resection for LGIB should be limited to patients likely to continue to bleed or rebleed and localized to the bleeding segment (50,51). Authors have disagreed about the morbidity of emergent subtotal colon resection (SCR). Cohn and Baker and others have suggested SCR is well tolerated and associated with a low rebleeding rate (22,52–54) (level IV evidence), whereas Setya has argued that it is associated with a high morbidity and mortality (55) (level IV evidence).

Not every patient with LGIB requires colonic resection. MacGuire showed that bleeding stopped in 99% of cases where 4 units or less were transfused (56) (level IV evidence). In retrospective series where the average transfusion requirement was 3 units or less, as many as 97% percent of patients could be managed nonoperatively (57–59) (level IV evidence). Curiously, therapeutic barium enema has been used in first episode of diverticular bleeding with good effect, allowing some patients to avoid resection (60) (level IV evidence).

Authors have varied on recommendations to resect based on transfusion requirements. Patients presenting to the emergency department with hypotension should be considered for earlier resection (61) (level IV evidence). Earlier resection (6–9 units) was associated with lower perioperative mortality (54, 62) (level IV evidence).

Answer: Patients who bleed 2 or more units of blood should receive an evaluation to localize the source of bleeding expeditiously (Grade C recommendation). Clinical stability and available testing options will determine to what extent localization studies can be performed so that excessive transfusion is avoided (>10 units). Persistent bleeding with true anatomic localization may allow for segmental resection otherwise subtotal colectomy with ileorectostomy should be performed (Grade C recommendation).

Summary of Evidence in the Diagnosis and Management of Lower Gastrointestinal Bleeding

Answer	Grade of recommendation	Question	Level of evidence	References
Tc-99-labeled RBCs appears superior to Tc-99 sulfur colloid injection.	B	What is the diagnostics accuracy of	Ib	5
For all comers, about half of the scans will be positive.	C	Tc-99 sulfur colloid injection versus	IV	7-19
Angiography is not indicated when scintigraphy is negative.		Tc-99-tagged red cells?		
Positive scans should be followed up with further localization studies to improve anatomic accuracy.				
Colonoscopy when available is the most accurate method of diagnosing LGIB and is the gold standard against which other studies are measured offering control of some lesions as well.	C	What is the diagnostic accuracy of	IV	30-32
Scintigraphy may offer valuable information for angiographic screening but is insufficient for operative planning alone.	C	colonoscopy,	IV	10-17, 20
MDCT is emerging as a valuable noninvasive modality but has not been sufficiently studied to determine whether it can be used as a sole modality for operative planning.	C	radionuclide scanning, and angiography in the setting of LGIB?	IIIb, IV	26-28
Colonoscopy is the ideal single test in the face of LGIB. In the event this is not available and an intervention is required, scintigraphy or MDCT should be performed to rule out proximal sources in the small bowel prior to angiographic embolization/vasopressin or surgical resection.	C	What is the ideal order of diagnostic test in the setting of LGIB?	IV	18, 21, 24,
	C		IV	30, 33, 34
				14-19, 27, 28
The major drawbacks of vasopressin therapy are coronary ischemia and rebleeding after cessation of therapy. Cessation of bleeding occurs in up to 90% of patients. Some studies have shown significant rebleeding after therapy is stopped.	No recommendations	What is the clinical effectiveness	IV	35-38
On the other hand, embolic therapy shows a similar rate of initial hemorrhage control with less early rebleeding, however, there is at about a 10% risk of significant colon ischemia. Super selective embolism has not eliminated ischemia as a risk.		intra-arterial	IV	36, 39-42,
The late rebleeding risk is 10-15% with either technique.		vasopressin infusion	IV	45, 47
		versus transcatheter embolization?		43
Patients who bleed 2 or more units of blood should receive an evaluation to localize the source of bleeding expeditiously.	C	What are the criteria for	IV	48, 51
Clinical stability and available testing options will determine to what extent localization studies can be performed so that excessive transfusion is avoided (>10 units).	C	surgical intervention in	IV	50, 51, 56-62
Persistent bleeding with true anatomic localization may allow for segmental resection otherwise subtotal colectomy with ileorectostomy should be performed.	C	LGIB and what operation should be done?	IV	22, 50, 52-54, 60

Abbreviations: LGIB, lower gastrointestinal bleeding; MDCT, multidetector computed tomography; RBCs, red blood cells.

REFERENCES

- Alavi A. Detection of gastrointestinal bleeding with 99mTc-sulfur colloid. *Semin Nucl Med* 1982; 12: 126-38.
- Winn M, Weissmann HS, Sprayregen S, et al. The radionuclide detection of lower gastrointestinal bleeding sites. *Clin Nucl Med* 1983; 8: 389-95.
- Miskowiak J, Nielsen SL, Munck O. Scintigraphic diagnosis of gastrointestinal bleeding with 99mTc-labeled blood-pool agents. *Radiology* 1981; 141: 499-504.
- Markisz JA, Front D, Royal HD, et al. An evaluation of 99mTc-labeled red blood cell scintigraphy for the detection and localization of gastrointestinal bleeding sites. *Gastroenterology* 1982; 83: 394-8.
- Siddiqui AR, Schauwecker DS, Wellman HN, et al. Comparison of technetium-99m sulfur colloid and in vitro labeled technetium-99m RBCs in the detection of gastrointestinal bleeding. *Clin Nucl Med* 1985; 10: 546-9.
- Thorne DA, Datz FL, Remley K, et al. Bleeding rates necessary for detecting acute gastrointestinal bleeding with technetium-99m-labeled red blood cells in an experimental model. *J Nucl Med* 1987; 28: 514-20.
- Friedman HI, Hilts SV, Whitney PJ. Use of technetium-labeled autologous red blood cells in detection of gastrointestinal bleeding. *Surg Gynecol Obstet* 1983; 156: 449-52.
- Rosenkilde Olsen P, Nielsen L, Dyrbye M, et al. Colorectal bleeding localized with gamma camera. *Acta Chir Scand* 1983; 149: 793-5.
- Orecchia PM, Hensley EK, McDonald PT, et al. Localization of lower gastrointestinal hemorrhage. Experience with red blood cells labeled in vitro with technetium Tc 99m. *Arch Surg* 1985; 120: 621-4.
- Bearn P, Persad R, Wilson N, et al. 99mTechnetium-labelled red blood cell scintigraphy as an alternative to angiography in the investigation of gastrointestinal bleeding: clinical experience in a district general hospital. *Ann R Coll Surg Engl* 1992; 74: 192-299.
- Wang CS, Tzen KY, Huang MJ, et al. Localization of obscure gastrointestinal bleeding by technetium 99m-labeled red blood cell scintigraphy. *J Formos Med Assoc* 1992; 91: 63-8.

12. Dusold R, Burke K, Carpentier W, et al. The accuracy of technetium-99m-labeled red cell scintigraphy in localizing gastrointestinal bleeding. *Am J Gastroenterol* 1994; 89: 345–8.
13. Rantis PC Jr., Harford FJ, Wagner RH, et al. Technetium-labelled red blood cell scintigraphy: is it useful in acute lower gastrointestinal bleeding? *Int J Colorectal Dis* 1995; 10: 210–15.
14. Dolezal J, Vizd'a J, Bures J. Detection of acute gastrointestinal bleeding by means of technetium-99m in vivo labelled red blood cells. *Nucl Med Rev Cent East Eur* 2002; 5: 151–4.
15. Howarth DM, Tang K, Lees W. The clinical utility of nuclear medicine imaging for the detection of occult gastrointestinal haemorrhage. *Nucl Med Commun* 2002; 23: 591–4.
16. Emslie JT, Zarnegar K, Siegel ME, et al. Technetium-99m-labeled red blood cell scans in the investigation of gastrointestinal bleeding. *Dis Colon Rectum* 1996; 39: 750–4.
17. Gutierrez C, Mariano M, Vander Laan T, et al. The use of technetium-labeled erythrocyte scintigraphy in the evaluation and treatment of lower gastrointestinal hemorrhage. *Am Surg* 1998; 64: 989–92.
18. Levy R, Barto W, Gani J. Retrospective study of the utility of nuclear scintigraphic-labelled red cell scanning for lower gastrointestinal bleeding. *ANZ J Surg* 2003; 73: 205–9.
19. Ng DA, Opelka FG, Beck DE, et al. Predictive value of technetium Tc 99m-labeled red blood cell scintigraphy for positive angiogram in massive lower gastrointestinal hemorrhage. *Dis Colon Rectum* 1997; 40: 471–7.
20. Hunter JM, Pezim ME. Limited value of technetium 99m-labeled red cell scintigraphy in localization of lower gastrointestinal bleeding. *Am J Surg* 1990; 159: 504–6.
21. Whitaker SC, Gregson RH. The role of angiography in the investigation of acute or chronic gastrointestinal haemorrhage. *Clin Radiol* 1993; 47: 382–8.
22. Cohn SM, Moller BA, Zieg PM, et al. Angiography for pre-operative evaluation in patients with lower gastrointestinal bleeding: Are the benefits worth the risks? *Arch Surg* 1998; 133: 50–5.
23. Junquera F, Quiroga S, Saperas E, et al. Accuracy of helical computed tomographic angiography for the diagnosis of colonic angiodysplasia. *Gastroenterology* 2000; 119: 293–9.
24. Ernst O, Bulois P, Saint-Drenant S, et al. Helical CT in acute lower gastrointestinal bleeding. *Eur Radiol* 2003; 13: 114–17.
25. Yamaguchi T, Yoshikawa K. Enhanced CT for initial localization of active lower gastrointestinal bleeding. *Abdom Imaging* 2003; 28: 634–6.
26. Jaekle T, Stuber G, Hoffmann MH, et al. Detection and localization of acute upper and lower gastrointestinal (GI) bleeding with arterial phase multi-detector row helical CT. *Eur Radiol* 2008; 18: 1406–13.
27. Yoon W, Jeong YY, Shin SS, et al. Acute massive gastrointestinal bleeding: detection and localization with arterial phase multi-detector row helical CT. *Radiology* 2006; 239: 160–7.
28. Duchesne J, Jacome T, Serou M, et al. CT-angiography for the detection of a lower gastrointestinal bleeding source. *Am Surg* 2005; 71: 392–7.
29. Butler ML, Johnson LF, Clark R. Diagnostic accuracy of fiberoptic panendoscopy and visceral angiography in acute upper gastrointestinal bleeding. *Am J Gastroenterol* 1976; 65: 501–11.
30. Chaudhry V, Hyser MJ, Gracias VH, et al. Colonoscopy: the initial test for acute lower gastrointestinal bleeding. *Am Surg* 1998; 64: 723–8.
31. Strate LL, Syngal S. Predictors of utilization of early colonoscopy vs. radiography for severe lower intestinal bleeding. *Gastrointest Endosc* 2005; 61: 46–52.
32. Haykir R, Karakose S, Karabacakoglu A, et al. Three-dimensional MR and axial CT colonography versus conventional colonoscopy for detection of colon pathologies. *World J Gastroenterol* 2006; 12: 2345–50.
33. Green BT, Rockey DC, Portwood G, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. *Am J Gastroenterol* 2005; 100: 2395–402.
34. Leitman IM, Paull DE, Shires GT III. Evaluation and management of massive lower gastrointestinal hemorrhage. *Ann Surg* 1989; 209: 175–80.
35. Athanasoulis CA, Baum S, Rosch J, et al. Mesenteric arterial infusions of vasopressin for hemorrhage from colonic diverticulosis. *Am J Surg* 1975; 129: 212–16.
36. Waltman AC. Transcatheter embolization versus vasopressin infusion for the control of arteriocapillary gastrointestinal bleeding. *Cardiovasc Intervent Radiol* 1980; 3: 289–95.
37. Sherman LM, Shenoy SS, Cerra FB. Selective intra-arterial vasopressin: clinical efficacy and complications. *Ann Surg* 1979; 189: 298–302.
38. Browder W, Cerise EJ, Litwin MS. Impact of emergency angiography in massive lower gastrointestinal bleeding. *Ann Surg* 1986; 204: 530–6.
39. Rahn NH III, Tishler JM, Han SY, et al. Diagnostic and interventional angiography in acute gastrointestinal hemorrhage. *Radiology* 1982; 143: 361–6.
40. Rosenkrantz H, Bookstein JJ, Rosen RJ, et al. Postembolic colonic infarction. *Radiology* 1982; 142: 47–51.
41. Patel TH, Cordts PR, Abcarian P, et al. Will transcatheter embolotherapy replace surgery in the treatment of gastrointestinal bleeding?(2)(2). *Curr Surg* 2001; 58: 323–7.
42. DeBarros J, Rosas L, Cohen JV, et al. The changing paradigm for the treatment of colonic hemorrhage: superselective angiographic embolization. *Dis Colon Rectum* 2002; 45: 802–8.
43. Gomes AS, Lois JF, McCoy RD. Angiographic treatment of gastrointestinal hemorrhage: comparison of vasopressin infusion and embolization. *Am J Roentgenol* 1986; 146: 1031–7.
44. Nawawi O, Young N, So S. Superselective coil embolization in gastrointestinal haemorrhage: Early experience. *Australas Radiol* 2006; 50: 21–6.
45. Kickuth R, Rattunde H, Gschossmann J, et al. Acute lower gastrointestinal hemorrhage: minimally invasive management with microcatheter embolization. *J Vasc Interv Radiol* 2008; 19: 1289–96.
46. Chin AC, Singer MA, Mihalov M, et al. Superselective mesenteric embolization with microcoils in a porcine model. *Dis Colon Rectum* 2002; 45: 212–18.
47. Burgess AN, Evans PM. Lower gastrointestinal haemorrhage and superselective angiographic embolization. *ANZ J Surg* 2004; 74: 635–8.
48. Rozycki GS, Tremblay L, Feliciano DV, et al. Three hundred consecutive emergent celiotomies in general surgery patients: influence of advanced diagnostic imaging techniques and procedures on diagnosis. *Ann Surg* 2002; 235: 681–8; discussion 688–9.
49. Kouraklis G, Misiakos E, Karatzas G, et al. Diagnostic approach and management of active lower gastrointestinal hemorrhage. *Int Surg* 1995; 80: 138–40.
50. So JB, Kok K, Ngoi SS. Right-sided colonic diverticular disease as a source of lower gastrointestinal bleeding. *Am Surg* 1999; 65: 299–302.
51. Strate LL, Saltzman JR, Ookubo R, et al. Validation of a clinical prediction rule for severe acute lower intestinal bleeding. *Am J Gastroenterol* 2005; 100: 1821–7.
52. Baker R, Senagore A. Abdominal colectomy offers safe management for massive lower GI bleed. *Am Surg* 1994; 60: 578–81; discussion 582.

53. Farner R, Lichliter W, Kuhn J, et al. Total colectomy versus limited colonic resection for acute lower gastrointestinal bleeding. *Am J Surg* 1999; 178: 587–91.
54. Field RJ Sr, Field RJ Jr, Shackelford S. Total abdominal colectomy for control of massive lower gastrointestinal bleeding. *J Miss State Med Assoc* 1994; 35: 29–33.
55. Setya V, Singer JA, Minken SL. Subtotal colectomy as a last resort for unrelenting, unlocalized, lower gastrointestinal hemorrhage: experience with 12 cases. *Am Surg* 1992; 58: 295–9.
56. McGuire HH Jr. Bleeding colonic diverticula. A reappraisal of natural history and management. *Ann Surg* 1994; 220: 653–6.
57. Bokhari M, Vernava AM, Ure T, et al. Diverticular hemorrhage in the elderly—is it well tolerated? *Dis Colon Rectum* 1996; 39: 191–5.
58. Al Qahtani AR, Satin R, Stern J, et al. Investigative modalities for massive lower gastrointestinal bleeding. *World J Surg* 2002; 26: 620–5.
59. Buttenschoen K, Buttenschoen DC, Odermath R, et al. Diverticular disease-associated hemorrhage in the elderly. *Langenbecks Arch Surg* 2001; 386: 8–16.
60. Koperna T, Kisser M, Reiner G, et al. Diagnosis and treatment of bleeding colonic diverticula. *Hepatogastroenterology* 2001; 48: 702–5.
61. Rios A, Montoya MJ, Rodriguez JM, et al. Severe acute lower gastrointestinal bleeding: risk factors for morbidity and mortality. *Langenbecks Arch Surg* 2007; 392: 165–71.
62. Clarke CS, Afifi AY. Impact of blood transfusion on outcome in patients admitted for gastrointestinal hemorrhage. *Curr Surg* 2000; 57: 493–6.

Diverticular Disease of the Colon

Brent Izu and Akpofure Peter Ekeh

Clinical Questions		
Question	Answer	Grade of recommendation
What is the appropriate indication for elective sigmoid resection after uncomplicated diverticulitis?	A case-by-case determination of the need for operative management is necessary.	C
Should younger patients (<40–50 years) undergo elective sigmoid colon resection after a single attack of acute diverticulitis?	Individualized decisions based on patients circumstance will need to be made prior to proceeding with surgery.	C
Are there any evidence-based dietary recommendations to prevent the recurrence of acute uncomplicated diverticulitis?	Dietary fiber can play a role in both the prevention of initial and recurrent attacks of uncomplicated diverticulitis.	A
What is the optimal operation for patients requiring surgery for complicated acute diverticulitis?	Primary resection of the inflamed colon (with or without primary anastomosis).	A
Is performing a primary anastomosis an option?	Primary anastomosis of the colon at the initial operation can be considered in Hinchey stage I and II patients.	B
Is laparoscopic colectomy equivalent or superior to open colectomy for diverticular disease? Is the overall cost different?	Laparoscopic colon resection is a safe and effective approach for the elective treatment of patients with diverticular disease.	B

Diverticular disease of the colon is considered is a disease of “modern times,” prevalent principally in Western societies. The appearance of diverticulosis in postmortem specimens basically paralleled both industrialization and the widespread use of refined wheat products (1).

Acute diverticulitis is the most frequent complication arising from the presence of colonic diverticula. The sigmoid colon is affected in 95% of cases. Patients may present initially with complications such as perforation, requiring immediate operative intervention. Most patients however recover following medical management with appropriate antibiotic therapy.

The methods of management of diverticulitis in the acute setting and subsequent to hospital discharge have evolved slowly over the past few decades. Several of the commonly accepted standards and guidelines are based on a small collection of studies generally with lower level evidence.

We will review the existing evidence in the literature regarding different facets of the management of colonic diverticular disease, ranging from indications for operative management, the importance of age in operative decision making, methods of operative management, the role of laparoscopy, and the prevention of recurrent attacks.

WHAT IS THE APPROPRIATE INDICATION FOR ELECTIVE SIGMOID RESECTION AFTER UNCOMPLICATED DIVERTICULITIS?

The appropriate indication for surgical intervention after uncomplicated acute diverticulitis, that is, disease in the absence of the complications of fistulas, strictures, abscess, or free perforation, has been subject to debate. The primary purpose of surgical intervention after acute attacks of diverticulitis is the prevention of recurrence and the accompanying morbidity. Consequently, recommendations are generally based on the risk of recurrence and the severity of subsequent attacks. Most studies assessing risk of repeat attacks are retrospective studies and have very wide variability of follow-up, making it difficult to establish an accurate recurrence rate.

Historically, clinical practice patterns and recommended guidelines have proposed elective colon resection after two or more acute attacks of diverticulitis successfully treated medically or after a single attack requiring in a patient less than 40 years of age (Level C recommendation).

The recommendation for surgery following two attacks in older patients is based primarily on dated case-series data indicating significant recurrence rates after medically managed acute diverticulitis (Level of evidence IV). Parks

published a review in 1969 of 455 patients admitted with acute diverticulitis. Of the patients treated medically, 24.6% subsequently had a second attack, 3.8% a third. Furthermore, the paper suggested medical management was less effective for symptom control with subsequent bouts (2). Makela et al. similarly showed recurrences of 22% of patients with diverticulitis managed medically and complications seen in 50% of patients who presented with a second attack (3) (Level of evidence IV).

More recent series have challenged the prevalence of recurrence and the severity of subsequent attacks stated in the older literature. This more recent data is however of the same evidence level—mostly retrospective studies yielding Level IV evidence. A recent large series involving over 3,000 patients showed 13.3% had a single recurrence and 3.9% had a second episode (4). This is lower than reported in older studies but has a longer follow-up period than any of the prior studies (8.9 years) (Level of evidence IV). Another retrospective review showed that only 2.7% of patients who presented emergently with acute diverticulitis and required surgery had a prior history of medical management. The majority of these cases were initial presentations (5) (Level of evidence IV). A retrospective study by Chapman et al. found multiple episodes of diverticulitis are not associated with increased risk of mortality or poor outcomes from complicated diverticulitis (6) (Level of evidence IV).

Salem and others used a statewide database to construct a Markov model to evaluate lifetime risks of death and colectomy, care costs, and quality of life associated with elective colectomy after subsequent episodes of diverticulitis using hypothetical cohorts of 35- and 50-year-old patients who recovered from a nonsurgically treated diverticulitis episode. They found that performing a colectomy after the fourth rather than the second episode in patients older than 50 years resulted in 0.5% fewer deaths, 0.7% fewer colectomies, and saved \$1,035 per patient. They concluded that expectant medical management after uncomplicated diverticulitis was associated with lower rates of death and colectomy and was cost saving compared with a strategy of elective prophylactic colectomy (Level of evidence II) (7).

To date, there are no randomized controlled trials pitting observation against elective sigmoid resection following episodes of complicated diverticular disease of the colon.

Summary: Though elective sigmoid resection has been traditionally recommended after two attacks of uncomplicated diverticulitis, a case-by-case determination of the need for operative management is necessary (Grade C recommendation). Waiting until at least the fourth episode attack of diverticulitis before elective surgery can result in lower colectomy and lower death rates (Grade B recommendation). Given the strength of these recommendations, there is no strong basis for the conventional decision to routinely proceed to a colectomy after two episodes of uncomplicated diverticulitis.

SHOULD YOUNGER PATIENTS (<40–50 YEARS) UNDERGO ELECTIVE SIGMOID COLON RESECTION AFTER A SINGLE ATTACK OF ACUTE DIVERTICULITIS?

Traditional clinical practice and expert guidelines have advocated elective sigmoid colectomy after the first attack of uncomplicated diverticulitis in patients less than 40 years

of age. This recommendation is based on multiple case series and retrospective studies from the 1960s and 1970s demonstrating more “virulent” presentation and more recurrences in patients less than 40. Studies confirming this notion and others challenging it are continuously presented in the literature—all similarly retrospective. There are no prospective studies comparing observation to elective surgery in patients under 40.

Multiple retrospective cohort studies have compared rates of complication and operation in younger patients to those of older patients. Some reports show that younger patients develop more subsequent complications, have more recurrences, and that the disease displays a more aggressive course compared with older patients (Level IIb evidence) (8–11). Other studies of comparable quality draw different conclusions, disputing the claim of a more “virulent” disease process in younger patients (12–14).

The decision tree analysis model described by Salem et al. specifically addressing younger patients concluded that performing colectomy after the fourth episode compared with the first episode resulted in 0.1% fewer deaths, 0.2% fewer colectomies, and saved \$5,429 per patient (Level II evidence) (7).

Summary: Given the conflicting conclusions based on evidence of similar quality (Level II) and studies of varying quality, no definite evidence-based recommendations can be made with regard to the indication for surgery after an uncomplicated attack of acute diverticulitis in younger patients. Individualized decisions based on patient’s circumstance will need to be made prior to proceeding with surgery (Grade C recommendation). However, as in older patients, there is a reduction in number of colectomies and death rate associated with holding elective surgery until after the fourth attack, if it ever occurs (Grade B recommendation).

ARE THERE ANY EVIDENCE-BASED DIETARY RECOMMENDATIONS TO PREVENT THE RECURRENCE OF ACUTE UNCOMPLICATED DIVERTICULITIS? IS THE PRACTICE OF PROHIBITING THE INTAKE OF “SEEDS” AFTER AN ACUTE EPISODE VALID?

In conjunction with standard antibiotic therapy for uncomplicated diverticulitis, patients are often given dietary recommendations. Fiber intake is the most significant dietary factor in preventing and reducing recurrence of diverticulitis. The progression of colonic diverticular disease has paralleled the drop in dietary fiber consumption in the United States, Europe, and Asia.

A number of studies have highlighted the benefits of fiber intake in the prevention and recurrence of diverticular disease. The original observations of the effect of fiber were published over 30 years ago by Burkitt, based on his experiences in rural Africa. He compared colonic transit times and stool weight in three populations with low-, mixed-, and high-residue diets. Colonic transit time was decreased and stool weight was increased in patients with high-residue diets. He further obtained epidemiological data from various countries, noting the very low prevalence of diverticular disease in populations with high-residue diets compared to those with low- and mixed residue diets (1).

A prospective questionnaire based study with a four-year follow-up by Aldoori et al. evaluated the effect of

various diets on the incidence of diverticular disease. The participants reporting diets high in fruit and vegetable fiber had a significantly lower incidence of symptomatic diverticulitis. Diets high in fat and red meat were also noted to augment the risk (15) (Level of evidence IIb). This is supported by findings from a cohort series from Greece in patients with radiologically confirmed diverticulitis in which patients with diverticulitis were demonstrated to have a lower intake of fiber and higher intake of red meat (16).

There is some good evidence that supports the clinical recommendation given to patients to increase fiber intake after acute attacks of diverticulitis as a means to lower recurrence rates. Brodribb demonstrated in a randomized controlled trial with fiber versus placebo that fiber improved symptoms of dyspepsia, bowel dysfunction, and pain in patients with symptomatic diverticular disease (17) (Level of evidence I). This is in line with another randomized controlled crossover trial by Taylor also performed in the 1970s, comparing bran tablets (18g/day) with a high-roughage diet and a laxative. The bran group was found to have better results in improving symptom score, stool weight, transit time, and motility (18).

The advice given against the consumption of popcorn, seeds, and nuts in an attempt to prevent obstruction of diverticula and subsequent inflammation has no basis in the medical literature.

Summary: Dietary fiber can play a role in both the prevention of initial and recurrent attacks of diverticulitis. Patients should be advised to increase their fiber content in their diet after a bout of uncomplicated diverticulitis (Grade A recommendation).

WHAT IS THE OPTIMAL OPERATION FOR PATIENTS REQUIRING SURGERY FOR COMPLICATED ACUTE DIVERTICULITIS? IS PERFORMING A PRIMARY ANASTOMOSIS AN OPTION?

The operative management of complicated acute diverticulitis has evolved over time. Historically, staged operations were commonly performed, involving the initial closure of the perforation with a proximal diversion (ileostomy or transverse colostomy) with subsequent delayed resection of the diseased portion and anastomosis. This approach has been largely supplanted by the Hartmann operation—resection of the acutely inflamed bowel, including the perforated portion of colon and a proximal end colostomy.

There has, however, been literature recently describing primary resection and immediate anastomosis in the acute setting. This has been described in some instances in conjunction with additional measures such as proximal protective ileostomies and intraoperative on-table colonic lavage.

In his 1978 paper on the treatment of diverticulitis, Hinchey divided acute diverticulitis into four stages, now referred to as the Hinchey stages I–IV, with increasingly severe clinical features and mortality in each successive stage. Stage IV disease involves feculent peritonitis and was described to be accompanied with a high mortality (19). This staging system has been widely adopted to provide a standard for comparison of the severity of disease.

In one of the very few randomized prospective trials that have been performed for the management of diverticulitis, Zeitoun et al compared primary resection with

suture, drainage and proximal colostomy followed by secondary resection. In this study, most of the patients in the primary resection group had Hartmann operations with a small minority (5%) undergoing primary anastomoses. They found postoperative peritonitis occurred less; fewer reoperations and a shorter hospital stay in the primary resection group (20) (Level of evidence I). This study only included patients with Hinchley stages III and IV. There was no difference in mortality between the two groups.

This study confirmed prior retrospective cohort studies that had arrived at similar conclusions. Finlay et al. compared outcomes in patients undergoing primary resection to proximal drainage and diversion. Morbidity was significantly higher in patients undergoing diversion without resection, including a higher incidence of fistula formation in the patients with staged operations (21).

More recently, several authors have published data on the use of primary resection and anastomosis in patients with perforated sigmoid diverticulitis. These are all retrospective studies. Stumpf et al. found 19 of 36 patients considered low risk (Hinchey stage I and II) had no complications following primary resection and anastomosis. They concluded that this method of management be considered in low-risk patients with acute diverticulitis (Level of evidence IIb) (22). Similarly, a small retrospective series from Australia comparing 33 patients with primary anastomosis with 64 who had Hartmann procedures revealed no marked difference in morbidity and no increased mortality. They also concluded that primary anastomosis has an acceptable morbidity and mortality (Level of evidence II). The patients in the primary anastomosis group were in earlier Hinchey Stages (23).

These two studies mentioned are representative of several others with similar findings and levels of evidence (24–27). Protective ileostomies and colonic lavage were used in some of these studies, but no recommendation can be made on these practices based on their irregular and random use.

Overall, the literature regarding primary anastomosis of acute complicated diverticulitis involves heterogeneous populations, differing methods (e.g., the use of protective ileostomy and intraoperative colonic lavage), and the inherent problems of selection bias. Two recent systemic reviews of the retrospective literature on this topic supported this observation, recognizing that patients selected for primary resection and anastomosis have a lower mortality than those treated by Hartmann's procedure. These factors limit clinically sound conclusions and demonstrate the need for prospective randomized studies in this area (28,29).

Summary: Primary resection of the inflamed colon (with or without primary anastomosis) is the optimal method of treating complicated sigmoid diverticulitis (Grade A recommendation). Primary anastomosis of the colon at the initial operation can be considered in Hinchey stage I and II patients (Grade B recommendation).

IS LAPAROSCOPIC COLECTOMY EQUIVALENT OR SUPERIOR TO OPEN COLECTOMY FOR DIVERTICULAR DISEASE? IS THE OVERALL COST DIFFERENT?

A clear role for laparoscopy in the management of colon cancer has been established by a multi-institutional

randomized prospective trial demonstrating noninferiority in recurrence rates as well as a shorter length of stay and less use of parenteral narcotics in the laparoscopic group (30). No such study has been performed specifically for diverticular disease. There are therefore no Level I evidence or Grade A recommendations regarding the use of laparoscopic colectomy for diverticular disease of the colon. A randomized prospective blinded trial addressing the use of laparoscopy in the management of diverticular disease is currently in progress in Europe (31).

There are a few retrospective cohort and case controlled studies offering Level II and III evidence on a range of outcome measures comparing laparoscopic sigmoid colectomy for diverticular disease with the traditional open procedure.

Compared with the open procedure, a number of these studies found no difference in complication rates or mortality (32). Furthermore, quicker return to diet, shorter time to first bowel movement, reduced length of hospital stay,

and reduced estimated blood loss have been consistently reported (33–36) (Level of evidence IIb).

Laparoscopic sigmoidoscopy, however, in most series had longer operative time although typically a shorter length of stay and charges (34,35) (Level of evidence II).

A single study from France comparing laparoscopic with open approaches in elderly patients concluded that laparoscopic colectomy can be safely applied to older patients with a reductions in complications, pain and hospital stay (37) (Level of evidence II).

Two studies examining cost per case report an overall reduction with laparoscopic sigmoid colectomies, possibly related to the reduced length of stay (35,36,38).

Summary: Laparoscopic colon resection is a safe and effective approach for the elective treatment of patients with diverticular disease demonstrating no increased morbidity and a shorter hospital stay, quicker resumption of bowel function, and reduced blood loss. It is appropriate for elderly patients (Grade B recommendation).

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Indication for elective colectomy after uncomplicated diverticulitis	2004	7	IIb	B	Expectant medical management after uncomplicated diverticulitis with lower cost, fewer deaths, and fewer colostomies.
Elective colectomy in younger patients following a single episode	2004	7	IIb	B	Colectomy after the fourth episode is associated with associated with lower rates of death and colostomy.
Dietary fiber intake and risk of diverticulitis	1994	15	IIb	B	Diets high in fruit and vegetable fiber had a significantly lower incidence of symptomatic diverticulitis.
Primary anastomosis for sigmoid diverticulitis	2007	22	IIb	B	Primary resection and anastomosis can be considered in low-risk patients (Hinchey stage I and II) with acute diverticulitis.
Laparoscopy for diverticular disease	2005	33	IIb	B	Laparoscopy associated with quicker return to diet, shorter time, and reduced length of hospital stay.

REFERENCES

- Burkitt DP, Walker AR, Painter NS. Effect of dietary fibre on stools and the transit-times, and its role in the causation of disease. *Lancet* 1972; 7792: 1408–12.
- Parks TG. Natural history of diverticular disease of the colon. A review of 521 cases. *Br Med J* 1969; 4: 639–45.
- Makela J, Vuolio S, Kiviniemi H, et al. Natural history of diverticular disease: When to operate? *Dis Colon Rectum* 1998; 41: 1523–8.
- Broderick-Villa G, Bruchette RJ, Collins JC, et al. Hospitalization for acute diverticulitis does not mandate routine elective colectomy. *Arch Surg* 2005; 140: 576–81.
- Somasekar K, Foster ME, Haray PN. The natural history of diverticular disease: is there a role for elective colectomy? *J R Coll Surg Edinb* 2002; 47: 481–4.
- Chapman JR, Dozois EJ, Wolff BG, et al. Diverticulitis: a progressive disease? Do multiple recurrences predict less favorable outcomes? *Ann Surg* 2006; 243: 876–83.
- Salem L, Veenstra DL, Sullivan SD, et al. The timing of elective colectomy in diverticulitis: a decision analysis. *J Am Coll Surg* 2004; 199: 904–12.
- Minardi AJ Jr, Johnson LW, Sehon JK, et al. Diverticulitis in the young patient. *Am Surg* 2001; 67: 458–61.
- Lahat A, Menachem Y, Avidan B, et al. Diverticulitis in the young patient—is it different? *World J Gastroenterol* 2006; 14: 2932–5.
- Pautrat K, Bretagnol F, Hutten N, et al. Acute diverticulitis in very young patients: a frequent surgical management. *Dis Colon Rectum* 2006; 50: 472–7.
- Anaya DA, Flum DR. Risk of emergency colectomy and colostomy in patients with diverticular disease. *Arch Surg* 2005; 140: 681.
- Biondo S, Parés D, Martí Ragué J, et al. Acute colonic diverticulitis in patients under 50 years of age. *Br J Surg* 2002; 89: 1137–41.
- Guzzo J, Hyman N. Diverticulitis in young patients: is resection after a single attack always warranted? *Dis Colon Rectum* 2004; 47: 1187–90.
- Nelson RS, Velasco A, Mukesh BN. Management of diverticulitis in younger patients. *Dis Colon Rectum* 2006; 49: 1341–5.
- Aldoori WH, Giovannucci EL, Rimm EB, et al. A prospective study of diet and the risk of symptomatic diverticular disease in men. *Am J Clin Nutr* 1994; 60: 757–64.
- Manousos O, Day NE, Tzonou A, et al. Diet and other factors in the aetiology of diverticulosis: an epidemiological study in Greece. *Gut* 1985; 26: 544–9.

17. Brodribb AJ. Treatment of symptomatic diverticular disease with a high-fibre diet. *Lancet* 1977; 1: 664–6.
18. Taylor I, Duthie HL. Bran tablets and diverticular disease. *Br Med J* 1976; 24: 988–90.
19. Hinchey EF, Schaal PG, Richards GK. Treatment of perforated diverticular disease. *Adv Surg* 1978; 12: 85–109.
20. Zeitoun G, Laurent A, Rouffet F, et al. Multicentre, randomized clinical trial of primary versus secondary sigmoid resection in generalized peritonitis complicating sigmoid diverticulitis. *Br J Surg* 2000; 87: 1366–74.
21. Finlay IG, Carter DC. A comparison of emergency resection and staged management in perforated diverticular disease. *Dis Colon Rectum* 1987; 30: 929–33.
22. Stumpf MJ, Vences FY, Edwards J. Is primary anastomosis safe in the surgical management of complications of acute diverticulitis? *Am Surg* 2007; 73: 787–90.
23. Blair NP, Germann E. Surgical management of acute sigmoid diverticulitis. *Am J Surg* 2002; 183: 525–8.
24. Schilling MK, Maurer CA, Kollmar O, et al. Primary vs. secondary anastomosis after sigmoid colon resection for perforated diverticulitis (Hinchey stage III and IV): a prospective outcome and cost analysis. *Dis Colon Rectum* 2001; 44: 699–703.
25. Richter S, Lindemann W, Kollmar O, et al. One-stage sigmoid colon resection for perforated sigmoid diverticulitis (Hinchey stages III and IV). *World J Surg* 2006; 30: 1027–32.
26. Regenet N, Pessaix P, Hennekinne S, et al. Primary anastomosis after intraoperative colonic lavage vs. Hartmann's procedure in generalized peritonitis complicating diverticular disease of the colon. *Int J Colorectal Dis* 2003; 18: 503–7.
27. Aydin HN, Tekkis PP, Remzi FH, et al. Evaluation of the risk of a nonrestorative resection for the treatment of diverticular disease: the Cleveland Clinic diverticular disease propensity score. *Dis Colon Rectum* 2006; 49: 629–39.
28. Salem L. Primary anastomosis or Hartmann's procedure for patients with diverticular peritonitis? A systematic review. *Dis Colon Rectum* 2004; 47: 1953–64.
29. Constantinides VA, Tekkis PP, Athanasiou T, et al. Primary resection with anastomosis vs. Hartmann's procedure in nonelective surgery for acute colonic diverticulitis: a systematic review. *Dis Colon Rectum* 2006; 49: 966–81.
30. Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med*. 2004; 350: 2050–9.
31. Klarenbeek BR, Veenhof AA, de Lange ES, et al. The Sigma-trial protocol: a prospective double-blind multi-centre comparison of laparoscopic versus open elective sigmoid resection in patients with symptomatic diverticulitis. *BMC Surg* 2007; 7: 16.
32. Gonzalez R, Smith CD, Mattar SG, et al. Laparoscopic vs open resection for the treatment of diverticular disease. *Surg Endosc* 2004; 18: 276–80.
33. Alves A, Panis Y, Slim K, et al. Association Française de Chirurgie. French multicentre prospective observational study of laparoscopic versus open colectomy for sigmoid diverticular disease. *Br J Surg* 2005; 92: 1520–5.
34. Lawrence DM, Pasquale MD, Wasser TE. Laparoscopic versus open sigmoid colectomy for diverticulitis. *Am Surg* 2003; 69: 499–503.
35. Dwivedi A, Chahin F, Agrawal S, et al. Laparoscopic colectomy vs. open colectomy for sigmoid diverticular disease. *Dis Colon Rectum* 2002; 45: 1309–14.
36. Senagore AJ, Duepre HJ, Delaney CP, et al. Cost structure of laparoscopic and open sigmoid colectomy for diverticular disease: similarities and differences. *Dis Colon Rectum* 2002; 45: 485–90.
37. Tuech JJ, Pessaix P, Rouge C, et al. Laparoscopic vs open colectomy for sigmoid diverticulitis: a prospective comparative study in the elderly. *Surg Endosc* 2000; 14: 1031–3.
38. Liberman MA, Phillips EH, Carroll BJ, et al. Laparoscopic colectomy vs traditional colectomy for diverticulitis. Outcome and costs. *Surg Endosc* 1996; 10: 15–18. numbered to 34, 35 and 36 respectively.

Large Bowel Obstruction

Jerry Lee Howard, John J. Hong, Michael M. Badellino, and Michael D. Pasquale

Clinical Questions		
Question	Answer	Grade
What is the clinical presentation?	Absence of passage of flatus (90%) and/or feces (80.6%) and abdominal distension (65.3%) were the most common symptoms and physical finding, respectively.	C
What is the differential diagnosis?	Large bowel cancer, adhesions, retroperitoneal tumors, and hernias were the most common causes of large bowel obstruction. Hernias, adhesions, strictures, endometriosis, ingested foreign bodies, phytobezoars, gallstones, and rectal foreign bodies have all been found to cause large bowel obstruction.	C
What is the proper diagnostic evaluation?	CT imaging is more accurate in making the diagnosis of large bowel obstruction than was contrast enema. CT imaging also allows for the evaluation of other disease processes and is more readily available. CT imaging in conjunction with contrast enema may yield superior results.	C
What is the preferred operative approach?	Stomas are preferred for patients with recurrent disease or for palliative resections. A primary anastomosis can be safely performed for obstructing colon lesions.	B
What are the nonoperative approaches?	Colonic stenting can be used as a bridge to surgery or as a palliative option. The success rate for relieving obstruction is around 90%. Three-quarters of patients in which colonic stents are used as a bridge to surgery go on to elective resection.	B
What are the outcomes?	Mortality rates for patients presenting with large bowel obstruction are 20–25%. If colonic stenting is available, the mortality rate can be significantly reduced.	B
Abbreviation: CT, computed tomography.		

Large bowel obstruction is a challenging and complex problem that can perplex the most experienced surgeon. This is mainly due to the wide range of causes and the physiologic derangements with which these patients present. Careful attention to pre- and postoperative management, anatomy, and operative technique will allow the surgeon to adequately manage this most challenging entity. Surgical decision making is made more difficult by the paucity of Level I evidence. When available, the most up-to-date and applicable research has been presented. Recent review articles were also used to support some of the points presented in other retrospective and prospective evaluations.

WHAT IS THE CLINICAL PRESENTATION?

The presentation of large bowel obstruction depends on the degree of intestinal luminal narrowing and duration of the obstruction. Very little evidence is available to firmly delineate the presentation of acute large bowel obstruction. Perhaps this is due to the plethora of causes ultimately leading to large bowel obstruction. The inciting pathologic process often dictates the patient's presentation. In a prospective observational study of 150 adult patients admitted with acute mechanical bowel obstruction to a surgical

specialty hospital in Greece over a 2 year period, it was noted that 36 (24%) patients had large bowel obstruction. Absence of passage of flatus (90%) and/or feces (80.6%) and abdominal distension (65.3%) were the most common symptoms and physical finding, respectively. These percentages are for all patients admitted with mechanical bowel obstruction (1). The top three causes for all patients with small or large bowel obstruction were adhesions, incarcerated hernias, and large bowel cancer (64.8%, 14.8%, and 13.4%, respectively). Large bowel cancer, adhesions, retroperitoneal tumors, and hernias were the most common causes in the large intestinal obstruction group retrospectively reviewed by Markogiannakis and colleagues (1) (47.4%, 36.3%, 5.5%, and 2.7%, respectively).

COLON CANCER

Approximately 10% of colon cancers present with obstruction (2). Sigmoid cancer accounted for 15 (75%) of the 20 patients with obstruction due to a large bowel cancer in the study by Markogiannakis et al. (1), whereas 2 (10%) patients had ascending colon cancer, 1 (5%) had transverse colon cancer, 1 (5%) had descending colon cancer, and 1 (5%) had rectal cancer. Of these 20 patients who presented with

obstruction due to large bowel cancer, 4 (20%) had ischemia, 3 (15%) had necrosis, and 2 (10%) had perforation (1). Of the 36 total patients with mechanical large bowel obstruction, 6 (16.6%) were diagnosed intraoperatively with ischemia, 6 (16.6%) with necrosis, and 4 (11.1%) with perforation. The incidence of ischemia, necrosis, and perforation in the patients with small bowel obstruction was similar. At the time of operation, no reversible ischemia was observed in the large bowel obstruction group. Although patients with small bowel obstruction and those with large bowel obstruction presented with similar ischemia rates, the incidence of necrosis and perforation was much higher in the large intestine obstruction group (1).

HERNIAS

Less than 3% of patients with large bowel obstruction will have a hernia as a root cause. Despite the rarity of this condition, it has a significant clinical impact. Hernias causing obstruction are associated with ischemia, necrosis, and perforation at a higher rate than other causes of obstruction (1). It seems prudent to carefully analyze all patient data (complete blood count for leukocytosis, lactic acidosis, metabolic acidosis) and look for erythema of the overlying skin to determine if bowel compromise is present. Any of these findings make the patient a candidate for early operative intervention (2).

INFREQUENT CAUSES

Stool impaction, strictures from Crohn's disease or diverticulitis, and acute diverticulitis with extracolonic abscess have been shown to cause colonic obstruction. Colonic pseudo-obstruction (a form of ileus) causes colonic dilatation that can be confused with a true mechanical colonic obstruction (2). The presentation, diagnosis, and management of these entities are covered elsewhere.

In summary, the most common clinical symptoms associated with large bowel obstruction are absence of passage of flatus (90%) and/or feces (80.6%) and abdominal distension (65.3%). A significant number of patients with large bowel obstruction will also have ischemia (16%), necrosis (16%), and perforation (11%) (1). Grade of recommendation: C.

WHAT IS THE DIFFERENTIAL DIAGNOSIS?

As previously mentioned, there is a wide range of causes for large bowel obstruction. No succinct Level I evidence was identified with regard to differential diagnosis. With such a broad differential diagnosis, the evaluation and treatment algorithm can become long and tedious. After gaining insight into the physiologic alterations caused by a large bowel obstruction, it is useful to have an appreciation for the variety of causes culminating in obstruction.

In an article by Jenkins et al. (3), the records of 73 patients with secondary causes of small and large bowel obstruction were reviewed. The etiology of intestinal obstruction was metastatic neoplastic obstruction (19%), colonic volvulus (18%), Crohn's disease (14%), hernia (11%), and diverticular disease (7%) (3). These, along with other

primary causes of bowel obstruction, must be considered. A variety of classification schemes have been derived to organize the causes of large bowel obstruction. A comprehensive and simple outline is illustrated in *Current Therapy in Colon and Rectal Surgery* (4). The categories are divided into lesions arising extrinsic to the bowel wall; within the bowel wall, the bowel lumen, and volvulus of the cecum; and in the transverse and sigmoid colons.

Extrinsic to Bowel Wall

Lesions extrinsic to the bowel trigger compression of the colon, causing obstruction. This could be due to a neoplastic growth from an adjacent organ or, more frequently, in the form of a retroperitoneal tumor as found by Markogiannakis and colleagues (1). As with small bowel obstruction, hernias and adhesions comprise the other two main causes of extrinsic large bowel obstruction.

Intrinsic to Bowel Wall

Colonic neoplasia is the most common cause of large bowel obstruction, accounting for just over 47% of cases (1). Other common causes arising from the bowel wall are strictures that could be from Crohn's disease, ulcerative colitis, chronic ischemia, diverticular disease, or radiation. Endometriosis has been known to cause large bowel obstruction (5).

Lesions Within the Bowel Lumen

Foreign bodies causing bowel obstruction can be a challenging entity. There are several routes by which a foreign body may enter the intestinal lumen. A biliary or colonic stent may have migrated from its intended position (6,7). An article by Small et al. (8) evaluated 23 patients who underwent stenting of the left colon for benign obstruction. Major complications occurred in 38% of the patients including migration ($n = 2$) and reobstruction ($n = 4$) (8). Another series of patients was evaluated by Seymour et al. (9) and showed that only 1 of 18 patients had migration of their colonic stent for obstructing left-sided colon cancer. There was no obstruction from stent migration in this single patient. This complication occurred at 250 days and resolved with stent removal (9). Phytobezoars, gallstones, and rectal foreign bodies are also known to cause colonic obstruction (10).

In summary, a plethora of causes can ultimately culminate in obstruction of the large bowel. The main three causes are large bowel cancer, adhesions, and retroperitoneal tumors. Another frequent cause is hernias. Hernias lead to an appreciable rate of nonreversible ischemia according to the data by Markogiannakis et al. (1). Grade of recommendation: C.

WHAT IS THE PROPER DIAGNOSTIC EVALUATION?

Options for confirming a radiographic diagnosis of a large bowel obstruction are limited and frequently require a multidisciplinary approach. Often, large bowel obstruction is diagnosed by clinical presentation, plain abdominal x-ray, and specialized radiographic tests. Plain abdominal radiographs are said to have 84% sensitivity and 72% specificity in diagnosing large bowel obstruction (2).

Often, a water-soluble contrast enema must be used to establish a diagnosis of large bowel obstruction. This has

a sensitivity of 96% and a specificity of 98% in diagnosing large bowel obstruction (2). However, computed tomography (CT) scanners are now readily available in most hospitals and can be accessed for diagnostic purposes in a timely fashion. In a single institution review over 7 years, it was noted that multidetector CT imaging was more accurate in making the diagnosis of large bowel obstruction than was contrast enema. CT imaging also allowed for the evaluation of other disease processes and was more readily available (11). In contrast, Cappell and Batke (2) state that the sensitivity and specificity of abdominopelvic CT in diagnosing large bowel obstruction is 90%. It is the opinion of the authors that even though multidetector CT imaging has a comparable diagnostic capability to a water-soluble enema, CT is more preferable due to its ability to evaluate for other disease and its availability.

In addition to radiographic studies, a thorough laboratory evaluation is useful in determining the patient's overall clinical status and may indicate intestinal ischemia, necrosis, or perforation. Although no Level I evidence can be found to support the routine ordering of certain laboratory tests, it is known that patients with large bowel obstruction often present with multiple metabolic derangements requiring correction prior to surgical intervention. Given that the most common cause of large bowel obstruction is cancer, it seems reasonable to obtain a baseline carcinoembryonic antigen level in addition to lactate level, arterial blood gases, coagulation profile, complete blood count, and complete metabolic panel.

Aside from routine hematologic and microbiologic testing, it is the opinion of the authors that the preferred test for diagnosing a large bowel obstruction is CT scan. This modality lends itself to being readily available, is quickly interpreted, allows for studying the extent of the primary process, and can be combined with water-soluble enemas if necessary (11). Grade of recommendation: C.

WHAT IS THE PREFERRED OPERATIVE APPROACH?

The initial treatment of large bowel obstruction is correction of fluid deficits and electrolyte disturbances. Foley catheter, nasogastric tube, and consideration of central venous pressure monitoring for those patients in which fluid overload are concerns. Careful attention to antibiotic and prophylactic (deep vein thrombosis and gastrointestinal) regimens is needed (2). To date there is little Level I evidence comparing one operative approach to another. With the gaining popularity of colonic stents, it is feasible that fewer large bowel obstructions will be taken emergently to the operating room (OR). If there is concern over ischemia or perforation, the patient has not clinically improved, or cecal diameter is increasing, laparotomy should be performed (12). Because most cases of colonic obstruction are due to colon cancer, we elaborate more thoroughly on this topic. In any case, it is incumbent on the operating surgeon to thoroughly evaluate the remaining colon for synchronous lesions.

Operative Management of Obstructing Colon Cancer

The debate over management in obstructing colorectal cancer is centered around two issues: nonoperative management using stents and whether to perform a primary

anastomosis. The role of stenting in colonic obstruction is covered later in the chapter. In right-sided colon cancer, a right hemicolectomy should be performed (2). The distal resection margin may include the right branch of the middle colic, especially if the cancer is located at the hepatic flexure (4). In stable patients, this can be done with a primary anastomosis. Those patients who are unstable, have perforation with peritonitis, or have a distended bowel should have an ileostomy performed (2). An article by Stoyanov et al. (13) looked at 232 cases of obstructing colorectal cancer requiring urgent surgical intervention. One hundred sixty tumors were located in the colon, and the remaining 72 had obstructing rectal lesions. In this group, there was a 25% mortality rate. It was noted that there was a slightly higher mortality in the primary anastomosis group (13).

A second series retrospectively reviewed the records of 23 patients with obstructing lesions of the left colon (14). The patients underwent different surgical procedures: 14 underwent one-stage colonic resection with intraoperative colonic lavage ($n = 10$) or subtotal colectomy ($n = 4$), which comprised the resection and primary anastomoses group. Nine patients underwent staged resection with either Hartmann's or loop colostomy and comprised the staged resection group. There was one case of anastomotic dehiscence in the resection and primary anastomoses group and two cases in the staged resection group. The authors concluded that a one-stage procedure is safe and may be indicated for the management of the majority of cases (14). For those patients who present with disseminated disease, a palliative resection should be performed. For recurrent disease, a bypass procedure or proximal stoma is most appropriate (2).

Operative Management of Other Causes

Benign strictures can be treated by segmental resection. In Crohn's disease, stricturoplasty may be more feasible. Preoperative screening colonoscopy is warranted to rule out malignancy. Strong consideration must be given to diverting colostomy in the presence of a radiation-induced stricture. Radiation history does not thoroughly exclude a primary anastomosis (2).

Multiple operative approaches are available to the operating surgeon. The decision on which, if any, procedure to perform is based on the preoperative imaging studies, the clinical status of the patients, and the disease process causing the obstruction. Because the overwhelming majority of colonic obstruction cases are due to colon cancer, standard oncologic operative technique is imperative. It is our opinion that hemodynamically compromised patients, those with gross peritonitis, grossly overdistended bowel, palliative procedures, and those with previous radiation are candidates for diverting ostomy. If none of these conditions are met, performing a primary anastomosis is reasonable. On-table colonic lavage does not appear to add any benefit (2,13,14). Grade of recommendation: C.

WHAT ARE THE NONOPERATIVE APPROACHES?

Great advances have been made in the nonoperative treatment of large bowel obstruction. Traditionally, surgery was the treatment of choice. The current widespread use and technical advancements of endoscopy have expanded the available armamentarium to treat this disease. The current

options for nonoperative management include photodynamic therapy, electrocoagulation, laser coagulation, and balloon dilation. However, the endoluminal stent has made a significant impact on the nonoperative treatment of large bowel obstruction. Given that patients with large bowel obstruction have a significant morbidity and mortality from diverting colostomy (16% and 5%, respectively), stents have become an acceptable treatment option for those patients with inoperable disease and for those who are poor surgical candidates (15). As such, Level I evidence to justify the use of laser coagulation and the other aforementioned methods is scarce. Articles are now appearing frequently on the benefits of colonic stents. We explore the indications, applications, and complications here. Outcomes for colonic stenting are covered in the next section.

The minimally invasive nature of colonic stents makes them a perfect adjunct for treating large bowel obstruction in poor surgical candidates and those needing palliative treatment from obstructing cancer. Benign strictures are also being treated by stenting (15). Some tout the widespread applicability of colonic stenting (15). To these authors, colonic stenting is indicated in all patients when technically feasible, thus allowing a one-stage procedure while also allowing full evaluation of disease extent (7,15,16).

The most recent series published in *Colorectal Disease* highlights 63 patients referred for large bowel obstruction (17). A prospective database was evaluated. Sixty-three patients had 71 stenting procedures performed. Thirty-two patients had metastatic disease discovered during their evaluation. Extrinsic compression caused seven strictures. The indication for stenting was palliation in 56 patients and served as a bridge to a one-stage procedure in 7 patients. Technical success was achieved 91% of the time. Obstructive symptoms were relieved in 89%. Twenty-four percent of the patients had complications, including overgrowth (8%), migration (6%), fistulation (4%), stent fracture (3%), tenesmus (3%), and fecal urgency (1%). No procedure-related deaths occurred, and there were no technical failures for lesions proximal to the descending colon. The authors concluded that combination endoscopic/fluoroscopic colorectal stenting is effective and safe (17).

Dauphine and colleagues (16) retrospectively reviewed 26 patients with malignant obstruction who underwent colonic stenting. The indications, success, and complication rates are mirrored in other studies. Fourteen patients had palliative procedures performed. Twelve patients had colonic stents placed as a bridge to surgery. First attempts were successful in 22 patients. In the remaining four individuals, three required emergency surgery, and one was successfully stented at the second attempt. Seventy-five percent of patients in the bridge-to-surgery group went on to elective colon resection. There was a 29% reobstruction rate and one (9%) stent migration. Patency was maintained in nine (64%) patients who underwent palliative treatment. Based on this, the authors concluded that colonic stents achieve immediate nonoperative decompression that is both safe and effective. Stenting is also a useful adjunct allowing

elective resection in the majority of resectable cases (16). A Cochrane review article published by Trompetas (18) found that colonic stenting is the best option for palliation or as a bridge to surgery. Morbidity, mortality, and colostomy rates are reduced by using stents. Stenting, depending on the health care system, is likely to be cost-effective (18). The literature focuses on descending colon, sigmoid, and rectal obstruction. As such, more information is needed on the applicability of stenting with regards to right colon and transverse lesions.

Colonic stenting is the most widely accepted method of nonoperative treatment. However, its use is limited by the small number of trained physicians and centers performing the procedure and its utility, at this point, seems to be most pronounced in treating rectal, sigmoid, left, and distal transverse colon lesions. Stenting allows for the relief of obstruction and the full evaluation of the primary process, and it can allow for a one-stage procedure. The complication rate is very low. Stenting is particularly helpful in those where treatment is palliative and for patients who are stable and can undergo resuscitation and primary disease evaluation as a bridge to a single operation (16–18). Grade of recommendation: B.

WHAT ARE THE OUTCOMES?

The outcomes for patients presenting with large bowel obstruction vary depending on the cause and whether the patient has compromised bowel at the time of operation. Outcomes for some causes of large bowel obstruction were alluded to in the corresponding sections. Mortality rates for those presenting with large bowel obstruction from colon cancer range from 5% to 25%. The mortality rates for those needing urgent operative Hartmann's procedure is similar (13,19). The mortality rate increases with findings of necrosis and perforation. Incarcerated hernias are more likely to cause necrosis or perforation (1). A study by Zorcolo et al. (20) retrospectively reviewed the records of 323 patients who presented acutely and underwent surgery over a 10-year period. The etiology of obstruction was left-sided colorectal cancer and diverticular disease. The aim of the review was to identify a difference in outcome of resection and primary anastomosis with Hartmann's procedure. Primary anastomosis was performed in 176 (55.7%) patients with a 30-day mortality of 5.7%. Nine patients (5.1%) had anastomotic breakdown. Hartmann's resection was associated with a higher incidence of systemic and surgical morbidity (39.5% and 24.3%, respectively). Mortality from primary anastomosis (5.7%) compared favorably with those undergoing Hartmann's resections (20.4%).

As mentioned previously, colonic stenting has the ability to convert an emergency procedure to an elective procedure with the ability to have a colon prep and evaluate the patient for other systemic disease. The aforementioned studies reveal a lower morbidity and mortality when colonic stents are used as a bridge to a single surgical procedure. Grade of recommendation: B.

Evidentiary Table

Ref.	Level of evidence	Groups	Design	Endpoint
1	III	Large and small bowel obstruction patients	Prospective cohort study	None
2	IV	None	Review article	None
3	III	All patients with intestinal obstruction	Retrospective cohort study	None
4	NA	None	Textbook	None
5	IV	None	Case report	None
6	III	All patients with migrated endoscopically placed endoprosthesis needing operative intervention	Retrospective cohort study	Surgical intervention
7	NA	0	Review paper	None
8	III	23 patients with benign colorectal strictures and all in the left colon	Retrospective review of prospectively collected data	Relief of obstruction
9	III	All patients had malignant left-sided colon cancer	Retrospective review	Relief of obstruction
10	IV	0	Case report	None
11	III	Patients with suspected lower bowel obstruction	Retrospective case note analysis	? Diagnosis confirmed by operative findings
12	IV	0	Review article	?
13	III	Acute, subacute, chronic, or recurring obstructions	Retrospective review	0
14	II	14 patients underwent one-stage colonic resection [intraoperative lavage of colon (n = 10) or subtotal colectomy (n = 4); resection and primary anastomoses group] and 9 patients underwent staged resection [Hartmann's operation (n = 4) or loop colostomy (n = 5); staged resection group]	Prospective	Anastomotic leak, mortality, hospital length of stay
15	II	11 consecutive patients with lower bowel obstruction and no peritonitis	Inception cohort study	Hospital length of stay, mortality, anastomotic leak, colostomy closure
16	III	26 patients with malignant left-sided large bowel obstruction	Retrospective cohort	Those who went to elective resection, stent migration, success at first-time stent placement with relief of obstruction
17	III	63 patients referred for treatment of malignant large bowel obstruction	Retrospective review of prospectively collected data	Technical success, clinical success (decompression), and procedure-related complications
18	IV	0	Review article	
19	III	93 patients with acute left colonic obstruction	Retrospective review	Mortality and morbidity rates, reoperation rate, hospital stay
20	III	323 patients who underwent emergency surgery for left-sided diverticulitis or colon cancer. Patients were stratified into three groups according to whether the presentation was with localized or generalized peritonitis, or with obstruction	Retrospective review	30-day mortality, wound infection, anastomotic leak, surgical morbidity, hospital stay

REFERENCES

- Markogiannakis H, Messaris E, Dardamanis D, et al. Acute mechanical bowel obstruction: clinical presentation, etiology, management and outcome. *World J Gastroenterol* 2007; 13: 432–7.
- Cappell MS, Batke M. Mechanical obstruction of the small bowel and colon. *Med Clin North Am* 2008; 92: 575–97.
- Jenkins JT, Taylor AJ, Behrns KE. Secondary causes of intestinal obstruction: rigorous preoperative evaluation is required. *Am Surg* 2000; 66: 662–6.
- Fazio V, Church J, Delaney C. *Current Therapy in Colon and Rectal Surgery*, 2nd edition. St. Louis, MO: Mosby, 2004.
- Varras M, Kostopanagiotou E, Katis K, et al. Endometriosis causing extensive intestinal obstruction simulating carcinoma of the sigmoid colon: a case report and review of the literature. *Eur J Gynaecol Oncol* 2002; 23: 353–7.
- Diller R, Senninger N, Kautz G, et al. Stent migration necessitating surgical intervention. *Surg Endosc* 2003; 17: 1803–7.
- Lopera JE, Ferral H, Wholey M, et al. Treatment of colonic obstructions with metallic stents: indications, technique, and complications. *Am J Roentgenol* 1997; 169: 1285–90.
- Small AJ, Young-Fadok TM, Baron TH. Expandable metal stent placement for benign colorectal obstruction: outcomes for 23 cases. *Surg Endosc* 2008; 22: 454–62.
- Seymour K, Johnson R, Marsh R, et al. Palliative stenting of malignant large bowel obstruction. *Colorectal Dis* 2002; 4: 240–5.
- Efrati Y, Freud E, Serour F, et al. Phytobezoar-induced ileal and colonic obstruction in childhood. *J Pediatr Gastroenterol Nutr* 1997; 25: 214–16.

11. Jacob SE, Lee SH, Hill J. The demise of the instant/unprepared contrast enema in large bowel obstruction. *Colorectal Dis* 2007.
12. Lopez-Kostner F, Hool GR, Lavery IC. Management and causes of acute large-bowel obstruction. *Surg Clin North Am* 1997; 77: 1265–90.
13. Stoyanov H, Julianov A, Valtchev D, et al. Results of the treatment of colorectal cancer complicated by obstruction. *Wien Klin Wochenschr* 1998; 110: 262–5.
14. de Aguilar-Nascimento JE, Caporossi C, Nascimento M. Comparison between resection and primary anastomosis and staged resection in obstructing adenocarcinoma of the left colon. *Arq Gastroenterol* 2002; 39: 240–5.
15. Tamim WZ, Ghellai A, Counihan TC, et al. Experience with endoluminal colonic wall stents for the management of large bowel obstruction for benign and malignant disease. *Arch Surg* 2000; 135: 434–8.
16. Dauphine CE, Tan P, Beart RW Jr, et al. Placement of self-expanding metal stents for acute malignant large-bowel obstruction: a collective review. *Ann Surg Oncol* 2002; 9: 574–9.
17. Baraza W, Lee F, Brown S, et al. Combination endo-radiological colorectal stenting: a prospective 5-year clinical evaluation. *Colorectal Dis* 2008; 10: 901–6.
18. Trompetas V. Emergency management of malignant acute left-sided colonic obstruction. *Ann R Coll Surg Engl* 2008; 90: 181–6.
19. Hennekine-Mucci S, Tuech JJ, Brehant O, et al. Management of obstructed left colon carcinoma. *Hepatogastroenterol* 2007; 54: 1098–101.
20. Zorcolo L, Covotta L, Carlomagno N, et al. Safety of primary anastomosis in emergency colo-rectal surgery. *Colorectal Dis* 2003; 5: 262–9.

Acute and Chronic Mesenteric Ischemia

Joshua B. Alley

Clinical Questions		
Question	Answer	Grade of recommendation
What is the ideal mode of imaging in CMI and AMI?	AMI: angio or CTA CMI: duplex, angio, CTA, MRA	B
Endovascular therapy for AMI?	Selective thrombolysis in early AMI	C
Open or endovascular treatment for CMI?	Open has better patency, both may be offered safely	B
Single- or multivessel open reconstruction?	Equivalent, may be tailored to patient	C
How to treat mesenteric venous thrombosis?	Anticoagulation +/- surgery for peritonitis; catheter-directed thrombolysis may be safe	C
How to treat NOMI?	Catheter-directed vasodilators +/- surgery for peritonitis	C
Abbreviations: AMI, acute mesenteric ischemia; CMI, chronic mesenteric ischemia; CTA, computed tomography angiography; MRA, magnetic resonance angiography; NOMI, nonocclusive mesenteric ischemia.		

Mesenteric ischemic syndromes remain a challenging and morbid spectrum of surgical diseases, despite advances in surgical critical care, diagnostic imaging, and minimally invasive techniques. The mesenteric ischemic syndromes include acute mesenteric ischemia (AMI) of all causes, chronic mesenteric ischemia (CMI), mesenteric venous thrombosis (MVT), and nonocclusive mesenteric ischemia (NOMI). Whereas lower extremity and carotid occlusive diseases may be more common, mesenteric ischemia carries higher morbidity and mortality rates. Delay in diagnosis is common and is the most serious shortcoming in current treatment of mesenteric ischemia. In one retrospective analysis, only one-third of patients with mesenteric ischemia were correctly diagnosed before surgery or death (1). Early diagnosis of mesenteric ischemia is a challenge, but the entity must be considered if acceptable outcomes are desired.

WHAT IS THE IDEAL MODE OF IMAGING IN THE DIAGNOSIS OF AMI OR CMI?

Duplex ultrasound: Transabdominal duplex exam performed in a competent vascular lab offers an accurate, noninvasive method of splanchnic vascular assessment, especially for screening in the ambulatory population. In a prospective validation study in which duplex was paired with angiography, a peak systolic velocity of ≥ 275 cm/s in the superior mesenteric artery (SMA) and ≥ 200 cm/s in the celiac artery (CA) was predictive of a 70–100% stenosis with sensitivity of 92% and specificity of 96% for the SMA and sensitivity of 87% and specificity of 80% for the CA (2) (Level Ib evidence). SMA stenosis greater than 50% or occlusion may

be predicted by an end-diastolic velocity greater than or equal to 45 cm/s. CA stenosis may be highly predicted by a finding of reversed flow in the common hepatic artery (3). Postprandial duplex was not found to increase the sensitivity of the exam (4). Duplex is significantly limited in several ways, however. Duplex ultrasound has not been evaluated in the setting of acute mesenteric ischemia, nor can it interrogate mesenteric vessels distal to the proximal main vessel, where emboli may lodge. Ultrasound findings must be interpreted in light of the patient's clinical scenario, because significant stenoses and occlusions of the mesenteric vessels can occur in the asymptomatic patient.

Angiography: Formal contrast angiography is considered the gold standard for diagnosis of AMI. Anteroposterior and lateral aortic views demonstrate the origins of the mesenteric arteries and are diagnostic of stenoses or occlusions. Case series report sensitivity of 74–100% and specificity of 100% in the diagnosis of AMI (5). Catheter access to the mesenteric vessels can also be obtained, allowing endovascular therapy of the offending lesion.

CT angiography: Although early studies of computed tomography (CT) angiography yielded less than encouraging results, more recent reviews using multidetector row CT angiography seem to indicate an acceptable sensitivity of 96% and specificity of 94% (6). CT angiography may also yield additional information about the condition of the bowel, assisting in the decision of whether to perform laparotomy. MVT can also be reliably diagnosed on CT angiography, with a sensitivity of 100% for acute MVT and 93% for chronic MVT (7). In summary, CT angiography may be considered as one of the first-line studies in mesenteric ischemic syndromes (Level IIIB).

MRA: Magnetic resonance angiography (MRA) in the setting of AMI is of limited value. MRA has been compared with digital subtraction angiography in the setting of CMI only in small retrospective series (8,9). Postprocedural imaging may be better using CT angiography rather than MRA because of faster acquisition times, better resolution, and the improved ability to visualize flow through metallic stents (10) (Level IIIb evidence in CMI).

Answer: For CMI, duplex ultrasound, CT angiography, and MRA offer acceptable results, with angiography as a potential confirmatory step. In AMI, only CT angiography or invasive angiography have been studied, and both are reliable (Grade B recommendation).

CAN ENDOVASCULAR THERAPY BE RECOMMENDED FOR ACUTE THROMBOEMBOLIC MESENTERIC ISCHEMIA?

It is generally agreed that endovascular therapy has a limited role in the setting of AMI with peritonitis, in which case immediate laparotomy is usually indicated. However, in that subset of patients with suspected early (and thus potentially reversible) mesenteric ischemia, some have advocated angiography with catheter-based therapy of the arterial lesion. In a review of 48 total published cases of thrombolysis in the setting of acute thromboembolic mesenteric ischemia from 1979 to 2002, technical success was achieved in 43 cases, but clinical success (defined as freedom from death or laparotomy) was seen in only 30 of 48 patients. Mortality in this highly select series of patients managed with combination of catheter-directed thrombolysis and surgery was 10.4% (11). No randomized comparison of open surgery versus endovascular therapy exists for the treatment of patients with acute mesenteric ischemia (Level IV evidence).

Answer: No head-to-head comparison exists comparing open surgery with endovascular treatment for acute thromboembolic mesenteric ischemia. Selective thrombolysis may be attempted, mandating postprocedure observation for signs of intestinal infarction (Grade C recommendation).

DOES EVIDENCE FAVOR OPEN BYPASS OR CATHETER-BASED ENDOVASCULAR INTERVENTION FOR CMI?

Many small case series of percutaneous angioplasty and/or stenting (PAS) have reported short-term results at least consistent with if not less morbid than open revascularization (OR) (12–15). Primary and primary assisted patency rates are consistently lower than in large series of patients undergoing OR (16). One case-control study attempted to compare similar cohorts of patients undergoing OR versus PAS. In-hospital morbidity and mortality were not different between the groups, but PAS was associated with statistically significantly decreased one-year primary patency (58% versus 90%, $p < 0.001$) and primary assisted patency (65% versus 96%, $p < 0.001$) and the need for earlier reintervention (17). (Level IIIb evidence).

Answer: PAS seems to offer greater patient convenience at the expense of diminished long-term patency. Both open and endovascular techniques can be safely offered to patients, but open surgery remains the gold standard (Grade B recommendation).

SHOULD OR FOR CMI INCLUDE SINGLE- OR MULTIPLE-VESSEL RECONSTRUCTION?

In multiple retrospective case series, no statistically significant difference in either primary patency or mortality has been shown between single (SMA) and multiple vessel reconstruction (18–20) (Level IV evidence, case series). Choice of revascularization technique is typically tailored to the patient's anatomy and physiologic state at surgery.

Answer: The data are inconclusive. Choice of OR technique may be tailored to the patient (Grade C recommendation).

WHAT IS THE IDEAL TREATMENT FOR ACUTE MVT?

MVT accounts for 5–15% of presentations of mesenteric ischemic syndromes. The mainstay of treatment has historically been immediate heparin anticoagulation with observation for signs of development of intestinal infarction, which then mandates abdominal exploration with resection of involved bowel. Mortality ranges from 15% to 50% (21,22). Some small but promising case series have been reported describing transhepatic or transjugular intrahepatic portal venous catheter access with thrombolysis of the portal vein and superior mesenteric vein, with low mortality rates (0–9%) (23,24). At this time, in the absence of trials comparing standard management with selective mesenteric venous thrombolysis, no strong recommendations can be made.

Answer: Systemic anticoagulation with serial observation for signs of bowel infarction. If resources allow, catheter-directed mesenteric venous thrombolysis may be considered (Grade C recommendation).

WHAT IS THE IDEAL TREATMENT FOR NOMI?

NOMI can be a diagnostic and therapeutic challenge, because patients who develop it may be in no condition for an operation or an extended visit to the angiography suite. Vasopressors, cocaine use, diuretics, and digitalis have all been implicated as contributing factors in NOMI and may exacerbate ischemia in the presence of preexisting atherosclerotic lesions of the mesenteric circulation or in low-flow states such as CHF, hemodialysis, or myocardial infarction.

Four small case series, totaling 42 patients, using intra-arterial infusion of vasodilators (papaverine hydrochloride or tolazoline) or intravenous prostaglandin E₂ as an adjunct to surgery demonstrated a mortality of 0–55%, compared with historic rates of mortality of 70% or more for NOMI (25–28) (Level IV evidence, case series).

Answer: Early angiography with intra-arterial infusion of vasodilators (typically papaverine) and selective laparotomy for gut infarction can be cautiously recommended (Grade C recommendation).

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Duplex versus angio in CMI	1997	2	Ib	B	Duplex sens/spec is 92% and 96% for SMA and 87% and 80% for CA
CTA	2003	6	IIb	B	Improved sens/spec when examining a constellation of findings
MRA for CMI	1997, 2001	8, 9	IIb	B	
Thrombolysis for AMI	2005	11	IV	C	Thrombolysis +/- laparotomy may be attempted for thromboembolic AMI
OR versus PAS for CMI	2007	17	IIb	B	OR more durable, similar morbidity and mortality
Single- or multivessel open reconstruction	1994, 2002, 1992	18-20	IV	C	No difference in single- and multiple-vessel open reconstruction
Catheter-directed thrombolysis for MVT	2005	23, 24	IV	C	Case series describe thrombolysis for venous thrombosis
Vasodilator therapy for NOMI	1984, 1995, 1977, 2007	25-28	IV	C	Case series describe vasodilator therapy for NOMI

Abbreviations: AMI, acute mesenteric ischemia; CA, celiac artery; CMI, chronic mesenteric ischemia; CTA, computed tomography angiography; MRA, magnetic resonance angiography; MVT, mesenteric venous thrombosis; NOMI, nonocclusive mesenteric ischemia; OR, open revascularization; PAS, percutaneous angioplasty and/or stenting.

REFERENCES

- Mamode N, Pickford I, Leiberman P, et al. Failure to improve outcome in acute mesenteric ischaemia: seven year review. *Eur J Surg* 1999; 165: 203-8.
- Nicoloff AD, Williamson WK, Moneta GL, et al. Duplex ultrasonography in evaluation of splanchnic artery stenosis. *Surg Clin N Amer* 1997; 77: 339-55.
- Zwolak RM, Fillinger MF, Walsh DB, et al. Mesenteric and celiac duplex scanning: a validation study. *J Vasc Surg* 1998; 27: 1078-88.
- Gentile AT, Moneta GL, Lee RW, et al. Usefulness of fasting and postprandial duplex ultrasound examinations for predicting high-grade superior mesenteric artery stenosis. *Am J Surg* 1995; 169: 476-9.
- Brandt LJ, Boley SJ. AGA technical review on intestinal ischemia. *Gastrointest* 2000; 118: 954-68.
- Kirkpatrick ID, Kroeker MA, Greenberg HM. Biphasic CT with mesenteric CT angiography in the evaluation of acute mesenteric ischemia: initial experience. *Radiology* 2003; 229: 91-8.
- Rhee RY, Gloviczki P, Mendonca CT, et al. Mesenteric venous thrombosis: still a lethal disease in the 1990s. *J Vasc Surg* 1994; 20: 688-97.
- Meaney JFM, Prince MR, Nostrant TT, et al. Gadolinium-enhanced MR angiography of visceral arteries in patients with suspected chronic mesenteric ischemia. *J Mag Reson Imag* 1997; 7: 171-6.
- Carlos RC, Stanley JC, Stafford-Johnson D, et al. Interobserver variability in the evaluation of chronic mesenteric ischemia with gadolinium-enhanced MR angiography. *Acad Radiol* 2001; 8: 879-87.
- Shih MP, Angle JF, Leung DA, et al. CTA and MRA in mesenteric ischemia: part 2, normal findings and complications after surgical and endovascular treatment. *Am J Roentgenol* 2007; 188: 462-71.
- Schoots IG, Levi MM, Reekers JA, et al. Thrombolytic therapy for acute superior mesenteric artery occlusion. *J Vasc Interv Radiol* 2005; 16: 317-29.
- Sharafuddin MJ, Olson CH, Sun S, et al. Endovascular treatment of celiac and mesenteric arteries stenoses: applications and results. *J Vasc Surg* 2003; 38: 692-8.
- Kasirajan K, O'Hara PJ, Gray BH, et al. Chronic mesenteric ischemia: open surgery versus percutaneous angioplasty and stenting. *J Vasc Surg* 2001; 33: 63-71.
- Landis MS, Rajan DK, Simons ME, et al. Percutaneous management of chronic mesenteric ischemia: outcomes after intervention. *J Vasc Interv Radiol* 2005; 16: 1319-25.
- AbuRahma AF, Stone PA, Bates MC, et al. Angioplasty/stenting of the superior mesenteric artery and celiac trunk: early and late outcomes. *J Endovasc Ther* 2003; 10: 1046-53.
- Park WM, Cherry KJ Jr, Chua HK, et al. Current results of open revascularization for chronic mesenteric ischemia: a standard for comparison. *J Vasc Surg* 2002; 35: 853-9.
- Atkins MD, Kwolek CJ, LaMuraglia GM, et al. Surgical revascularization versus endovascular therapy for chronic mesenteric ischemia: a comparative experience. *J Vasc Surg* 2007; 45: 1162-71.
- Gentile AT, Moneta GL, Taylor LM Jr, et al. Isolated bypass to the superior mesenteric artery for intestinal ischemia. *Arch Surg* 1994; 129: 926-31.
- Park WM, Cherry KJ Jr, Chua HK, et al. Current results of open revascularization for chronic mesenteric ischemia: A standard for comparison. *J Vasc Surg* 2002; 35: 853-9.
- McAfee MK, Cherry KJ Jr, Naessens JM, et al. Influence of complete revascularization on chronic mesenteric ischemia. *Am J Surg* 1992; 164: 220-4.
- Chang RW, Chang JB, Longo WE. Update in management of mesenteric ischemia. *World J Gastroenterol* 2006; 12: 3243-7.
- Kumar S, Sarr MG, Kamath PS. Mesenteric venous thrombosis. *N Engl J Med* 2001; 345: 1683-8.
- Kim HS, Patra A, Khan J, et al. Transhepatic catheter-directed thrombectomy and thrombolysis of acute superior mesenteric venous thrombosis. *J Vasc Interv Radiol* 2005; 16: 1685-91.
- Hollingshead M, Burke CT, Mauro MA, et al. Transcatheter thrombolytic therapy for acute mesenteric and portal vein thrombosis. *J Vasc Interv Radiol* 2005; 16: 651-61.
- Clark RA, Gallant TE. Acute mesenteric ischemia: angiographic spectrum. *Am J Roentgenol* 1984; 142: 555-62.
- Ward D, Vernava AM, Kaminski DL, et al. Improved outcome by identification of high-risk nonocclusive mesenteric ischemia, aggressive reexploration, and delayed anastomosis. *Am J Surg* 1995; 170: 577-81.
- Boley SJ, Sprayregen S, Siegelman SS, et al. Initial results from an aggressive approach to acute mesenteric ischemia. *Surgery* 1977; 82: 848-55.
- Mitsuyoshi A, Obama K, Shinkura N, et al. Survival in nonocclusive mesenteric ischemia: early diagnosis by multidetector row computed tomography and early treatment with continuous intravenous high-dose prostaglandin E1. *Ann Surg* 2007; 246: 229-35.

Ogilvie's Syndrome and Colonic Volvulus

Raymond P. Compton

OGILVIE'S SYNDROME

History and Pathogenesis

Ogilvie's syndrome or colonic pseudo-obstruction was first described by W. H. Ogilvie in 1948 (1). It is manifested by abdominal distention, poor rectal output, and colonic distension without anatomic obstruction. Ogilvie's syndrome has been reported in relation to many conditions. These include post-cesarean section, pregnancy, trauma, orthopedic surgery, cancer, herpetic infection, and other systemic infections, among other events (2–24). This is by no means an exhaustive list of associations. It is currently held that colonic pseudo-obstruction occurs due to an imbalance of sympathetic and parasympathetic input to the colon (25–28).

Though there are well over 1,000 articles that have been published regarding Ogilvie's syndrome since its original description, the vast majority of these are simple case reports, uncontrolled case series, and narrative reviews. The Level I, II, and III data are unfortunately sparse. The important articles are summarized in Table 54.1.

Should Neostigmine Be Used for Treatment of Ogilvie's Syndrome?

All treatments for Ogilvie's syndrome are predicated on the idea that the patient does not have peritoneal signs or peritonitis. Although the risk of spontaneous perforation is low, only about 3%, the mortality of this event is about 40% (29,30). This is compared to only 15% mortality when ischemia or perforation do not occur (30). The risk of perforation seem to vary with duration, progression, and cecal diameter of more than 12 cm (31).

Older studies have shown upward of 90% resolution with conservative measures alone (32–38). These measures have been nicely elucidated in a consensus panel/treatment guideline statement from the American Society for Gastrointestinal Endoscopy (33). Conservative measures include, in some combination, nasogastric tube placement, rectal tube placement, enemas, aggressive positioning, correcting electrolyte abnormalities, serial exam and radiographs, discontinuation of potentiating drugs, and exclusion of true obstruction by water-soluble contrast enema. Aggressive positioning is taken to mean prone positioning with the hips elevated or knee chest positions. When appropriate, this type of positioning should alternate sequentially with left and right lateral decubitus positioning. These maneuvers will often help with the evacuation of flatus (33). Essentially all of the current and historical studies on acute colonic pseudo-obstruction have a uniform starting point

of 24–48 hours of conservative, noninterventional treatment. So given the overall preponderance of Level I, II, and III data. A trial of conservative management, in the absence of signs of peritoneal inflammation, carries a category A recommendation.

Saunders and Kimmey, in their well-done systematic review of acute colonic pseudo-obstruction, recommend intervention for patients with a cecal diameter >10 cm present for three to four days who have not responded to 24–48 hours of conservative treatment (31). Interventions to relieve acute colonic pseudo-obstruction can be divided into two broad categories: prokinetic medications and instrumentations (endoscopic and surgical).

Prokinetic agents such as erythromycin, metaclopramide, and cisapride, have been used but do not have any Level I, II, or III data to support their use (33). Neostigmine remains the only well studied drug for the treatment of acute colonic pseudo-obstruction.

Neostigmine was first reported in 1992 but Hutchinson et al. (38). Several nonrandomized studies have since been reported (39–44). Ponc et al. have reported a randomized control trial showing excellent results (45). Even though this trial had small numbers (21 patients), it was well done and blinded. A similar study by van der Spoel and colleagues randomized 30 critically ill patients with colonic ileus to treatment with neostigmine (46). Nonresponders in each group were treated subsequently in a cross-over fashion with either neostigmine or placebo. Placebo caused no passage of stool, and neostigmine caused defecation in 19 of 24 patients treated. Interestingly, neostigmine in this study was given as a continuous infusion of 0.4–0.8 mg/hour instead of slow bolus treatment as in other studies. In 2000, Amaro and Rogers reported a prospective randomized blinded trial of neostigmine compared with placebo in patients unresponsive to conservative measures (47). In this study, neostigmine was administered as 2 mg IV over three to five minutes. Ten of 11 patients treated with neostigmine resolved the colonic ileus versus none in the placebo-treated patients. Nonresponders were eligible for treatment with unblinded neostigmine. Eight patients were treated in this group (seven from the placebo group and the one neostigmine nonresponder). Seven responded, with only a single patient (from the original placebo group) not responding.

A subsequent systematic review by De Giorgio et al. has summarized the current evidence for neostigmine use very nicely, as well as other prokinetic agents (48). They have proposed a well-evidenced case for neostigmine as the drug of choice for acute colonic pseudo-obstruction.

Most commonly neostigmine is administered in a 2–2.5 mg dose (38,40–45). It is expected that 88% of patients unresponsive to conservative treatment will respond to treatment with neostigmine with only a 7% recurrence rate (31). There is no clear consensus on how quickly this medication should be given. However, given the side effect profile, a slower infusion (30–60 minutes or longer) would seem prudent. Althausen has shown that even in patients with Ogilvie's syndrome after spinal surgery, neostigmine has been safely tolerated with the same level of response (49). Bench research, as reported by Law and colleagues, has

shown that neostigmine not only increased colonic transit but also increased colonic contractile force (50).

Recommendation: Given the level of evidence available, including prospective trials, systematic review, and consensus statements, in addition to the growing number of case reports on the subject, neostigmine must be considered the drug of choice for the treatment of acute colonic pseudo-obstruction unresponsive to conservative treatment. When this is coupled with the almost complete lack of negative data regarding the use of neostigmine for the treatment of acute colonic pseudo-obstruction, this must be given a category A recommendation.

Table 54.1 Summary of Pertinent Articles Regarding Ogilvie's Syndrome

Ref.	Year	Comment
Treatment of Ogilvie's syndrome with neostigmine		
31	2005	Systematic review with an excellent compilation of data up to 2005
33	2002	ASGE Standards of Practice; review of the topic with good recommendations
38	1992	Original report of neostigmine use
45	1999	PRCT of 21 patients; good results with neostigmine treatment
46	2001	PRCT with 30 patients
47	2000	PRCT of 11 patients
48	2001	Systematic review of the pharmacologic treatment
Role of colonoscopy in the treatment of Ogilvie's syndrome		
52	1996	50 patients from Mayo Clinic with 88% success rate
53	1992	45 patients treated with colonoscopy
54	1982	22 patients treated
55	1983	44 patients treated over 8 years
56	1984	22 patients decompressed
57	1997	28 patients added to the literature
Prevention of recurrence of Ogilvie's syndrome		
59	2006	PRCT of polyethylene glycol vs placebo to prevent recurrence

Abbreviations: ASGE, American society for gastrointestinal endoscopy; PRCT, prospective randomized controlled trial.

What Is the Role of Colonoscopy in the Treatment of Ogilvie's Syndrome?

Instrumentation to relieve acute colonic pseudo-obstruction is usually colonoscopy. This treatment has a twofold purpose. One is to decompress the distended bowel, and the second is to assess viability. Colonoscopic decompression has been shown in retrospective study to decrease length of stay (51). In a retrospective series from the Mayo Clinic, 50 patients underwent colonoscopic decompression with an 88% overall success rate, but in-hospital mortality was 30% (52). There was one perforation in this group. Overall, there have been numerous retrospective studies that have shown the safety and efficacy of colonoscopic decompression (52–57). These have been well summarized by Saunders and Kimmey, showing a success rate varying between 73% and 88%. Farinon's report of another 28 patients treated with colonoscopy brings the total to well over 300 patients with fairly uniform results over time and among reviewers (31,57). Additionally, consensus panel and systematic review have supported this course of treatment (31,33).

Maintaining decompression has been a goal as well. Placement of a colonic decompression tube at the time of colonoscopy has been effective in decreasing recurrences. However, in comparison to the numbers of patients sited for colonoscopic decompression, there is a relative paucity of patients in this group. Geller, Farinon, and Berger have all reported retrospective reviews but the only recommendation that can be generated is that it is probably not

Table 54.2 Resection with Primary Anastomosis Versus Colostomy or Pexy in the Literature

Ref.	No. PA	No. HC	No. Pexy	Comment
60	21			Single surgeon experience; no anastomotic failures or deaths. No intraoperative lavage.
61	91	45		No difference between groups for mortality or complications.
62	51	146	56	Several groups; no difference between PA and HC. 15% mortality and 37% overall complication rates. Almost 7% recurrence with pexy alone.
63	9	16	7	HC group more complications and comorbidities than PA group. Sigmoidopexy high recurrence rate. Abstract review due to language.
64	44	33	7	Mortality varied not with procedure but with colon viability.
65	57			Compared PA in gangrenous and viable bowel. High leak rate, 27% and 15%.
66	197			1% anastomotic leak and 1% mortality.
67	13	37		Mortality 31% PA versus 5% HC; morbidity similar. Article in French, so only abstract for review.
68	57	49		6% mortality (11% if gangrenous bowel), 4 leaks. No decompression performed preop.
Total patients	540	326	70	

Abbreviations: HC, Hartmann's type procedure (resection with colostomy); PA, Primary anastomosis; Pexy, fixation of the volvulized portion of the colon.

necessary to reach proximal to the hepatic flexure for tube placement (52,57,58).

There have been a number of case reports concerning percutaneous colostomy. However, there are insufficient data contained in these trials to make any recommendation of evidenced based care.

Based on consensus panel, systematic review, and large amounts of retrospective cohorts, colonoscopic decompression of patients not responding to conservative measures is given a category A recommendation. However, the use of a decompression tube is given a category B recommendation due to the lack of data concerning this. Given the low numbers of patients that fail neostigmine treatment, it would seem unlikely that the question of the use of a decompression tube will ever be able to be answered in a prospective randomized manor.

Can Recurrence of Ogilvie's Syndrome Be Prevented?

Recommendation: Although it would seem an obvious choice to aim research at trying to prevent recurrence of acute colonic pseudo-obstruction, there has been little work in this arena. One nicely done prospective randomized blinded trial has looked at this topic. Sgouros et al. randomized 30 patients with acute colonic pseudo-obstruction to receive polyethylene glycol daily or placebo after resolution of the pseudo-obstruction (59). Treatment was continued for a week, with nonresponders eligible to receive open-label polyethylene glycol subsequently. Essentially all of the polyethylene glycol-treated patients responded and had no recurrence. Five of the placebo-treated patients recurred. However, the number of patients is low, and the follow-up is short. We do not know how long the polyethylene glycol should be continued. Due to these limitations and lack of corroborating data, this can only be given a category B recommendation.

COLONIC VOLVULUS

There is essentially no prospective randomized data regarding colonic volvulus (sigmoid, cecal, or otherwise) published within the last 10 years. There are a number of retrospective articles with large patient volumes that do, however, compare two distinct treatments—resection with primary anastomosis versus resection with colostomy. These are summarized in Table 54.2.

All of the reviews listed are retrospective. There is some heterogeneity among the patients groups, mainly in terms of preoperative decompression and on-table lavage. The mortality rates in these series varies widely, from 1% to more than 30%. Anastomotic leaks have almost the same variance (0–27%). These points only illustrate the wide variation in patient presentation and illness and the heterogeneity of these studies. The recommendations that can be made from these reports are narrow. Resection is better than simple pexy—due to a high recurrence rate of volvulus. This is category B. Primary anastomosis can be undertaken. This is category C due to the wide range of variation in the available literature.

Clearly, prospective data are needed to make any clear recommendations on this subject. Areas of research would include decompression prior to surgery versus

decompression alone and primary anastomosis versus resection with colostomy, among other topics.

REFERENCES

- Ogilvie WH. Large-intestine colic due to sympathetic deprivation. *Br Med J* 1948; 2: 671–3.
- Kim TS, Lee JW, Kim MJ, et al. Acute colonic pseudo-obstruction in postchemotherapy complication of brain tumor treated with neostigmine. *J Pediatr Hematol Oncol* 2007; 29: 420–2.
- Rausch ME, Troiano NH, Rosen T. Use of neostigmine to relieve a suspected colonic pseudoobstruction in pregnancy. *J Perinatol* 2007; 27: 244–6.
- Kakarla A, Posnett H, Jain A, et al. Acute pseudo-obstruction of the colon (Ogilvie's syndrome) following instrumental vaginal delivery. *Int J Clin Pract* 2006; 60: 1303–5.
- Göral V, Uyar A, Müftüoğlu E, et al. Ogilvie's syndrome in a patient with multiple myeloma. *Turk J Gastroenterol* 2002; 13: 115–18.
- Nguyen HT, Cobbs EL. Chronic colonic pseudo-obstruction associated with recurrent congestive heart failure. *J Am Geriatr Soc* 2005; 53: 171–2.
- Busch FW, Hamdorf JM, Carroll CS, et al. Acute colonic pseudo-obstruction following cesarean delivery. *J Miss State Med Assoc* 2004; 45: 323–6.
- Hamilton SW, Jabbar AA. Ogilvie's syndrome: a rare complication of inguinal hernia repair. *Hosp Med* 2004; 65: 562–3.
- Coskun H, Mihmanli M. Neostigmine for the treatment of acute colonic pseudo-obstruction (Ogilvie's syndrome) in a patient on CAPD. *Perit Dial Int* 2004; 24: 85–7.
- Pui JC, Furth EE, Minda J, et al. Demonstration of varicella-zoster virus infection in the muscularis propria and myenteric plexi of the colon in an HIV-positive patient with herpes zoster and small bowel pseudo-obstruction (Ogilvie's syndrome). *Am J Gastroenterol* 2001; 96: 1627–30.
- Shapiro AM, Bain VG, Preiksaitis JK, et al. Ogilvie's syndrome associated with acute cytomegaloviral infection after liver transplantation. *Transpl Int* 2000; 13: 41–5.
- Caner H, Bavbek M, Albayrak A, et al. Ogilvie's syndrome as a rare complication of lumbar disc surgery. *Can J Neurol Sci* 2000; 27: 77–8.
- Estela CM, Burd DA. Conservative management of acute pseudo-obstruction in a major burn. *Burns* 1999; 25: 523–5.
- O'Malley KJ, Flechner SM, Kapoor A, et al. Acute colonic pseudo-obstruction (Ogilvie's syndrome) after renal transplantation. *Am J Surg* 1999; 177: 492–6.
- Teh SH, O'Riordain DS, O'Connell PR. Colonic pseudo-obstruction following acute pancreatitis. *Ir J Med Sci* 1998; 167: 41–2.
- Marinella MA. Acute colonic pseudo-obstruction complicated by cecal perforation in a patient with Parkinson's disease. *South Med J* 1997; 90: 1023–6.
- Polignano FM, Caradonna P, Maiorano E, et al. Recurrence of acute colonic pseudo-obstruction in selective adrenergic dysautonomia associated with infectious toxoplasmosis. *Scand J Gastroenterol* 1997; 32: 89–94.
- Brubacher JR, Levine B, Hoffman RS. Intestinal pseudo-obstruction (Ogilvie's syndrome) in theophylline overdose. *Vet Hum Toxicol* 1996; 38: 368–70.
- Pecha RE, Danilewitz MD. Acute pseudo-obstruction of the colon (Ogilvie's syndrome) resulting from combination tocolytic therapy. *Am J Gastroenterol* 1996; 91: 1265–6.
- Jucgla A, Badell A, Ballesta C, et al. Colonic pseudo-obstruction: a complication of herpes zoster. *Br J Dermatol* 1996; 134: 788–90.

21. Meland NB, Edel C, Devine RM. Ogilvie's syndrome as a complication after abdominoplasty: a case report and review. *Plast Reconstr Surg* 1995; 96: 721-4.
22. Thessen CC, Kreder KJ. Ogilvie's syndrome: a potential complication of vaginal surgery. *J Urol* 1993; 149: 1541-3.
23. Ripps B, Muram D, Winer-Muram HT. Large bowel obstruction: an uncommon complication of a tubo-ovarian abscess. *J Tenn Med Assoc* 1992; 85: 103-4.
24. Post AB, Falk GW, Bukowski RM. Acute colonic pseudo-obstruction associated with interleukin-2 therapy. *Am J Gastroenterol* 1991; 86: 1539-41.
25. Di Giorgio R, Barbara G, Stanghellini V, et al. The pharmacologic treatment of acute colonic pseudo-obstruction. *Aliment Pharm Ther* 2001; 15: 1717-27.
26. Vanek VW, Al-Salti M. Acute pseudo-obstruction of the colon (Ogilvie's syndrome): an analysis of 400 cases. *Dis Col Rect* 1986; 29: 203-10.
27. Khelif K, Scaillon M, Govaerts MJ, et al. Bilateral thorascopic splanchnicectomy in chronic intestinal pseudo-obstruction: report of two paediatric cases. *Gut* 2006; 55: 293-4.
28. Polignano FM, Caradonna P, Maiorano E, et al. Recurrence of acute colonic pseudo-obstruction in selective adrenergic dysautonomia associated with infectious toxoplasmosis. *Scand J Gastroenterol* 1997; 32: 89-94.
29. Rex DK. Acute colonic pseudo-obstruction: ogilvie's syndrome. *Gastrointest* 1994; 2: 233-8.
30. Rex DK. Colonoscopy and acute colonic pseudo-obstruction. *Gastrointest Clin N Am* 1997; 7: 499-508.
31. Saunders MD, Kimmey MB. Systematic review: acute colonic pseudo-obstruction. *Aliment Pharm Ther* 2005; 22: 917-25.
32. Sloyer AF, Panella VS, Demas BE, et al. Ogilvie's syndrome. Successful management without colonoscopy. *Dig Dis Sci* 1988; 33: 1391-6.
33. Eisen GM, Baron TH, Dominitz JA, et al. Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy: acute colonic pseudo-obstruction. *Gastr Endosc* 2002; 56: 789-92.
34. Wandeo H, Mathewson C, Conolly B. Pseudo-obstruction of the colon. *S G O* 1971; 133: 44.
35. Meyers MA. Colonic ileus. *Gastr Rad* 1977; 2: 37-40.
36. Bschulis BL, Smith PE. Pseudo-obstruction of the colon. *Am J Surg* 1978; 136: 66-72.
37. Baker DA, Morin ME, Tan A, et al. Colonic ileus. Indication for prompt decompression. *JAMA* 1979; 241: 2633-4.
38. Hutchinson R, Griffiths C. Acute colonic pseudo-obstruction: a pharmacologic approach. *Ann R Coll Surg Eng* 1992; 74: 364-7.
39. Loftus CG, Harewood GC, Baron TH. Assessment of predictors of response to neostigmine for acute colonic pseudo-obstruction. *Am J Gastroenterol* 2002; 97: 3118-22.
40. Stephenson BM, Morgan AR, Salaman JR, et al. Ogilvie's syndrome: A new approach to an old problem. *Dis Colon Rectum* 1995; 38: 424-7.
41. Trevisani GT, Hyman NH, Church JM. Neostigmine: safe and effective treatment for acute colonic pseudo-obstruction. *Dis Colon Rectum* 2000; 43: 599-603.
42. Turégano-Fuentes F, Muñoz-Jiménez F, Del Valle-Hernández E, et al. Early resolution of Ogilvie's syndrome with intravenous neostigmine: a simple, effective treatment. *Dis Colon Rectum* 1997; 40: 1353-7.
43. Paran H, Silverberg D, Mayo A, et al. Treatment of acute colonic pseudo-obstruction with neostigmine. *J Am Coll Surg* 2000; 190: 315-18.
44. Abeyta BJ, Albrecht RM, Schermer CR. Retrospective study of neostigmine for the treatment of acute colonic pseudo-obstruction. *Am Surg* 2001; 67: 265-8.
45. Ponc RJ, Saunders MD, Kimmey MB. Neostigmine for the treatment of acute colonic pseudo-obstruction. *N Engl J Med* 1999; 341: 137-41.
46. van der Spoel JI, Oudemans-van Straaten HM, Stoutenbeek CP, et al. Neostigmine resolves critical illness-related colonic ileus in intensive care patients with multiple organ failure—a prospective, double-blind, placebo-controlled trial. *Intensive Care Med* 2001; 27: 822-7.
47. Amaro R, Rogers AI. Neostigmine infusion: new standard of care for acute colonic pseudo-obstruction? *Am J Gastroenterol* 2000; 95: 304-5.
48. De Giorgio R, Barbara G, Stanghellini V, et al. Review article: the pharmacological treatment of acute colonic pseudo-obstruction. *Aliment Pharmacol Ther* 2001; 15: 1717-27.
49. Althausen PL, Gupta MC, Benson DR, et al. The use of neostigmine to treat postoperative ileus in orthopedic spinal patients. *J Spinal Disord* 2001; 14: 541-5.
50. Law NM, Bharucha AE, Undale AS, et al. Cholinergic stimulation enhances colonic motor activity, transit, and sensation in humans. *Am J Physiol Gastrointest Liver Physiol* 2001; 281: G1228-G1237.
51. Nelson JD, Urban JA, Salisbury TL, et al. Acute colonic pseudo-obstruction (Ogilvie syndrome) after arthroplasty in the lower extremity. *J Bone Joint Surg Am* 2006; 88: 604-10.
52. Geller A, Petersen BT, Gostout CJ. Endoscopic decompression for acute colonic pseudo-obstruction. *Gastrointest Endosc* 1996; 44: 144-50.
53. Jetmore AB, Timmcke AE, Gathright BJ Jr, et al. Ogilvie's syndrome: colonoscopic decompression and analysis of predisposing factors. *Dis Colon Rectum* 1992; 35: 1135-42.
54. Nivatvongs S, Vermeulen FD, Fang DT. Colonoscopic decompression of acute pseudo-obstruction of the colon. *Ann Surg* 1982; 196: 598-600.
55. Strodel WE, Nostrant TT, Eckhauser FE, et al. Therapeutic and diagnostic colonoscopy in non-obstructive colonic dilatation. *Ann Surg* 1983; 19: 416-21.
56. Bode WE, Beart RW, Spencer RJ, et al. Colonoscopic decompression for acute pseudo-obstruction of the colon (Ogilvie's syndrome): report of 22 cases and review of the literature. *Am J Surg* 1984; 147: 243-5.
57. Farinon AM, Stroppa I, Torquati A, et al. Acute pseudo-obstruction of the colon (Ogilvie's syndrome): Advances in management. *Ann Ital Chir* 1997; 68: 331-6.
58. Berger WL, Saeian K. Sigmoid stiffener for decompression tube placement in colonic pseudo-obstruction. *Endoscopy* 2000; 32: 54-7.
59. Sgouros SN, Vlachogiannakos J, Vassiliadis K, et al. Effect of polyethylene glycol electrolyte balanced solution on patients with acute colonic pseudo obstruction after resolution of colonic dilation: a prospective, randomised, placebo controlled trial. *Gut* 2006; 55: 638-42.
60. Sule AZ, Misauno M, Opaluwa AS, et al. One stage procedure in the management of acute sigmoid volvulus without colonic lavage. *Surgeon* 2007; 5: 268-70.
61. Akcan A, Akyildiz H, Artis T, et al. Feasibility of single-stage resection and primary anastomosis in patients with acute noncomplicated sigmoid volvulus. *Am J Surg* 2007; 193: 421-6.
62. Oren D, Atamanalp SS, Aydinli B, et al. An algorithm for the management of sigmoid colon volvulus and the safety of primary resection: experience with 827 cases. *Dis Colon Rectum* 2007; 50: 489-97.
63. Ağaoğlu N, Yücel Y, Türkyılmaz S. Surgical treatment of the sigmoid volvulus. *Acta Chir Belg* 2005; 105: 365-8.
64. Bhuiyan MM, Machowski ZA, Linyama BS, et al. Management of sigmoid volvulus in Polokwane-Mankweng Hospital. *S Afr J Surg* 2005; 43: 17-19.

65. Raveenthiran V. Restorative resection of unprepared left-colon in gangrenous vs. viable sigmoid volvulus. *Int J Colorectal Dis* 2004; 19: 258–63.
66. De U, Ghosh S. Single stage primary anastomosis without colonic lavage for left-sided colonic obstruction due to acute sigmoid volvulus: a prospective study of one hundred and ninety-seven cases. *ANZ J Surg* 2003; 73: 390–2.
67. Touré CT, Dieng M, Mbaye M, et al. Results of emergency colectomy in the management of the colon volvulus in Dakar hospital. *Ann Chir* 2003; 128: 98–101; discussion 102.
68. Kuzu MA, Aşlar AK, Soran A, et al. Emergent resection for acute sigmoid volvulus: results of 106 consecutive cases. *Dis Colon Rectum* 2002; 45: 1085–90.

Hemorrhoids

Clarence E. Clark III

Clinical Questions		
Question	Answer	Grade of recommendation
Is observation alone a viable option?	No. Clear benefit with intervention for grade II and greater hemorrhoids.	A
Is there a clear advantage of one nonoperative management strategy over the others?	Yes. Rubber band ligation is superior to anal dilation, sclerotherapy, and infrared photocoagulation.	A
Is one operative strategy superior to the others?	Yes. Conventional hemorrhoidectomy is superior to procedure for prolapse and hemorrhoids but no significant difference between Milligan Morgan (open) hemorrhoidectomy and Ferguson hemorrhoidectomy.	B
What is the best management strategy for symptomatic external hemorrhoids?	Excision over topical agents and incision.	B

INTRODUCTION

There are a million new cases of hemorrhoids per year in the United States (1). Sixteen million people total are affected annually (2,3), and 168,000 people are hospitalized for complications related to this disease (4). Nearly 2 million ambulatory care visits per year are reported for hemorrhoids in the United States (9), making this disease a significant health care issue.

Hemorrhoids are classified as internal, external, or mixed. Internal hemorrhoids (IHs) are vascular cushions found above the dentate line, and external hemorrhoids are found below the dentate line (1). IHs are further classified based on their symptoms: first degree are those that cause bleeding but do not prolapse; second-degree hemorrhoids prolapse out of the anal canal during defecation and spontaneously return to their anatomical position; third-degree hemorrhoids prolapse and require digital replacement; and fourth-degree hemorrhoids are permanently prolapsed and cannot be reduced.

Evaluation starts with history and physical exam, paying close attention to complaints of anal bleeding, itching, discharge, discomfort, pain, or prolapse. Anoscopy is included to help classify the type of hemorrhoids.

Because this disease is commonly seen in general and colorectal surgical practices, evidence-based data are essential for guiding nonoperative and operative treatment decisions. Conservative measures (topical agents, stool softeners, and dietary/lifestyle modifications) are effective first-line treatments, but the focus of this chapter is treatment of hemorrhoids after the failure of conservative

management. I examine recent evidence-based data on the treatment modalities for internal and external hemorrhoids. Details of techniques for the listed interventions can be found in their original articles.

MANAGEMENT INTERNAL HEMORRHOIDS

Is Observation Alone a Viable Option?

The potential impact of doing nothing for symptomatic hemorrhoids should be discussed with the patient along with described nonoperative and operative treatment options. An examination of the natural history of a first-episode symptomatic grade II hemorrhoids showed that treatment with rubber band ligation had a better prognosis over observation alone over 48 months, including need to treat (hemorrhoidectomy for recurrent symptoms in 29.6% versus 40.2%) and relief of symptoms after treatment (48% versus 19.8%) (5). The authors note, however, that 25% of the observation group did remit within their 48 month follow-up period.

Early intervention with rubber band ligation is superior to observation of internal hemorrhoids. Level of evidence Ib. Strength of recommendation: A.

Summary: This study shows observation significantly increases the risk of developing symptomatic hemorrhoids requiring surgery. Intervention should be considered early in these patients in light of the clear benefit of symptom relief.

Anal dilation, injection sclerotherapy (IS), cryotherapy, infrared coagulation (IRC), laser therapy, diathermy

coagulation, and rubber band ligation (RBL) have been described as outpatient options for treating hemorrhoids. Here we discuss the evidence-based data of these treatment modalities.

IS THERE A CLEAR ADVANTAGE OF ONE NON-OPERATIVE MANAGEMENT STRATEGY OVER THE OTHERS?

A randomized prospective study in Europe with a 17-year follow-up compared anal dilation to surgical hemorrhoidectomy for grade II–III hemorrhoids (6). Three groups were assigned: group A underwent Milligan (23) hemorrhoidectomy (41 patients) with no retractor, group B was had the original Lord's six-finger dilation with a dilator (46 patients), and group C underwent anal dilation as described previously without the dilator (51 patients). More patients were symptom-free in group A (52%) versus group B (23%) and group C (27%) after treatment. Recurrence of hemorrhoids was lower for the hemorrhoidectomy group. Fecal incontinence was the major complication found during follow-up for groups B and C (52% of the total patients).

A meta-analysis by MacRae et al. compared several of the nonoperative treatment methods and surgical hemorrhoidectomy with a no treatment (7). Overall, patients undergoing hemorrhoidectomy had a significantly better response to treatment than did patients treated with RBL ($p = 0.001$), although this was at a cost of a significantly greater risk of complications ($p = 0.02$) and pain ($p < 0.0001$). For grade III hemorrhoids alone, no difference was shown. RBL was shown to be significantly better than injection sclerotherapy in response to treatment ($p = 0.005$). This difference was shown for both grades I and II hemorrhoids ($p = 0.007$) and grade III hemorrhoids ($p = 0.042$), with no significant difference in the complication rate. Patients treated with RBL were less likely to require further therapy than those treated with either sclerotherapy ($p = 0.031$) or IRC ($p = 0.0014$), although pain was significantly more likely to occur following RBL (IS, $p = 0.03$; IRC, $p < 0.0001$). No difference was found between sclerotherapy and infrared photocoagulation for any of the outcome measures.

Recommendations from this article are that RBL should be the first-line treatment for grade III prolapsing hemorrhoids, reserving hemorrhoidectomy for patients whose symptoms are not relieved, and RBL appears to be the therapy of choice for grades I to II hemorrhoids.

A more recent meta-analysis of randomized controlled trial (RCT) of RBL versus excisional hemorrhoidectomy (closed or open) (8) found RBL to be as effective for grade II hemorrhoids. For grade III hemorrhoids, the recurrence rate was improved with hemorrhoidectomy. Symptoms (incontinence, anal stenosis, sepsis, and significant bleeding), time from intervention to return to work, and complications were higher for excisional hemorrhoidectomy.

RBL is preferred over anal dilation, sclerotherapy, and infrared photocoagulation. Level of evidence: Ib. Strength of recommendation: A.

Summary: RBL is the therapy of choice for grades I and II internal hemorrhoids. RBL should be the first-line treatment for grade III prolapsing hemorrhoids, reserving hemorrhoidectomy for patients whose symptoms are not relieved. Anal dilation should be abandoned due

to significant morbidity associated with this treatment modality.

IS ONE OPERATIVE STRATEGY SUPERIOR TO THE OTHERS?

If nonoperative management fails, surgery may be required. Specific technical aspects of various hemorrhoid procedures have been prospectively analyzed, including open versus closed hemorrhoidectomy, stapled hemorrhoidectomy or hemorrhoidopexy, and hemorrhoidectomy with bipolar diathermy and harmonic scalpel.

Open versus Closed Hemorrhoidectomy

Many RCTs have compared open versus closed hemorrhoidectomy with no clear advantage of one technique over another. Recent RCTs have shown closed hemorrhoidectomy offers faster healing time. Arberman et al. found that at three weeks, 86% of patients in the Ferguson group (closed, $n = 38$) had completely healed wounds compared with 18% in the Milligan-Morgan (open, $n = 39$) group ($p < 0.001$) (13). Arroyo and colleagues also found healing during the first postoperative month was faster in the closed hemorrhoidectomy group ($n = 100$) compared to open ($n = 100$) (90% versus 40%; $p < 0.05$) (14). Another RCT of 80 patients (40 open, 40 closed) showed the mean operating time in the open group (35 ± 7 minutes) was significantly shorter than in the closed group (45 ± 8 minutes; $p < 0.001$) (15). No significant differences were observed in the duration of hospital stay or the mean duration of inability to work. They also found mean healing time was significantly shorter in the closed group (2.8 ± 0.5 weeks) than in the open group (3.5 ± 0.6 weeks; $p < 0.001$).

The data for closed versus open hemorrhoidectomy do not favor one procedure over another. No clear difference is seen with regard to postoperative pain. Closed hemorrhoidectomy appears to offer faster wound healing, but open hemorrhoidectomy offers shorter operative time and possibly improved morbidity (15). It is important to note that most of these studies did include internal and external hemorrhoids.

Harmonic Scalpel, Bipolar Diathermy

The original description of Milligan-Morgan hemorrhoidectomy (MMH) used scissors for excision (23). Harmonic scalpel hemorrhoidectomy (HSH) and bipolar diathermy hemorrhoidectomy (BSH) are alternative modalities for hemorrhoid excision. Recently, a prospective double-blind randomized trial of 86 patients with prolapsing hemorrhoids looked at MMH versus BSH versus HSH (22). There was no significant difference in the complication rates among the three groups. There was no case of failure of hemostasis in the BSH and HSH groups. HSH and BSH were found to be associated with less operative blood loss when compared with MMH ($p = 0.036$, $p = 0.028$, respectively), though this has little clinical relevance. Cheung et al. note HSH is as safe and effective, with similar complication and recurrence rates, as diathermy or scissors excision–ligation hemorrhoidectomy. They also note that HSH has less postoperative pain.

Stapled Hemorrhoidopexy

A more recent, novel approach to hemorrhoidectomy is stapled hemorrhoidopexy, also known as procedure for prolapse and hemorrhoids (PPH) and stapled hemorrhoidectomy. Longo's hemorrhoidopexy, as described in 1998, does not involve removing mucosa or hemorrhoidal tissue (11,12). The purpose of the procedure is to remove the feeding vessels to treat symptomatic hemorrhoids. Jayaraman et al. (10) looked at the outcomes of this technique by performing a meta-analysis of 12 RCTs of stapled circular hemorrhoidopexy (SH) versus conventional open or closed hemorrhoidectomy (CH) for the treatment of grade III and IV hemorrhoids. Follow-up periods ranged from 6 to 39 months with a median follow-up period of 7–14 months.

A trend indicating patients with SH were more likely to complain of hemorrhoidal bleeding at all time points was seen [9 trials, 699 patients, odds ratio (OR) 1.33, confidence interval (CI) 0.84–2.08] as well as a significantly higher proportion of patients with SH complained of prolapse at all time points (8 studies, 798 patients, OR 2.96, CI 1.33–6.58, $p = 0.008$). A nonsignificant trend showed that patients with SH were less likely to complain of pruritus and at final follow-up for all time points than those with CH (4 studies, 273 patients, OR 0.66, CI 0.29–1.50).

A nonsignificant trend showing patients with SH were more likely to complain of difficulties with soiling, hygiene, or incontinence. Trends showing a higher proportion of patients with perianal skin tags were seen in the SH group as compared to CH at all time points. A nonsignificant trend demonstrated that patients with SH were more likely to require repeat operations of any nature in long-term follow-up for their hemorrhoids. Patients with SH were significantly more likely to have recurrent hemorrhoids in long-term follow-up at all time points than those with CH (7 trials, 537 patients, OR 3.85, CI 1.47–10.07, $p = 0.006$).

Chung et al. analyzed 88 patients with grade III hemorrhoids (HSH = 45, PPH = 43) and median follow-up period of 15 months (range, 6–30) (16). Comparing the two groups, the authors found no significant observable difference in operation time, blood loss, or time to first bowel movement. They state PPH derive greater short-term benefits, with reduced pain, shorter length of hospital stay, and earlier return to work. Recommendations cannot be drawn from this data due to the short follow-up and small sample size.

Computer-guided bipolar diathermy (LigaSure) has also been compared with PPH (17) showing that postoperative pain scores, patient satisfaction, and self-assessment of activity was almost identical in both treatment groups. They also note 9 of 25 PPH patients had skin tags and prolapsed hemorrhoids removed with conventional diathermy. The authors revealed the inability of PPH to address these additional findings is a disadvantage of this treatment modality. Kraemer et al. use LigaSure whenever there is a need for more extensive excision or anodermal reconstruction, such as in fourth-degree piles. The design of the RCT prevents one to draw definitive recommendations regarding use of PPH. The data do confirm findings that PPH is not a good choice for grade IV hemorrhoids.

Conventional excisional hemorrhoidectomy is preferred over PPH. Level of evidence: Ib. Strength of recommendation: B.

Summary: Conventional excisional surgery is the gold standard in the surgical treatment of grade III and IV internal hemorrhoids. The data for CH versus open hemorrhoidectomy does not favor one procedure over the other. PPH is not a good choice for grade IV internal hemorrhoids. No clear recommendations can be made based on the current data favoring PPH over BSH or HSH for the treatment of symptomatic hemorrhoids. Recommendations could not be made favoring BSH or HSH over traditional MMH. Trends of intraoperative bleeding, however, do favor the use of newer technologies over scissors for excision.

MANAGEMENT OF THROMBOSED EXTERNAL HEMORRHOIDS

What Is the Best Management Strategy for Symptomatic External Hemorrhoids?

The most common findings with external hemorrhoids are pain and/or ulceration of a thrombus through the skin (1). Conservative measures are often used, which includes a combination of localized hygiene, tub baths, dietary changes, stool softeners, and oral and topical analgesics. There are very few quality studies looking at the management of external hemorrhoids exclusively.

Greenspon et al. (18) retrospectively reviewed outcomes of 231 patients with thrombosed external hemorrhoids. One hundred nineteen (51.5%) were initially treated conservatively, and 112 (48.5%) were treated surgically with mean follow-up at 7.6 months (up to 7 years). Most (97.3%) of the surgical patients had excision of their external hemorrhoids and 2.7% had incision. Time to symptom resolution was 24 days for conservatively managed patients versus 3.9 days for surgical patients ($p < 0.0001$). The frequency of recurrence was significantly higher for the conservative group (25.4%) than for the surgical group (6.3%; $p < 0.0001$). These data favor excision of thrombosed external hemorrhoids over conservative therapy.

Jongen et al. focused on the clinical outcomes of the 340 patients who underwent outpatient office excision of symptomatic external hemorrhoids (19). All wounds were left open, and follow-up was achieved in 70% of the patients. Postoperative complications are rare (1.3–7.7%). Anal stenosis, urinary retention, and fecal retention were not seen in this series. Recurrence rate was 9.2%. Based on their analysis, the authors recommend excision under local anesthesia in the office for thrombosed external hemorrhoids.

A prospective randomized trial examined conservative therapy versus surgery for the treatment of thrombosed external hemorrhoids (22). Three arms each had 50 patients: the first group was treated conservatively with 0.2% glyceryl trinitrate ointment; the second group by incision, and the third by excision of the thrombosed external hemorrhoid. At four days, there was significantly less pain in patients treated by excision compared to those treated with glyceryl trinitrate or incision ($p < 0.001$). At one year, all clinical outcomes significantly favored excision

of thrombosed hemorrhoids. Based on their data, the authors recommend excision of perianal thrombosis under local anesthesia as the method of choice because it prevents recurrence of perianal thrombosis and development of anal skin tags.

Excision of symptomatic external hemorrhoids is preferred over observation with topical agents or incision

of hemorrhoid. Level of evidence: Ib. Strength of recommendation: B.

Summary: Excision of external hemorrhoids under local anesthesia is the method of choice for symptomatic external hemorrhoids due to improved symptom relief. Practitioners can safely perform this procedure in the outpatient office setting.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
First-line treatment of internal hemorrhoids	2005	8	Ib	A	Rubber band ligation is the first-line therapy followed by hemorrhoidectomy if symptoms persist or grade IV.
Open or closed technique	2002	15	IIb	B	Both are acceptable operative strategies with no significant difference in outcomes.
Conventional hemorrhoidectomy or procedure for prolapse and hemorrhoids	2006	10	Ia	A	Conventional hemorrhoidectomy is superior to procedure for prolapse and hemorrhoids.
Management of symptomatic external hemorrhoids	2004	18	IIb	B	Excision is superior to topical agents and incision of external hemorrhoids.

REFERENCES

- Kaidar-Person O, Person B, Wexner S. Hemorrhoidal disease: a comprehensive review. *J Am Coll Surg* 2007; 204: 102–17.
- Adams P, Hendershot G, Marano M. Current estimates from the National Health Interview Survey, 1996. National Center for Health Statistics. *Vital Health Stat* 1999; 10.
- Johanson, J. Evidence based approach to the treatment of hemorrhoidal disease. *Ev Based Gastroenterol* 2002; 3: 26–31.
- Kozak L, Owings M, Hall M. National Hospital Discharge Survey: 2002 annual summary with detailed diagnosis and procedure data. National Center for Health Statistics. *Vital Health Stat* 2005; 13: 1–207.
- Jensen S, Harling H, Arseth-Hansen P, et al. The natural history of symptomatic hemorrhoids. *Int J Colorectal Dis* 1989; 4: 41–4.
- Konsten J, Baeten C. Hemorrhoidectomy vs. Lord's method: 17-year follow-up of a prospective, randomized trial. *Dis Colon Rectum* 2000; 43: 503–6.
- MacRae H, McLeod R. Comparison of hemorrhoidal treatment modalities: a meta-analysis. *Dis Colon Rectum* 1995; 38: 687–94.
- Shanmugam V, Thaha M, Rabindranath K, et al. Rubber band ligation versus excisional haemorrhoidectomy for haemorrhoids. *Cochrane Database of Systematic Reviews* 2005; 1: CD005034.y
- Burt C, Schappert S. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1999–2000. National Center for Health Statistics. *Vital and Health Stat* 2004; 13: 1–78.
- Jayaraman S, Colquhoun P, Malthaner R. Stapled versus conventional surgery for hemorrhoids. *Cochrane Database of Systematic Reviews* 2006; 4: CD005393.
- Longo A. Treatment of hemorrhoids disease by reduction of mucosa and hemorrhoidal prolapse with a circular suturing device: A new procedure. *Proceedings of the 6th World Congress of Endoscopic Surgery*, 1998.
- Corman M, Gravié T, Hager M, et al. Stapled haemorrhoidopexy: a consensus position paper by an international working party—indications, contra-indications and technique. *Colorectal Dis* 2003; 5: 304–10.
- Arbman G, Krook H, Haapaniemi S. Closed vs. open hemorrhoidectomy—is there any difference? *Dis Colon Rectum* 2000; 43: 31–4.
- Arroyo A, Perez F, Miranda E, et al. Open versus closed day-case haemorrhoidectomy: is there any difference? Results of a prospective randomized study. *Int J Colorectal Dis* 2004; 19: 370–3.
- Gencosmanoglu R, Sad O, Koc D, et al. Hemorrhoidectomy: open or closed technique? A prospective, randomized clinical trial. *Dis Colon Rectum* 2002; 45: 70–75.
- Chung C, Cheung H, Chan E, et al. Stapled hemorrhoidopexy vs. harmonic scalpel hemorrhoidectomy: a randomized trial. *Dis Colon Rectum* 2005; 48: 1213–19.
- Kraemer M, Parulava T, Roblick M, et al. Prospective, randomized study: proximate PPH stapler vs. LigaSure for hemorrhoidal surgery. *Dis Colon Rectum* 2005; 48: 1517–22.
- Greenspon J, Williams S, Young H, et al. Thrombosed external hemorrhoids: outcome after conservative or surgical management. *Dis Colon Rectum* 2004; 47: 1493–8.
- Jongen J, Bach S, Stubinger S, et al. Excision of thrombosed external hemorrhoid under local anesthesia: a retrospective evaluation of 340 patients. *Dis Colon Rectum* 2003; 46: 1226–31.
- Chung C, Ha J, Tai Y, et al. Doubleblind, randomized trial comparing Harmonic Scalpel™ hemorrhoidectomy, bipolar scissors hemorrhoidectomy and scissors excision: ligation technique. *Dis Colon Rectum* 2002; 45: 789–94.
- Milligan E, Morgan C, Jones L, et al. Surgical anatomy of the anal canal, and the operative treatment of haemorrhoids. *Lancet* 1937; 1120–4.
- Cavcic J, Turcic J, Martinac P, et al. Comparison of topically applied 0.2% glyceryl trinitrate ointment, incision and excision in the treatment of perianal thrombosis. *Dig Liver Dis* 2001; 33: 335–40.

Anal Fissure, Fistula, and Abscess

W. Brian Perry

Anorectal Fissure, Fistula, and Abscess: Question Summary		
Question	Answer	Grade
How do nonoperative medical therapies (nitroglycerin, calcium channel blockers, and botulinum toxin) compare with placebo and lateral internal sphincterotomy in the treatment of anal fissures?	Nonsurgical therapies are superior to placebo but inferior to lateral internal sphincterotomy for healing anal fissures.	A
What is the impact of technique on the outcomes of patients undergoing surgery for anal fissure?	Lateral internal sphincterotomy (open or closed) is the surgical treatment of choice for chronic anal fissures.	A
What is the healing and incontinence rate for fistulotomy for simple fistula-in-ano?	Fistulotomy is appropriate for simple fistula-in-ano with high rates of healing and low rates of incontinence.	B
What is the healing and incontinence rate for more complex fistulas treated with fibrin glue, fistula plug, or a seton?	Complex fistulas-in-ano may be successfully treated with fibrin glue, fistula plug, or a seton. Success and incontinence rates vary widely.	C
What is the healing and incontinence rate for more complex fistulas treated with an endorectal advancement flap?	Complex fistulas-in-ano may be successfully treated with an endorectal advancement flap. Success rates vary widely, but incontinence is infrequent.	C
Are antibiotics unnecessary for most patients undergoing routine incision and drainage of perirectal abscesses?	Antibiotics are unnecessary for most patients following adequate abscess drainage.	B

INTRODUCTION

Anorectal complaints are common, but often poorly understood. Most physicians seem to have missed “anus day” in medical school. More often than not, a referral for “hemorrhoids” can mean any number of perineal maladies. Proper treatment absolutely depends on proper diagnosis. Once an accurate assessment is made, therapy can be based on evidence-based guidelines for the treatment of anorectal abscess, fistula, and fissure. Hemorrhoids and pilonidal disease are covered in other chapters.

HOW DO NONOPERATIVE MEDICAL THERAPIES (NITROGLYCERIN, CALCIUM CHANNEL BLOCKERS, AND BOTULINUM TOXIN) COMPARE WITH PLACEBO AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF ANAL FISSURES?

Multiple randomized prospective trials have examined the role of various nonoperative therapies in the treatment of anal fissures. All effective modalities are aimed at decreasing the hypertonicity found in the internal anal sphincter of fissure patients. Therapies that do not lower sphincter

pressures have been uniformly found to be no better than placebo. Most studies focus on chronic fissures (1).

Glyceryl trinitrate (GTN) and its derivatives are smooth muscle relaxants that have been shown to decrease internal anal sphincter pressures. In controlled trials, application of these nitric oxide donors is associated with a greater than 50% fissure healing rate, compared with only 30–35% for placebo. A recent Cochrane review combining 15 studies showed a statistically better healing rate with GTN (49% versus 37%). Headache is the principal adverse event with GTN use, causing about a quarter of patients to stop therapy; incontinence was not observed in any study. Interestingly, one small study showed no difference between anal application and distant transdermal delivery. In studies with follow-up periods of more than one year, recurrence after cessation of therapy approaches 50% (2).

Calcium channel blockers, either topically or orally given, have been shown to heal fissures in 65–95% of patients. Comparisons to GTN show similar results. Headache is less frequently reported with topical use, but oral administration has more side effects and less efficacy (2).

Botulinum toxin (botox) induces a temporary “chemical sphincterotomy” that initially heals approximately two-thirds of fissures with a single application.

There is little consensus on dosing, injection sites, or repeated use. Transient incontinence to flatus and minor stool leakage is reported in up to 10% of patients. At one year, fissure recurrence rates are 40–50% (2).

Surgical sphincterotomy outperforms all medical therapies in numerous randomized, controlled trials with an overall healing rate greater than 90%. A minor incontinence rate of less than 10% compares favorably with topical therapy (3).

Nonsurgical therapies are superior to placebo but inferior to lateral internal sphincterotomy for healing anal fissures. Level of evidence: Ia, Grade of recommendation: A.

WHAT IS THE IMPACT OF TECHNIQUE ON THE OUTCOMES OF PATIENTS UNDERGOING SURGERY FOR ANAL FISSURE?

Surgical options for the treatment of anal fissure include anal stretch, open or closed lateral internal sphincterotomy (LIS), and posterior sphincterotomy, with or without papillae excision or dermal flap coverage (1). Meta-analysis of stretch versus LIS clearly favors LIS for both recurrence [odds ratio (OR) = 3.08, 95% confidence interval (CI) 1.26–7.54] and incontinence (OR = 4.22, 95% CI 1.89–9.42). Randomized trials of surgical technique may suffer from performance variations. Nevertheless, multiple trials comparing open LIS to closed LIS show no difference in either recurrence or incontinence. Posterior sphincterotomy has been shown to be inferior to LIS for both persistence of the fissure and incontinence (4). Additional procedures such as papillae excision and dermal flap coverage show a trend toward increased patient satisfaction in small trials (5,6). Overall, the risk of incontinence is low and patient satisfaction following LIS is high, even in those patients with minor continence disturbances (7).

LIS (open or closed) is the surgical treatment of choice for chronic anal fissures. Level of evidence: Ia, Grade of recommendation: A.

WHAT IS THE HEALING AND INCONTINENCE RATE FOR FISTULOTOMY FOR SIMPLE FISTULA-IN-ANO?

Anal fistulas vary in complexity from short, straight tracks involving primarily internal sphincter to branching complexes through a large amount of the external sphincter. With proper identification of the internal opening, fistulotomy is effective for simple fistulas, with recurrence rates less than 10% and minor incontinence rates of 0–17%. Although recurrence rates are similar, fistulectomy has shown to be inferior to fistulotomy due to longer healing times and a greater risk of incontinence (8). Marsupialization of the wound edges following fistulotomy has been shown in a small study to speed final healing and decrease bleeding (9). Most functional problems following surgery for simple fistulas improve in one to two years.

Fistulotomy is appropriate for simple fistula-in-ano with high rates of healing and low rates of incontinence. Level of evidence: IIb, Grade of recommendation: B.

WHAT IS THE HEALING AND INCONTINENCE RATE FOR MORE COMPLEX FISTULAS TREATED WITH FIBRIN GLUE, FISTULA PLUG, OR A SETON?

Fistulotomy alone is contraindicated when a significant amount of external sphincter is divided, due to an increased risk of permanent incontinence. Several surgical treatment modalities have been developed to increase the likelihood of durable fistula closure while reducing the risk of post-operative functional problems.

Using fibrin glue to obliterate fistula tracts was initially considered an attractive option because no sphincter muscle is divided. Early series with short follow-up reported fistula closure rates of 60–70% (8). However, this has not been borne out in subsequent trials with longer periods of evaluation. Singer randomized patients to fibrin sealant plus closure of the internal opening, fibrin sealant plus antibiotics, or fibrin sealant plus both; failures were offered retreatment. At one year, the rates of durable fistula closure were only 44%, 25%, and 35%, respectively, with no significant difference between groups (10).

In response to these findings, a bioabsorbable xenograft fistula plug made from lyophilized porcine intestinal submucosa (Surgisis, Cook Surgical, Bloomington, IN) was developed. Initially, Champagne et al. demonstrated an overall success rate of 83% with a median follow-up of 12 months (11). Subsequent studies have not been as encouraging, with success rates of 40–55%, depending on length of follow-up and fistula complexity, with simple fistulas faring better (12,13). A consensus statement of experts sponsored by Cook has delineated patient selection and technical factors for fistula plug use in hopes of improving outcomes (14).

A seton is a flexible foreign body placed through a fistula and secured to itself to keep the track open, preventing subsequent abscess formation. It may be place-holding or cutting, depending on how it is used. The fibrosis induced is thought to lessen subsequent incontinence. Overall recurrence rates are low—less than 10% in most series—but the rates of incontinence can be significant, up to 60% for minor disturbances in some cases (15).

There is a paucity of well-done randomized controlled trials addressing fistula-in-ano, especially comparing different techniques. As Malik and Nelson noted, a properly conducted randomized controlled trial comparing a variety of accepted and newer techniques using a pre- and post-treatment validated incontinence assessment tool is needed (15).

Complex fistulas-in-ano may be successfully treated with fibrin glue, fistula plug, or a seton. Success and incontinence rates vary widely. Levels of evidence: IIb–IV, Grade of recommendation: C.

WHAT IS THE HEALING AND INCONTINENCE RATE FOR MORE COMPLEX FISTULAS TREATED WITH AN ENDORECTAL ADVANCEMENT FLAP?

An endorectal advancement flap treats fistula-in-ano by obliterating the internal opening with a sliding “patch” of healthy tissue; no sphincter muscle need be divided.

Numerous small case series demonstrate successful fistula closure in 55–98% of patients, with low rates of major continence disturbance (<10%). Durable cure rates decrease with increasing fistula complexity—Crohn's disease, radiation, large rectovaginal, and multiply recurrent fistulas fare worse than simpler ones (8,15). There have been few randomized controlled trials involving flap fistula repair. Perez found little difference in patients with complex fistulae between flap repair and fistulotomy with immediate sphincter reconstruction, noting similar healing times, recurrences (10%), and incontinence rates (32%) (16). Ellis found that adding fibrin glue as an adjunct for an endorectal advancement flap is actually detrimental, as recurrence rates were 46% in the fibrin glue group, compared with 20% in the flap alone group (17).

Complex fistulas-in-ano may be successfully treated with an endorectal advancement flap. Success rates vary widely but incontinence is infrequent. Level of evidence: III; Grade of recommendation: C.

ARE ANTIBIOTICS UNNECESSARY FOR MOST PATIENTS UNDERGOING ROUTINE INCISION AND DRAINAGE OF PERIRECTAL ABSCESES?

Neither time to complete healing nor recurrence rates are improved by treating patients with antibiotics following incision and drainage of uncomplicated perirectal abscesses. These studies specifically excluded patients considered higher risk—those with diabetes, immunosuppression, or extensive cellulitis. Although there are no large trials in these patients, antibiotics should be considered for this subset on a case-by-case basis (8). According to American Heart Association guidelines, patients identified as high risk for the development of endocarditis should receive antibiotics prior to perirectal abscess incision and drainage (18).

Antibiotics are unnecessary for most patients following adequate abscess drainage. Level of evidence: IIc, Grade of recommendation: B.

Anorectal Fissure, Abscess, and Fistula: Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Nonoperative fissure therapy	2006	2	Ia	A	Nonop therapy is better than placebo but worse than LIS.
Fissure surgical technique	2005	4	Ia	A	LIS, open or closed, is the treatment of choice.
Fistulotomy for simple fistula-in-ano	2005	8	IIb	B	Fistulotomy is appropriate for simple fistulas.
Fibrin glue, plug, seton for complex fistulas	2005	8	III	C	Incontinence and success rates vary widely.
Endorectal advancement flap for complex fistulas	2005	8	III	C	Success is variable, but incontinence is rare.
Antibiotics for perianal abscesses	2005	8	IIb	B	Not indicated for most patients.

Abbreviation: LIS, lateral internal sphincterotomy.

REFERENCES

- Orsay CO, Rakinic J, Perry WB, et al. Practice parameters for the management of anal fissures (revised). *Dis Colon Rectum* 2004; 47: 2003–7.
- Nelson R. Non surgical therapy for anal fissure. *Cochrane Database of Systematic Reviews* 2006; 4: CD003431.
- Nicholls J. Anal fissure: surgery is the best treatment. *Colorectal Dis* 2008; 10: 529–30.
- Nelson R. Operative procedures for fissure in ano. *Cochrane Database of Systematic Reviews* 2005; 2: CD002199.
- Gupta PJ, Kalaskar S. Removal of hypertrophied anal papillae and fibrous anal polyps increases patient satisfaction after anal fissure surgery. *Tech Coloproctol* 2003; 7: 155–8.
- Leong AF, Seow-Choen F. Lateral internal sphincterotomy compared with anal advancement flap for chronic anal fissure. *Dis Colon Rectum* 1995; 38: 69–71.
- Hyman N. Incontinence after lateral internal sphincterotomy: a prospective study and quality of life assessment. *Dis Colon Rectum* 2004; 47: 35–8.
- Whiteford MH, Kilkenny J III, Hyman N, et al. Practice parameters for the treatment of perianal abscess and fistula-in-ano (revised). *Dis Colon Rectum* 2005; 48: 1337–42.
- Ho YH, Tan M, Leong, et al. Marsupialization of fistulotomy wounds improves healing: a randomized controlled trial. *Br J Surg* 1998; 85: 105–7.
- Singer M, Cintron J, Nelson R, et al. Treatment of fistulas-in-ano with fibrin sealant in combination with intra-adhesive antibiotics and/or surgical closure of the internal fistula opening. *Dis Colon Rectum* 2005; 48: 799–808.
- Champagne BJ, O'Connor LM, Ferguson M, et al. Efficacy of anal fistula plug in closure of cryptoglandular fistulas: Long term follow-up. *Dis Colon Rectum* 2006; 49: 1817–21.
- van Koperen PJ, D'Hoore A, Wolthuis AM, et al. Anal fistula plug for closure of difficult anorectal fistula: a prospective study. *Dis Colon Rectum* 2007; 50: 2168–72.
- Ky AJ, Sylla P, Steinhagan R, et al. Collagen fistula plug for the treatment of anal fistulas. *Dis Colon Rectum* 2008; 51: 838–43.
- The Surgisis® AFP™ anal fistula plug: report of a consensus conference. *Colorectal Dis* 2007; 10: 17–20.
- Malik AI, Nelson RL. Surgical management of anal fistulae: a systematic review. *Colorectal Dis* 2008; 10: 420–30.
- Perez F, Arroyo A, Serrano P, et al. Randomized clinical and manometric study of advancement flap versus fistulotomy with sphincter reconstruction in the management of complex fistula-in-ano. *Am J Surg* 2006; 192: 34–40.
- Ellis CN, Clark S. Fibrin glue as an adjunct to flap repair of anal fistulas: a randomized, controlled study. *Di Colon Rectum* 2006; 49: 1736–40.
- Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *Circulation* 1997; 96: 358–66.

Evidence-Based Surgery: Pilonidal Disease

Matthew J. Eckert, Joel E. Goldberg and Scott R. Steele

Pilonidal Disease: Question Summary		
Question	Answer	Grade
What is the optimal treatment of acute pilonidal disease?	Incision and drainage of abscess only	B
Do antibiotics have a role in the treatment of pilonidal disease?	Only with significant cellulitis or special situations (i.e., immunosuppressed)	D
How does gluteal cleft shaving influence pilonidal disease recurrence?	Evidence supports its use in sinus disease with limited downside	C
What is the expected outcome with respect to wound healing and recurrence of excision of pilonidal cyst/sinus with primary closure versus healing by secondary intention versus excision with marsupialization?	Excision with primary closure is associated with faster healing and higher recurrence. Secondary intention closures are associated with delayed healing but lower recurrence rates	B
Should a flap be required, what is the optimal type of flap reconstruction following excision?	There is insufficient evidence to support one flap over another. They do have a role in complex or recurrent disease	C
What is the optimal strategy for the treatment of recurrent pilonidal disease?	There is insufficient evidence to support one strategy. Surgeon comfort and ability may guide the use of flaps versus more conservative strategies. Recurrent abscesses should be drained	C
What is the role of nonoperative management of chronic pilonidal disease	Phenol injection has shown some success with limited data. Local care including is an adjunctive measure for this strategy	C

INTRODUCTION

Gluteal pilonidal disease is a potentially debilitating condition affecting 70,000 patients annually in the United States (1). The etiology and optimal treatment of this disease process have remained controversial since its first description by William Mayo in 1833 (2). Originally, Hodges and others believed this to be a congenital condition secondary to abnormal skin in the gluteal cleft (3), although the current consensus holds that pilonidal disease is an acquired condition intimately related to the presence of hair in the cleft (4). This hypothesis involves loose hairs inserted into the natal cleft skin create a foreign body reaction, ultimately leading to formation of midline pits and, in some cases, development of subcutaneous abscesses (5,6). Additional risk factors associated with the presence of pilonidal disease include obesity, a sedentary lifestyle, repetitive trauma or irritation to the gluteal cleft skin, familial history of pilonidal disease, and a hirsute body habitus (1,7).

The spectrum of pilonidal disease presentation varies from a chronic pilonidal cyst and sinus with persistent drainage to the more acute presentation of an associated abscess that may contain extensive subcutaneous tracts. Numerous treatment options have been previously described for each of these situations. In this chapter we systematically review the available literature concerning the treatment of acute, recurrent, and chronic disease, as well as nonoperative

adjunct measures to provide treatment recommendations as supported by the current level of evidence.

WHAT IS THE OPTIMAL TREATMENT OF ACUTE PILONIDAL DISEASE?

To answer this question, the term *acute pilonidal disease* should first be more properly defined as to the acute pilonidal abscess. Although patients may “acutely” present with pilonidal sinus disease, as often noted by increased drainage or even tenderness, the most common acute pilonidal condition (i.e., abscess) presents with significant pain and tenderness with an area of fluctuance and coexistent local cellulitis. As with any abscess elsewhere in the body, the mainstay of treatment is adequate surgical drainage. Jensen and Harling prospectively followed 73 patients after simple cruciate incision and drainage for first-episode acute pilonidal abscesses (8). The authors reported overall successful healing after simple drainage in 58%, whereas 42% required a second definitive procedure to address excess granulation prior to wound closure. Nine patients developed recurrent disease after complete healing, where the presence of multiple pits and lateral sinus tracts corresponded with recurrence. Their overall cure rate at a median follow-up of 60 months was reported to be 76%.

Within most abscess cavities, there exists extensive inflammatory and granulation tissue. The role that this debris plays on wound healing (or lack thereof) is controversial—as evidenced in part by Jensen's study. Vahedian and colleagues attempted to address this aspect more closely by prospectively randomizing 150 patients with acute abscesses to incision and drainage with or without curettage of the abscess cavity and removal of the inflammatory remains (9). Curettage was associated with significantly greater complete healing at 10 weeks (96% versus 79%, $p = 0.001$) and lower incidence of recurrence up to 65 months postoperatively (10% versus 54%, $p < 0.001$). Proponents of curettage cite the postulated benefit of the additional removal of hair and abscess debris, thought to be the nidus for recalcitrant and recurrent disease. Opponents of this practice anecdotally state that the base of the ulcer needs to be kept intact to provide adequate healing.

With this in mind, some authors have evaluated the use of local excision of both the abscess and the midline pits during the treatment of the acute pilonidal abscess, allowing healing by secondary intent as a way of eliminating all potential for future disease. Matter et al. retrospectively reviewed 58 patients treated with incision and drainage of the abscess alone versus complete excision with healing by secondary intent, finding no difference in disease recurrence (55% versus 41%, $p > 0.05$), length of hospital stay (3 versus 4 days, $p > 0.05$), or time to healing (30 versus 30 days, $p > 0.05$), when followed for a minimum of three years (10). The authors did find that patients treated with local excision of diseased tissue had a nearly significant trend to require more time off of work (14 versus 7 days, $p = 0.06$). Although the results of this study suggest no difference in disease recurrence, they must be interpreted with caution, as the majority of follow-up in this retrospective study was conducted with phone interviews without physical examination.

Hosseini and colleagues prospectively randomized 76 patients with first-time acute pilonidal abscesses to excision with healing by secondary intention or incision and drainage of the abscess followed by delayed cyst excision and primary closure at three weeks (11). The authors found no difference in disease recurrence between the groups after six months. Yet at 12-month follow-up, which included clinical examinations, the primary closure group demonstrated a 14% recurrence rate compared to no recurrences among those healing by secondary intention ($p < 0.05$). Although the authors did not specifically report on the overall rate of healing, they did allude to faster healing after delayed primary closure.

Recommendation: The primary treatment of the acute pilonidal abscess remains adequate surgical drainage. Whether drainage performed with a cruciate incision, abscess unroofing, curettage, or using an incision lateral to the abscess cavity confers any additional benefit cannot be clearly answered by available evidence. A lack of Level I evidence precludes Grade A treatment recommendations by current standards. However, the bulk of surgical literature supporting drainage of abscess collections elsewhere in the body may rightfully be extrapolated to the treatment of the acute pilonidal abscess. The current literature also demonstrates a reduction in local recurrence following concomitant complete excision of all associated disease, although at the cost of increased morbidity and delayed healing.

DO ANTIBIOTICS HAVE A ROLE IN THE TREATMENT OF PILONIDAL DISEASE?

The utility of antibiotics in conjunction with surgical drainage of the acute pilonidal abscess or definitive treatment of the chronic pilonidal sinus has been evaluated in few clinical trials. More specifically, antibiotic use has been studied in three discrete settings: perioperative prophylaxis, postoperative treatment courses, and topical postoperative use. Sondenaa and colleagues assessed the effect of a single dose of preoperative cefoxitin before excision and primary closure of chronic pilonidal disease tissues, excluding acute presentations. The authors found no difference in wound complication or healing rates up to 30 months post-operatively compared to those not receiving antibiotics (12).

Kronborg and associates randomized 88 patients with chronic pilonidal disease to excision with healing by secondary intention, excision with primary closure, and excision with primary closure and two weeks of clindamycin therapy (13). The authors found no difference between the primary excision groups with median time to healing 64 versus 14 versus 11 days, respectively ($p > 0.10$ for primary closure versus primary closure with antibiotics). Only secondary intention was associated with delayed healing. Recurrence rates after three years of follow-up were 13% versus 25% versus 19%, respectively ($p > 0.05$). Thus, the addition of antibiotics did not convey a statistically significant decrease in either closure or recurrence compared to primary closure alone.

Marks et al. evaluated 100 patients who underwent excision of a chronic pilonidal sinus tract and were prospectively assigned to healing by secondary intention, with or without 14 days of outpatient metronidazole therapy or metronidazole with the addition of erythromycin depending on wound appearance during the follow-up period (14). Although mean time to wound healing was significantly shorter in the group randomized to postoperative metronidazole compared to those without antibiotics (18 ± 22 versus 38 ± 44 days, $p = 0.05$), the significantly large standard deviation precludes definitive conclusions. In addition, the authors found no difference in wound healing with the addition of erythromycin therapy ($p = 0.14$).

The use of topical antibiotic regimens has also been evaluated in the treatment of pilonidal disease. Vogel and associates reported significantly higher wound healing rates (86% versus 35%, $p < 0.001$) after excision of chronic or previously drained acute pilonidal abscesses and packing with or without an absorbable gentamicin impregnated collagen-based sponge with primary wound closure (15). Although these data seemed promising, the contributions of gentamicin could not be separated from the potential role of the sponge material itself. Williams et al. randomized 75 patients with abscesses or chronic sinuses to excision with wound packing with a flavine-soaked sponge for four days, followed by either a silastic foam dressing pack or daily chlorhexadine-soaked gauze packing (16). The authors reported no significant differences in healing [66 versus 58 days, effective size (ES) 8.5, -1.97 – 18.97 95% confidence interval (CI)] or duration of hospital admission (8.5 versus 7.3, $p > 0.05$). In a similar study, Walker et al. treated patients initially with a sodium hypochlorite solution packing following excision of chronic sinus disease and subsequently randomized them to either a silastic foam

packing or continued hypochlorite-based packing (17). The authors found no difference in healing rates, wound complications, or hospital admission duration.

Thus, the utility of antibiotics in topical or systemic formulations remains controversial in both the treatment of acute and chronic pilonidal disease—whether used in a perioperative or postoperative treatment regimen. Nevertheless, numerous authors have suggested the potential role for adjunctive antibiotic treatment in the setting of immunosuppression, severe associated cellulitis, or associated systemic illness, despite a lack of evidence-based support as described (18–22).

Recommendation: There is inadequate evidence to suggest the use of routine topical or systemic antibiotic therapies in the setting of either acute or chronic pilonidal disease. Anecdotal support may suggest a potential role of systemic therapy in the setting of an associated abscess with significant cellulitis in a patient with coexistent systemic illnesses. However, there is no existing supportive data specifically addressing this situation (Grade D).

HOW DOES GLUTEAL CLEFT SHAVING INFLUENCE PILONIDAL DISEASE RECURRENCE?

The importance of gluteal cleft shaving is directly related to the significance of hair in the cleft as a major contributing factor to the development of pilonidal disease. Whether the development of pilonidal abscesses and sinuses is secondary to local pressure on the tissues, ruptured hair follicles, hypoxic tissue beds, or a potentially congenital vulnerability of the natal skin, this central role of hair in the cleft has led most authors to emphasize the importance of local shaving (6,21–25). Yet when examining the literature, it is first important to distinguish among the potential roles that shaving plays in each series—as an adjunctive form of treatment in active disease, as a sole agent of therapy, or as a preventive tool in the setting of chronic sinus disease to avoid recurrent flares and abscess formation.

A limited number of studies have examined the usefulness of gluteal shaving both as an adjunct to surgical treatment and as a measure to prevent recurrence. Armstrong and Barcia conducted a prospective study of 101 patients treated with shaving, hygiene enforcement, and limited lateral incision and drainage of abscesses with comparison to a retrospective analysis of 229 patients treated with a variety of more invasive surgical techniques over a two-year period preceding this conservative treatment pilot study (26). The authors found that the conservative treatment group required significantly fewer total hospital admission days (83 versus 4,760 days) and fewer total surgical procedures (0 versus 240) with a significantly lower occupational-absence rate (data not reported). The authors subsequently analyzed the results of the conservative protocol over the ensuing 17 years, reporting 110 incision and drainage procedures, 23 excisional procedures, and only 150 hospital admissions. Because the authors did not provide a specific denominator of total patients treated, definitive comparisons are difficult. Instead, they cited the potential patient population at risk for pilonidal disease and compared these results to their own initial two-year period of aggressive excisional management. Clearly, the descriptive data presented in this study seem to suggest a more

favorable result with the conservative methods described; however, the lack of basic statistical analysis significantly weakens the authors' conclusions and limits the ability to assess the total contribution of shaving in pilonidal disease.

Several additional studies have included shaving as a standard component of postoperative treatment while comparing other surgical techniques, making discerning the actual contribution of shaving as an individual treatment difficult. Chinn (22), Solla and Rothenberger (27), Al-Naami (28), and others used regular gluteal strip shaving in their studies comparing various surgical techniques. Despite the promising results suggested by these authors, further studies will be necessary to fully assess the utility and efficacy of shaving as an individual treatment strategy. In addition, the most effective frequency and extent of shaving have yet to be clarified, because most series have an arbitrary manner and method for this practice.

Recently, numerous small retrospective series have been published evaluating the role of laser epilation in the setting of pilonidal disease (29–31). The majority of these studies included patients with recurrent disease who have previously been treated with one or more surgical procedures. The 43 patients included in these studies all demonstrated improvement in local folliculitis and pilonidal sinus drainage, but this required multiple treatment sessions with only temporary effect. Although laser epilation may serve as an adjunct treatment modality, there is insufficient evidence to date to make any assessment of the significance of this technique.

Recommendation: The importance of gluteal cleft shaving is emphasized by the central role that natal hairs play in the genesis of pilonidal disease. We recommend routine shaving during the treatment of all types of pilonidal disease (acute, chronic, and recurrent) given the relative simplicity, likely beneficial role of this adjunct treatment, and limited downside to its use (Grade C). Though we acknowledge there is limited evidence to support this recommendation, it coincides with the majority opinion and limited available data. The duration, frequency, and extent of shaving for optimal effect remain unknown. The role of depilatory agents, though somewhat promising, requires further accumulation of data with increased patient numbers to fully evaluate their use.

WHAT IS THE EXPECTED OUTCOME WITH RESPECT TO WOUND HEALING AND RECURRENCE OF EXCISION OF PILONIDAL CYST/SINUS WITH PRIMARY CLOSURE VERSUS HEALING BY SECONDARY INTENTION VERSUS EXCISION WITH MARSUPIALIZATION?

The surgical treatment of pilonidal cyst and sinus disease is generally divided into two categories: excision of diseased tissue with primary closure attempt versus excision with a form of healing by secondary intention. The technique of marsupialization or suturing the skin margins to the fibrotic wound base after debridement is intended to decrease the total area that will need to heal by secondary intention and prevent premature reepithelialization over a persistent wound cavity. Advocates of the marsupialization technique cite the favorable decrease in wound area required to heal by secondary intention and the fact that

should the suture line break down, the wound is converted to simple healing by secondary intent without requirement for any further surgical treatment (21). Thus, a potential abscess cavity is avoided altogether. Proponents of the primary closure point to a faster rate of wound healing in the absence of complications and the technical ease to open the wound should an infection occur, in those rare cases that the cavity does not spontaneously drain.

Several studies have prospectively compared excision with primary midline closure versus excision with healing by secondary intention. Despite variability in sample size, study design, and patient follow-up, there is a uniform significant trend toward faster median healing rates following primary closure in multiple prospective randomized trials: Rao et al. (32) (14 versus 79 days, $p < 0.001$), Khawaja et al. (33) (14 versus 41 days, median difference -23 , 95% CI -28 to 20), Sondenna et al. (34) (14 versus 70 days, $p < 0.001$), and Hameed et al. (35) (14.5 versus 70 days, $p < 0.05$). Additional studies of variable quality support these findings as well (12,36). In addition to a more rapid rate of closure, a few studies have also shown a more rapid return to work after primary closure (33,36–37). This is likely a benefit of not only faster healing but also less pain and decreased need for continued care with open wounds.

Despite these benefits, primary closure does have some drawbacks. With respect to disease recurrence after initial treatment by excision with primary closure versus excision with healing by secondary intention, a 2007 literature review by McCallum and colleagues demonstrated a significantly lower recurrence after healing by secondary intention (38). Reported recurrence rates ranged from 0% to 12% after healing by secondary intention versus 0% to 24% after primary midline closure. The authors analyzed nine individual studies, finding an estimated 60% reduction in the risk of recurrent disease after healing by secondary intention when compared to primary midline closure after excision, but they stressed the moderate methodological quality of the included studies. Unfortunately, there remains no good data explaining this phenomenon, as presumably in both methods the diseased tissue has been adequately removed.

Two studies have previously evaluated the efficacy of excision with marsupialization compared to primary closure. Spivak et al. retrospectively reviewed their series of 56 patients treated by excision with primary midline closure versus 26 treated by excision with wound marsupialization (39). Median time to healing after primary closure was 14 days versus 5 weeks with marsupialization, without statistical comparison. Disease recurrence was similar in each group, documented in 6% of primary closure patients compared with 4% of patients treated with marsupialization. The authors also included 47 patients treated by excision with healing by secondary intent, demonstrating a median of eight weeks to heal and 13% experiencing recurrent disease after three years' mean follow-up. The authors concluded that although they felt no definitive data exist to support the surgical treatment of chronic pilonidal disease, they prefer to treat small, uncomplicated cysts with excision and primary closure, with marsupialization for larger cysts and excision with healing by second intent for large complicated or grossly infected cases. Genencosmanoglu et al. compared 73 marsupialization and 69 primary midline

closure patients, reporting median times to healing of 79 versus 14 days, respectively ($p < 0.001$) (40). Unlike Spivak's group, disease recurrence was significantly lower in the marsupialization group, occurring in 1.5% versus 17% after primary closure (p -value not reported). Similar results showing less recurrence at a slightly prolonged time to heal over primary closure were reported by Solla and Rothenberger in their series of 150 patients (27). Average time to healing after primary midline closure, healing by secondary intent, and marsupialization were two, eight, and four weeks, with recurrence in 22%, 19%, and 6%, respectively, without statistical comparison.

Recommendation: The available clinical evidence suggests that excision with primary midline repair leads to faster healing but a potentially higher rate of disease recurrence (Grade B). Given the divergence in results, the decision to use either treatment must weigh the potential weakness of each with respect to the individual patient. The available data following marsupialization suggest favorable recurrence rates but slower healing, however, the data limitations preclude treatment recommendations. It remains up to the discretion of the surgeon to determine the risks and expected outcomes with each method prior to embarking on a single approach.

SHOULD A FLAP BE REQUIRED, WHAT IS THE OPTIMAL TYPE OF FLAP RECONSTRUCTION FOLLOWING EXCISION?

In the setting of chronic pilonidal disease, often with multiple previous surgical treatments, several flap-based treatment strategies have been described. The goal of flap-based procedures is to excise disease while simultaneously providing healthy tissue coverage in the defect. In some settings, soft tissue reconstruction with the intent of altering the contour of the natal cleft as a measure to reduce further disease recurrence has been attempted.

Multiple authors have evaluated the efficacy of the rhomboid or Limberg flap, in which all sinuses are excised down to the presacral fascia, with rotation of a fasciocutaneous flap that results in flattening of the gluteal cleft. The rhomboid flap has been used extensively in the treatment of refractory pilonidal disease. Overall results are favorable with respect to disease recurrence (1.5–5%) and patient tolerance (41–42). Potentially unfavorable points of this surgical procedure include large tissue mobilization, increased risk of hematoma/seroma formation, and wound dehiscence (18). Unalp and colleagues reported significantly lower recurrence after rhomboid flap versus V-Y advancement (1.5% versus 11%, $p = 0.039$) in their retrospective review of 111 patients, finding no differences in wound complications, seroma formation, or hospital admission duration (43).

The Karydakias flap is an additional technique based on excision of diseased tissue from the midline with soft tissue coverage in the form of a mobilized fasciocutaneous flap secured to the sacrococcygeal fascia with lateral suture lines to reduce recurrence in the midline. Karydakias reviewed his personal series of over 6,000 patients treated with this technique in 1992, with a recurrence rate less than 2% and wound complications in 8% (44). More recently, Akinci and associates prospectively followed 112 patients

treated with the Karydakís flap procedure, reporting wound complications in 7% and recurrence in a single patient (0.9%) (45). Kitchen reported similar findings (4% recurrence, 9% local complications) in his review of 141 patients who underwent the Karydakís procedure (46). Similar to the Karydakís procedure, the Bascom cleft lip technique aims to excise all diseased tissues with minimal removal of healthy tissue by creating a flap-based coverage off the midline, thus obliterating the cleft. Bascom reported successful healing in all patients in a series of 28 complicated pilonidal presentations; however, no further in-depth studies of the effectiveness of this technique have been performed (47).

The V-Y advancement and Z-plasty techniques are plastic surgical reconstructions patterns that have been employed to provide tissue coverage for many different areas of the body, including following excision of pilonidal disease. Schoeller et al. reported no disease recurrence, universal healing, and only two minor wound complications in a series of 24 patients managed with V-Y advancement (48). The comparison of V-Y advancement with the Limberg flap by Unalp et al., already described, suggests that recurrence may be more frequent after the V-Y technique (43). The Z-plasty technique has been described in numerous studies, but with generally higher rates of wound complications and disease recurrence, as discussed in the review by Nelson and Billingham (18). The prospective, randomized trial comparing Z-plasty with excision with or without marsupialization by Hodgson and Greenstein demonstrated significantly decreased need for further surgical treatment after Z-plasty compared to healing by secondary intent (49).

Recommendation: The efficacy of flap-based techniques for the treatment of complicated or chronic pilonidal disease has been well described in numerous case series. Available evidence is insufficient to make any recommendation as to which type of flap is superior. Flap-based procedures appear to have a predominant role in the setting of complex and multiple recurrent pilonidal disease when other techniques have failed (Grade C). Surgeon ability and experience, along with patient preference, should heavily influence the extent of tissue manipulation.

WHAT IS THE OPTIMAL STRATEGY FOR THE TREATMENT OF RECURRENT PILONIDAL DISEASE?

Recurrent pilonidal disease implies previous surgical treatment for either the acute pilonidal abscess or symptomatic pilonidal cyst and sinus. Previously reported recurrence rates of up to 50% following initial intervention suggest the lack of a single optimal treatment strategy for pilonidal disease. In addition, secondary and tertiary recurrence rates are reported to be as high as 10–30%, suggesting that a small percentage of patients will continue to experience failure regardless of the management. Despite this, therapy for the patient with recurrence in many aspects is similar to that with de novo presentation. Much like the initial presentation of pilonidal disease, perianal hygiene and shaving are cornerstones in outpatient management in recurrent disease. In addition, recurrent abscesses are drained just as if they were sentinel acute presentations. In the face of

nonacute recurrence or chronically recurring pilonidal sinus disease, the goal should be a treatment strategy that allows the patient to resume a normal lifestyle and occupational duties as soon as possible. Definitive flap-based procedures may be indicated if previous local excisions or multiple drainage procedures have been performed or a minimally invasive approach may be entertained, with no strong evidence for either strategy (50). However, with multiple, recurrent presentations, the surgeon needs to remain vigilant for abnormal underlying etiologies of chronic perirectal pathology to include inflammatory bowel disease, immunosuppression, and cutaneous neoplasms.

Recommendation: Recurrent pilonidal disease of the acute nature should be treated with adequate surgical drainage similar to the sentinel acute pilonidal abscess (Grade C). Chronic recurrent disease may be approached with a conservative or more aggressive approach, depending on the goals and desires of the patient and experience and expertise of the surgeon. There is no significant evidence to guide the treatment of recurrent disease, and all recommendations should be based on the individual technique chosen as stated in the individual sections.

WHAT IS THE ROLE OF NONOPERATIVE MANAGEMENT OF CHRONIC PILONIDAL DISEASE?

In addition to shaving, other nonoperative measures have been described for chronic pilonidal disease. The use of phenol solution injections for the treatment of the chronic pilonidal sinus was first described by Maurice and Greenwood in 1964 (51). Through a protocol that involved one or more injections of phenol solution into the sinus tract until filled, with cautious protection of the surrounding normal skin, removal of sinus hairs and debris with forceps, as well as local shaving, the authors reported successful healing in 17 of 21 patients up to 18 months after injection, with disease recurrence in 4 patients. Stephens and colleagues reported no disease recurrence in 30 patients treated with phenol injection and local depilatory cream application on a weekly basis, up to six years after initial treatment (52). All 30 patients had previously presented with acute abscesses, received surgical drainage, and subsequently developed chronic pilonidal sinus tracts. Stansby and Greatorex reported an 11% recurrence rate in their series of 104 patients treated with phenol, with significantly shorter hospital lengths of stay and time to healing when compared to 65 patients treated with excision and healing by secondary intention (53).

The goal of this nonoperative treatment strategy is removal of all hair and debris that potentially acts as stimulus for maintaining a chronic low-grade inflammatory state that allows the tract to remain open. After removal of the debris, the phenol application eliminates granulation tissue and additional debris, allowing sinus closure. However, all authors reporting on this technique stress the importance of regular local hair removal techniques to ensure prevention of hair accumulation in the natal cleft. In addition, proponents of this technique stress the importance of protecting adjacent normal skin with a thick coat of petroleum jelly to prevent skin irritation and avoiding

overfilling the sinus tract to prevent spillage. Thus, the degree to which each component plays a role in the overall success remains to be determined.

Recommendation: The promising technique of phenol injection for the nonoperative treatment of the chronic pilonidal sinus is likely most appropriate for simple cyst/sinus disease when patients wish to avoid surgical treatment

(Grade C). Available retrospective series demonstrate favorable results while avoiding the wound care, hospitalization time, and patient inconvenience associated with operative treatment. This technique may be applicable to those patients with medical comorbidities that compromise effective wound healing, but existing data do not specifically address this situation.

Literature Summary for Pilonidal Disease

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoints
Akinci	45	2000	IV	Karydakias flap series review	CS	NR, mean 2.4 years	Healing, recurrence, hospital stay, wound complications
Armstrong	26	1994	IIIb	Shaving and limited I&D, open	RCS	4 years	Hospital days, procedures required
Fuzun	36	1994	IIb	Open, primary midline closure	RCT	Mean 23 months	RTW, recurrence
Gencosmanoglu	40	2005	IIb	Open, marsupialization	RCT	2 years	Healing, recurrence
Hameed	35	2001	IIb	Open, primary midline closure	RCT	NR	Healing, recurrence
Hosseini	11	2006	IIb	Open, I&D with delayed excision and closure	RCT	12 months	Healing, recurrence
Jensen	8	1988	IV	I&D	CS	60 months	Healing, recurrence, additional procedures
Karydakias	4, 25, 44	1992	IV	Karydakias flap series review	CS	NR, 2–24 years	Healing, recurrence
Khawaja	33	1992	IIb	Open, primary midline closure	RCT	12 months	Healing, recurrence, RTW
Kitchen	46	1996	IV	Karydakias flap series review	CS	22 months	Healing, recurrence, wound complications
Kronborg	13	1985	IIb	Open, primary midline closure, Primary closure with antibiotics	RCT	3 years	Healing, recurrence
Marks	14	1985	IIb	Open $\pm$ metronidazole $\pm$ metronidazole with erythromycin	PCS	NR, 20–221 days	Healing, recurrence
Matter	10	1995	IV	Open, I&D	CS	6 years	Healing, recurrence, RTW
Maurice	51	1964	IV	Phenol injection	CS	NR, 18 months minimum	Healing, recurrence, additional procedures
Rao	32	2001	IIb	Open, marsupialization, primary midline closure	RCT	NR	Healing
Schoeller	48	1997	IV	V-Y advancement	CS	NR, mean 4.5 years	Healing, recurrence, RTW, wound complications
Solla	27	1990	IV	Open, primary closure, marsupialization	CS	NR	Healing, recurrence
Sondenna	37	1992	IIb	Open, primary midline closure	RCT	NR, 6–30 months	Healing, recurrence, RTW
Sondenna	1, 12	1995	IIb	Primary midline closure $\pm$ preoperative antibiotics	RCT	NR, 6–30 months	Healing, recurrence
Spivak	39	1996	IIb	Open, primary closure, marsupialization	RCT	NR, mean 3.3 years	Healing, recurrence
Stansby	53	1989	IV	Phenol injection	CS	NR, mean 8 months	Healing, recurrence
Stephens	52	1969	IV	Phenol injection	CS	NR, 6 months–3 years	Healing, recurrence
Topgul	42	2003	IV	Limberg flap series review	CS	NR, mean 5 years	Healing, recurrence, wound complications
Unalp	43	2007	IV	Limberg, V-Y flap	CS	NR, mean 47 months	Healing, recurrence, wound complications
Urhan	41	2002	IV	Limberg flap series review	CS	NR, mean 2.9 years	Healing, recurrence, wound complications
Vahedian	9	2005	IIb	I&D $\pm$ curettage	RCT	NR, 65 month mean	Healing, recurrence

Abbreviations: CS, case series (retrospective); I&D, incision and drainage; NR, not reported; PCS, prospective cohort study; RCS, retrospective cohort study; RCT, randomized controlled trial; RTW, return to work.

REFERENCES

1. Sondenaar K, Andersen E, Nesvik I, et al. Patient characteristics and symptoms in chronic pilonidal sinus disease. *Int J Colorect Dis* 1995; 10: 39–42.
2. Mayo OH. Observations on injuries and diseases of the rectum. London: Burgess and Hill, 1833: 45–6.
3. Hodges RM. Pilonidal sinus. *Boston Med Surg J* 1880; 103: 485–6.
4. Karydakos GE. Easy and successful treatment of pilonidal sinus after explanation of its causative process. *Aust N Z J Surg* 1992; 62: 385–9.
5. Patey DH, Scraff RW. Pathology of post-anal pilonidal sinus: its bearing on treatment. *Lancet* 1946; ii: 484–6.
6. Hull TL, Wu J. Pilonidal disease. *Surg Clin North Am* 2002; 82: 1169–85.
7. da Silva JH. Pilonidal cyst: cause and treatment. *Dis Colon Rectum* 2000; 43: 1146–56.
8. Jensen SL, Harling H. Prognosis after simple incision and drainage for a first-episode acute pilonidal abscess. *Br J Surg* 1988; 75: 60–1.
9. Vahedian J, Nabavizadeh F, Nakhaee N, et al. Comparison between drainage and curettage in the treatment of acute pilonidal abscess. *Saudi Med J* 2005; 26: 553–5.
10. Matter I, Kunin J, Schein M, et al. Total excision versus non-resectional methods in the treatment of acute and chronic pilonidal disease. *Br J Surg* 1995; 82: 752–3.
11. Hosseini SV, Bananzadeh AM, Rivaz M, et al. The comparison between drainage, delayed excision and primary closure with excision and secondary healing in management of pilonidal abscess. *Int J Surg* 2006; 4: 228–31.
12. Sondenaar K, Nesvik I, Gullaksen F, et al. The role of cefoxitin prophylaxis in chronic pilonidal sinus treated with excision and primary suture. *J Am Coll Surg* 1995; 180: 157–60.
13. Kronborg O, Christensen K, Zimmermann-Neilsen C. Chronic pilonidal disease: a randomized trial with a complete 3-year follow-up. *Br J Surg* 1985; 72: 303–4.
14. Marks J, Harding K, Hughes L, et al. Pilonidal sinus excision-healing by open granulation. *Br J Surg* 1985; 72: 63–640.
15. Vogel P, Lenz J. Treatment of pilonidal sinus with excision and primary suture using a local, absorbable antibiotic carrier. Results of a prospective randomized trial. *Chirurg* 1992; 63: 748–53.
16. Williams R, Wood R, Mason M, et al. Multicentre prospective trial of silastic foam dressing in management of open granulating wounds. *Br J Med* 1981; 282: 21–2.
17. Walker A, Shouler P, Leicester R, et al. Comparison between Eusol and silastic foam dressing in the postoperative management of pilonidal sinus. *J R Coll Surg Edinburgh* 1991; 36: 105–6.
18. Nelson J, Billingham R. Pilonidal disease and hidradenitis suppurativa. In: *The ASCRS Textbook of Colon and Rectal Surgery*. New York: Springer, 2007; 228–35.
19. Hull TL, Wu J. Pilonidal disease. *Surg Clin N Am* 2002; 82: 1169–85.
20. Hanley PH. Acute pilonidal abscess. *Surg Gyn Obst* 1980; 150: 9–11.
21. Notaro JR. Management of recurrent pilonidal disease. *Semin Colon Rectal Surg* 2003; 14: 173–85.
22. Chinn BT. Outpatient management of pilonidal disease. *Semin Colon Rectal Surg* 2003; 14: 166–72.
23. Surrell JA. Pilonidal disease. *Surg Clin N Am* 1994; 74: 1309–15.
24. Talbott TM. Pilonidal disease. *Semin Colon Rectal Surg* 1990; 224–7.
25. Karydakos GE. Easy and successful treatment of pilonidal sinus after explanation of its causative process. *Aust N Z J Surg* 1992; 62: 385–9.
26. Armstrong JH, Barcia PJ. Pilonidal sinus disease. The conservative approach. *Arch Surg* 1994; 129: 914–17.
27. Solla JA, Rothenberger DA. Chronic pilonidal disease: an assessment of 150 cases. *Dis Colon Rectum* 1990; 33: 758–61.
28. Al-Naami MY. Outpatient pilonidal sinotomy complemented with good wound and surrounding skin care. *Saud Med J* 2005; 26: 285–8.
29. Odili J, Gault D. Laser depilation of the natal cleft—an aid to healing the pilonidal sinus. *Ann R Coll Surg Engl* 2002; 84: 29–32.
30. Schulze SM, Patel N, Hertzog D, et al. Treatment of pilonidal disease with laser epilation. *Am Surg* 2006; 72: 534–7.
31. Landa N, Aller O, Landa-Gundin N, et al. Successful treatment of recurrent pilonidal sinus with laser epilation. *Dermatol Surg* 2005; 31: 726–8.
32. Rao M, Zawislak W, Gilliland R. A prospective randomized trial comparing two treatment modalities for chronic pilonidal sinus. *Int J Colorect Dis* 2001; 3(Suppl 1 Oral): 102.
33. Khawaja HT, Bryan S, Weaver PC. Treatment of natal cleft sinus: a prospective clinical and economical evaluation. *Br Med J* 1992; 304: 1282–3.
34. Sondenaar K, Nesvik E, Soreide J. Recurrent pilonidal sinus after excision with closed or open treatment: final result of a randomized trial. *Acta Chirurg* 1996; 162: 237–40.
35. Hameed KK. Outcome of surgery for chronic natal cleft pilonidal sinus: a randomized trial of open compared with closed technique. *Med Forum Monthly* 2001; 12: 20–3.
36. Fuzun M, Bakir H, Soylu M, et al. Which technique for treatment of pilonidal sinus—open or closed? *Dis Colon Rectum* 1994; 37: 1148–50.
37. Sondenaar K, Andersen E, Soreide J. Morbidity and short term results in a randomized trial of open compared with closed treatment of chronic pilonidal sinus. *Acta Chirurg* 1992; 158: 351–5.
38. McCallum I, King P, Bruce J. Healing by primary versus secondary intention after surgical treatment for pilonidal sinus. *Cochrane Database of Systematic Reviews* 2007; 4: CD006213.
39. Spivak H, Brooks P, Nussbaum M, et al. Treatment of chronic pilonidal disease. *Dis Colon Rectum* 1996; 39: 1136–9.
40. Gencosmanoglu R, Inceoglu R. Modified lay-open versus total excision with primary closure in the treatment of chronic sacrococcygeal pilonidal sinus. *Int J Colorect Dis* 2005; 20: 415–22.
41. Urhan M, Kucukel F, Topgul K, et al. Rhomboid excision and Limberg flap for managing pilonidal sinus: results of 102 cases. *Dis Colon Rectum* 2002; 45: 656–9.
42. Topgul K, Ozdemir E, Kilic K, et al. Long-term results of Limberg flap procedure for treatment of pilonidal sinus: a report of 200 cases. *Dis Colon Rectum* 2003; 46: 1545–8.
43. Unalp H, Derici H, Kamer E, et al. Lower recurrence rate for Limberg vs. V-Y flap for pilonidal sinus. *Dis Colon Rectum* 2007; 50: 1436–44.
44. Karydakos GE. Easy and successful treatment of pilonidal sinus disease after explanation of its causative process. *Aust N Z J Surg* 1992; 62: 385–9.
45. Akinci O, Coskun A, Uzunkoy A. Simple and effective surgical treatment of pilonidal sinus. *Dis Colon Rectum* 2000; 43: 701–7.
46. Kitchen P. Pilonidal sinus: experience with the Karydakos flap. *Br J Surg* 1996; 83: 1452–5.
47. Bascom J, Bascom T. Failed pilonidal surgery: new paradigm and new operation leading to cures. *Arch Surg* 2002; 137: 1146–50.
48. Schoeller T, Wechselberger G, Otto A, et al. Definite surgical treatment of complicated recurrent pilonidal disease with a modified fasciocutaneous V-Y advancement flap. *Surgery* 1997; 121: 258–63.

49. Hodgson W, Greenstein R. A comparative study between Z-plasty and incision and drainage or excision with marsupialization for pilonidal sinus. *Surg Gynecol Obstet* 1981; 153: 842-4.
50. Notaro J. Management of recurrent pilonidal disease. *Semin Colon Rectal Surg* 2003; 14: 173-85.
51. Maurice B, Greenwood R. A conservative treatment of pilonidal sinus. *Br J Surg* 1964; 51: 510-12.
52. Stephens F, Sloane D. Conservative management of pilonidal sinus. *Surg Gynecol Obstet* 1969; 129: 786-8.
53. Stansby G, Greated R. Phenol treatment of pilonidal sinuses of the natal cleft. *Br J Surg* 1989; 76: 729-30.

Rectal Prolapse: Evidence-Based Outcomes

Scott R. Steele and Joel E. Goldberg

Rectal Prolapse: Question Summary		
Question	Answer	Grade
What is the optimal preoperative evaluation for those patients with rectal prolapse—i.e., what are the data on colonoscopy, anorectal physiology studies, manometry, transit studies, and defecography?	Anorectal physiology studies have little correlation with postoperative outcomes and rarely impact operative management. Colonoscopy should be performed on those at-risk patients by current screening/surveillance recommendations for colorectal cancer.	C, B
What is associated with better perioperative outcomes: abdominal or perineal approaches?	There is insufficient evidence to support one approach over the other due to significant selection bias. In general, perineal approaches are associated with higher recurrence.	I, B
When considering abdominal approaches, which technique is associated with improved outcomes: mobilization with suture rectopexy, suture rectopexy with the addition of mesh, or resection rectopexy?	Results for all abdominal procedures are comparable in terms of postoperative morbidity and recurrence. Resection rectopexy is associated with less postoperative constipation.	B, B
Does laparoscopy provide superior outcomes to open repair?	Laparoscopy has equivalent morbidity, mortality, and recurrence rates, with similar postoperative functional outcomes as open surgery. Laparoscopy is associated with decreased length of stay and longer operative times.	B
How does rectal prolapse surgery affect postoperative function in those patients with preoperative fecal incontinence?	Repair via either the perineal or abdominal approach, regardless of method, is associated with improved continence and a smaller degree of complete resolution.	B
How does rectal prolapse surgery affect postoperative function in those patients with preoperative constipation?	Repair via either the perineal or abdominal approach is associated with improved constipation, though rates widely vary. Patients with significant preoperative constipation should avoid a Ripstein procedure and likely benefit more from addition of a sigmoid resection.	B, B
What is the optimal treatment for recurrence?	The abdominal approach is associated with lower subsequent recurrence rates when compared to the perineal approach, and should be considered when the patient's risk profile permits it.	B

INTRODUCTION

In this era of evidence-based medicine, it is more important than ever to formulate clinical decisions on reliable information. The dilemma that clinicians too often face is how to fully evaluate patients without performing unnecessary testing and then best manage them to achieve optimal outcomes. This decision is particularly difficult in patients presenting with rectal prolapse for a number of reasons: the complex nature of the condition, the frequency of concomitant pelvic floor conditions contributing to the

symptoms, and, in general, a lack of correlation among many of the available tests. In addition, despite its relative frequency, quality data regarding the best outcome and management for both primary and recurrent rectal prolapse are lacking. Yet full-thickness rectal prolapse remains a distressing condition for both the patient and surgeon alike. The prolapse results in difficulties not only with the actual condition itself (i.e., pain, bleeding, seepage) but also with function (constipation and incontinence), as well as quality of life. Full-thickness external prolapse occurs when the rectum descends beyond the anal verge, manifesting

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concentric rings of rectal mucosa to the examiner. Varying degrees of prolapse exist, from mucosa only and progression through presence with increased abdominal pressure, to continual prolapse with inability to reduce. As time passes, the chronic prolapse through the sphincter complex, along with the often present concomitant pelvic floor dysfunction, leads to progressive problems with incontinence, from chronic stretching and neuropathy, as well as constipation from outlet obstruction.

With over 130 different procedures described for the surgical treatment of rectal prolapse and its recurrence, it is not surprising to find disagreement about the ideal management. This likely more accurately emphasizes the lack of an ideal option for all patients and highlights the need for proper patient counseling regarding outcome and expectations following operative repair. This chapter systematically reviews the available literature concerning the treatment and outcomes of initial and recurrent prolapse and provides recommendations as supported by the current level of evidence.

WHAT IS THE OPTIMAL PREOPERATIVE EVALUATION FOR THOSE PATIENTS WITH RECTAL PROLAPSE; THAT IS, WHAT ARE THE DATA ON COLONOSCOPY, ANORECTAL PHYSIOLOGY STUDIES, MANOMETRY, TRANSIT STUDIES, AND DEFECOGRAPHY?

In terms of preoperative evaluation, it is clear that not all aspects of patient care require a prospective, randomized trial to determine what is best. As with any disease process, the initial approach to the patient remains a standard history and physical examination. Though lacking any true Level I evidence, no one would doubt the necessity to perform a thorough history and physical examination prior to embarking on the surgical repair of rectal prolapse. In addition, rectal prolapse has a high rate of concomitant undiagnosed pelvic floor conditions that may contribute to symptoms or need to be addressed at the time of the operation (1), thus making a comprehensive preoperative evaluation essential. Yet “comprehensive” does not necessarily mean “all-inclusive,” leading to the underlying principle of this question.

The exact role and benefit of ancillary studies remain controversial. Although colonoscopy is often recommended by many authors prior to surgical repair to evaluate for neoplasia, solitary rectal ulcer, or anastomotic stricture in those patients with a prior resection, the benefits of endoscopy as it specifically relates to rectal prolapse are lacking. Extrapolating the data from screening guidelines for colorectal cancer, endoscopic evaluation in those patients at risk for malignancy has very strong evidence to support its use (2,3). Very rarely does it provide information that may lead to a change in management as it pertains to rectal prolapse. Certainly there are case reports of colorectal cancer presenting as rectal prolapse, though these are in patients already deemed at risk and should be appropriately screened outside of their unusual presentation (4–6). In our review of the literature, we were unable to identify additional rationale to justify colonoscopy apart from the

standard screening and surveillance guidelines or work-up of unusual signs or symptoms.

Preoperative symptoms have also been used to help stratify patients and guide surgeons in choosing the ideal operative procedure. Those patients complaining of a large amount of constipation may benefit from undergoing transit marker studies to exclude or diagnose slow-transit constipation. Yet the exact role of colonic transit has had minimal evaluation specifically for rectal prolapse. Prokesch et al. demonstrated prolonged total colonic transit time and rectosigmoid transit time in a study that included five patients with rectal prolapse compared to those with internal intussusception—though total colonic transit time was not significantly different from those with idiopathic constipation (7). Huber and associates evaluated colonic transit in the postoperative setting and noticed mean transit time and rectosigmoid transit time significantly decreased following rectopexy and sigmoid resection; though again, they did not specifically evaluate the use of these tests preoperatively to either manage or decide operative approach (8). Likewise, Brown and associates noted prolonged transit time occurred more often following suture rectopexy when compared to a group of normal controls (9). In one study assessing the preoperative predictive value of transit studies, Schultz and colleagues evaluated 17 patients with rectal prolapse undergoing Ripstein’s rectopexy, and found a slight correlation between the numbers of markers retained preoperatively with higher rates of emptying difficulties following surgery (10). Thus, although some expert opinion suggests performing preoperative transit studies in patients with “severe” constipation (11), the added value is unknown—especially when accounting for the significant percentage of patients who have improved or resolved constipation following prolapse repair (see later discussion).

Cinedefecography may also be used to identify obstructive defecation pathology such as paradoxical puborectalis, anismus, or internal intussusception. In addition, it may diagnose concomitant pelvic floor abnormalities, such as cystocele, enterocele, or vaginal vault prolapse in 15–30%, which may contribute to symptoms and lead to higher recurrence if not addressed (12). Yet there is very limited data with no controlled trials, and evidence to support its use outside of expert opinion is lacking.

Anorectal physiology studies include manometry, electromyography (EMG), and pudendal nerve terminal motor latency (PNTML) testing. Whereas they have been commonly used in patients with fecal incontinence secondary to other conditions (i.e., obstetrical injuries), their use in rectal prolapse patients with incontinence has been less extensively studied. Like constipation, there are conflicting reports as to the correlation between preoperative testing with postoperative outcomes. In one of the few studies demonstrating an association, Williams and colleagues found preoperative use of anorectal manometry may help predict postoperative continence (13). In their prospective study of 23 patients, those with higher preoperative resting (>10 mmHg) and maximum squeeze anal pressure (>50 mmHg) had better rates of postoperative continence. Yet in this small study, the entire cohort demonstrated improvements in postoperative pressures, and

the preoperative results did not change the operative plan. In another study showing some value of manometry, Glasgow and colleagues retrospectively evaluated the use of EMG and manometry in 45 patients with rectal prolapse undergoing perineal proctectomy (14). Of these, 35 patients complained of fecal incontinence preoperatively, while one-third had symptoms of obstructive defecation. Preoperative PNTML abnormalities were identified in 56% of all patients, whereas the mean resting pressure (34.2 mmHg, normal >40) and mean squeeze pressure (60.4 mmHg, normal >80) were decreased. The authors found that the degree of incontinence *did not* correlate with manometry studies. In addition, whereas the total rate of incontinence fell from 78% preoperatively to 36% postoperatively, mean preoperative resting pressure and presence of pudendal neuropathy also did not correlate with functional outcome. Only preoperative squeeze pressures >60 mmHg were associated with a lower rate of postoperative fecal incontinence (10.5 versus 54.8%, $p = 0.004$). The authors tested only 45 out of the original 106 patients, and the cohort consisted of purely perineal resections—thus confounding the applicability to those undergoing either a Delorme procedure or abdominal operation that spares the rectum and its associated compliance and storage. The same group 10 years prior had reported the utility of postoperative PNTML testing for predicting postoperative outcomes in a study of 24 patients evaluated prospectively by manometry and PNTML before and after surgery. Of 19 total patients with postoperative EMG testing, those with postoperative bilateral or unilateral pudendal neuropathy had higher rates of postoperative incontinence (83% and 38%, respectively) than those with normal PNTML (20%) (15). Thus, although postoperative testing demonstrated some predictive value, preoperative testing was unable to predict outcome or influence treatment. Unfortunately, most other authors have failed to demonstrate an association of PNTML or manometry with postoperative functional outcome via either perineal or abdominal approaches (16–18).

Finally, there are limited data to support the use of ultrasound evaluation in those patients presenting with incontinence in the setting of rectal prolapse. In a retrospective review of 21 patients with full-thickness rectal prolapse, 71% were found to have sphincter defects on ultrasound evaluation, leading the authors to theorize a contribution to persistent or recurrent fecal incontinence following successful repair of the rectal prolapse (19). Rarely is the sphincter defect addressed at the time of rectal prolapse surgery. Rather, the patient is more commonly followed postoperatively to evaluate functional outcome.

Recommendation: Although there are some data suggesting a correlation of preoperative testing with postoperative functional outcome to aid in counseling or research, most studies do not find a correlation and rarely do these results impact operative strategy (Grade C). A lack of Level I evidence specifically for the use of endoscopy in the setting of rectal prolapse precludes a Grade A recommendation by current standards. However, the bulk of literature supporting the utility and need for screening and surveillance endoscopy in those specific patients at risk for colorectal cancer may rightfully be extrapolated to patients prior to the surgical treatment of rectal prolapse.

WHAT IS ASSOCIATED WITH BETTER PERIOPERATIVE OUTCOMES: ABDOMINAL OR PERINEAL APPROACHES?

The ideal surgical procedure for full-thickness rectal prolapse should be one of minimal morbidity, improve postoperative function, and have a low rate of recurrence over an extended time period. Unfortunately, as evident from the large number of surgical options for prolapse, it is not surprising to find a lack of a single uniform solution. Therefore, when determining what procedure is associated with improved outcomes, it is imperative to focus on the specific endpoint in question—that is, morbidity, mortality, function, or recurrence. For example, recurrence rates vary widely in the literature with older studies reporting rates as high as 50%, though perioperative morbidity in the same cohort may be <5% (20). Variation is widely perceived to reflect the differences in procedures, although some authors suggest technique itself cannot fully account for these differences (21). Instead, they may more accurately be explained by nonuniform endpoint definitions (i.e., recurrence), varying length of follow-up, and sample size (22).

In general, perineal procedures have been reserved for older patients and those with comorbid conditions who would gain the most benefit from a less morbid operation, shorter length of hospital stay, and faster recovery. Unfortunately, perineal repairs have not been as durable as abdominal procedures, with higher recurrence rates of 5–40% reported, depending on the particular procedure and length of follow-up (23). This may be especially evident in young patients who would otherwise outlive their repair (24). Other factors also play a role in selecting the optimal approach that may not be accounted for in the literature—such as the young male wanting to minimize the potential risk of sexual dysfunction from autonomic nerve damage during the pelvic dissection with an abdominal procedure versus the increased risk of recurrence with perineal techniques.

Nevertheless, it is generally accepted that recurrence rates following an abdominal repair (0–10%) are less than after a perineal approach (21,24–26). Regardless of initial procedure performed, most recurrences are detected one to three years postoperatively, with up to one-third developing within the first seven months (27–29). Though the pathophysiology of recurrence is not entirely clear, potential causes include division of the lateral ligaments with abdominal approaches (30,31), technical errors associated with rectopexy or mesh placement (28), unclear endpoint of resection with perineal resection (29), incomplete mucosectomy with Delorme's procedure (32), and a failure to address concomitant pelvic floor defects (33). Other risk factors reported include concomitant psychiatric disease (34), male gender (35), older age, and higher body mass index (36).

Unfortunately, there is limited Level I evidence with a paucity of randomized series to compare outcomes between the two surgical approaches. Of the five prospective, randomized trials in publication regarding rectal prolapse, only one study directly compares abdominal with perineal approaches (37). The authors randomized 10 patients in each group to either resection rectopexy with pelvic floor repair or perineal rectosigmoidectomy with pelvic floor repair. Recurrence rates were similar in the two cohorts,

with only one patient (perineal group) developing a recurrence, although two patients in each group developed mucosal prolapse. Soiling was more frequent in the perineal group [60% versus 20%, odds ratio (OR) 8.07], with a corresponding higher anal mean resting pressure and better compliance in the abdominal group. Finally, morbidity rates were similar with one anastomotic stricture in the perineal group, and ileus ($n = 2$), wound infection ($n = 1$), and colostomy ($n = 1$) in the abdominal group.

The largest prospective, randomized study to date is still under way, being plagued by difficulty with patient enrollment. Although still in abstract form, the PROSPER trial (prolapse surgery; perineal or rectopexy) from the Association of Coloproctology of Great Britain and Ireland aims to compare both abdominal and perineal approaches, as well as resection versus no resection for the abdominal cohort and Delorme's operation versus the perineal rectosigmoidectomy for the perineal approach (38). With target recruitment at 1,000 patients, as of June 2005, only 201 patients were enrolled, with 153 having undergone surgery. In this study, patients are initially randomized between abdominal or perineal approaches or surgeons can elect to enroll in either the abdominal or perineal cohort, with subsequent randomization regarding resection. At the last update, unfortunately only 11% of all patients had been randomized between abdominal and perineal approaches. With 115 patients in the perineal group and only 35 patients in the abdominal cohort, higher complication rates were seen in the perineal group (24% versus 8%). Out of the entire cohort, 23 patients have developed a recurrence (11 mucosal and 12 full-thickness). However, with so few patients randomized between the two approaches, the authors have been unable to adequately compare outcomes.

Finally, in 2005, Madiba and colleagues performed a review of all prospective and retrospective comparison studies demonstrating that abdominal operations are associated with a lower rate of recurrence and similar rates of improvement in functional outcomes when compared to the perineal approach (25). They concluded that suture and mesh rectopexy result in essentially equivalent outcomes, though the addition of resection is associated with lower rates of postoperative constipation. The authors deemed all patients should be offered an abdominal approach, except for those patients too old or frail to tolerate a general anesthetic, who should then undergo a perineal procedure.

Recommendation: The literature is limited by a paucity of true comparative studies between both approaches. From the two prospective, randomized trials and large review available, despite small numbers, it appears the two approaches are fairly similar with regard to outcomes. In general, prospective (Level II) and retrospective (Level III–IV) cohort series demonstrate that most patients selected to undergo a perineal approach tend to be older with more comorbidities and lack the physiological capacity to safely tolerate an abdominal operation in many cases. Thus, the morbidity, mortality, and especially recurrence rates in this group are, on average, higher than their abdominal counterpart (Grade B). Yet the lack of large-scale sample populations and true randomization makes it difficult to discern the obvious selection bias associated with this type of analysis and determine the optimal approach (Grade I).

WHEN CONSIDERING ABDOMINAL APPROACHES, WHICH TECHNIQUE IS ASSOCIATED WITH BETTER OUTCOMES: MOBILIZATION WITH SUTURE RECTOPEXY, SUTURE RECTOPEXY WITH THE ADDITION OF MESH, OR RESECTION RECTOPEXY?

Though again largely devoid of large-scale data, in addition to multiple prospective and retrospective series, there are four small prospective, randomized trials that have attempted to further clarify this question. The basic tenets of an abdominal approach remain the same—mobilization of the rectum down to the pelvic floor and suspension of the rectum to hold/scar it in place and improve overall functional outcome. Yet the technical aspects of different operations may lead to differences in results. These involve issues such as the extent of dissection both laterally and anteriorly, how best to adequately ensure fixation to the sacrum—via mesh, sutures, or scarring alone—and when to add a resection to the mobilization.

First, to evaluate both the functional aspects and recurrence rates associated with the degree of mobilization, Speakman and colleagues randomized 26 patients undergoing abdominal rectopexy to either division ($n = 14$) or no division ($n = 12$) of the lateral ligaments (30). The authors demonstrated a statistically significant increase in postoperative constipation in those undergoing division of the ligaments, however they had a lower recurrence rate (0% versus 50%, $p < 0.01$). Scaglia and colleagues also found worsening constipation with division of the ligaments in their comparison of the Wells procedure (posterior mesh with division of lateral ligaments, $n = 16$) and Ripstein procedure (anterior mesh with preserved lateral ligaments, $n = 16$) (31). Limited dissection in only the posterior and anterior planes with anterolateral mesh fixation to the sacral promontory (Orr-Loygue ventral rectopexy) has also been shown to be successful in a prospective series of 73 patients, including 51 with full-thickness rectal prolapse (39). Using this technique, the authors demonstrated a 6% recurrence, with improvement in continence in 58%, and constipation in 52%. Like the previous two studies, the authors recommended avoidance of lateral dissection, but proposed an anterolateral placement of mesh to avoid posterior-lateral immobilization of the rectum by the mesh, which they theorize can lead to increased constipation.

Raftopoulos and associates specifically evaluated different abdominal approaches in a multicenter review of 623 patients using the primary endpoint of recurrence (21). At a median follow-up of 43 months, recurrence occurred in 38 patients (6.1%). Interestingly, six centers including 281 patients identified no recurrences. By procedure, 46 patients had mobilization only, 130 patients had resection with rectopexy, and 467 had mobilization with rectopexy. Mesh was used in 320 patients, with 98% of these placed posteriorly. In evaluating the 307 patients from the nine centers that reported recurrence, the 1-, 5-, and 10-year recurrence rates were 1.06%, 6.61%, and 28.92%, respectively. Neither surgical technique (mobilization-pexy, resection-pexy, or mobilization only), method of rectopexy (mesh versus suture), nor means of access (open versus laparoscopic) had any impact on the rate of recurrence—only length of follow-up. One drawback to this study is

the low number of mobilization-only patients that led to difficulty with definitive conclusions regarding that technique. The large number of patients from multiple centers provides insight into the similarity in recurrence rates between the different methods. Nelson and colleagues in a retrospective review of 13 patients with mobilization only demonstrated one early and one late recurrence at a mean follow-up of 33.4 months, correlating somewhat to the findings of Raftopolous's cohort (40).

The theory behind mesh use is to help ensure adequate fixation and scarring, although location of the mesh has resulted in slightly different outcomes. Schultz and colleagues demonstrated long-term success with Ripstein's repair in 112 patients, including 69 with rectal prolapse and 43 with internal intussusception over nearly two decades (41). With almost six years of follow-up, there were no perioperative deaths, although early (<30 days) and late (>30 days) complications were common. The majority of the 33% early complication rate was due to minor complications such as urinary tract, wound, or respiratory infections. However, significant complications requiring intervention included presacral hemorrhage, fecal impaction requiring subtotal colectomy with ileorectal anastomosis, and obstructive hydronephrosis requiring reexploration. Of delayed complications, small bowel obstruction, rectovaginal fistula, and severe constipation requiring hospitalization were the most common. In this series, only one patient had recurrence of rectal prolapse. Overall, although incontinence did improve, patients continued to have problems with mostly constipation.

In a prospective trial, Novell and group randomized 63 patients (62 females) to either Ivalon sponge rectopexy ($n = 31$) or suture rectopexy alone ($n = 32$) (42). The authors found no difference in perioperative morbidity (6/31 versus 3/32) and no mortality at 30 days within the entire cohort. Just as in the Raftopoulos series, recurrence was also similar, with one patient in each group at a median follow-up of 47 months. Other authors have examined the role of absorbable versus nonabsorbable mesh ($n = 37$), finding no significant differences in either recurrence or postoperative complications (43). Similarly, Winde and associates found no difference in complications, recurrence, or functional outcomes in a prospective randomized trial comparing two types of absorbable mesh ($n = 47$) (44). Some authors have even demonstrated no infectious complications with absorbable mesh (45), although certainly mesh use raises the concern for infection or erosion of the mesh, both of which have been described (25,46,47). Athanasiadis and associates demonstrated a 2% rate of pelvic infection in 145 patients undergoing resection rectopexy versus 5% without resection ($n = 77$) (46). Despite using mesh in all cases, the authors found no difference in infectious complications between polyvinyl alcohol (Ivalon), vicryl, or Gore-Tex mesh. Unfortunately, technical differences among various series, including mesh location and whether a colonic resection was used, make it difficult to draw widespread conclusions.

Finally, the role of resection is also of considerable debate. Most single-institution studies have identified the rate of postoperative constipation to be significantly lower with resection rectopexy when compared to nonresectional abdominal procedures. In addition, those patients with preexisting constipation are likely more apt to benefit from

the addition of a resection to rectopexy (24,48–50). Despite this vast body of literature, there have been only two randomized prospective trials evaluating the role of rectopexy alone (one with mesh and one with suture rectopexy) versus the addition of resection. McKee and associates randomized 18 patients to suture rectopexy versus resection rectopexy (51). In comparing constipation rates, seven of nine patients in the suture rectopexy cohort had severe constipation at a follow-up of three months, versus only two of nine in the resection rectopexy group. This correlated with a higher rate of colonic Sitz marker retention in the rectopexy group compared to preoperatively. Luukkainen and colleagues also performed a randomized trial of 30 patients to either suture rectopexy with resection ($n = 15$) versus mesh without resection ($n = 15$) (52). Both groups had equivalent rates of morbidity and improvement in continence following surgery, although new worsening constipation occurred in one-third of the mesh patients following repair. Although difficult to put side by side accurately, because two different control groups were used, the combined rate of postoperative constipation in the resection group was significantly lower than the rectopexy alone patients (2/23 versus 12/23).

Recommendation: Despite the abundance of literature, there remains a paucity of high-quality trials, leaving mainly single-institution studies using different surgical procedures to draw conclusions from, thus making it difficult to directly compare results. In general, full rectal mobilization down to the levators is an integral component for ensuring the best outcomes. There is some Level II and III evidence to suggest that division of the lateral ligaments increases postoperative constipation with slightly lower recurrence rates (Grade B). Neither mobilization alone, rectopexy with suture or mesh, nor resection rectopexy appear to offer an advantage with regard to prevention of recurrence or postoperative morbidity (Grade B). However, resection rectopexy in patients with increased preoperative constipation appears to convey a benefit of better postoperative function (Grade B).

DOES LAPAROSCOPY PROVIDE SUPERIOR OUTCOMES TO OPEN REPAIR?

As with other medical conditions, a minimally invasive approach also offers patients undergoing surgery for rectal prolapse the potential advantages of reduced postoperative pain, early return of bowel function, and shortened length of stay (53). Unfortunately, the trend of a lack of a plethora of comparative evidence continues with this section as well. The single Cochrane review in 2000 by Bachoo et al. (updated February 2003) concluded there were too few data to adequately evaluate the open versus laparoscopic approaches (54). In fact, only two acceptable trials were available at that time—one a retrospective review of 21 participants (55), and the other, a randomized controlled trial of 40 patients—both using the technique of a Well's rectopexy (56). In addition, neither of the trials shared the same primary endpoint (recurrence of full-thickness or mucosal prolapse) or secondary outcomes (postoperative function, morbidity, length of stay, and operative time), and both groups used mesh rectopexy with no cases of suture rectopexy alone or resection rectopexy. Thus, it is

difficult to not only compare outcomes but also provide generalized recommendations. An additional Cochrane review discussing the short-term benefits for laparoscopy in colorectal resection that included a small number of patients with rectal prolapse demonstrated that laparoscopy is associated with decreased blood loss, decreased pain, decreased postoperative ileus (-1 day), shorter length of hospital stay (-1.4 days), improved short-term quality of life (10 points on 0–100 scale on day 7), and decreased morbidity [RR 0.72, 95% confidence interval (CI) 0.55–0.95] (57). Yet only the Solomon trial (56) was used for rectal prolapse evaluation, again lacking widespread specificity to rectal prolapse.

Subsequently, a meta-analysis including six studies and 195 patients (98 open versus 97 laparoscopic) of abdominal rectopexy was published in 2005, in which Purkayastha and colleagues found no difference in recurrence (OR = 0.94, 95% CI 0.26–3.44) or morbidity (OR = 0.56, 95% CI 0.24–1.29) between the two groups (58). Laparoscopy was also associated with a significant decrease in length of stay by 3.5 days (95% CI 3.08–4.01) at the down-side of approximately 60 minutes longer operative time. Interestingly, again, the only prospective randomized trial included was Solomon et al.'s review of 40 patients (56). In this study, the authors compared 20 laparoscopic with 20 open patients and demonstrated an increase in morbidity in the open cohort (6 of 20 laparoscopic versus 14 of 19 open, $p < 0.001$). Also of note, the authors found a reduction in operative time occurred from their prior study of laparoscopic rectopexy from 70 to 50 minutes. Thus, the surgical learning curve that comes with increasing experience may mitigate the longer operative times and create even fewer differences between the two approaches. These authors also demonstrated an increase in the ability to tolerate a solid diet in the laparoscopic cohort (16 of 20 laparoscopic versus 2 of 19 open, $p < 0.01$). In another of the included articles in the meta-analysis, Kairaluoma and colleagues found similar results in study of 106 patients, and also demonstrated decreased intraoperative bleeding for both the resection rectopexy (lap 35 ml versus open 300 ml) and rectopexy alone (laparoscopic 15 ml versus open 100 ml; both $p < 0.05$) with the use of laparoscopy (59).

Other authors have demonstrated the feasibility and effectiveness of the laparoscopic approach using different techniques in retrospective reviews of their data. Benoist and colleagues showed that laparoscopic approaches have comparable results between rectopexy alone, mesh repair, or the addition of a resection with no mortality, low morbidity rates (11–19%), and improvement in continence in 75% for all procedures combined (60). Similarly, Dulucq and colleagues demonstrated good functional outcomes with 89% improvement in continence and 36% improvement in constipation, with only 1 of their 77 patients developing a recurrence following a laparoscopic posterior (Well's) rectopexy (61). Kariv demonstrated a shorter hospital stay (3.9 days versus 6 days, $p < 0.001$), with equivalent functional and recurrence rates at 59 months' follow-up in a case-control study of 111 laparoscopic (suture rectopexy, $n = 67$; mesh rectopexy, $n = 42$; and resection rectopexy, $n = 32$) with 86 open repairs (36). Possibly even more important, some have shown the ability to extend traditional boundaries by allowing higher risk patients to undergo an abdominal procedure via laparoscopy, who would have

been historically relegated to a perineal procedure, both safely and effectively. Carpelan-Holmstrom described their results of laparoscopic rectopexy that included 51 female patients with a median age of 70 years and 50% deemed high risk (either ASA III or IV), finding less blood loss, decreased length of stay, no mortality, and equivalent morbidity as the open cohort (62). In addition, only 6% required conversion to open surgery. Salkeld and associates took a different angle, and despite their longer operative times (mean 51 minutes) and disposable instrument cost (mean £291/patient), the savings associated with a decreased length of stay following laparoscopy resulted in an overall cost savings of £357/patient when compared to an open cohort (63). Finally, an even larger series of resection rectopexy have demonstrated that laparoscopy is safe and feasible. Ashari et al., in their series of 117 patients undergoing a laparoscopic resection rectopexy, had comparable mortality (0.9%) and morbidity (9%) rates to open procedures (49). With a low 2.5% recurrence rate and an overall 69% improvement in continence, even beyond smaller incisions, the function and durability were equivalent to the open counterpart.

Recommendation: Laparoscopy is associated with decreased length of stay and longer operative times when compared to open approaches. There is some evidence to suggest that with increasing use, the difference in operative time can be less dramatic. Yet the perioperative morbidity and mortality rates, development of recurrence, and functional outcomes for all abdominal techniques (suture rectopexy, mesh rectopexy, and resection rectopexy) are equivalent between the two approaches (Grade B).

HOW DOES RECTAL PROLAPSE SURGERY AFFECT POSTOPERATIVE FUNCTION IN THOSE PATIENTS WITH PREOPERATIVE FECAL INCONTINENCE?

As stated in the opening section regarding use of preoperative testing, many studies have attempted to identify factors that may accurately predict which patients will have improvement in continence following repair of their rectal prolapse. Due to the multifactorial nature of the condition, this has remained largely elusive. Therefore, most surgeons will perform the operation and take a "wait-and-see" approach to evaluate for subsequent improvement, resolution, or even worsening of symptoms.

In general, fecal incontinence continues to be a major problem associated with long-standing rectal prolapse. Whether it is secondary to underlying sphincter tears, chronic stretch, or associated neuropathy, the majority of series have demonstrated some degree of fecal incontinence to be present in up to 75% of patients (64). Knowledge of expected outcomes is then essential for accurate preoperative counseling, though it may depend in part by the operative approach.

Simple suture rectopexy alone has been shown to improve continence in 15–82% of patients, with most studies demonstrating over 50% success rates (42,60,65–70). With the addition of mesh, Aitola and colleagues found ~60% of patients to have restoration of continence in their retrospective review of 123 patients following mostly abdominal approaches (91%) (71). Other authors have demonstrated similar rates (3–92%) in continence improvement

with the use of mesh, with the variability, in part, secondary to the type and location of mesh placement (31,42,72,73). Again, most studies demonstrate improvement rates between 20–60%. Following resection rectopexy, the literature is also scattered with wide ranges of improved continence (11–100%) though similar mean rates (8,24,37,52,60,72,74–77).

Those studies specifically evaluating the Ripstein repair, while consistently associated with increased rates of postoperative constipation (see next section), have demonstrated continence is improved after surgery in 15–80% (44,75,78–80). Postoperative anorectal manometry following the Ripstein technique has also demonstrated an increase in maximal sphincteric resting pressure (80). This may represent partial recovery of internal sphincter function following reduction of the prolapsed rectum and may also occur following other abdominal approaches. Thus, although the mechanisms for this improved function following any of the abdominal procedures are not currently known, generalized improvement in continence can normally be expected regardless of the repair performed.

With perineal procedures, continence also has widely varying improvement rates from 20–100% and complete resolution in 20–50% (81). Just like the abdominal approach, rates vary among studies and depend also on the technique used. Delorme's procedure is associated with improvement in continence from 25% to 70%, with the vast majority of these studies retrospective in nature (32,82–86). One prospective study of 43 patients undergoing a Delorme procedure included 40 patients with preoperative fecal incontinence and demonstrated complete resolution of the incontinence in 50% (87). Possible reasons behind this improved continence are those listed above for abdominal repair, and, specific to Delorme's procedure, Oliver and colleagues postulated increased bulk in the anal canal provided by the plicated muscularis propria (32).

Following perineal rectosigmoidectomy, continence rates improve from 20% to 90%; though, again, the majority of studies are retrospective in nature and include between 10 and 183 patients (16,24,74,81,88). The single prospective randomized trial that demonstrated 80% continence improvement in the perineal sigmoidectomy group was limited by inclusion of only 10 patients (37). Glasgow and associates noted a drop in incontinence rates from 77% preoperatively to 42% postoperatively in a larger retrospective study of 103 patients undergoing perineal rectosigmoidectomy at a median follow-up of 21 months (89). Despite these consistent success rates, a study from the University of Minnesota involving 33 patients undergoing perineal rectosigmoidectomy noted continence improvement in only 6%; although more important, 22% developed worsened symptoms (74). In one of the few studies comparing the two perineal approaches, Agachan and colleagues evaluated 61 patients retrospectively, and found a significant improvement in both cohorts between preoperative and postoperative mean incontinence scores, although differences in anal manometry did not significantly differ between the two groups (90).

Results may also in part depend on the addition of pelvic floor repair. Concomitant performance of a levatorplasty has been reported to improve postoperative continence, with small cohorts demonstrating up to 90% in short-term follow-up (81,90–92). This levatorplasty creates subsequent lengthening of the anal canal and has been demonstrated to provide even greater improvements in

postoperative continence when compared to perineal rectosigmoidectomy alone. This is not uniformly appreciated, though, as Chun and colleagues noted no significant difference of continence rates with the addition of a levatorplasty in their retrospective review of 120 perineal procedures, although each group did have significant improvements in postoperative incontinence scores (93). In addition, the authors demonstrated that recurrence rates were lower in the levatorplasty group, although the groups differed in length of follow-up (21% at 45 months, no levatorplasty versus 8% at 13 months, levatorplasty, $p = 0.049$).

Furthermore, although controversial, surgeons should be aware of associated pelvic floor findings that may need to be addressed at the time of surgery. Concomitant pelvic floor pathology such as enteroceles or rectoceles may be present in up to 10–50% of patients with rectal prolapse or internal intussusception depending on method of evaluation (94). In a study of 22 patients, Mellgren and colleagues found that continence was improved in 94%; however, functional improvements in emptying difficulties are more varied (95). Yet there are limited data regarding this practice, and many expert opinions feel it is best to address only the prolapse and follow symptoms postoperatively.

Recommendation: Repair of rectal prolapse via either a perineal or abdominal approach is associated with a wide range of reported success rates. However, in general, the majority of studies demonstrate improved continence, whereas a lower percentage will have complete resolution of their incontinence (Grade B).

HOW DOES RECTAL PROLAPSE SURGERY AFFECT POSTOPERATIVE FUNCTION IN THOSE PATIENTS WITH PREOPERATIVE CONSTIPATION?

Obstructive defecation with symptoms of constipation is also frequently present in patients with rectal prolapse, reported in 15–65% (24,25). In this setting, constipation is postulated to be secondary to either associated proximal colonic dysmotility resulting in slow-transit constipation (96), or from the intussusception of the bowel itself—creating a functional blockage that is exacerbated with chronic straining (41). In addition, concomitant pelvic floor disorders may also lead to symptoms of obstruction (97–99). As per the discussion pertaining to the patient with rectal prolapse and fecal incontinence, one of the main outcomes associated with surgical repair is improvement or resolution of these debilitating symptoms of constipation and obstruction. Yet in contrast to the patient with fecal incontinence, there is a slightly higher, albeit small, number of patients that may have new-onset or worsening of constipation following repair—especially following abdominal approaches. Outcomes therefore vary, depending on both surgical approach (abdominal versus perineal) and chosen technique.

For those patients that do not complain of a significant component of preoperative constipation, mobilization with rectopexy alone has a low rate of new-onset constipation (69,100). In general, most prospective studies have also demonstrated improvement in constipation ranging from 14–83% (66,68–70). There are a small but not insignificant percentage of patients (11–31%) that will notice worsening of symptoms (42,60,65). Unfortunately, the exact etiology of this worsening or new-onset constipation remains elusive.

It probably involves multiple factors ranging from neuropathy with division of the lateral ligaments (30), to the redundant sigmoid colon kinking at the proximal rectum, resulting in increased outlet resistance (51). Nevertheless, the surgeon should be aware and counsel patients accordingly.

Rectopexy with use of mesh is similarly associated with a wide range of functional results in constipated patients. In a prospective study of 77 patients undergoing laparoscopic posterior (Wells) rectopexy, Dulucq and colleagues found improvement of constipation in 36% of cases, although 18% of patients demonstrated new-onset constipation (61). Broadly speaking, mesh use has slightly higher rates of worsening constipation (14–50%) when compared to suture rectopexy (31,42,60,72,73). Surgeons encountering constipated patients need to be especially aware of the potential for worsening symptoms following Ripstein's rectopexy. In a study of 30 patients, Schultz et al. found whole-gut transit time to be prolonged following Ripstein's repair (10). Although only 13% had documented delayed transit time preoperatively, 43% had abnormal postoperative retention of transit markers distributed in the left, rectosigmoid colon, or both following surgery. Not surprisingly, the literature has discordant findings, with some authors reporting worsening constipation postoperatively in up to 45% (78,101), whereas others have found constipation unchanged (75) or even decreased (44,79). Regardless, clinically significant postoperative constipation ranges from 15% to 71% despite careful patient selection (10,41,75,79,80,101). Ripstein repair may be especially plagued by constipation secondary to fecal impaction at the level of the narrow net as a result of a technical error in which the mesh is secured too tightly to the rectum, thereby creating a mechanical outlet resistance (102).

Unlike the Ripstein repair, rectopexy with sigmoid resection appears to have the strongest evidence suggesting decreased rates of constipation following surgery (18–80% improvement) (8,24,52,72,75,76). Even in those patients that continue to have postoperative constipation, individual symptoms such as the feeling of incomplete evacuation, time spent on the commode, use of enemas, and painful evacuation have all been shown to be decreased (48). Therefore, the literature suggests the addition of a sigmoid resection is the preferred option for those patients with significant preoperative constipation who are able to tolerate an abdominal procedure.

Perineal procedures have also shown a significant improvement in constipation following surgery, as well as a very low rate of new onset of constipation. In part, this is probably secondary to the loss of capacitance of the rectum for the perineal rectosigmoidectomy. Yet Delorme's procedure has found similar success, suggesting that relief of the intussusception and functional obstruction also plays a role. Largely based on retrospective series, functional improvement has been consistently demonstrated for Delorme's procedure in reducing constipation in 13–100% of patients (82,103–106), with only 1–15% developing new-onset constipation (83–86). Interestingly, many of the retrospective series do not report the rate of functional improvement for constipation following perineal rectosigmoidectomy. Of the previously cited studies evaluating perineal rectosigmoidectomy, only Kim and colleagues report a reduction in 61% (24), whereas one other review from Oschner Clinic found all six of

their patients had improved constipation following a perineal resection (107).

Recommendation: Repair of rectal prolapse via either a perineal or abdominal approach is associated with a wide range of reported success rates for constipation, with the majority of studies suggesting improvement (Grade B). Those patients undergoing an anteriorly based mesh procedure (Ripstein) tend to have more residual or worsening constipation than the other approaches, and surgeons should consider another approach if this is a significant component of a patient's preoperative symptoms (Grade B). In general, the addition of a sigmoid resection is associated with less postoperative constipation and is the preferred option in those patients with rectal prolapse and severe constipation (Grade B).

WHAT IS THE OPTIMAL TREATMENT FOR RECURRENCE?

Unfortunately, recurrent rectal prolapse continues to be a major problem, with rates ranging from 0–47%, depending on a multitude of factors, including patient comorbidities, surgical approach, follow-up length, and accurate data reporting and censoring (22). When evaluating these patients, surgeons should first decide whether anything needs to be done operatively at all. Depending on the degree of prolapse and symptoms, observation or band ligation of mucosal prolapse have shown excellent results (108). Notwithstanding, for those that require more invasive intervention, the surgical options for recurrent rectal prolapse remain the same as in primary disease. Abdominal repairs can be performed via laparoscopy or traditional open routes, although only case reports currently exist for the minimally invasive approach in the setting of recurrent disease (109). It is important to again emphasize that when attempting to determine the optimal treatment for the patient with recurrence, surgeons need to consider the outcome of evaluation—that is, morbidity, mortality, functional results, length of stay, or subsequent recurrences. For example, Delorme's procedure has been limited by its high rate of recurrence (up to 53% at 16 months) in the setting of recurrent disease, yet the morbidity is often <10% (85). Thus, achieving optimal outcomes in one endpoint may mean accepting worse results in another.

Currently, there are five retrospective reviews specifically focusing on the approach to the patient with recurrent rectal prolapse (27–29,85,110). Fengler et al. described 14 patients over a 10-year period in which 13 patients had an initial perineal approach, and 1 patient had an abdominal operation (27). The authors noted a mean time to initial recurrence of 14 months. In treating the recurrences, they performed a repeat perineal approach (Altemeier, Delorme, or anal encirclement) in nine patients and an abdominal approach (rectopexy with and without resection) in the remaining five patients, finding no second recurrences after a mean follow-up of 50 months. Specific complications included one mucosal sloughing between two anastomotic lines, and three patients with preoperative fecal incontinence had no resolution of symptoms.

Hool and associates described 24 patients over a 30-year period in which they performed 29 operations for recurrent prolapse (28). The vast majority were abdominal (72% Ripstein) with only four perineal procedures.

The overall subsequent recurrence rate was 17% at approximately seven years' follow-up. Major postoperative complications were only seen among those who had abdominal procedures, occurring in 24% of cases (6/25). Like Fengler's series, subsequent surgery rarely altered preoperative bowel function, with incontinence improvement in only 3 of 10 patients and new-onset constipation developing in 1 patient. Pikarsky and associates matched 27 cases of reoperative recurrent prolapse with an equal number of primary repairs (110). The authors performed a mixture of abdominal and perineal procedures, demonstrating similar recurrence rates (recurrent repair 15% versus primary repair 11%), morbidity, and incontinence score at two years.

In the largest series to date, Steele and colleagues evaluated a cohort of 685 patients over a 16-year period, identifying 78 recurrences that underwent subsequent operative repair via a perineal approach ($n = 51$) or abdominal operation ($n = 27$) (29). At a mean follow-up of nine months, 29% of all patients developed a second recurrence. When stratified by operative approach, there was a statistically higher second recurrence rate in the group who underwent a perineal procedure compared to those who had an abdominal procedure (37% versus 15%, $p = 0.03$). This trend also held up when comparing the results of all patients who underwent a third repair, with 50% (3/6) of perineal approaches recurring and only 8% (1/12) of abdominal approaches ($p = 0.07$). Thus, evaluating the overall

recurrence rate following any repair (first, second, or third repair) for recurrent prolapse, patients undergoing an abdominal procedure had a significantly lower recurrence rate when compared to those undergoing a perineal repair (13% versus 39%, $p < 0.01$) at a mean follow-up of 10 months. Rates of major and minor postoperative complication were similar between perineal and abdominal approaches.

Recommendation: Though based exclusively on retrospective data, an abdominal approach for the treatment of recurrent rectal prolapse, when the patient's risk profile permits, is associated with a lower rate of subsequent recurrences. Given the baseline differences in these cohorts, both perineal and abdominal approaches have similar safety profiles in selected patients, though obvious selection bias makes direct comparison of morbidity impossible (Grade B).

CONCLUSION

Careful evaluation of the literature provides important information on which to base clinical decision making. Although there remains a paucity of both randomized controlled trials and large-scale cohort series for rectal prolapse, when evaluated as a whole, the vast experience of many authors can provide insight into expected outcomes for clinically important scenarios when confronted with patients with this condition.

Rectal Prolapse: Levels of Evidence

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Boccasanta	55	1998	IIIb	Laparoscopic mesh rectopexy versus open mesh rectopexy	PCS	29.5 months (mean)	Recurrence, incontinence, morbidity, constipation, ARPS
Deen	37	1994	IIb	Perineal rectosigmoidectomy and pelvic floor repair versus abdominal resection rectopexy with pelvic floor repair	RCT	17 months	Recurrence, incontinence, morbidity
Galili	43	1997	IIIb	Open mesh rectopexy (polyglycolic) versus open mesh rectopexy (polypropylene)	PCS	3.7 years	Recurrence, incontinence, morbidity
Glasgow	14	2006	IV	Perineal proctectomy value of PNTML and manometry	RCS	33.8 months	Incontinence
Jan (PROSPER)	38	2005	IIb	Abdominal rectopexy versus open rectopexy and resection versus no resection (in both groups)	RCT	36 months	Recurrence, incontinence, morbidity, constipation, QOL
Kellokumpu	68	2000	IIIb	Laparoscopic resection rectopexy versus laparoscopic suture rectopexy	PCS	2 years	Recurrence, incontinence, morbidity, constipation
Kim	24	1999	IV	Rectal prolapse patients undergoing surgery	RCS	98 months (ABD); 47 months (PER)	Recurrence, incontinence, morbidity, constipation
Luukkonen	52	1992	IIb	Open resection rectopexy versus open mesh rectopexy	RCT	6 months	Recurrence, incontinence, morbidity, constipation
McKee	51	1992	IIb	Open resection rectopexy versus open suture rectopexy	RCT	20 months (mean)	Recurrence, incontinence, morbidity, constipation, ARPS
Novell	42	1994	IIb	Open mesh rectopexy versus open suture rectopexy	RCT	47 months	Recurrence, incontinence, morbidity, constipation
Purkayastha	58	2005	Ia	Laparoscopic versus open rectopexy	MA	12–31 months	Recurrence, morbidity, operative time, LOS

(Continued)

Rectal Prolapse: Levels of Evidence (Continued)

Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Raftopoulos	21	2005	IV	Abdominal surgery for rectal prolapse (multicenter pooled data)	RCS	43 months	Recurrence
Ramanujam	88	1994	IV	Rectal prolapse undergoing perineal rectosigmoidectomy and levatorplasty	RR	48 months (mean)	Recurrence, incontinence, morbidity, constipation
Schultz	10	1999	IIb	Ripstein rectopexy value of transit studies	PCS	6 years	Constipation, marker retention
Schultz	18	1998	IIIb	Ripstein rectopexy value of EMG and PNTML	PCS	4.5 years	Continence, PNTML, EMG, nerve fiber density
Solomon	56	2002	IIb	Laparoscopic mesh rectopexy versus open mesh rectopexy	RCT	24 months (mean)	Recurrence, incontinence, morbidity, constipation
Steele	29	2006	IV	Recurrent rectal prolapse	RCS	9 months	Recurrence, morbidity
Watts	85	2000	IV	Rectal prolapse undergoing Delorme's procedure (primary and secondary)	RR	36 months (mean)	Recurrence, incontinence, morbidity, constipation
Williams	13	1991	IIb	Rectal prolapse and fecal incontinence value of manometry	PCS	7 months	Incontinence
Winde	44	1993	IIb	Open mesh rectopexy (polyglycolic) versus open mesh rectopexy (polyglactin)	RCT	50.5 months (mean)	Recurrence, incontinence, morbidity, constipation

Abbreviations: ABD, abdominal approach; ARPS, anorectal physiology; LOS, length of stay; MA, meta-analysis; PCS, prospective cohort study; PER, perineal approach; PNTML, pudendal nerve terminal motor latencies; QOL, quality of life; RCS, retrospective cohort study (review and case series); RCT, randomized controlled trial; RR, retrospective review.

REFERENCES

- Pescatori M, Spyrou M, Pulvirenti d'Urso A. A prospective evaluation of occult disorders in obstructed defecation using the "iceberg diagram." *Colorectal Dis* 2007; 9: 452-6.
- Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med* 1993; 329: 1977-81.
- Citarda F, Tomaselli G, Capocaccia R, et al. Italian Multicentre Study Group. Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence. *Gut* 2001; 48: 812-15.
- Chen CW, Hsiao CW, Wu CC, Jao SW. Rectal prolapse as initial clinical manifestation of colon cancer. *Z Gastroenterol* 2008; 46: 348-50.
- Yamazaki T, Sakai Y, Sekine Y, et al. Sigmoid colon cancer presenting as complete rectal prolapse: report of a case. *Surg Today* 1999; 29: 266-7.
- Bounovas A, Polychronidis A, Laftsidis P, et al. Sigmoid colon cancer presenting as complete rectal prolapse. *Colorectal Dis* 2007; 9: 665-6.
- Prokesch RW, Breitensteiner MJ, Kettenbach J, et al. Assessment of chronic constipation: Colon transit time versus defecography. *Eur J Radiol* 1999; 32: 197-203.
- Huber FT, Stein H, Siewert JR. Functional results after treatment of rectal prolapse with rectopexy and sigmoid resection. *World J Surg* 1995; 19: 138-43.
- Brown AJ, Nicol L, Anderson JH, McKee RF, et al. Prospective study of the effect of rectopexy on colonic motility in patients with rectal prolapse. *Br J Surg* 2005; 92: 1417-22.
- Schultz I, Mellgren A, Oberg M, et al. Whole gut transit is prolonged after Ripstein rectopexy. *Eur J Surg* 1999; 165: 242-7.
- Safar B, Vernava AM. Abdominal approaches for rectal prolapse. *Clin Colon Rectal Surg* 2008; 21: 94-9.
- Altman D, Zetterstrom J, Schultz I, et al. Pelvic organ prolapse and urinary incontinence in women with surgically managed rectal prolapse: a population-based case-control study. *Dis Colon Rectum* 2006; 49: 28-35.
- Williams JG, Wong WD, Jensen L, et al. Incontinence and rectal prolapse: a prospective manometric study. *Dis Colon Rectum* 1991; 34: 209-16.
- Glasgow SC, Birnbaum EH, Kodner IJ, et al. Preoperative anal manometry predicts continence after perineal proctectomy for rectal prolapse. *Dis Colon Rectum* 2006; 49: 1052-8.
- Birnbaum EH, Stamm L, Rafferty JF, et al. Pudendal nerve motor latency influences surgical outcome in treatment of rectal prolapse. *Dis Colon Rectum* 1996; 39: 1215-21.
- Johansen OB, Wexner SD, Daniel L, et al. Perineal rectosigmoidectomy in the elderly. *Dis Colon Rectum* 1993; 36: 767-72.
- Sainio AP, Voutilainen PE, Husa AI. Recovery of anal sphincter function following transabdominal repair of rectal prolapse: cause of improved continence? *Dis Colon Rectum* 1991; 34: 816-21.
- Schultz I, Mellgren A, Nilsson BY, et al. Preoperative electrophysiologic assessment cannot predict continence after rectopexy. *Dis Colon Rectum* 1998; 41: 1392-8.
- Woods R, Voyvodic F, Schlothe AC, et al. Anal sphincter tears in patients with rectal prolapse and faecal incontinence. *Colorectal Dis* 2003; 5: 544-8.
- Karulf RE, Madoff RD, Goldberg SM. Rectal prolapse. *Curr Prob Surg* 2001; 38: 771-832.
- Raftopoulos Y, Senagore AJ, Di Giuro G, et al. Rectal Prolapse Recurrence Study Group. Recurrence rates after abdominal surgery for complete rectal prolapse: a multicenter pooled analysis of 642 individual patient data. *Dis Colon Rectum* 2005; 48: 1200-6.
- DiGiuro G, Ignjatovic D, Brogger J, et al. Rectal Prolapse Recurrence Study Group. How accurate are published recurrence rates after rectal prolapse surgery? A meta-analysis of individual patient data. *Am J Surg* 2006; 191: 773-8.
- Azimuddin K, Khubchandani IT, Rosen L, et al. Rectal prolapse: a search for the "best" operation. *Am Surg* 2001; 67: 622-7.
- Kim DS, Tsang CB, Wong WD, et al. Complete rectal prolapse: Evolution of management and results. *Dis Colon Rectum* 1999; 42: 460-6.

25. Madiba TE, Baig MK, Wexner SD. Surgical management of rectal prolapse. *Arch Surg* 2005; 140: 63–73.
26. Jacobs LK, Lin YJ, Orkin BA. The best operation for rectal prolapse. *Surg Clin North Am* 1997; 77: 49–70.
27. Fengler SA, Pearl RK, Prasad ML, et al. Management of recurrent rectal prolapse. *Dis Colon Rectum* 1997; 40: 832–4.
28. Hool GR, Hull TL, Fazio VW. Surgical treatment of recurrent complete rectal prolapse: a thirty-year experience. *Dis Colon Rectum* 1997; 40: 270–2.
29. Steele SR, Goetz LH, Minami S, et al. Management of recurrent rectal prolapse: surgical approach influences outcome. *Dis Colon Rectum* 2006; 49: 440–5.
30. Speakman CT, Madden MV, Nicholls RJ, et al. Lateral ligament division during rectopexy causes constipation but prevents recurrence: results of a prospective randomized study. *Br J Surg* 1991; 78: 1431–3.
31. Scaglia M, Fasth S, Hallgren T, et al. Abdominal rectopexy for rectal prolapse. Influence of surgical technique on functional outcome. *Dis Colon Rectum* 1994; 37: 805–13.
32. Oliver GC, Vachon D, Eisenstat TE, et al. Delorme's procedure for complete rectal prolapse in severely debilitated patients. An analysis of 41 cases. *Dis Colon Rectum* 1994; 37: 461–7.
33. Uhlig BE, Sullivan ES. The modified Delorme operation: its place in surgical treatment for massive rectal prolapse. *Dis Colon Rectum* 1979; 22: 513–21.
34. Marceau C, Parc Y, Debroux E, et al. Complete rectal prolapse in young patients: psychiatric disease a risk factor for poor outcome. *Colorectal Dis* 2005; 7: 360–5.
35. Zbar AP, Takashima S, Hasegawa T, et al. Perineal rectosigmoidectomy (Altemeier's procedure): a review of physiology, technique and outcome. *Tech Coloproctol* 2002; 6: 109–16.
36. Kariv Y, Delaney CP, Casillas S, et al. Long-term outcome after laparoscopic and open surgery for rectal prolapse: a case-control study. *Surg Endosc* 2006; 20: 35–42.
37. Deen KI, Grant E, Billingham C, et al. Abdominal resection rectopexy with pelvic floor repair versus perineal rectosigmoidectomy and pelvic floor repair for full thickness rectal prolapse. *Br J Surg* 1994; 81: 302–4.
38. Jan S, Gross L, Hills RK, Gray R, et al. Persistent benefits in bowel function and quality of life following rectal prolapse surgery—the ACPGBI PROSPER trial. Available at www.bctu.bham.ac.uk/propser, accessed June 2008.
39. Portier G, Iovino F, Lazorthes F. Surgery for rectal prolapse: Orr-Loygue ventral rectopexy with limited dissection prevents postoperative-induced constipation without increasing recurrence. *Dis Colon Rectum* 2006; 49: 1136–40.
40. Nelson R, Spitz J, Pearl RK, et al. What role does full rectal mobilization alone play in the treatment of rectal prolapse? *Tech Coloproctol* 2001; 5: 33–5.
41. Schultz I, Mellgren A, Dolk A, et al. Long-term results and functional outcome after Ripstein rectopexy. *Dis Colon Rectum* 2000; 43: 35–43.
42. Novell JR, Osborne MJ, Winslet MC, et al. Prospective randomized trial of Ivalon sponge versus sutured rectopexy for full thickness rectal prolapse. *Br J Surg* 1994; 81: 904–6.
43. Galili Y, Rabau M. Comparison of polyglycolic acid and polypropylene mesh for rectopexy in the treatment of rectal prolapse. *Eur J Surg* 1997; 163: 445–8.
44. Winde G, Reers B, Nottberg H, et al. Clinical and functional results of abdominal rectopexy with absorbable mesh-graft for treatment of complete rectal prolapse. *Eur J Surg* 1993; 159: 301–5.
45. Arndt M, Pircher W. Absorbable mesh in the treatment of rectal prolapse. *Int J Colorectal Dis* 1988; 3: 141–3.
46. Athanasiadis S, Weyand G, Heiligers J, et al. The risk of infection of three synthetic materials used in rectopexy with or without colonic resection for rectal prolapse. *Int J Colorectal Dis* 1996; 11: 42–4.
47. Sullivan ES, Longaker CJ, Lee PY. Total pelvic mesh repair: A ten-year experience. *Dis Colon Rectum* 2001; 44: 857–63.
48. Johnson E, Stangeland A, Johannessen HO, et al. Resection rectopexy for external rectal prolapse reduces constipation and anal incontinence. *Scand J Surg* 2007; 96: 56–61.
49. Ashari LH, Lumley JW, Stevenson AR, et al. Laparoscopically-assisted resection rectopexy for rectal prolapse: ten years' experience. *Dis Colon Rectum* 2005; 48: 982–7.
50. Brown AJ, Anderson JH, McKee RF, et al. Strategy for selection of type of operation for rectal prolapse based on clinical criteria. *Dis Colon Rectum* 2004; 47: 103–7.
51. McKee RF, Lauder JC, Poon FW, et al. A prospective randomized study of abdominal rectopexy with and without sigmoidectomy in rectal prolapse. *Surg Gynecol Obstet* 1992; 174: 145–8.
52. Luukkonen P, Mikkonen U, Jarvinen H. Abdominal rectopexy with sigmoidectomy vs. rectopexy alone for rectal prolapse: A prospective, randomized study. *Int J Colorectal Dis* 1992; 7: 219–22.
53. Delaney CP. Laparoscopic management of rectal prolapse. *J Gastrointest Surg* 2007; 11: 150–2.
54. Bachoo P, Brazzelli M, Grant A. Surgery for complete rectal prolapse in adults. *Cochrane Database Syst Rev* 2000; 2: CD001758.
55. Boccasanta P, Rosati R, Venturi M, et al. Comparison of laparoscopic rectopexy with open technique in the treatment of complete rectal prolapse: clinical and functional results. *Surg Laparosc Endosc* 1998; 8: 460–5.
56. Solomon MJ, Young CJ, Eysers AA, et al. Randomized clinical trial of laparoscopic versus open abdominal rectopexy for rectal prolapse. *Br J Surg* 2002; 89: 35–9.
57. Schwenk W, Haase O, Neudecker J, et al. Short term benefits for laparoscopic colorectal resection. *Cochrane Database Syst Rev* 2005; 3: CD003145.
58. Purkayastha S, Tekkis P, Athanasiou T, et al. A comparison of open vs. laparoscopic abdominal rectopexy for full thickness rectal prolapse: a meta-analysis. *Dis Colon Rectum* 2005; 48: 1930–40.
59. Kairaluoma MV, Viljakka MT, Kellokumpu IH. Open vs. laparoscopic surgery for rectal prolapse: a case-controlled study assessing short-term outcome. *Dis Colon Rectum* 2003; 46: 353–60.
60. Benoist S, Taffinder N, Gould S, et al. Functional results two years after laparoscopic rectopexy. *Am J Surg* 2001; 182: 168–73.
61. Dulucq JL, Wintringer P, Mahajna A. Clinical and functional outcome of laparoscopic posterior rectopexy (Wells) for full-thickness rectal prolapse. A prospective study. *Surg Endosc* 2007; 21: 2226–30.
62. Carpelan-Holmstrom M, Kruuna O, Scheinin T. Laparoscopic rectal prolapse surgery combined with short hospital stay is safe in elderly and debilitated patients. *Surg Endosc* 2006; 20: 1953–9.
63. Salkeld G, Bagia M, Solomon M. Economic impact of laparoscopic versus open abdominal rectopexy. *Br J Surg* 2004; 91: 1188–91.
64. Madoff RD, Mellgren A. One hundred years of rectal prolapse surgery. *Dis Colon Rectum* 1999; 42: 441–50.
65. Graf W, Karlhom U, Pahlman L, et al. Functional results after abdominal suture rectopexy for rectal prolapse or intussusception. *Eur J Surg* 1996; 162: 905–11.
66. Khanna AK, Misra MK, Kumar K. Simplified sutured sacral rectopexy for complete rectal prolapse in adults. *Eur J Surg* 1996; 162: 143–6.
67. Briel JW, Schouten WR, Boerma MO. Long-term results of suture rectopexy in patients with fecal incontinence associated with incomplete rectal prolapse. *Dis Colon Rectum* 1997; 40: 1228–32.
68. Kellokumpu IH, Vironen J, Scheinin T. Laparoscopic repair of rectal prolapse: a prospective study evaluating surgical

- outcome and changes in symptoms and bowel function. *Surg Endosc* 2000; 14: 634–40.
69. Heah SM, Hartely JE, Hurley J, et al. Laparoscopic suture rectopexy without resection is effective treatment for full-thickness rectal prolapse. *Dis Colon Rectum* 2000; 43: 638–43.
 70. Bruch HP, Herold A, Schiedeck T, et al. Laparoscopic surgery for rectal prolapse and outlet obstruction. *Dis Colon Rectum* 1999; 42: 1189–94.
 71. Aitola PT, Hiltunen KM, Matikainen MJ. Functional results of operative treatment of rectal prolapse over an 11-year period: emphasis on transabdominal approach. *Dis Colon Rectum* 1999; 42: 655–60.
 72. Sayfan J, Pinho M, Alexander-Williams J, et al. Sutured posterior abdominal rectopexy with sigmoidectomy compared with Marlex rectopexy rectal prolapse. *Br J Surg* 1990; 77: 143–5.
 73. Himpens J, Cadere GB, Bruyns J, et al. Laparoscopic rectopexy according to Wells. *Surg Endosc* 1999; 13: 139–41.
 74. Watts JD, Rothenberger DA, Buls JG, et al. The management of procidentia. 30 years' experience. *Dis Colon Rectum* 1985; 28: 96–102.
 75. Tjandra JJ, Fazio VW, Church JM, et al. Ripstein procedure is an effective treatment for rectal prolapse without constipation. *Dis Colon Rectum* 1993; 36: 501–7.
 76. Stevenson AR, Stitz RW, Lumley JW. Laparoscopic-assisted resection-rectopexy for rectal prolapse: early and medium follow-up. *Dis Colon Rectum* 1998; 41: 46–54.
 77. Xynos E, Chrysos J, Tsiaoussis J, et al. Resection rectopexy for rectal prolapse: the laparoscopic approach. *Surg Endosc* 1999; 13: 862–4.
 78. Launer DP, Fazio VW, Weakley FL, et al. The Ripstein procedure: a 16-year experience. *Dis Colon Rectum* 1982; 25: 41–5.
 79. Roberts PL, Schoetz DJ Jr., Collier JA, et al. Ripstein procedure. Lahey Clinic experience: 1963–1985. *Arch Surg* 1988; 123: 554–7.
 80. Schultz I, Mellgren A, Dolk AJ, et al. Continence is improved after the Ripstein rectopexy. Different mechanisms in rectal prolapse and rectal intussusception? *Dis Colon Rectum* 1996; 39: 300–6.
 81. Williams JG, Rothenberger DA, Madoff RD, et al. Treatment of rectal prolapse in the elderly by perineal rectosigmoidectomy. *Dis Colon Rectum* 1992; 35: 830–4.
 82. Pescatori M, Interisano A, Stolfi VM, et al. Delorme's operation and sphincteroplasty for rectal prolapse and fecal incontinence. *Int J Colorectal Dis* 1998; 13: 223–7.
 83. Lechaux JP, Lechaux D, Perez M. Results of Delorme's procedure for rectal prolapse: advantages of a modified technique. *Dis Colon Rectum* 1995; 38: 301–7.
 84. Kling KM, Rongione AJ, Evans B, et al. The Delorme procedure: a useful operation for complicated rectal prolapse in the elderly. *Am Surg* 1996; 62: 857–60.
 85. Watts AM, Thompson MR. Evaluation of Delorme's procedure as a treatment for full-thickness rectal prolapse. *Br J Surg* 2000; 87: 218–22.
 86. Liberman H, Hughes C, Dippolito A. Evaluation and outcome of the Delorme procedure in the treatment of rectal outlet obstruction. *Dis Colon Rectum* 2000; 43: 188–92.
 87. Tobin SA, Scott IH. Delorme operation for rectal prolapse. *Br J Surg* 1994; 81: 1681–4.
 88. Ramanujam PS, Venkatesh KS, Fietz MJ. Perineal excision of rectal procidentia in elderly high-risk patients. A ten-year experience. *Dis Colon Rectum* 1994; 37: 1027–30.
 89. Glasgow SC, Birnbaum EH, Kodner IJ, et al. Recurrence and quality of life following perineal proctectomy for rectal prolapse. *J Gastrointest Surg* 2008.
 90. Agachan F, Pfeifer J, Joo JS, et al. Results of perineal procedures for the treatment of rectal prolapse. *Am Surg* 1997; 53: 9–12.
 91. Yoshioka K, Hyland G, Keighley MR. Physiological changes after postanal repair and parameters predicting outcome. *Br J Surg* 1988; 75: 1220–4.
 92. Habr-Gama A, Jacob CE, Jorge JM, et al. Rectal procidentia treatment by perineal rectosigmoidectomy combined with levator ani repair. *Hepatogastroenterology* 2006; 43: 213–17.
 93. Chun SW, Pikarsky AJ, You SY, et al. Perineal rectosigmoidectomy for rectal prolapse: role of levatorplasty. *Tech Coloproctol* 2004; 8: 3–8.
 94. Dippolito A, Esser S, Reed J III. Anterior modification of Delorme procedure provides equivalent results to Delorme procedure in treatment of rectal outlet obstruction. *Curr Surg* 2005; 62: 609–12.
 95. Mellgren A, Dolk A, Johansson C, et al. Enterocoele is correctable using the Ripstein rectopexy. *Dis Colon Rectum* 1994; 37: 800–4.
 96. Keighley MR, Shouler PJ. Abnormalities of colonic function in patients with rectal prolapse and faecal incontinence. *Br J Surg* 1984; 71: 892–5.
 97. Mellgren A, Johansson C, Dolk A, et al. Enterocoele demonstrated by defaecography is associated with other pelvic floor disorders. *Int J Colorectal Dis* 1994; 9: 121–4.
 98. Okamoto N, Maeda K, Kato R, et al. Dynamic pelvic three-dimensional computed tomography for investigation of pelvic abnormalities in patients with rectocele and rectal prolapse. *J Gastroenterol* 2006; 41: 802–6.
 99. Salzano A, Nocera V, Rossi E, et al. Radiologic investigation of external rectal prolapse. Assessment in 48 patients with defecography, seven of them also with dynamic CT of the pelvis. *Radiol Med (Torino)* 2000; 100: 348–53.
 100. Hsu A, Brand MI, Saclarides TJ. Laparoscopic rectopexy without resection: a worthwhile treatment for rectal prolapse in patients without prior constipation. *Am Surg* 2007; 73: 858–61.
 101. Holmstrom B, Broden G, Dolk A. Results of the Ripstein operation in the treatment of rectal prolapse and internal rectal procidentia. *Dis Colon Rectum* 1986; 29: 845–8.
 102. Gordon PH, Hoexter B. Complications of the Ripstein procedure. *Dis Colon Rectum* 1978; 21: 277–80.
 103. Pascual Montero JA, Martinez Puente MC, Pascual I, et al. Complete rectal prolapse clinical and functional outcome with Delorme's procedure. *Rev Esp Enferm Dig* 2006; 98: 837–43.
 104. Tsunoda A, Yasuda N, Yokoyama N, et al. Delorme's procedure for rectal prolapse: clinical and physiological analysis. *Dis Colon Rectum* 2003; 46: 1260–5.
 105. Senapati A, Nicholls RJ, Thomson JP, et al. Results of Delorme's procedure for rectal prolapse. *Dis Colon Rectum* 1994; 37: 456–60.
 106. Marchal F, Bresler L, Ayav A, et al. Long-term results of Delorme's procedure and Orr-Loygue rectopexy to treat complete rectal prolapse. *Dis Colon Rectum* 2005; 48: 1785–90.
 107. Whitlow CB, Beck DE, Opelka FG, et al. Perineal repair of rectal prolapse. *J La State Med Soc* 1997; 149: 22–6.
 108. Kleinubing H Jr, Pinho MS, Ferreira LC. Longitudinal multiple rubber band ligation: an alternative method to treat mucosal prolapse of the anterior rectal wall. *Dis Colon Rectum* 2006; 49: 876–8.
 109. Tsugawa K, Sue K, Koyanagi N, et al. Laparoscopic rectopexy for recurrent rectal prolapse: a safe and simple procedure without a mesh prosthesis. *Hepatogastroenterology* 2002; 49: 1549–51.
 110. Pikarsky AJ, Joo JS, Wexner SD, et al. Recurrent rectal prolapse: what is the next good option? *Dis Colon Rectum* 2000; 43: 1273–6.

Evidence-Based Practice: Acute Cholecystitis

Juliane Bingener

Acute Cholecystitis: Question Summary		
Question	Answer	Grade
Should laparoscopic or open cholecystectomy be performed in acute and complicated acute cholecystitis?	Laparoscopic attempt is preferred.	C
What should the timing of surgical intervention be?	Early cholecystectomy preferred to delayed cholecystectomy.	B
What are the indications and outcomes for nonsurgical intervention?	Unclear.	D
Indications for drain placement?	Drains may harm the patient, does not confer benefit.	B
Which antibiotic therapy is warranted?	Several are appropriate.	B
Which perioperative pain therapy is effective?	Stepwise multimodality approach.	A

HISTORY AND EPIDEMIOLOGY

Today 3–9% of all patients admitted to a hospital for acute abdominal pain in the United States are diagnosed with acute cholecystitis; 15–30% of all cholecystectomies are performed for acute cholecystitis. Urgent cholecystectomy adds 90% of the cost to an elective cholecystectomy (1).

Langenbuch first sought to ease the suffering of his patients in 1882 by removing the offending organ and reported a single case. Over the next several years, 39 more patients underwent cholecystectomy through a subcostal incision, and the reported case series changed the approach to patients with acute gallstone disease. Another case report, of the first laparoscopic cholecystectomy by Erich Muehe in 1985, had detrimental consequences for his career. A case series by Mouret two years later initiated the advent of laparoscopic cholecystectomy as the accepted treatment, as it is known today.

ANATOMY AND PHYSIOLOGY

Retrospective cohort studies delineate the frequency of anatomic variations in the extrahepatic biliary tree. Ectopic gallbladders (1/1,600 autopsies), duplication or triplication of the gallbladder (1/4,000 autopsies), and even gallbladder agenesis with biliary symptoms (<1 in 6,000 live births) can all contribute to the therapeutic difficulty in a patient with acute cholecystitis (2). Furthermore, textbook-like lateral cystic duct drainage in patients undergoing cholecystectomy was only encountered in 17% of several thousand cholangiograms reviewed (3). Premature or delayed developmental separation, duplication or malrotation of the cystic duct lead to the large number of variations in the biliary

anatomy. A prospective study of 186 consecutive laparoscopic cholecystectomies found that when the dissection was limited to the neck of the gallbladder and Calot's triangle, the variations in ductal anatomy were rarely visualized, the variations in arterial anatomy were more readily apparent (4). There is increasing evidence that the visual perceptions and "biased confirmation" of anatomic patterns contribute significantly to bile duct injury mechanisms (5,6).

Obstruction of the cystic duct by a calculus is most often the cause of acute cholecystitis, but it can also be caused by blood clots or infectious organisms in immune-suppressed patients. Calculus obstruction is thought to be correlated with sterile bile in >50% of patients. Stewart et al. have demonstrated a subset of patients with slime-forming bacteria embedded into the gallstones (7).

INITIAL EVALUATION AND DIAGNOSIS

What Are the Clinical Criteria Required for the Diagnosis of Acute Cholecystitis?

Textbook criteria for acute cholecystitis are gallstones, right upper abdominal quadrant pain, nausea, vomiting, fever, and elevated white blood cell count. A patient lacking most of these signs and symptoms is often not deemed to have acute cholecystitis, and the diagnosis may be delayed. Trowbridge et al. performed a MEDLINE search for the period between 1955 and 2002 to determine if aspects of the history and physical exam or basic laboratory testing could clearly identify patients who required imaging to identify or rule out acute cholecystitis. Of the 195 studies retrieved, 17 included groups with and without cholecystitis. In these studies, outcomes of 3,490 patients were assessed. No clinical sign showed a reasonable likelihood ratio to predict or

rule out acute cholecystitis. Possible exceptions were the Murphy's sign and right upper quadrant pain. However, the confidence interval on both variables included 1, and Murphy's sign appeared especially prone to verification bias in the authors' estimation (8). The authors did not assess the combination of clinical signs for their likelihood ratios.

Answer: No one clinical criterion is sufficient to predict or rule out acute cholecystitis (Grade B recommendation).

What Is the Value of Imaging Studies for the Diagnosis of Acute Cholecystitis?

Confirmation bias is a factor in many study designs evaluating the imaging modalities for acute cholecystitis. Often, only patients that have positive imaging findings will undergo a gold standard confirmation (e.g., cholecystectomy), and patients with (false) negative findings may not be diagnosed. Ultrasound has 98% sensitivity for gallstone detection. A meta-analysis from 1994 found the sensitivity for real-time ultrasound for the detection of acute cholecystitis to be 94% with a specificity of 78% (9). When mathematically adjusted for confirmation bias, sensitivity for acute cholecystitis was 88%, with a specificity of 80% (8). A small prospective study of 50 patients with the clinical suspicion of acute cholecystitis found the ultrasound diagnosis to be correct in about 60% of patients, when the ultrasound was performed by a technician and read by a two radiologists (10). Blaivas et al. reviewed their experience with bedside Emergency Department (ED) ultrasound in comparison to subsequent hepatobiliary iminodiacetic acid (HIDA) scan and found agreement in 77% of 99 patients examined [confidence interval (CI), 68–84%]. Forty-seven percent of the patients with acute cholecystitis on HIDA scan were missed by the ED ultrasound (11). A pilot study of 33 patients using contrast-enhanced sonography of the gallbladder suggested that improved ultrasonographic differentiation between acute and chronic cholecystitis may be available in the future (12). Reviewing 22 radionuclide scanning studies with 2,542 patients, Shea et al. found the sensitivity for HIDA scan to detect acute cholecystitis to be between 0.93 (95% CI, 0.90–0.97) and 0.97 (95% CI, 0.96–0.98) depending on the classification of indeterminate patients. The specificity for radionuclide scanning in the diagnosis of acute cholecystitis was between 0.90 (95% CI, 0.86–0.95) and 0.91 (95% CI, 0.86–0.95). Computed tomography exhibited a sensitivity of 0.79 and a specificity of 0.99, not adjusted for confirmation bias (9).

Answer: Radionuclide scan remains the gold standard; ultrasound may miss up to 47% of patients with acute cholecystitis (Grade B recommendation).

MANAGEMENT

Should Laparoscopic or Open Cholecystectomy Be Performed in Acute and Complicated Acute Cholecystitis?

Although acute cholecystitis was initially regarded as a contraindication for laparoscopic cholecystectomy, over the past two decades that opinion has changed. The evidence-based guidelines published by the European Association for Endoscopic Surgery (13) state that the laparoscopic

approach is preferred for patients with acute cholecystitis, although no major differences between laparoscopy and laparotomy in clinical trials have been reported when evaluation of outcomes was blinded (14). A meta-analysis by Borzellino et al. reported on results regarding the treatment of severe acute cholecystitis (such as gangrenous and empyematous cholecystitis) (15). No studies comparing laparoscopic cholecystectomy with open cholecystectomy or cholecystostomy for severe acute cholecystitis were found. Seven studies comparing acute and nonacute cholecystitis were included in the analysis, with a total of 1,408 patients, 469 with severe acute cholecystitis and 939 with nonsevere acute cholecystitis. The risk of conversion was higher in patients with severe acute cholecystitis [relative risk (RR) 3.2, 95% CI 2.5–4.2] and overall postoperative complications (RR 1.6, 95% CI 1.2–2.2) were increased. No difference was encountered in local postoperative complications. Early conversion to the open procedure has been suggested to allow for reduction of postoperative complications (15), however a cohort study evaluating the timing of conversion, early versus late found no difference in the morbidity rates (16). Several studies have suggested that the outcome for patients undergoing laparoscopic cholecystectomy by surgeons with a specific interest in laparoscopy have improved outcomes compared to surgeons without laparoscopic interest (17,18).

Answer: Laparoscopic cholecystectomy should be attempted (Grade C recommendation).

What Should the Timing of Surgical Intervention Be?

In 2007, the Cochrane group reviewed five trials evaluating early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Two hundred twenty-three patients were in the early and 228 patients in the delayed group (19). Four of the five trials were of high methodological quality. No mortality was reported and no statistical difference in any measured outcomes (e.g., bile duct injury [odds ratio (OR) 0.63, 95% CI 0.15–2.70] and conversion (OR 0.84, 95% CI 0.53–1.34) were seen (Fig. 59.1) (19). However, the early group had a shorter length of hospital stay (by three days), and 18% of patients in the delayed group required early intervention with 45% conversion rate.

These findings confirmed a meta-analysis by Papi et al. (20). Here nine trials of open cholecystectomy with 915 total patients were included. The pooled rate difference for complications in early surgery was 1.37% (95% CI, 3.78–6.53%, $p = 0.2$) (Fig. 59.2) (20).

One randomized clinical trial evaluated the impact of early versus delayed cholecystectomy for acute cholecystitis on patient's health-related quality of life (21). A total of 145 patients were enrolled and randomly assigned to the early or delayed surgery group. Assessments of quality of life with a validated instrument were obtained at one, three, and six months after surgery. The conversion rate was 31% in the early and 29% in the delayed group; 26% of patients in the delayed group failed conservative treatment. The gastrointestinal symptom scores were significantly better in three dimensions (diarrhea, indigestion, abdominal pain) in the early group at one month, but evened out at three and six months.

It can be concluded that with failure rates of initial nonoperative treatment occurs in up to 32% of patients and

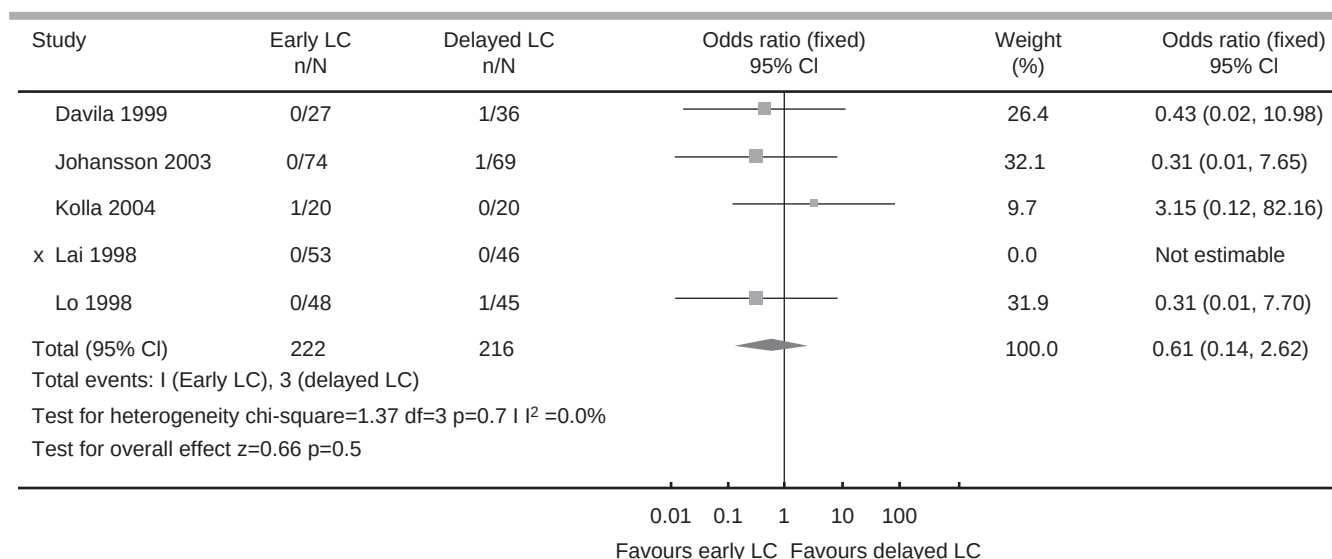


Figure 59.1 Comparison of early versus delayed LC (number of people operated), outcome bile duct injury.

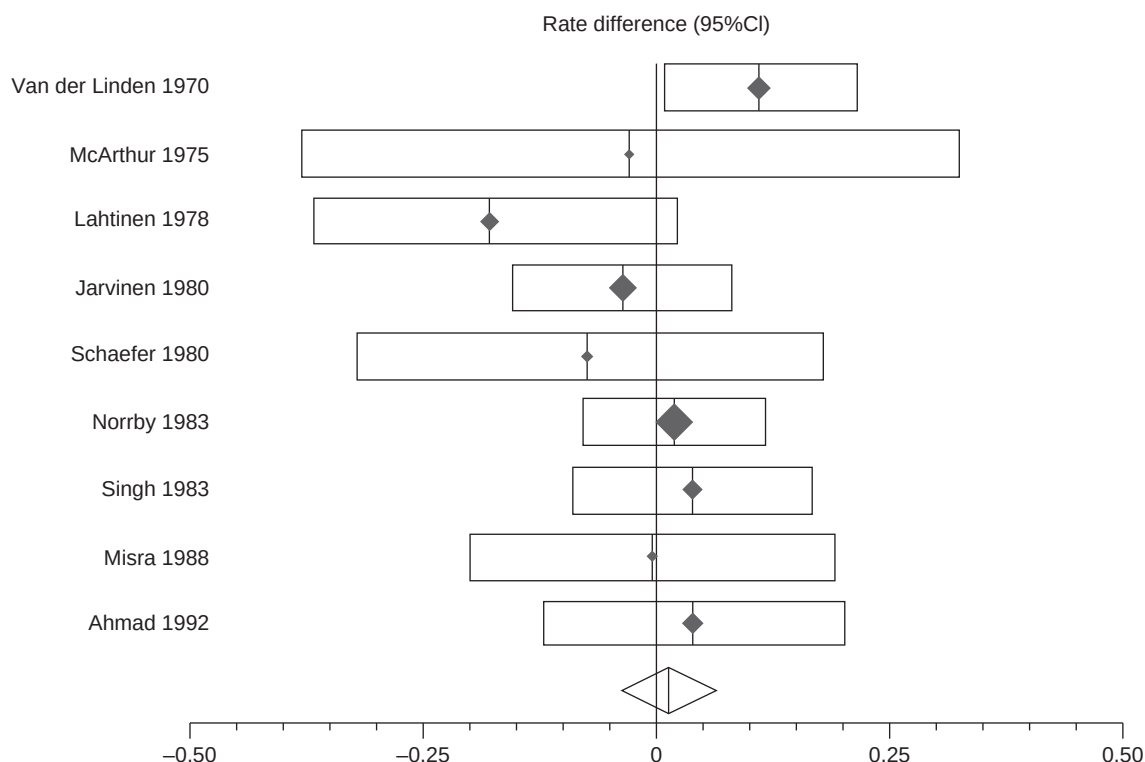


Figure 59.2 Rate differences (95% CI) for operative and perioperative complications in prospective randomized trials addressing early versus delayed open cholecystectomy for acute lithiasic cholecystitis. The pooled rate differences for complications in early surgery is 1.37% (95% CI 3.78–6.53%; $p = 0.2$).

an equally high conversion rate but shorter hospital stay attributed to early cholecystectomy, and better patient quality of life, it appears prudent to proceed swiftly.

Answer: Early cholecystectomy is the preferred approach (Grade B recommendation).

What Are the Indications and Outcomes for Nonsurgical Intervention?

Some patients with acute cholecystitis are severely ill and have a high operative risk. Cholecystostomy or gallbladder aspiration have been reported as temporizing measures or

definitive treatment for those patients. High-level evidence for these treatment modalities is scarce, however. Between 1972 and 2005, 785 cases were published of operative cholecystectomy for complex acute cholecystitis; many patients needed reintervention. Approximately 70 MEDLINE citations report on percutaneous cholecystostomy case series with 25–65 patients each and reveal the feasibility of the procedure under local anesthesia. A 14% mortality rate in this severely ill patient population is reported, and many require subsequent cholecystectomy. One randomized controlled trial evaluated the use of percutaneous cholecystostomy in 123 patients with APACHE scores >12 (22). No significant difference in morbidity or symptom improvement was noted between the groups. The authors, however, recommended cholecystostomy tube placement in intensive care patients with acute cholecystitis if no clinical improvement is seen after three days. Another randomized trial allocated 30 patients to cholecystostomy and 28 patients to gallbladder aspiration only. A “good clinical result” was realized in 90% of patients with cholecystostomy and 61% of patients with gallbladder aspiration, which led the authors to recommend cholecystostomy placement for most patients (23).

Answer: The best approach remains unclear (Grade D recommendation).

What Are the Indications for Drain Placement?

Gurumsamy et al. assessed the use of routine abdominal drainage for uncomplicated open cholecystectomy in a systematic review for the Cochrane database in 2007 (24). Included were 28 open cholecystectomy trials (3,659 patients), of which 20 trials evaluated the comparison of no drain placement versus drain placement and 12 trials evaluated one drainage method versus another (e.g., closed suction versus Penrose). In addition, the drain placement through the wound versus a separate stab incision was evaluated for its effect on each outcome. No significant differences were encountered for intra-abdominal fluid collections, however, wound and chest infections were more frequent with drain placement (Table 59.1) (24). Five laparoscopic trials with 591 patients confirmed those findings (Table 59.2) (25).

Answer: Drain placement may harm the patient (Grade B recommendation).

Which Antibiotic Therapy Is Warranted?

A number of randomized prospective trials have evaluated the role of prophylactic perioperative antibiotic administration for patients undergoing elective laparoscopic cholecystectomy. Choudare et al. reported on a meta-analysis of eight randomized controlled trials with a total of 1,361 patients. Prophylactic antibiotics did not prevent superficial or deep surgical site or distant infections in low-risk patients undergoing elective cholecystectomy. In addition, antibiotic administration did not decrease the hospital stay (26).

An additional meta-analysis is planned by the Cochrane group to evaluate the harmful effects of antibiotics in patients undergoing elective cholecystectomy (27).

For acute cholecystitis, several trials were reported comparing one antibiotic regimen versus another regimen, more recently cephalosporins have been compared. It appears that a second-generation cephalosporin for five

Table 59.1 Findings of Systematic Review Regarding Outcomes of Drain Placement in Open Cholecystectomy (24)

Open cholecystectomy (27 trials)	No drain	Drain
Mortality	No difference	
Bile peritonitis	No difference	
Total abdominal collections	No difference	
Abdominal collection requiring treatment	No difference	
Infected abdominal collections	No difference	
Wound infection	Less without drain (OR 0.61, 95% CI 0.43–0.87)	
Chest infection	Less without drain (OR 0.59, 95% CI 0.42–0.84)	

Abbreviations: CI, confidence interval; OR, odds ratio.

Table 59.2 Findings of Systematic Review Regarding Outcomes of Drain Placement in Laparoscopic Cholecystectomy (25)

Laparoscopic cholecystectomy (5 trials)	No drain	Drain
Wound infection	Lower	Higher (OR 15.38, 95% CI 0.86 to 275.74)
Shoulder and abdominal pain	More	Less (NS)
Hospital stay	Shorter	Longer

Abbreviations: CI, confidence interval; NS, not significant; OR, odds ratio.

to seven days may be just as effective as other regimen (28–30). On literature review, no randomized controlled trials or cohort studies were encountered evaluating the duration of antibiotic therapy for patients with acute cholecystitis. No data were encountered that elucidate if antibiotic administration for more than 24 hours is necessary or if 24-hour antibiotic administration might be sufficient.

Answer: Several regimens are appropriate; duration of therapy has not been evaluated (Grade B recommendation).

Which Perioperative Pain Therapy Is Effective?

Kehlet et al. (31) published a procedure-specific systematic review and consensus recommendations for postoperative analgesia following laparoscopic cholecystectomy in 2005. Sixty-nine randomized trials were evaluated in their review, and an attempt was made to stratify for operative and anesthesia technique used during the procedure to assess the postoperative pain outcomes.

Recommendations that resulted from the review for the management of postoperative pain following laparoscopic cholecystectomy were as follows. Analgesic medication should be instituted in time to secure sufficient analgesia when the patient is waking following the procedure. Dexamethasone was an effective adjunct for pain control and also had antiemetic effects. Regarding the anesthetic techniques, inhalational, total intravenous, or balanced techniques were effective. Intravenous anesthesia was associated with reduced postoperative nausea and vomiting in the reviewed studies.

An operative technique that was associated with better postoperative pain control was a low-pressure CO₂ pneumoperitoneum. Relative weak evidence also supported CO₂ pneumoperitoneum with peritoneal lavage and subsequent suction.

For intraoperative analgesia short-acting strong opioids and intraperitoneal local anesthetic at the end of surgery were recommended. In addition, incisional local anesthetic at the end of surgery was effective, but care needs to be taken with the total dose if combined with intraperitoneal local anesthetic.

For the postoperative analgesia, a stepwise approach was recommended, using nonsteroidal anti-inflammatory drugs, acetaminophen, and weak opioids to affect pain control through a variety of mechanisms and limit side effects. In high-risk patients and if laparoscopic cholecystectomy was converted to open surgery, epidural analgesia with local anesthetics and opioids was effective. If insufficient analgesia was obtained, ketamine should be considered in multimodal regimens.

A separate meta-analysis on the intraperitoneal administration of local anesthesia was conducted by Boddy et al. (32) to establish the efficacy of this technique in reducing early postoperative abdominal pain. Their systematic literature search revealed 24 randomized controlled trials assessing intraperitoneal local anesthetic use in laparoscopic cholecystectomy that met inclusion criteria. Of these, 16 studies reported sufficient data to allow pooled quantitative analysis. Overall, the use of intraperitoneal local

anesthesia resulted in a significantly reduced pain score at four hours [weighted mean difference (WMD), -9 mm; 95% CI, -13 to -5]. Subgroup analysis suggested that the effect was greater when the local anesthetic was given at the start of the operation (WMD, -13 mm; 95% CI, -19 to -7) compared with instillation at the end (WMD, -6 mm; 95% CI, -10 to -2). No adverse events related to local anesthetic toxicity were reported. They concluded that the use of intraperitoneal local anesthesia was safe, and it resulted in a statistically significant reduction in early postoperative abdominal pain.

Answer: A stepwise multimodality approach is effective (Grade A recommendation).

DISCUSSION

Given the fact that acute cholecystitis is a frequent occurrence many routine steps in its management are not necessarily evidence-based, starting from diagnosis to postoperative antibiotic regimen. Laparoscopic cholecystectomy for acute cholecystitis has become the standard of care in many institutions, supported by weak evidence. The postoperative pain regimen has been evaluated extensively, and good evidence supports pathways that should become the standard of care. The history of cholecystectomy started with good judgment and a case report; we will need to apply good judgment to implement findings from randomized trials and meta-analyses and to provide care where guidance from those is not yet available.

Acute Cholecystitis: Levels of Evidence

Subject	Year	Refs.	Level of evidence	Strength of recommendation	Findings
Laparoscopic or open cholecystectomy for acute cholecystitis	2006	13	IIb	C	Laparoscopic attempt is recommended.
Timing of surgical intervention	2006	19–21	Ia	B	Early cholecystectomy preferred.
Indications for nonsurgical intervention	2002 2004	22, 23	IV	D	Unclear.
Postoperative drain placement	2007	24, 25	Ia	B	Drains may harm the patient, no benefit.
Antibiotic therapy	1993	26–28	IIb	B	Several are appropriate.
Perioperative pain therapy	2005	31, 32	Ia	A	Stepwise multimodality approach.

REFERENCES

- Chen SL, Comstock MC, Taheri PA. The added cost of urgent cholecystectomy to health systems. *J Am Coll Surg* 2003; 197: 16–21.
- Lamah M, Karanjia ND, Dickson GH. Anatomical variations of the extrahepatic biliary tree: review of the world literature. *Clin Anat* 2001; 14: 167–72.
- Berci G. Biliary ductal anatomy and anomalies. The role of intraoperative cholangiography during laparoscopic cholecystectomy. *Surg Clin North Am* 1992; 72: 1069–75.
- Laborina M, Nottle PD. Extrahepatic biliary anatomy at laparoscopic cholecystectomy: is aberrant anatomy important? *ANZ J Surg* 2005; 75: 392–5.
- Way LW, Stewart L, Gantert W, et al. Causes and prevention of laparoscopic bile duct injuries: analysis of 252 cases from a human factors and cognitive psychology perspective. *Ann Surg* 2003; 237: 460–9.
- Hugh TB. New strategies to prevent laparoscopic bile duct injury—surgeons can learn from pilots. *Surgery* 2002; 132: 826–35.
- Stewart L, Griffiss JM, Jarvis GA, et al. Gallstones containing bacteria are biofilms: bacterial slime production and ability to form pigment solids determines infection severity and bacteremia. *J Gastrointest Surg* 2007; 11: 977–83; discussion 983–4.
- Trowbridge RL, Rutkowski NK, Shojania KG. Does this patient have acute cholecystitis? *JAMA* 2003; 289: 80–6.
- Shea JA, Berlin JA, Escarce JJ, et al. Revised estimates of diagnostic test sensitivity and specificity in suspected biliary tract disease. *Arch Intern Med* 1994; 154: 2573–81.

10. Bingener J, Schwesinger WH, Chopra S, et al. Does the correlation of acute cholecystitis on ultrasound and at surgery reflect a mirror image? *Am J Surg* 2004; 188: 703–7.
11. Blaivas M, Adhikari S. Diagnostic utility of cholescintigraphy in emergency department patients with suspected acute cholecystitis: comparison with bedside RUQ ultrasonography. *J Emerg Med* 2007; 33: 47–52.
12. Adamietz B, Wenkel E, Uder M, et al. Contrast enhanced sonography of the gallbladder: a tool in the diagnosis of cholecystitis? *Eur J Radiol* 2007; 61: 262–6.
13. Sauerland S, Agresta F, Bergamaschi R, et al. Laparoscopy for abdominal emergencies: evidence based guidelines of the European Association for Endoscopic Surgery. *Surg Endosc* 2006; 20: 14–29.
14. Johansson M, Thune A, Nelvin L, et al. Randomized clinical trial of open versus laparoscopic cholecystectomy in the treatment of acute cholecystitis. *Br J Surg* 2005; 92: 44–9.
15. Borzellino G, Sauerland S, Minicozzi AM, et al. Laparoscopic cholecystectomy for severe acute cholecystitis. A meta-analysis of results. *Surg Endosc* 2008; 22: 8–15.
16. Bingener J, Stefanidis D, Richards ML, et al. Early conversion for gangrenous cholecystitis: impact on outcome. *Surg Endosc* 2005; 19: 1139–41.
17. Feldman LS, Medeiros LE, Hanley J, et al. Does a special interest in laparoscopy affect the treatment of acute cholecystitis? *Surg Endosc* 2002; 16: 1697–703.
18. Mercer SJ, Knight JS, Toh SK, et al. Implementation of a specialist-led service for the management of acute gallstone disease. *Br J Surg* 2004; 91: 504–8.
19. Gurusamy KS, Samraj K. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Cochrane Database of Systematic Reviews* 2006; 4: CD005440. DOI: 10.1002/14651858.CD005440.pub2.
20. Papi C, Catarci M, D'Ambrosio L, et al. Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. *Am J Gastroenterol* 2004; 99: 147–55.
21. Johansson M, Thune A, Blomqvist A, et al. Impact of choice of therapeutic strategy for acute cholecystitis on patient's health-related quality of life. Results of a randomized controlled clinical trial. *Dig Surg* 2004; 21: 359–62.
22. Hatzidakis AA, Prassopoulos P, Petinarakis I, et al. Acute cholecystitis in high-risk patients: percutaneous cholecystostomy vs conservative treatment. *Eur Radiol* 2002; 12: 1778–84.
23. Ito K, Fujita N, Noda Y, et al. Percutaneous cholecystostomy versus gallbladder aspiration for acute cholecystitis: a prospective randomized controlled trial. *Am J Roentgenol* 2004; 183: 193–6.
24. Gurusamy KS, Samraj K. Routine abdominal drainage for uncomplicated open cholecystectomy. *Cochrane Database of Systematic Reviews* 2007; 2: CD006003.
25. Gurusamy KS, Samraj K, Mullerat P, et al. Routine abdominal drainage for uncomplicated laparoscopic cholecystectomy. *Cochrane Database of Systematic Reviews* 2007; 4: CD006004.
26. Choudhary A, Bechtold ML, Karpman C, et al. Role of prophylactic antibiotics in laparoscopic cholecystectomy: A meta-analysis. 49th Annual Meeting of the Society for Surgery of the Alimentary Tract, May 17–21, 2008. San Diego, CA, Digestive Disease Week, 2008. Program Book, abstract 249: 103.
27. Sanabria A, Valdivieso E, Gomez G. Antibiotic prophylaxis for patients undergoing elective laparoscopic cholecystectomy. (Protocol) *Cochrane Database of Systematic Reviews* 2004; 4: CD005265.
28. Yellin AE, Berne TV, Appleman MD, et al. A randomized study of cefepime versus the combination of gentamicin and mezlocillin as an adjunct to surgical treatment in patients with acute cholecystitis. *Surg Gynecol Obstet* 1993; 177(Suppl): 23–9; discussion 35–40.
29. Mueller EL, Pitt HA, Thompson JE Jr, et al. Antibiotics in infections of the biliary tract. *Surg Gynecol Obstet* 1987; 165: 285–92.
30. Thompson JE Jr, Bennion RS, Roettger R, et al. Cefepime for infections of the biliary tract. *Surg Gynecol Obstet* 1993; 177 Suppl: 30–4; discussion 35–40.
31. Kehlet H, Gray AW, Bonnet F, et al. A procedure-specific systematic review and consensus recommendations for post-operative analgesia following laparoscopic cholecystectomy. *Surg Endosc* 2005; 19: 1396–415.
32. Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anesthesia in laparoscopic cholecystectomy: a systematic review and meta-analysis. *Anesth Analg* 2006; 103: 682–8.

Acute Cholangitis

Adrian W. Ong and Charles F. Cobb

Questions to be Addressed	
Question	Recommendation
What is the optimal antibiotic strategy for acute cholangitis?	Antibiotics should be initiated early (Grade A). Blood and bile cultures should be routinely obtained to guide therapy (Grade B). There is insufficient evidence to recommend a specific antibiotic regimen or duration of therapy. Duration of therapy should be guided by clinical response and disease severity (Grade B). There is insufficient evidence that biliary penetration is a factor that influences clinical outcome. However, antibiotic therapy should be used in conjunction with expeditious clearance of obstructed bile ducts to derive maximum benefit (Grade C).
What is the preferred mode of biliary decompression for cholangitis due to biliary stones? What is the optimal timing for biliary decompression?	Endoscopic biliary decompression is preferred over surgery (Grade A). Percutaneous transhepatic biliary drainage is an alternative where endoscopic decompression is not possible (Grade C). Patients who do not respond to medical management after 6–24 hours should undergo urgent drainage (Grade C). Certain patients are at high risk for failure of medical therapy and should undergo urgent drainage even before clinical deterioration (Grade C).
Is cholecystectomy warranted after ES and clearance of bile duct stones with or without cholangitis? If so, when should it be performed?	Prophylactic cholecystectomy should be offered to patients after ES unless prohibited by patient-related factors, in patients with proven gallbladder stones (Grade A). The optimal time after ES for cholecystectomy is unclear but earlier LC may be associated with a lower conversion rate to open cholecystectomy (Grade C). In patients with no gallbladder stones, cholecystectomy may not be necessary (Grade C).
Does MRCP play a role in the management of acute cholangitis due to biliary stones?	There is insufficient evidence to support the use of MRCP in the management of acute cholangitis due to bile duct stones (Grade D).
Abbreviations: ES, endoscopic sphincterotomy; LC, laparoscopic cholecystectomy; MRCP, magnetic resonance cholangiopancreatography.	

INTRODUCTION

Acute cholangitis due to biliary stones remains a common surgical emergency. Bacteremia from biliary tract infections accounts for approximately 5% of all bacteremias (1). The mortality rate from cholangitis ranges from 10% to 20% (2–4). Despite advances in our knowledge of the management of this disease, it is still associated with significant morbidity and mortality.

METHODS

We examined questions faced by the clinician in the management of acute cholangitis due to biliary stones. Specific discussion of cholangitis associated with other benign or malignant biliary tract disease, stricture, recurrent pyogenic cholangitis, and prior instrumentation of the biliary tract was beyond the scope of this chapter. An online search of PubMed was performed for all English-language articles

on human subjects from January 1986 to June 2008 using the terms “acute cholangitis,” “endoscopic retrograde cholangiopancreatography,” and “magnetic retrograde cholangiopancreatography.” Abstracts were reviewed and selected for suitability with regard to the questions being examined, and the relevant articles were obtained for further review. We also performed an online search of the Cochrane library and the U.S. National Guidelines Clearinghouse using similar key phrases.

Review articles that were not systematic reviews, expert opinion without explicit critical appraisal, and case series including fewer than five subjects were excluded.

Suitable articles were graded according to the levels of evidence developed by the Oxford Centre for Evidence Based Medicine, and grades of recommendations were formulated based on the same system. Articles with Level V evidence based on this system were excluded.

The two authors reviewed the suitable articles and rated each article independently. A consensus was reached as to constructing the evidentiary tables for the questions.

QUESTIONS TO BE ADDRESSED

1. What is the optimal antibiotic strategy for acute cholangitis?
2. What is the preferred mode of biliary decompression for cholangitis due to biliary stones? What is the optimal timing for biliary decompression?
3. Is cholecystectomy warranted after endoscopic treatment of bile duct stones with or without cholangitis? If so, when should it be performed?
4. Does magnetic resonance cholangiopancreatography (MRCP) play a role in the management of acute cholangitis due to biliary stones?

WHAT IS THE OPTIMAL ANTIBIOTIC STRATEGY FOR ACUTE CHOLANGITIS?

Early initiation of antibiotics are recommended by the 2008 guidelines of the Surviving Sepsis Campaign (5): initiation as early as one hour after recognition of the septic state is recommended. In a prospective study, the overwhelming majority of blood stream infections were found to be due to Gram-negative bacteria (*Escherichia coli*, *Klebsiella*, *Enterobacter*), with a substantial proportion (27%) having polymicrobial infection. Gram-positive species included *Enterococcus* (10%), *Streptococcus* (6%), and anaerobes (7%). *Aeromonas hydrophilia* and *Pseudomonas aeruginosa* accounted for 8% (6). No one antibiotic regimen has been shown to be clinically superior to another. Tanaka et al., in the Tokyo Guidelines, found that third-generation cephalosporins, carbapenems, and fluoroquinolones were as effective as ampicillin plus aminoglycoside (7). The positive rates of blood cultures obtained ranged from 50% to 76% (7). Englesbe et al. found a high rate (36%) of resistant pathogens when blood cultures were drawn, underscoring the importance of obtaining bile and blood cultures to guide therapy (8).

The importance of choosing an antibiotic with good biliary penetration is unclear, with lack of data correlating biliary penetration to clinical outcome. However, it is recognized that biliary penetration is poorer when bile ducts are obstructed (9,10).

The optimal duration of antimicrobial therapy is as yet unclear. Tanaka et al. recommended two to three days for mild acute cholangitis and five to seven days for moderate to severe antibiotics, but this recommendation was not based on high-level evidence (7). Van Lent et al. (11) found that short-duration therapy (three days or less) could be sufficient if clinical improvement was seen and blood cultures were negative, and the Surviving Sepsis Campaign guidelines recommended a 7- to 10-day course for sepsis.

Recommendation: Antibiotics should be initiated early (Grade A). Blood and bile cultures should be routinely obtained to guide therapy (Grade B). There is insufficient evidence to recommend a specific antibiotic regimen or duration of therapy. Duration of therapy should be guided by clinical response and disease severity (Grade B). There is insufficient evidence that biliary penetration is a factor that influences clinical outcome. However, antibiotic therapy should be used in conjunction with expeditious clearance of obstructed bile ducts to derive maximum benefit (Grade C).

WHAT IS THE PREFERRED MODE OF BILIARY DECOMPRESSION FOR CHOLANGITIS DUE TO BILIARY STONES? WHAT IS THE OPTIMAL TIMING FOR BILIARY DECOMPRESSION?

Endoscopic decompression is effective—it has been shown to promptly decrease bile and serum endotoxin levels after decompression (12). Bile and serum endotoxin correlated with the presence of the components of Charcot's triad. Endoscopic decompression involve endoscopic sphincterotomy (ES) with stone extraction or placement of a nasobiliary catheter or stent. Nasobiliary drainage is equally as effective as stent placement (13,14). A randomized trial comparing duct clearance by ES to placement of a biliary stent found that stent placement was an effective and safe alternative to duct clearance in the immediate period, but in the long run biliary complications were more prevalent in the stent group. In the immediate period, drainage was safer than ES (15–17).

Whether surgery or endoscopic drainage should be performed was addressed by Lai et al. in a randomized trial. Of 82 patients randomized to receive early endoscopic drainage via nasobiliary catheter, endoscopic drainage was associated with lower mortality and lower period of ventilatory support. Mode of drainage was a significant predictor of mortality in their analysis. Other factors such as serum albumin, creatinine, leukocyte count, platelet count, age, serum urea nitrogen, and concomitant medical problems were also significant predictive factors for mortality in their series. The authors concluded that urgent endoscopic drainage should be considered for patients with adverse prognostic factors (2). That endoscopic drainage is the preferred method over surgery is also noted by other nonrandomized studies and systematic reviews (18–23).

There is no high-level evidence in the literature comparing the effectiveness and safety of percutaneous transhepatic biliary drainage (PTBD) to endoscopic and surgical drainage. Pessa et al. (24) studied 42 patients who underwent percutaneous transhepatic drainage for acute cholangitis. Only 12 patients had cholangitis due to bile duct stones. All were successful, despite a 17% incidence of nondilated ducts. Sepsis began to resolve in 22 of 24 after 24 hours. There was a 7% complication rate. PTBD is considered an alternative option if endoscopic drainage is not possible. A consensus conference (Tokyo Guidelines) has considered both these modes of drainage (endoscopic and PTBD) as preferred therapies over open surgery (14).

Timing of biliary decompression was addressed by Yeung et al. (4), who studied 171 patients with cholangitis. Thirty-one patients did not respond to conservative measures after six hours, and emergent biliary drainage was undertaken (ERCP, PTBD, surgery). Logistic regression demonstrated five factors: age >75, history of smoking, prothrombin time, size of the common bile duct and blood glucose as predictors for need for emergent ERCP. The authors concluded that age >75 and smoking history were important factors that predicted failure of conservative management and that subset of patients could benefit from emergent intervention before deterioration. Another prospective study of 142 consecutive patients with acute cholangitis found that 31 (21.8%) required emergency ERCP. Linear regression demonstrated four factors (heart rate >100/min, albumin <30g/dl, bilirubin >50mcmol/L, and

prothrombin time of >14 seconds) were associated with failure of medical treatment. When one or more of the factors were present, emergent ERCP was required in 40% of patients. The proportion was 82% if two or more factors were present (25). Another retrospective study found that 13 patients who did not respond to antibiotics after 24 hours did not have complications if they were drained <72 hours. On the other hand, 12 patients where antibiotics had failed and who were not drained until >three days later developed a 33% rate of septic complications. The authors conclude that urgent biliary decompression was indicated in patients who do not respond early (<24 hours) to antibiotics (26). At the Tokyo consensus conference, no evidence-based recommendations were produced with regard to timing of drainage (20).

Recommendation: Endoscopic biliary decompression is preferred over surgery (Grade A). PTBD is an alternative where endoscopic decompression is not possible (Grade C). Patients who do not respond to medical management after 6–24 hours should undergo urgent drainage (Grade C). Certain patients are at high risk for failure of medical therapy and should undergo urgent drainage even before clinical deterioration (Grade C).

IS CHOLECYSTECTOMY WARRANTED AFTER ES AND CLEARANCE OF BILE DUCT STONES WITH OR WITHOUT CHOLANGITIS? IF SO, WHEN SHOULD IT BE PERFORMED?

In a systematic review, McAlister et al. examined the role of cholecystectomy after ES. The authors recommended proceeding with cholecystectomy due to the higher rate of biliary complications in patients managed expectantly (27). Method of cholecystectomy or patient ASA class did not seem to influence outcome. Williams et al. (19) reached a similar conclusion in another systematic review. Boerma et al. (28) randomized patients with proven gallbladder stones to expectant management versus laparoscopic cholecystectomy after ES. The wait-and-see group had a 47% incidence of recurrent biliary complications versus 2% in the cholecystectomy group, with a median follow-up time of 30 months (range 15–67 months). Lau et al. (29) similarly randomized older patients (>60 years) after ES and found that at 5 years, 5.8% of patients in the cholecystectomy group versus 25.4% in the group with gallbladders in situ had recurrent biliary events. Both trials contained patients with proven gallstones. On the other hand, in a retrospective study comprising patients treated for cholangitis, those who underwent ES had a lower incidence of recurrent cholangitis than patients who did not undergo ES, and cholecystectomy was not a factor predicting recurrent cholangitis (30). Ando et al. (31) followed 1,042 patients prospectively and found that patients with acalculous gallbladders had a lower risk of recurrent stones when cholecystectomy was not performed than patients with calculous gallbladders after a 20-year follow-up. Nagino et al. (20), in the Tokyo Guidelines, came to a similar conclusion that patients with acalculous gallbladders need not have cholecystectomy after sphincterotomy.

There is no high-level evidence on when cholecystectomy should be performed. Schiphorst et al. found that of 167 consecutive patients who underwent ES then cholecystectomy, 33 patients had recurrent biliary complications, with a median time to complications of 22 days (3–225 days)

after ES. Seventy-six percent of the complications occurred more than one week after ES, with acute cholecystitis accounting for 11% of complications. Complications were associated with increased hospital length of stay. Their conclusion was that cholecystectomy should be done within a week (32). DeVries et al. (33) also studied 83 patients after ERCP who underwent laparoscopic cholecystectomy (LC). Of the three time interval groups (LC <2, 2–6, and >6 weeks after ERCP), adhesions, operation time, and bile duct damage did not significantly differ between the groups. However, the conversion rate in group 2 was significantly higher compared to group 1. They concluded that a higher conversion rate of LC was found if LC was done two to six weeks after ERCP compared to LC within two weeks (33). The two randomized trials (28,29) did also report a significantly higher conversion rate for LC in the group managed expectantly when cholecystectomy was needed, compared to the group managed with prophylactic cholecystectomy (approximately 50% versus 20%).

Recommendation: Prophylactic cholecystectomy should be offered to patients after ES unless prohibited by patient-related factors in patients with proven gallbladder stones (Grade A). The optimal time after ES for cholecystectomy is unclear, but earlier laparoscopic cholecystectomy may be associated with a lower conversion rate to open cholecystectomy (Grade C). In patients with no gallbladder stones, cholecystectomy may not be necessary (Grade C).

DOES MRCP PLAY A ROLE IN THE MANAGEMENT OF ACUTE CHOLANGITIS DUE TO BILIARY STONES?

The accuracy of MRCP in the detection of common bile duct stones and ductal dilation had been studied. MRCP was shown to have excellent sensitivity and specificity for the detection of common bile duct stones and biliary dilatation compared to ERCP (34,35). Although it is noninvasive and safe, MRCP requires special expertise in interpretation and is solely a diagnostic modality in contrast to ERCP. Hence, few studies have examined the role of MRCP in the management of acute calculous cholangitis, whereas ERCP is recognized as the preferred modality for biliary decompression. Farrell et al. (36) examined the potential impact of MRCP on ERCP workload in a single tertiary referral center. Of 1,148 patients, only 84 presented for ERCP for acute cholangitis. Of 118 ERCPs done in this subgroup, 10 were unsuccessful, 22 were normal, and 53 found biliary stones. According to their analysis, 29% of patients could have avoided ERCP if MRCP had been used as the first imaging modality. This percentage contrasted with 44% for abdominal pain, 77% for asymptomatic dilated ducts, 55% for asymptomatic abnormal liver function tests, and 10% for jaundice. The authors concluded that the majority of patients with cholangitis would still require ERCP performed by an experienced endoscopist. Shanmugam et al. (37) suggested that MRCP could replace ERCP in the initial diagnosis of bile duct stones and suggested an algorithm where MRCP was used after ultrasound to assess patients with jaundice, pancreatitis, or cholangitis. However, it was unclear from their analysis of the 7.4% of patients in their series presenting with acute cholangitis whether ERCP could have been avoided.

Recommendation: There is insufficient evidence to support the use of MRCP in the management of acute cholangitis due to bile duct stones (Grade D).

Evidentiary Table for Questions to be Addressed

First author	Ref.	Level of evidence	Design	Summary of findings
Van Lent	11	IV	R	80 patients who underwent successful ERCP for cholangitis were studied. Antibiotic therapy was given for median duration of 3 days (range 0–42 days): 41 patients had <3 days, 19 had 4–5 days, and 20 had >5 days. Endpoints of recurrent cholangitis, procedures, death, new course of antibiotics were not different between the three groups. Conclusion: Short-duration antibiotic therapy appears sufficient. Patients with positive blood cultures may need longer periods of therapy.
Tanaka	7	Ila	SR	Tokyo Guidelines: Bile and blood cultures should be performed at all available opportunities (recommendation Grade B). Varying durations of antibiotics were recommended depending on the severity of cholangitis (mild, 2–3 days, moderate to severe, minimum 5–7 days, recommendation Grade A). Clinical trials involving single-agent therapy were compared to the combination of ampicillin and an aminoglycoside, and found to have comparable efficacy.
Englesbe	8	IV	R	30 patients with cholangitis were studied (18 had gallstones, 5 had benign strictures, 7 had malignant obstruction). Of the patients with bile duct stones, 78% had blood cultures, 64% had positive cultures, and 36% had organisms resistant to ≥ 3 antibiotics from the blood isolates. The most common organisms were <i>Enterococcus</i> , <i>E. coli</i> , <i>Enterobacter</i> . Conclusion: Blood and bile cultures should routinely be performed in acute cholangitis. Broad spectrum antibiotics should be initiated. Polymicrobial infections are common.
Melzer	1	IV	R	The biliary tract accounted for 4.1% of hospital-acquired and 6.1% of community-acquired bacteremias. Gram-negative bacteremias were responsible for 55 of 58 episodes, with Gram-positive organisms accounting for 3. 30-day mortality was 14%. Drainage of bile was attempted in only 23/49 of cases. The most common isolated were <i>E. coli</i> and <i>Klebsiella</i> , with <i>Enterococcus</i> accounting for only one episode. 13% of the isolated were extended spectrum β -lactamase producers.
Lee	6	IIc	P	All patients admitted to the emergency department with documented blood stream infection were prospectively followed. Of 145 patients with biliary tract bacteremias (15.5%), 77.2% were due to cholangitis. Emergent biliary decompression was done on 60% of the patients. Of the blood isolates, 88% had Gram-negative bacteria, with 27% being polymicrobial. Gram-positive species included <i>Enterococcus</i> (10.3%), <i>Streptococcus</i> (6.2%), and anaerobes (6.9%). <i>A. hydrophilia</i> and <i>P. aeruginosa</i> accounted for 8.3%. Of bile isolates, 37% had <i>E. coli</i> , 20.3% had <i>Klebsiella</i> , 34% had <i>Enterococcus</i> , and 12.2% had anaerobes. Mortality for cholangitis was 13.4% versus 6.1% for acute cholecystitis. Acute renal failure, septic shock, biliary tract malignant obstruction, Carlson comorbidity index of ≥ 6 and serum bilirubin level were independent factors associated with increased 30-day mortality. Conclusion: Certain prognostic factors may allow clinicians to recognize high-risk patients. Critique: No examination of prognostic significance of different antibiotic regimens.
Dhalluin-Venier	9	IIb	P	62 patients treated with endoscopic biliary drainage were given intravenous ciprofloxacin or cefotaxime for more than 24 hours before exploration. Biliary penetration was assessed by the bile to plasma ratio of the concentration of antibiotic. Biliary penetration was more than 1 in only 35% of the ciprofloxacin group and 9% in the cefotaxime group. Conclusion: Biliary penetration of antibiotics is poor in obstructed bile ducts.
Schwab	10	IIb	P	Biliary excretion of moxifloxacin was determined in plasma and bile of 10 patients with biliary obstruction and cholangitis and 10 patients without biliary obstruction 30 min after IV administration of 400 mg moxifloxacin. The concentration of moxifloxacin in the bile was significantly lower in patients with biliary obstruction than without (4.63 mcg/ml, range 0.71–14.40 versus 16.90 mcg/ml; range 1.79–42.50; $p = 0.043$). Although significantly different, the penetration index was extensively high in those without biliary obstruction (4.41, range 0.35–14.45) but still sufficient in those patients with obstructive cholangitis (1.02, range 0.29–2.83; $p = 0.035$). Conclusion: Moxifloxacin administration produces biliary concentration sufficiently above the minimal inhibitory concentrations.
Dellinger	5	Ia	SR	Recommendations from a consensus conference: IV antibiotic should be started as early as possible and within the first hour of recognition of septic shock (Ib) and severe sepsis without septic shock (Id). Appropriate cultures should be obtained before initiating antibiotic therapy but should not prevent prompt administration of antimicrobials. The duration of therapy should typically be 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, or immunologic deficiencies, including neutropenia (Id).
Chijiwa	18	IV	R	Of 362 patients with bile duct stones, 27 had AOSC. In this subset, stone removal rates were >95% in both surgery versus ES, with morbidity rate 4/6 (67%) versus 5/21 (24%) and mortality rate of 2/6 (33%) versus 1/21 (5%) in the surgery group versus endoscopy (not significant). Conclusion: ES is recommended in AOSC. Critique: Of the 27 patients, 10 underwent “elective” treatment.
Lai	2	IV	R	Of 86 patients who underwent open bile duct exploration, 42 (49%) were done in first 24 hours, with 10 (12%) explored after 72 hours. Septic shock present in 55 (64%) prior to surgery. Blood cultures were positive in 43 of 58 with collected samples. <i>E. coli</i> was the most common organism. Mortality rate was 20%. Conclusion: Nonsurgical method of biliary decompression may be preferable in those with highest risk of death. Critique: Timing of surgery not considered in the analysis.

(Continued)

Evidentiary Table for Questions to be Addressed (Continued)

First author	Ref.	Level of evidence	Design	Summary of findings
Williams	19	Ila	SR	Consensus recommendations: patients with acute cholangitis who fail to respond to antibiotic therapy or who have signs of septic shock require urgent biliary decompression. Radiologically guided percutaneous drainage is an alternative but open surgery should be avoided (evidence Grade Ib, recommendation Grade A).
Boender	26	IV	P	Of 95 patients, complete CBD stone clearance was achieved in 85 by ERCP. 85 patients had cholangitis prior to ES. 60 patients with good response to antibiotics had a lower morbidity rate than 12 patients with poor response to antibiotics in 24 hours that were drained >72 hours. In 13 patients with poor response in 24 hours that were drained <72 hours, there were no complications. Conclusion: Patients who fail to respond to antibiotics within 24 hours require urgent biliary drainage.
Nagino	20	Ila	SR	At the Tokyo consensus meeting, endoscopic drainage was recommended over surgery or percutaneous transhepatic drainage (second choice). The discussion of the timing of biliary drainage produced no evidence-based recommendations.
Sugiyama	21	IV	R	191 patients with CBD stones underwent urgent biliary drainage for cholangitis (154 were <80 years). Urgent drainage was used in patients with septic shock, mental confusion, or those that did not respond to antibiotics. Severe cholangitis found in 43% of elderly patients versus 25% of younger patients. In both older and younger patients, surgery was associated with poorer outcomes than endoscopy or percutaneous transhepatic drainage. Endoscopy in elderly patients yielded better outcomes than surgery or percutaneous drainage. Conclusion: Endoscopic drainage should be the treatment of choice for elderly patients with cholangitis.
Leese	22	IV	R	94 patients were admitted with cholangitis (87% due to stones). 71 patients underwent early decompression (39% surgically versus 61% endoscopically). 11 did not undergo intervention because they clinically improved with antibiotics or were moribund. There was a higher 30-day mortality with surgery (21%) versus ES (4.7%), despite older patients undergoing ES. Conclusion: Patients who do not respond to antibiotics should undergo early ES with surgery reserved for those who did not respond to ES. Critique: no definition of "early" was made.
Lai	3	Ib	PR	Trial of surgery versus endoscopic drainage, all had ERCP to delineate anatomy prior to randomization. Of 82 patients, 43 had all features of Charcot's triad, 17 had mental confusion. All 82 had CBD stones, 8 had strictures. All 41 randomized to endoscopic drainage had successful drainage, and 12 later underwent cholecystectomy. 79 of 82 had bile cultures with 80% positive, and 50 (63%) had positive blood cultures. In the surgery arm, there was a longer period of ventilator support, with higher mortality rate (13/41 versus 4/41 in the endoscopy arm). Method of drainage was a discriminant factor in a multivariate analysis of mortality, together with serum albumin, creatinine, age, leucocyte count, platelet count, and concomitant comorbidities. Time to randomization was 23 versus 27 hours in the two arms. Conclusion: For patients with adverse prognostic factors, urgent endoscopic drainage should be considered.
Yeung	4	IV	R	171 patients with acute cholangitis were studied. Conservative treatment was continued for 6 hours and emergency biliary drainage arranged if there was no improvement. Logistic regression identified five variables associated with emergency drainage in 31 patients (ERCP 11, PTD 10, surgical 10): age >75, chronic smoking history, prothrombin time, blood glucose, and size of CBD. Conclusion: Urgent biliary drainage should be considered for patients >75 year and/or with a chronic smoking history as these patient are less likely to respond to conservative treatment.
Lai	23	IV	R	15 patients who underwent urgent endoscopic drainage via nasobiliary tube were compared to 20 patients undergoing surgical drainage in the same period. Patients who underwent endoscopic drainage were significantly older and had worse jaundice. No differences in morbidity and mortality were noted. Conclusion: Endoscopic drainage may provide a safe and effective method of biliary decompression.
Khuroo	38	Iib	PR	22 patients were randomized to receive endoscopic nasobiliary drainage versus surgery after emergency ERCP was performed. Hospital stay was significantly longer in the group undergoing endoscopic drainage with no differences in mortality. Surgical morbidity was equivalent. 11 of the 12 patients in the endoscopy group required definitive surgical procedures. Conclusion: There was no advantage of performing prior nasobiliary drainage in patients with acute cholangitis.
Neoptolemos	39	IV	R	32 patients with acute pancreatitis and cholangitis were identified. ERCP was attempted in 24 patients and was successful in 23. 9 underwent ERCP at 3 days or less and 14 at 5–28 days. Mortality rate between surgery and ERCP/ES was comparable, but numbers were too small to draw conclusions. Only 5.7% patients with cholangitis alone had evidence of passed CBD stones versus 25% of patients who had also acute pancreatitis ($p < 0.05$). Mortality rate was similar. Conclusion: In patients with acute cholangitis, ERCP/ES should be done irrespective of whether acute pancreatitis is an additional feature.

(Continued)

Evidentiary Table for Questions to be Addressed (Continued)

First author	Ref.	Level of evidence	Design	Summary of findings
Hui	25	Ib	P	31 patients received emergent ERCP (usually 24–48 hours after admission) versus 111 with elective ERCP. The majority (68%) had ES while the rest had stenting. Using regression, prothrombin time >14 s, maximal heart rate >100/min, bilirubin >50 $\mu\text{mol/L}$, and albumin <30 g/L were found to be predictive of failure to respond to medical treatment, and a scoring system was devised. Conclusion: Emergency ERCP should be performed on patients with one or more of these factors because they are less likely to respond to medical treatment.
Pessa	24	IV	R	42 patients with acute cholangitis (54% had Charcot's triad, 14% had Reynolds' pentad) underwent PTD. 40% had prior biliary tract surgery. Sepsis began to resolve within 24 hours in 40 of the 42 patients. Mortality was 5% with complications noted in 7%. Conclusion: PTD allows rapid control of sepsis with minimal morbidity.
McAlister	27	Ia	SR	5 RCTs with 662 participants were included. The wait-and-see group had a higher mortality rate (CI 1.15–2.75), with higher rates of recurrent biliary pain, jaundice, or cholangitis. Stratified by method of cholecystectomy or patient ASA class, outcome was not different. Conclusion: Prophylactic cholecystectomy should be offered to patients after ES and CBD clearance.
Hui	30	IV	P	210 consecutive patients presenting with acute cholangitis due to CBD stones were studied. 90 did not require ES because no CBD stones were detected. 41 patients agreed to cholecystectomy. Recurrent cholangitis developed in 22% in group 1 (cholecystectomy) versus 13% in group 2 (no cholecystectomy), $p = 0.149$. In both groups, patients who underwent ES had a lower rate of recurrent cholangitis than those who did not undergo ES. Acute cholecystitis occurred in 1.2% of the patients who declined cholecystectomy. Conclusion: Cholecystectomy did not lower the rate of recurrent cholangitis, but ES did.
Schiphorst	32	IV	R	Of 167 consecutive patients who underwent ES then cholecystectomy, 33 patients had recurrent biliary complications. Median time to complications was 22 days (3–225 days) after ES. 30 of 33 required repeat ERCP or emergent cholecystectomy. Patients who developed complications during waiting had no increase in complications but an increase in hospital stay compared to patients with an uncomplicated waiting period. 76% of the complications occurred more than 1 week after ES. Acute cholecystitis accounted for 11% of complications. Conclusion: 20% of all patients after ES developed biliary complications. Cholecystectomy within a week may prevent complications.
Lai	40	IV	R	279 patients were admitted for ES for CBD stones. (Group A underwent cholecystectomy soon after ES; group B did not.) Of 140 followed after discharge, there were no significant differences in the incidence of recurrent bile duct stones or biliary symptoms in the two groups over a 43-month median follow-up period. In group B, the presence of cholelithiasis was not a factor predicting recurrent biliary complications. Acute cholecystitis occurred in 6 (6.3%) of the patients with gallbladders left in situ. Conclusion: Cholecystectomy after ES does not reduce the incidence of recurrent biliary complications. Critique: The incidence of cholelithiasis was significantly different between the two groups.
Boerma	28	Ib	PR	This study randomized 108 patients 18–80 years who underwent endoscopic stone clearance with cholelithiasis present to elective LC within 6 weeks after sphincterotomy versus a wait-and-see policy. Median follow-up time was 30 months. The wait-and-see group had 47% rate of recurrent biliary events versus 2% in the cholecystectomy group. Conclusion: A wait- and-see policy cannot be routinely recommended.
Lau	29	Ib	PR	This study randomized 178 patients >60 years who underwent sphincterotomy to elective cholecystectomy or expectant management. Mean follow-up was at least 58 months. About 40% of each group presented with cholangitis. Those who underwent cholecystectomy had fewer biliary events (7% versus 24%) with similar late mortality rates. Conclusion: Cholecystectomy should be recommended after endoscopic treatment of bile duct stones.
Williams	19	III	SR	In patients with gallbladder stones and bile duct stones, endoscopic stone extraction as the sole treatment should be avoided unless there are patient-related factors that make cholecystectomy inappropriate.
Ando	31	Ib	P	1,042 consecutive patients who underwent ES for bile duct stones from December 1975 to September 1998 were prospectively followed up. Patients were divided into four groups according to GB status: acalculous GB group, calculous GB group, cholecystectomy group, and prior cholecystectomy group. Reliable follow-up information was obtained for 983 (94.3%) of the 1,042 patients. Recurrence occurred in 111 patients. The acalculous GB group was less prone to recurrence than the prior cholecystectomy group and the calculous GB group. The RR for the latter two compared with the former group were 2.26 ($p = 0.0078$) and 2.16 ($p = 0.0093$), respectively. Other prognostic factors were lithotripsy (RR 2.37, $p = 0.0004$) and pneumobilia (RR 1.57, $p = 0.044$). Conclusion: GB status, lithotripsy, and pneumobilia were significantly related to bile duct stone recurrence after ES.

(Continued)

Evidentiary Table for Questions to be Addressed (Continued)

First author	Ref.	Level of evidence	Design	Summary of findings
DeVries	33	IV	R	83 patients with choledochocystolithiasis were studied with regard to the timing of LC after ERCP in three time interval groups: LC <2, 2–6, and >6 weeks after ERCP. Adhesions, operation time, and bile duct damage did not significantly differ between the groups. The conversion rate in (the LC2-6 group) was significantly higher compared to the LC < 2 group ($p = 0.027$, odds ratio 11 (1.13–106.8). Conclusion: A higher conversion rate of LC was found 2–6 weeks after ERCP compared to LC within 2 weeks.
Farrell	36	IV	R	Of 118 ERCPs done for cholangitis, 10 failed. Excluding those, 22 of the 108 ERCPs were normal, and 53 showed biliary stones. The proportion of potentially avoidable ERCPs was 22/108. Of 84 patients, 29% could have potentially avoidable ERCPs. Conclusion: The majority of patients with cholangitis still require ERCP.
Shanmugam	37	IV	P	374 consecutive patients underwent MRCP, of which 26 patients had cholangitis. Overall positive predictive value for all biliary pathology was 83.6%, and the negative predictive value was 98.1%. An algorithm was devised for patients with cholangitis, deranged LFTs, or jaundice using MRCP and ultrasound as first-line modalities for evaluation prior to ERCP. Critique: Devised pathway for cholangitis was not supported by authors' findings.

Abbreviations: AOSC, acute obstructive suppurative cholangitis; CBD, common bile duct; CI, confidence interval; EPT, endoscopic papillotomy; ERCP, endoscopic retrograde cholangiopancreatography; ES, endoscopic sphincterotomy; GB, gallbladder; LC, laparoscopic cholecystectomy; MRCP, magnetic resonance cholangiopancreatography; PTD, percutaneous transhepatic drainage; RCT, randomized controlled trial; RR, relative risk; LFTs, liver function tests; P, prospective non-randomized; PR, prospective randomized; R, retrospective; SR, systematic review.

REFERENCES

- Melzer M, Toner R, Lacey S, et al. Biliary tract infection and bacteremia: presentation, structural abnormalities, causative organisms and clinical outcomes. *Postgrad Med J* 2007; 83: 773–6.
- Lai ECS, Tam PC, Paterson IA, et al. Emergency surgery for severe acute cholangitis. *Ann Surg* 1990; 211: 55–9.
- Lai ECS, Mok FPT, Tan ESY, et al. Endoscopic biliary drainage for severe acute cholangitis. *N Engl J Med* 1992; 326: 1582–6.
- Yeung YP, Yip AWC. Predictors for emergency biliary decompression in acute cholangitis. *Eur J Gastroenterol Hepatol* 2006; 18: 727–31.
- Dellinger RP, Levy MM, Carlet JM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008; 36: 296–327.
- Lee CC, Chang IJ, Lai YC, et al. Epidemiology and prognostic determinants of patients with bacteremic cholecystitis or cholangitis. *Am J Gastroenterol* 2007; 102: 563–9.
- Tanaka A, Takada T, Kawarada Y, et al. Antimicrobial therapy for acute cholangitis: Tokyo guidelines. *Hepatobiliary Pancreat Surg* 2007; 14: 59–67.
- Englesbe MJ, Dawes LG. Resistant pathogens in biliary obstruction: Importance of cultures to guide antibiotic therapy. *HPB (Oxford)* 2005; 7: 144–8.
- Dhalluin-Venier V, Bazin C, Massias L, et al. Effects of biliary obstruction on the penetration of ciprofloxacin and cefotaxime. *Eur J Gastroenterol Hepatol* 2008; 20: 127–30.
- Schwab D, Grauer M, Hahn EG, et al. Biliary secretion of moxifloxacin in obstructive cholangitis and the non-obstructed biliary tract. *Aliment Pharmacol Ther* 2005; 22: 417–22.
- Van Lent AUG, Bartelsman JFW, Tytgat GNJ, et al. Duration of antibiotic therapy for cholangitis after successful endoscopic drainage of the biliary tract. *Gastrointest Endosc* 2002; 55: 518–22.
- Lau JYW, Ip SM, Chung SCS, et al. Endoscopic drainage aborts endotoxaemia in acute cholangitis. *Br J Surg* 1996; 83: 181–4.
- Lee DWH, Chan ACW, Lam YH, et al. Biliary decompression by nasobiliary catheter or biliary stent in acute suppurative cholangitis: a prospective randomized trial. *Gastrointest Endosc* 2002; 56: 361–5.
- Tsuyuguchi T, Takada T, Kawarada Y, et al. Techniques of biliary drainage for acute cholangitis: Tokyo guidelines. *J Hepatobiliary Pancreat Surg* 2007; 14: 35–45.
- Chopra KB, Peters RA, O'Toole PA, et al. Randomised study of endoscopic biliary endoprosthesis versus duct clearance for bile duct stones in high-risk patients. *Lancet* 1996; 348: 791–3.
- Hui CK, Lai KC, Yuen MF, et al. Does the addition of endoscopic sphincterotomy to stent insertion improve drainage of the bile duct in acute suppurative cholangitis? *Gastrointest Endosc* 2003; 58: 500–4.
- Sharma BC, Agarwal DK, Baijal SS, et al. Endoscopic management of acute calculous cholangitis. *J Gastroenterol Hepatol* 1997; 12: 874–6.
- Chijiwa K, Kozaki N, Naito T, et al. Treatment of choice for choledocholithiasis in patients with acute obstructive suppurative cholangitis and liver cirrhosis. *Am J Surg* 1995; 170: 356–60.
- Williams EJ, Green J, Beckingham I, et al. Guidelines on the management of common bile duct stones (CBDS). *Gut* 2008; 57: 1004–21.
- Nagino M, Takada T, Kawarada Y, et al. Methods and timing of biliary drainage for acute cholangitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg* 2007; 14: 68–77.
- Sugiyama M, Atomi Y. Treatment of acute cholangitis due to choledocholithiasis in elderly and younger patients. *Arch Surg* 1997; 132: 1129–33.
- Leese T, Neoptolemos JP, Baker AR, et al. Management of acute cholangitis and the impact of endoscopic sphincterotomy. *Br J Surg* 1986; 73: 988–92.
- Lai ECS, Paterson IA, Tam PC, et al. Severe acute cholangitis: the role of emergency nasobiliary drainage. *Surgery* 1990; 107: 268–72.
- Pessa ME, Hawkins IF, Vogel SB. The treatment of acute cholangitis. Percutaneous transhepatic biliary drainage before definitive therapy. *Ann Surg* 1987; 205: 389–92.
- Hui CK, Lai KC, Yuen MF, et al. Acute cholangitis-predictive factors for emergency ERCP. *Aliment Pharmacol Ther* 2001; 15: 1633–7.

26. Boender J, Nix GAJJ, de Ridder MAJ, et al. Endoscopic sphincterotomy and biliary drainage in patients with cholangitis due to common bile duct stones. *Am J Gastroenterol* 1995; 90: 233–8.
27. McAlister VC, Davenport E, Renouf E. Cholecystectomy deferral in patients with endoscopic sphincterotomy. *Cochrane Database Syst Rev* 2007; 4: CD006233.
28. Boerma D, Rauws EAJ, Keulemans YCA, et al. Wait-and-see policy or laparoscopic cholecystectomy after endoscopic sphincterotomy for bile-duct stones: a randomized trial. *Lancet* 2002; 360: 761–5.
29. Lau JYW, Leow CK, Fung TMK, et al. Cholecystectomy or gallbladder in situ after endoscopic sphincterotomy and bile duct stone removal in Chinese patients. *Gastroenterol* 2006; 130: 96–103.
30. Hui CK, Lai KC, Yuen MF, et al. Role of cholecystectomy in preventing recurrent cholangitis. *Gastrointest Endosc* 2002; 56: 55–60.
31. Ando T, Tsuyuguchi T, Okugawa T, et al. Risk factors for recurrent bile duct stones after endoscopic papillotomy. *Gut* 2003; 52: 116–21.
32. Schiphorst AH, Besselink MGH, Boerma D, et al. Timing of cholecystectomy after endoscopic sphincterotomy for common bile duct stones. *Surg Endosc* 2008; 22: 2046–50.
33. De Vries A, Donkervoort SC, Van Geloven AA, et al. Conversion rate of laparoscopic cholecystectomy after endoscopic retrograde cholangiography in the treatment of choledocholithiasis: does the time interval matter? *Surg Endosc* 2005; 19: 996–1001.
34. Pamos S, Benages A, Medina E, et al. Prospective evaluation of magnetic resonance cholangiopancreatography in patients with biliary disease: comparative study with conventional ultrasonography and endoscopic retrograde cholangiopancreatography. *Dig Liver Dis* 2003; 35: 186–92.
35. Hintze RE, Adler A, Veltzke W, et al. Clinical significance of magnetic resonance cholangiopancreatography (MRCP) compared to endoscopic cholangiopancreatography (ERCP). *Endoscopy* 1997; 29: 182–7.
36. Farrell RJ, Noonan N, Mahmud N, et al. Potential impact of magnetic resonance cholangiopancreatography on endoscopic retrograde cholangiopancreatography workload and complication rate in patients referred because of abdominal pain. *Endoscopy* 2001; 33: 668–75.
37. Shanmugam V, Beattie GC, Yule SR, et al. Is magnetic resonance cholangiopancreatography the new gold standard in biliary imaging? *Br J Radiol* 2005; 78: 888–93.
38. Khuroo MS, Mahajan R, Zargar SA. Endoscopic vs surgical drainage of biliary tract in acute pyogenic cholangitis: a controlled study. *Ind J Gastroenterol* 1989; 8: 119.
39. Neoptolemos JP, Carr-Locke DL, Leese T, et al. Acute cholangitis in association with acute pancreatitis: incidence, clinical features and outcome in relation to ERCP and endoscopic sphincterotomy. *Br J Surg* 1987; 74: 1103–6.
40. Lai KH, Lin LF, Lo GH, et al. Does cholecystectomy after endoscopic sphincterotomy prevent the recurrence of biliary complications? *Gastrointest Endosc* 1999; 49: 483–7.

Acute Pancreatitis

Stephen W. Behrman

Clinical Questions		
Question	Answer	Grade
Scoring systems: is one superior to another in predicting the clinical course of AP?	No. Systems are complimentary not mutually exclusive.	B
What is the role of ERCP in acute biliary pancreatitis?	Only if evidence of cholangitis or biliary obstruction exists.	A
What is the role of prophylactic antibiotics in severe AP?	Studies do not show a benefit. May be reasonable in severe AP.	B
Is EN safe and superior to TPN in AP?	Safe and less expensive but clinical benefit unclear.	B
Is gastric feeding safe and equivalent to jejunal feeding in AP?	Safe in hemodynamically stable patients if tolerated.	B
Can the inflammatory cascade of AP be alleviated?	Not with current drug regimens.	A
Abbreviations: AP, acute pancreatitis; EN, enteral nutrition; ERCP, endoscopic retrograde cholangiopancreatography; TPN, total parenteral nutrition.		

Acute pancreatitis (AP) is responsible for approximately a quarter of a million hospital admissions in the United States on a yearly basis (1). Although most cases are self-limiting, about 10–20% of patients will develop severe inflammation of the pancreas, defined as organ failure persisting beyond 72 hours, and/or develop complications of the disease such as pseudo-cyst formation and pancreatic necrosis that may require surgical intervention (2). These latter entities prolong recovery, increase hospital length of stay, and can have morbidity and mortality rates approaching 40% and 10%, respectively (3). Recognition and early therapeutic intervention of those with severe pancreatitis is paramount to maintain end-organ integrity, mitigate the inflammatory response, minimize infectious complications, and maintain metabolic needs. Whereas basic concepts of therapy in those with severe AP have not changed (fluid resuscitation, hemodynamic monitoring, electrolyte homeostasis, etc.), the last decade or so has been noteworthy for new concepts in patient care that represent, in many instances, a significant deviation from previous management schemes.

SCORING SYSTEMS: IS ONE SUPERIOR TO ANOTHER IN PREDICTING THE CLINICAL COURSE OF AP?

Scoring systems in AP have proven to be quite valuable in terms of assessing those at risk for severe disease, identifying patients that require intensive monitoring (intensive care unit) and predicting individuals likely to develop complications. Ideally, such a system would allow standardization and comparison of similar patients with AP between different centers as well as offer an accurate assessment of prognosis in terms of morbidity and mortality. One problem in common with all systems is identification of a critical value that will uniformly differentiate mild from severe pancreatitis without exception. Given the myriad etiologies of AP, age, and patient comorbidities, it is unlikely a specific threshold value will be identified with any system. Nonetheless, scores associated with severe pancreatitis have proven, in general, to be reasonably predictive of the clinical course.

Several scoring systems have been commonly employed in those with AP. The Acute Physiology and Chronic Health Evaluation (APACHE) II and III systems use clinical and laboratory data gathered in a 24-hour time period, whereas Ranson criteria are tabulated during the initial 48 hours following admission (4–6). The Balthazar system focuses on computed tomography (CT) findings within 72 hours of admission (7). All systems with the exception of the APACHE are specific to those presenting with AP. The APACHE scoring system is dynamic and may be recalculated for any 24-hour time period. Other scoring systems have been developed (modified Glasgow, Multiple Organ System Score, etc.) but have not been studied in head-to-head comparisons as well as those just mentioned (8,9). There are no randomized control trials comparing one scoring system to another and assessing patient outcome. Several cohort studies have compared different scoring systems applied to all patients in an attempt to ascertain one that might be superior.

Yeung et al. compared APACHE II scores at 24 and 48 hours versus Ranson criteria in 101 patients admitted to a single hospital followed in a prospective fashion (10). Severe ($n = 12$) pancreatitis was defined by the Atlanta criteria (2). The authors found that the positive predictive value, sensitivity, and specificity of APACHE II for the development of severe pancreatitis was greater than that of Ranson criteria. Furthermore, this difference was exaggerated when the APACHE II was calculated at 48 hours versus 24 hours of admission.

Leung and colleagues reported on a retrospective review of 107 patients presenting with AP having CT scanning within 48 hours of admission (11). Results of the Balthazar scoring system were compared to Ranson criteria and the APACHE II system. In this study, a Balthazar score of > 5 ($n = 22$) indicated severe pancreatitis. In comparison to those with mild disease, those with severe pancreatitis as defined by Balthazar scoring had a significant increase in complications (pseudo-cyst, etc.), mortality, and length of stay (LOS). In contrast, these same 22 patients with severe pancreatitis did not have significantly higher APACHE II scores or Ranson criteria compared with those with mild disease. The authors concluded that the sensitivity of Ranson and APACHE II scoring systems to predict complications, mortality, and LOS from AP were inferior to the Balthazar system.

In a more neutral manner, Chatzicostas et al. prospectively studied 78 patients admitted with AP receiving a CT scan within 72 hours of admission (12). Severe pancreatitis (34 of 78 patients) was as defined per the Atlanta criteria. These authors subsequently applied the Balthazar and Ranson criteria (within 48 hours of admission) and APACHE II and III (within 24 hours of admission) scoring systems to these patients and followed their clinical course. They found a significant difference in all scoring systems differentiating mild from severe disease. Ranson and APACHE criteria were superior in predicting organ failure. However, the Balthazar system was superior to all other scoring schemes with respect to predicting AP severity and the development of pancreatic necrosis—factors that might be more clinically relevant.

In summary, there are no randomized control studies comparing various scoring systems. Numbers reported in comparison studies are small. Current data would suggest that these systems are not mutually exclusive but rather complementary—particularly a combination of physiologic, chemical, and radiology analyses (Grade B recommendation).

WHAT IS THE ROLE OF EARLY ERCP IN ACUTE BILIARY PANCREATITIS?

The need for, and timing of endoscopic retrograde cholangiopancreatography (ERCP) in biliary pancreatitis has been a subject of much controversy in both the gastroenterology and surgical literature. The vast majority of stones pass spontaneously into the duodenum and thus neither exacerbate the ensuing pancreatitis nor present a risk for the development of concurrent cholangitis. Indeed, early ERCP may exacerbate pancreatitis. However, the development of cholangitis in the face of severe AP would most certainly contribute substantially to morbidity and mortality, favoring early endoscopic evaluation. Perhaps more controversial is the role of early ERCP in ameliorating the degree of pancreatitis and the ensuing inflammatory cascade. Several randomized controlled studies and meta-analyses have addressed issues that are key in the management of these often critically ill patients.

In an early study, Neoptolemos and colleagues prospectively randomized 121 patients with presumed biliary pancreatitis to early (< 72 hours from admission) ERCP with sphincterotomy and stone extraction if necessary versus conservative management alone with selective

ERCP “if it was indicated” (13). The severity of pancreatitis was assessed via the modified Glasgow criteria with severe disease defined as a score of 3 or higher (8). Interpretation of the data in this study is somewhat clouded by the fact that gallstones could not be confirmed in 18 patients despite the availability of ultrasound and CT. With this limitation in mind, early ERCP was successful in 52 of 59 (88%) patients, choledocholithiasis was confirmed in 19 (32%) (versus 3 of 14, 21% in the conservative group), and successful stone extraction was accomplished in all. Early ERCP was associated with a statistically significant decrease in disease related complications (pseudo-cyst, organ failure) and a reduction (not significant) in mortality in those with severe but not mild pancreatitis.

Fan et al. studied the role of ERCP in AP of all causes (predominantly biliary in this Oriental population) in a prospective randomized trial of 197 patients in an early study (14). The purpose of this study was to compare the efficacy of early (< 24 hours) ERCP with papillotomy if stones were identified versus initial conservative treatment with ERCP +/- papillotomy reserved for those with clinical deterioration. Indications of clinical deterioration included rising fever, tachycardia, worsening leukocytosis, and/or an increase in bilirubin. Outcome was assessed on the basis of local and systemic complications as well as death. Severe pancreatitis was defined as a Ranson score of 4 or more. Impacted stones were found in 37 of 97 (38%) patients having early ERCP. In contrast, 27 of 98 patients initially followed conservatively required ERCP for deterioration, with stones found in the common bile duct or ampulla in only 12 (12%), confirming that the vast majority of stones pass spontaneously. Complications were higher in those with initial conservative treatment (29% versus 18%) but this difference was not significant ($p = 0.07$). With the exception of those developing cholangitis in the conservative group (eight versus zero patients), other complications did not differ dramatically. Mortality was higher in those treated conservatively (nine versus five patients) but did not reach statistical significance. All deaths occurred in those with severe pancreatitis—the vast majority of whom had no stone found on endoscopic evaluation. Early ERCP did not seem to either worsen or improve the progression of pancreatitis. The authors, surprisingly, conclude that emergency ERCP is indicated in all patients with AP although their data seem to suggest otherwise.

Folsch and colleagues conducted a prospective, randomized, multicenter study comparing early ERCP (< 72 hours) versus conservative management in those with acute biliary pancreatitis *without* evidence of obstructive jaundice (15). Disease severity was measured by the modified Glasgow criteria (> 3 severe). Indications for ERCP in the conservatively managed group were similar to those described by Fan et al. (14). Fifty-eight of 126 patients undergoing early ERCP had documented bile duct stones, versus 13 of 112 in the conservative group. Of note, 22 of 112 patients in the conservatively managed group developed indications for ERCP, and the incidence of choledocholithiasis in this group was 60 percent. Overall, morbidity and mortality did not differ between groups, including the risk of developing pancreatic-related complications such as pseudo-cyst and necrosis. The authors conclude that early ERCP is not indicated in those with acute biliary pancreatitis in the absence of clinical evidence of biliary obstruction or sepsis.

In a more recent study, Oria et al. examined the role of early (<48–72 hours) ERCP in those presenting with acute gallstone pancreatitis and evidence of biliopancreatic obstruction defined as a common bile duct >8mm or serum bilirubin >1.2mg/dl (16). Importantly, patients with clinical evidence of cholangitis (Charcot's triad) were excluded because this condition was felt to mandate early ERCP in this randomized, prospective study. Severe pancreatitis was defined as an APACHE II score >6. The specific aims of this study were to determine if early ERCP could reduce the severity of pancreatitis and thereby limit organ failure and complications of pancreatitis. The safety of early endoscopy was also assessed. Fifty-one of 103 patients were randomized to early ERCP with choledocholithiasis noted on 47 (72%) successful cannulations with minimal complications. When comparing the two groups, early clearance of the common duct did not reduce organ failure, local complications of the pancreas, or mortality in either mild or severe pancreatitis. The authors concluded that early ERCP did not alter the course of acute gallstone pancreatitis and was not indicated in the absence of cholangitis. Two recent meta-analyses have yielded the same conclusions while recognizing the heterogeneity of patient populations, enrollment criteria, the arbitrary assignment of mild and severe pancreatitis, and the definition of early ERCP (17,18).

In conclusion, ERCP has proven to be safe when performed in the face of acute biliary pancreatitis. If performed early, the incidence of choledocholithiasis is substantially higher than if ERCP is performed selectively when there is evidence of persistent biliary obstruction based on routine radiologic and chemical analysis. However, in the studies to date, early clearance of the common bile duct has not correlated with a reduction in organ failure, pancreatic-related complications, or mortality. For these reasons, in the absence of cholangitis or evidence of significant biliary obstruction, early ERCP in gallstone pancreatitis is not recommended (Grade A recommendation).

WHAT IS THE ROLE OF PROPHYLACTIC ANTIBIOTICS IN SEVERE AP?

Severe pancreatitis, by any grading system, is associated with a substantial risk for the development of pancreatic fluid collections and/or pancreatic necrosis as defined by the Atlanta classification (2). If these processes remain sterile, there is a good probability that patients will recover without the need for operative intervention. In contrast, secondary pancreatic infections mandate the need for operative drainage and debridement, markedly increase hospital LOS, and are associated with significant morbidity and mortality (19). In theory, prophylactic antibiotics in those with severe AP might prevent the progression of a sterile process into an infected milieu. Questions remain if this mode of therapy is chosen. When should antimicrobial therapy be initiated, and for how long? What antibiotic best penetrates pancreatic tissue? Finally, there may be a price to pay for such a strategy, including antibiotic-associated colitis and the potential selection of resistant or fungal organisms given prolonged therapy that may worsen, rather than protect against, the risk for mortality (20).

A review of antimicrobial agents with satisfactory tissue concentrations in the pancreatic bed is appropriate.

In a classic study, Buchler and colleagues measured the tissue (not serum) concentrations of 10 different but appropriate antibiotics in 89 patients having elective pancreatic surgery (21). Antimicrobial agents with the highest tissue concentrations as well as bactericidal activity included ciprofloxacin, ofloxacin, and imipenem. Further work from Bassi and colleagues examined the utility of these favored antibiotics in the face of human necrotizing pancreatitis. Tissue (not serum) levels of antimicrobials were obtained by needle biopsy, samples obtained at the time of surgery, or surgically placed drains in 12 patients (22). In this study, fluoroquinolones and metronidazole had concentrations in pancreatic tissue higher than the minimal inhibitory concentration (MIC) for the most commonly cultured organisms. Carbapenem concentrations in necrotic tissue did not always exceed the MIC for common pathogens. The liposolubility of these agents proved to be a common trait, and repeated administration enhanced their penetration in necrotic pancreatic tissue. In common with the study by Buchler, aminoglycosides proved inadequate presumably due to their limited liposolubility. Thus, the fluoroquinolones and the carbapenems have formed the basis of clinical studies investigating the role of antimicrobial prophylaxis in severe pancreatitis.

In an early, small, multicenter, nonblinded trial, Penderzoli and colleagues randomized 74 patients with evidence of pancreatic necrosis noted on CT scan within 72 hours of admission to medical management alone versus the addition of prophylactic imipenem-cilastin for 14 days (41 patients) (23). Mean Ranson criteria for all patients was 3.7, and about one-half had pancreatitis on the basis of biliary disease. More patients receiving prophylaxis had >50% necrosis (14 versus 2). Only five patients receiving antimicrobial prophylaxis developed pancreatic sepsis (confirmed by culture) statistically different than those who were medically managed. However, mortality and the need for surgical debridement of the pancreas did not differ. Curiously, in addition to the five septic patients in the prophylaxis group, seven additional patients had laparotomy for reasons not stated. Culture data on those with pancreatic sepsis suggests that prophylaxis did not select out resistant organisms.

Frey et al. conducted a retrospective review from 1982–96 of a cohort of patients with severe AP defined by an APACHE II score >6 and necrosis documented by CT scan of >15% (24). They compared three groups of patients treated during three different, consecutive time periods: 50 patients in the early (1982–89) period did not receive antibiotics, 55 patients received antimicrobials in a nonprotocol fashion, and 75 patients received 4 weeks (or until discharge) of the carbapenem imipenem-cilastin (1993–96). The etiology of pancreatitis was not noted. Among the time periods, the incidence of secondary pancreatic infection was reduced from 76% to 27%—a significant reduction comparing all subgroups. The mortality rate was reduced from 16% to 5%, a reduction that approached (but did not reach) statistical significance. The bacterial flora cultured was not noted, and thus the influence of prolonged antimicrobial prophylaxis on the development of resistant organisms is not known. This study is marred by the fact it is retrospective and took place during an extended time period when critical care treatment of those with AP no doubt improved. Nonetheless, it is suggested the

prophylactic carbapenem use may be beneficial to prevent pancreatic sepsis.

Isenmann and colleagues performed a multicenter, randomized, placebo-controlled, double-blind study on the effect of ciprofloxacin and flagyl, administered for a minimum of 14 days, in preventing infected pancreatic necrosis and thereby reducing mortality (25). One hundred fourteen patients with severe AP defined as a C-reactive protein (CRP) level >150 mg/L and/or the presence of pancreatic necrosis on contrast-enhance CT and entering within 72 hours of admission were studied. Study patients were converted to open antibiotic therapy if extra or *de novo* pancreatic sepsis was documented, multiple organ failure developed, or CRP levels increased. The etiology of pancreatitis was predominantly biliary and alcohol-related. Of the 58 patients randomized to treatment, only 16 required conversion to open antimicrobial administration versus 26 in the placebo group—a significant difference. However, the incidence of secondary and extrapancreatic infections was not different, nor was the mortality rate. Approximately one-half of the isolates in both groups with infected necrosis were Gram-positive organisms. However, it was not noted how these isolates were obtained—open versus percutaneous. Thus, although empiric antibiotic treatment did not lead to development of resistant or fungal organisms, it failed to prevent pancreatic and systemic infections, and it did not reduce mortality in this study. It should be noted, however, that the initial power analysis called for a study population of 200 patients assuming an incidence of pancreatic infection of 40%. Surprisingly, this study was terminated after an interim analysis because, the authors state, infected pancreatic necrosis occurred in 7/53 treated patients versus 5/52 receiving placebo, and this was a reverse trend. Certainly it could be argued that study recruitment should have continued.

Dellinger and colleagues reported a multicenter similarly designed study and patient population to that of Isenmann comparing prophylactic meropenem infusion to placebo in 40 patients each within 5 days of onset of severe acute pancreatitis and delivered for 7–21 days (26). In contrast to the study by Isenmann, most patients in this study had documented pancreatic necrosis $>30\%$ consistent with severe disease. The incidence of developing pancreatic infection, the number of operative interventions on the pancreas, and the mortality rate were not different between groups. The utilization of prophylaxis did not increase the incidence of resistant organisms with Gram-positive and -negative flora predominating. The authors concluded the antibiotic prophylaxis did not reduce septic pancreatic infections in those with severe AP, as was confirmed in a most recent meta-analysis (27). This study again did not reach its desired power analysis assuming an incidence of pancreatic infection of 40%, and it was not continued to reach the desired number of patients due to a “restriction of resources.”

To summarize, the utilization of prophylactic antibiotics in severe necrotizing pancreatitis is well tolerated and may alter the flora recovered if infection ensues but is not associated with the development of resistant organisms. Randomized, double-blinded, placebo-controlled studies to date have failed to recruit enough patients to establish a statistically significant difference, if it exists, between prophylaxis and placebo. It is unlikely that given the low

incidence of severe pancreatitis as well as the heterogeneity of patients and the treatment they receive that future studies might improve on those reported to date. Given the morbidity and mortality associated with infected necrosis, it would seem reasonable to employ antimicrobial prophylaxis in those with severe pancreatitis *and* significant necrosis if there is evidence of organ failure or hemodynamic instability (Grade B recommendation).

IS ENTERAL NUTRITION SAFE AND SUPERIOR TO TOTAL PARENTERAL NUTRITION IN AP?

Nutritional support in severe AP is vital due to the local and systemic inflammatory response that increases metabolic demands, resulting in hypercatabolism (28). In an attempt to rest the pancreas and not worsen its severity, hyperalimentation has traditionally provided the backbone of therapy to meet nutritional needs. In addition, severe pancreatitis is often associated with gastric stasis and/or intestinal ileus, limiting enteral feeding, and many patients are simply too ill to consume adequate calories. It has long been recognized that enteral nutrition (EN) is superior to the parenteral route in terms of immune competence, metabolic homeostasis, reducing catheter-related sepsis, as well as the overall cost of support, and its utilization in other areas of surgical care has been well established (29). Most recently, the paradigm that EN in severe pancreatitis exacerbates the disease or will not be tolerated has been challenged. The utilization of this mode of nutritional support, however, must not present its own set of complications *and* it must prove superior outcomes to standard therapy with total parenteral nutrition (TPN).

In the setting of severe AP, the utilization of jejunal nutrition has its own inherent limitations and potential associated complications beyond just intolerance secondary to disease associated ileus. Nasojejunal tube placement typically requires either radiologic or endoscopic advancement, either of which can be problematic in an unstable intensive care unit patient. Bedside placement can be used but is cumbersome and time-consuming (30). In addition, jejunal feedings in the hypotensive patient, those with large volume fluid requirements, and those with clinical evidence of an ileus have been associated with the development of catastrophic small bowel necrosis (31). With these caveats in mind, jejunal feedings have been successfully implemented in AP in several comparison studies with TPN.

Windsor et al. investigated the impact of EN on decreasing the acute phase response and thereby the disease severity of AP when compared with TPN in a randomized trial of 34 patients (32). Severe pancreatitis was defined as an Imrie score >3 , and nasojejunal tubes were placed radiologically (8). Enrollment was within 48 hours of admission, and the influence of nutritional support was assessed after seven days of implementation. The degree of inflammation was assessed by serial Imrie and APACHE II scores, CRP levels, measurement of immunoglobulin M anticore endotoxin antibodies (EndoCAB) (a higher level suggesting continued endotoxin exposure), and total antioxidant potential (TAC) (a lower level suggesting a continued inflammatory response) (5). Patients were followed clinically for the development of the systemic inflammatory response

syndrome, intra-abdominal sepsis, multiple organ failure, the need for operative intervention and mortality. Four of 16 patients in the EN group required a temporary reduction in their goal rate due to intolerance. The EN group had a significant reduction in CRP levels and APACHE II scores—a trend *not* found in the TPN group. EndoCAB antibodies significantly increased in those receiving TPN but remained unchanged in those fed enterally. Similarly, TAC levels were significantly higher in those receiving EN. The clinical parameters assessed demonstrated a superior trend favoring EN. The authors conclude that EN is superior to TPN in attenuating the acute phase response of pancreatitis that may translate to an improved clinical course.

McClave et al. randomized 32 well-matched patient admissions to EN via a nasojejunal tube placed endoscopically or TPN within 48 hours (33). Ranson scores were only modestly elevated, suggesting these patients did not have severe pancreatitis. The vast majority of patients in both groups reached goal calories by day 4 of implementation. There was no mortality and no difference between groups with respect to pain scores, serum albumin level, hospital LOS, and the incidence of nosocomial infection. Serial Ranson and APACHE III scores were reduced in the EN group and increased in the TPN group, but this difference reached significance on only one occasion and it is unclear how to interpret “serial” Ranson criteria. EN was significantly less expensive. In a cautionary note, one patient had an exacerbation of pancreatitis when the nasojejunal tube migrated back into the stomach, and three patients in the EN group had recurrent pancreatitis on initiation of an oral diet. LOS was not improved. The authors tenuously conclude that EN may promote more rapid resolution of the toxicity and stress response of pancreatitis and that this should be the preferred method of caloric delivery.

The issue was reexamined in those with severe pancreatitis in a well-performed randomized study of 38 patients by Kalfarentzos and colleagues (34). Severe pancreatitis was defined as 3 or more Imrie criteria or an APACHE II score >8 combined with a CRP concentration >120 mg/L within 48 hours of admission and Grade D or E findings by Baltazar criteria (4,7,8). All patients received antibiotic prophylaxis with imipenem. The 18 patients randomized to EN had a nasenteric tube placed fluoroscopically within 48 hours of admission (2 patients had unsuccessful placement and were excluded from analysis). Feedings were initiated immediately thereafter in resuscitated, “stable” patients. There was no difference in the clinical course of either group with respect to the need for operation, LOS, and mortality. Target nutritional goals were reached, and nitrogen balance improved progressively and equally in both groups. The mean number of infections per patient as well as the overall complication rate was significantly less in those receiving EN; however, few pancreatic infections were noted. EN was significantly less expensive. The authors conclude that early EN in those with severe pancreatitis is safe and preferential to TPN.

Petrov et al. examined the impact of EN on reducing secondary pancreatic infections and mortality in a randomized trial of 69 well-matched patients presenting with severe AP defined as an APACHE II score >8 and/or a CRP concentration >150 mg/dl (35). Nutritional support

was initiated within 72 hours of presentation with enteral catheters positioned radiologically. The hemodynamic stability (or lack thereof) of patients receiving EN was not reported. Prophylactic antibiotics were routinely used in both groups. When compared with TPN, EN was associated with a statistically significant reduction in pancreatic and extrapancreatic septic morbidity. Because pancreatic infection mandated operative intervention, the need for surgery was significantly reduced in those receiving EN as well. Mortality from pancreatic sepsis and/or multiple organ failure was significantly worse in those receiving TPN. The need for additional feeding tube positioning, abdominal bloating, diarrhea, and a reduction in the rate of administration of support were all more common in those receiving EN. The authors conclude that EN could be an important adjunct in reducing pancreatic infectious complications and thereby mortality in those with severe AP.

In conclusion, when compared with TPN, careful utilization of EN is well tolerated, reduces the inflammatory response of AP, reduces infectious morbidity, and is less expensive. Data demonstrating a clinical improvement with respect to the need for operative intervention, a shorter hospital LOS, and lower disease-related mortality when EN is used remain sparse but promising due to the small number of patients reported in comparative studies to date. Although further study is needed and with the acknowledged difficulty in feeding tube placement, EN in the hemodynamically stable patient with severe pancreatitis is favored with close monitoring of tolerance (Grade B recommendation). In those undergoing surgical debridement, a surgically placed jejunostomy tube is strongly recommended (36). If jejunal feeding is not tolerated due to hemodynamic instability or ileus, TPN remains an important therapy.

IS GASTRIC FEEDING SAFE AND EQUIVALENT TO JEJUNAL FEEDING IN AP?

With the aforementioned benefits of jejunal feedings, a reasonable extrapolation would be to simplify the limitations of tube placement by feeding directly into the stomach. As previously noted, such a management scheme may be associated with its own inherent complications—specifically, intolerance due to gastric stasis, the possibility of aspiration in those without airway protection, and an exacerbation of pancreatitis due to stimulation of the pancreas. Several clinical trials have compared these routes of administration.

Eatock and colleagues randomized 49 well-matched patients with severe AP defined as an Imrie score >3 , and APACHE II score >6 or a CRP >150 mg/dl to nasogastric (NG) versus endoscopically placed nasojejunal (NJ) feedings beginning within 72 hours of onset of symptoms (37). All but one patient tolerated the enteral route, and the majority of patients in both groups were receiving at least 75% of goal calories within 48 hours of initiation of feedings. Groups did not differ with respect to follow-up APACHE II scores, CRP levels, or pain analog scales and mortality was not statistically different (24.5% of study population). Gastrointestinal complications were equivalent between groups. One patient required repeat endoscopy to replace

an NJ tube. The authors conclude that NG feeding is simpler, less expensive, and equivalent to the NJ route.

Kumar et al. randomized 31 evenly matched patients with severe AP defined as organ failure and an APACHE II score >8 or Balthazar score >7 to NG ($n = 15$) or NJ (placed endoscopically) feedings (38). Importantly, patients in shock (systolic blood pressure <90 mmHg) were appropriately excluded, and feedings were gradually increased over a seven-day period. Patients were assessed for study accrual up to four weeks after onset of symptoms—a delay in initiation that might allow better tolerance of feedings. No patient required TPN once the goal rate of feeding was achieved (day 7). When compared with the NJ route, NG feedings were associated with similar rates of pancreatic infection and operative intervention, and the LOS and mortality was not different between groups. Anthropometric and nutritional parameters declined regardless of route of administration, and complications were similar. Neither modality exacerbated pancreatitis. The authors conclude that both routes of administration, when gradually delivered, are well tolerated but fail to reverse the catabolism associated with the disease.

Eckerwall and colleagues compared NG feedings to TPN in 48 well-matched patients with severe AP defined as an APACHE II score >8 and/or a CRP level >150 mg/dl (39). The goal of the study was to assess the impact of nutrient delivery on the inflammatory response of AP during the first 10 days of illness. Nutritional support was started within 24 hours of admission with a target goal reached in 66% of the entire population with no difference between groups. No patient receiving NG feeds had aspiration. EndoCAB concentrations decreased equally in both groups during the study period. Only one patient in the entire series required pancreatic surgery. The authors concluded that NG feedings were tolerated well in those with predicted severe AP but did not attenuate the inflammatory response associated with the disease when compared with TPN.

In summary, these preliminary studies suggest that NG feeding seems to be tolerated as well as NJ feeding in those with severe AP in the hemodynamically stable patient without exacerbating the disease process provided close assessment of tolerance is made (Grade B recommendation). Tube placement is easier and less costly. The relationship of NG feedings to a decline in secondary pancreatic infections and disease related mortality has yet to be ascertained.

CAN THE INFLAMMATORY CASCADE OF AP BE ALLEVIATED?

Given the complications associated with severe AP, much attention has focused on the potential application of inflammatory modulators in both experimental and human studies that might ameliorate the severity of disease and thereby reduce morbidity and mortality. Whereas a substantial amount of data has focused on prophylactic utilization of these agents (such as prior to ERCP), this review focuses on human studies after the onset of AP.

Somatostatin and its analogs strongly inhibit the production of pancreatic enzymes and theoretically might attenuate the degree of inflammation associated with AP if

instituted early in its clinical course. In the only large, double-blind, prospective multicenter study to date of patients with moderate to severe AP, Uhl et al. randomized 251 patients from 32 hospitals within 96 hours of admission to placebo, 100 or 200 mcg of octreotide three times daily for a seven-day course in attempt to alleviate complications and mortality associated with this disease (40). Moderate and severe pancreatitis were not defined by traditional grading systems, but the acuity as assigned seemed appropriate. Importantly, patients on an as-needed basis received peritoneal lavage, ERCP, and interventional or surgical procedures during this study that had the obvious potential to skew study results. Nonetheless, APACHE II scores, the need for surgical intervention, LOS, and mortality did not differ between groups. The authors concluded that octreotide does not offer treatment benefit in AP.

The use of protease inhibitors could theoretically reduce the intracellular activation of pancreatic proteolytic enzymes, thereby attenuating the inflammatory response of AP. The majority of clinical experience has been with the synthetic protease inhibitor gabexate mesilate (GM), an agent that reduces, in addition to other inflammatory mediators, trypsin activity. In an early study from Spain, Valderrama et al. randomized 100 patients to continuous infusion GM administered within 12 hours of onset of symptoms for a 4–12-day time period (41). In this double-blind study, the majority of patients had mild pancreatitis. No difference was found with respect to disease-related complications, LOS, or mortality. In a further double-blind study by Buchler and colleagues, 223 patients beginning treatment within seven days of onset of symptoms with moderate to severe AP (mean Ranson criteria 3.7) from 29 hospitals were randomized to GM or placebo for seven days (42). There was no difference with respect to mortality or complications associated with AP between groups. Opposite results were found by Chen et al. in a prospective study of 52 patients with severe AP (Ranson criteria >5) randomized to GM ($n = 26$) for seven days versus placebo within 72 hours of the onset of symptoms (43). The incidence of complications requiring surgical intervention and mortality were reduced in those receiving GM. A recent meta-analysis specifically examining mortality following AP concluded there might be a survival benefit to GM therapy in those with moderate to severe pancreatitis (44).

Oxidative stress is likely contributory to the early development of AP and depletion of favorable antioxidants correlating with the severity of disease and has been demonstrated in humans (45). Siriwardena et al. examined the impact of combination antioxidant therapy delivered for seven days beginning within 72 hours of admission in a randomized, double blind, placebo controlled series of 43 patients with severe predicted AP (APACHE II score >8) (46). Patients receiving therapy had higher antioxidant levels and a diminution of markers of oxidative stress, although this difference did not reach significance. The incidence of organ failure at seven days and mortality were also not different. The authors conclude this mode of therapy fails to benefit those with severe AP.

Platelet-activating factor (PAF) is an inflammatory mediator that both induces AP and is released during AP in experimental pancreatitis (47,48). Such findings formed the basis for human studies with the use of the PAF antagonist

that binds to the PAF receptor. Kingsnorth et al. assessed a three-day regimen of lexipafant delivered within 48 hours of the onset of symptoms in a randomized, double-blind study of 83 patients with AP, 29 of whom had severe disease (49). Organ failure significantly improved from baseline in those receiving study medication. CRP levels were not different between treatment arms. The need for surgical intervention, LOS, and mortality were not analyzed in this study. McKay and colleagues studied the role of lexipafant in a randomized, placebo-controlled trial of 50 well-matched patients with severe predicted AP (APACHE II score >6, CRP level >120 mg/L) (50). Study medication was received within 72 hours of onset of symptoms and continued for five to seven days. The mortality rate in this study was 18% (testifying to the severity of disease of those enrolled) but was not different between treatment arms. There was an improvement in organ failure at day 7, the

significance of which is unclear in this small study. Johnson et al. randomized 186 patients with severe AP (APACHE II >6) to receive lexipafant within 72 hours of onset of symptoms for seven days in a double-blind, placebo-controlled study (51). The incidences of organ failure, local complications, LOS, and death were not different between treatment arms. The authors conclude that PAF was ineffective in ameliorating the inflammatory response in severe AP.

In summary, despite the theoretic and experimental advantages of blocking the inflammatory cascade of AP, randomized placebo-controlled trials in humans to date have failed to demonstrate an advantage over standard supportive care in terms of reducing organ failure, local complication, LOS, and mortality (Grade A recommendation). Further work with novel agents and perhaps combination therapy are necessary.

Level of Evidence

Question	Answer	Levels of evidence	Grade	Refs.
Scoring systems: is one superior to another in predicting the clinical course of AP?	No. Systems are complimentary not mutually exclusive.	IIb	B	10-12
What is the role of ERCP in acute biliary pancreatitis?	Only if evidence of cholangitis or biliary obstruction exists.	Ia	A	13-16
What is the role of prophylactic antibiotics in severe AP?	Studies do not show a benefit. May be reasonable in severe AP.	Ib	B	23-27
Is EN safe and superior to TPN in AP?	Safe and less expensive but clinical benefit unclear.	IIb	B	32-35
Is gastric feeding safe and equivalent to jejunal feeding in AP?	Safe in hemodynamically stable patients if tolerated.	IIb	B	40-46
Can the inflammatory cascade of AP be alleviated?	Not with current drug regimens.	Ib	A	49-51

Abbreviations: AP, acute pancreatitis; EN, enteral nutrition; ERCP, endoscopic retrograde cholangiopancreatography; TPN, total parenteral nutrition.

REFERENCES

- Whitcomb DC. Acute pancreatitis. *N Engl J Med* 2006; 354: 2142-50.
- Bradley EL. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, GA, September 11-13, 1992. *Arch Surg* 1993; 128: 586-90.
- Gloor B, Muller CA, Worni M, et al. Late mortality in patients with severe acute pancreatitis. *Br J Surg* 2001; 88: 975-9.
- Knaus WA, Draper EA, Wagner DP, et al. APACHE II. A severity of disease classification system. *Crit Care Med* 1985; 13: 818-29.
- Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest* 1991; 100: 1619-36.
- Ranson JHC, Rifkind KM, Roses DF, et al. Prognostic signs and the role of operative management in acute pancreatitis. *Surg Gynecol Obstet* 1974; 139: 69-81.
- Balthazar EJ, Robinson DL, Megibow AJ, et al. Acute pancreatitis: value of CT in establishing prognosis. *Radiology* 1990; 174: 331-6.
- Blamey S, Imrie C, O'Neill J, et al. Prognostic factors in acute pancreatitis. *Gut* 1984; 25: 1340-6.
- Taylor SI, Morgan DL, Denson KD, et al. A comparison of Ranson, Glasgow and APACHE II systems to a multiple organ system score in predicting patient outcome in pancreatitis. *Am J Surg* 2005; 189: 219-22.
- Yeung YP, Lam BYK, Yip AWC. APACHE system is better than Ranson system in the prediction of severity of acute pancreatitis. *Hepatobil Pancreat Dis Int* 2006; 5: 294-9.
- Leung T, Lee C, Chen H, et al. Balthazar computed tomography severity index is superior to Ranson criteria and APACHE II scoring system in predicting acute pancreatitis outcome. *World J Gastroenterol* 2005; 11: 6049-52.
- Chatzicostas C, Roussomoustakaki M, Vardas E, et al. Balthazar computed tomography severity index is superior to Ranson criteria and APACHE II and III scoring systems in predicting acute pancreatitis outcome. *J Clin Gastroenterol* 2003; 36: 253-60.
- Neoptolemos JP, Carr-Locke DL, London NJ, et al. Controlled trial of urgent endoscopic cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. *Lancet* 1988; 2: 979-83.
- Fan S, Lai E, Mok F, et al. Early treatment of acute biliary pancreatitis by endoscopic papillotomy. *N Engl J Med* 1993; 328: 228-32.
- Folsch UR, Nitsche R, Ludtke R, et al. Early ERCP and papillotomy compared with conservative treatment for acute biliary pancreatitis. The German Study Group on acute biliary pancreatitis. *N Engl J Med* 1997; 336: 237-42.
- Oria A, Cimmino D, Ocampo C, et al. Early endoscopic intervention versus early conservative management in patients with acute gallstone pancreatitis and biliopancreatic obstruction: a randomized clinical trial. *Ann Surg* 2007; 245: 10-17.
- Behrns KE, Ashley SW, Hunter JG, et al. Early ERCP for gallstone pancreatitis: for whom and when? *J Gastrointest Surg* 2008; 12: 629-33.
- Petrov MS, van Santvoort HC, van der Heijden GJ, et al. Early endoscopic retrograde cholangiopancreatography versus

- conservative management in acute biliary pancreatitis: a meta-analysis of randomized trials. *Ann Surg* 2008; 247: 250–7.
19. Rodriguez JR, Razo AO, Targarona J, et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. *Ann Surg* 2008; 247: 294–9.
 20. Hoerauf A, Hammer S, Muller Myhsok B, et al. Intra-abdominal *Candida* infection during acute necrotizing pancreatitis has a high prevalence and is associated with increased mortality. *Crit Care Med* 1998; 26: 2010–15.
 21. Buchler M, Malfertheiner P, Friess, H et al. Human pancreatic tissue concentration of bactericidal antibiotics. *Gastroenterology* 1992; 103: 1902–8.
 22. Bassi C, Pederzoli P, Vesentini S, et al. Behavior of antibiotics during human necrotizing pancreatitis. *Antimicrob Agents Chemother* 1994; 38: 830–6.
 23. Penderzoli P, Bassi C, Vesentini S, et al. A randomized multicenter clinical trial of antibiotic prophylaxis of septic complications in acute necrotizing pancreatitis with imipenem. *Surg Gynecol Obstet* 1993; 176: 480–3.
 24. Ho HS, Frey CF. The role of antibiotic prophylaxis in severe acute pancreatitis. *Arch Surg* 1997; 132: 487–3.
 25. Isenmann R, Runzi M, Kron M, et al. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled, double-blind trial. *Gastroenterology* 2004; 126: 997–1004.
 26. Dellinger EP, Tellado JM, Soto NE, et al. Early antibiotic treatment for severe necrotizing pancreatitis: a randomized, double-blind, placebo-controlled study. *Ann Surg* 2007; 245: 674–83.
 27. Bai Y, Gao J, Zou D, et al. Prophylactic antibiotics cannot reduce infected pancreatic necrosis and mortality in acute necrotizing pancreatitis: evidence from a meta-analysis of randomized controlled trials. *Am J Gastroenterol* 2008; 103: 104–10.
 28. Dickerson RN, Vehe KL, Mullen JL, et al. Resting energy expenditure in patients with pancreatitis. *Crit Care Med* 1991; 19: 484–90.
 29. Kudsk KA. Beneficial effect of enteral nutrition. *Gastrointest Endosc Clin N Am* 2007; 17: 647–62.
 30. Zaloga GP. Bedside method for placing small bowel feeding tubes in critically ill patients. A prospective study. *Chest* 1991; 100: 1643–6.
 31. Schunn CD, Daly JM. Small bowel necrosis associated with postoperative jejunal tube feeding. *J Am Coll Surg* 1995; 180: 410–16.
 32. Windsor A, Kanwar S, Li A, et al. Compared with parenteral nutrition, enteral feeding attenuates the acute-phase response and improves disease severity in acute pancreatitis. *Gut* 1998; 42: 431–5.
 33. McClave SA, Greene LM, Snider HL, et al. Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. *J Parenter Enter Nutr* 1997; 21: 14–20.
 34. Kalfarentzos F, Kehagias J, Mead N, et al. Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. *Br J Surg* 1997; 84: 1665–9.
 35. Petrov MS, Kukosh MV, Emelyanov NV. A randomized controlled trial of enteral versus parenteral feeding in patients with predicted severe acute pancreatitis shows a significant reduction in mortality and in infected pancreatic complications with total enteral nutrition. *Dig Surg* 2006; 23: 336–45.
 36. Kudsk K, Campbell S, O'Brien T, et al. Postoperative jejunal feedings following complicated pancreatitis. *Nutr Clin Pract* 1990; 5: 14–17.
 37. Eatock F, Chong P, Menezes N, et al. A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis. *Am J Gastroenterol* 2005; 100: 432–9.
 38. Kumar A, Singh N, Prakash S, et al. Early enteral nutrition in severe acute pancreatitis: a prospective randomized controlled trial comparing nasojejunal and nasogastric routes. *J Clin Gastroenterol* 2006; 40: 431–4.
 39. Eckerwall G, Axelsson J, Andersson R. Early nasogastric feeding in predicted severe acute pancreatitis: a clinical randomized study. *Ann Surg* 2006; 244: 959–67.
 40. Uhl W, Buchler MW, Malfertheiner P, et al. A randomized, double blind, multicentre trial of octreotide in moderate to severe acute pancreatitis. *Gut* 1999; 45: 97–104.
 41. Valderrama R, Perez-Mateo M, Navarro S, et al. Multicenter double-blind trial of gabexate mesilate (FOY) in unselected patients with acute pancreatitis. *Digestion* 1992; 51: 65–70.
 42. Buchler M, Malfertheiner P, Uhl W, et al. Gabexate mesilate in human acute pancreatitis. German pancreatitis study group. *Gastroenterology* 1993; 104: 1165–70.
 43. Chen HM, Chen JC, Hwang TL, et al. Prospective and randomized study of gabexate mesilate for the treatment of severe acute pancreatitis with organ dysfunction. *Hepatogastroenterology* 2000; 47: 1147–50.
 44. Seta T, Noguchi Y, Shimada T, et al. Treatment of acute pancreatitis with protease inhibitors: A meta-analysis. *Eur J Gastroenterol Hepatol* 2004; 16: 1287–93.
 45. Bonham MJ, Abu-Zidan FM, Simovic MO, et al. Early ascorbic acid depletion is related to the severity of acute pancreatitis. *Br J Surg* 1999; 86: 1296–301.
 46. Siriwardena AK, Mason JM, Balachandra S, et al. Randomized, double blind, placebo controlled trial of intravenous antioxidant (n-acetylcysteine, selenium, vitamin C) therapy in severe acute pancreatitis. *Gut* 2007; 56: 1439–44.
 47. Yatsumoto F, Manabe T, Kyogoku T, et al. Platelet-activating factor involvement in the aggravation of acute pancreatitis in rabbits. *Digestion* 1994; 55: 260–7.
 48. Kald B, Kald A, Ihse I, et al. Release of platelet-activating factor in acute experimental pancreatitis. *Pancreas* 1993; 8: 440–2.
 49. Kingsnorth AN, Galloway SW, Formela LJ. Randomized, double-blind phase II trial of lexipafant, a platelet-activating factor antagonist, in human acute pancreatitis. *Br J Surg* 1995; 82: 1414–20.
 50. McKay CJ, Curran F, Sharples C, et al. Prospective placebo-controlled randomized trial of lexipafant in predicted severe acute pancreatitis. *Br J Surg* 1997; 84: 1239–43.
 51. Johnson CD, Kingsnorth AN, Imrie CW, et al. Double-blind, randomized, placebo controlled study of a platelet activating factor antagonist, lexipafant, in the treatment and prevention of organ failure in predicted severe acute pancreatitis. *Gut* 2001; 48: 62–69.

Pancreatic Pseudo-cysts

Olga N. Tucker and Raul J. Rosenthal

Clinical Questions		
Question	Answer	Grade of recommendation
What is the definition of a pancreatic pseudo-cyst?	The Atlanta classification system provides a definition for pancreatic pseudo-cyst. However, this system has been recently criticized.	C
What is the incidence of pancreatic pseudo-cysts?	The true incidence of pancreatic pseudo-cyst is unknown.	C
What is the incidence of complicated pancreatic pseudo-cysts?	The true incidence of complicated pancreatic pseudo-cyst is unknown.	C
What is the optimal time for intervention once the diagnosis of pancreatic pseudo-cyst has been confirmed?	The optimal time of intervention for pancreatic pseudo-cysts is unknown.	C
What are the optimal imaging modalities for diagnosis of a pancreatic pseudo-cyst?	Contrast-enhanced computed tomography is the imaging modality of choice.	C
What is the optimal method of therapeutic intervention?	The optimal approach to pancreatic pseudo-cyst drainage remains controversial.	C
Do delays in surgical intervention affect outcome?	Yes.	C

INTRODUCTION

Pancreatic pseudo-cysts comprise $\geq 75\%$ of all cystic lesions of the pancreas. They generally arise as a complication of acute or chronic pancreatitis, however, other causes exist. Acute pancreatitis is usually a mild and self-limiting disorder, but approximately 20% of patients develop a severe form with local and systemic complications. Fluid collections representing an exudative or serous reaction to injury of the pancreas occur in approximately 50% of patients with moderate to severe pancreatitis. Approximately 50% of these collections resolve spontaneously within six weeks. However, 5–15% progress to pseudo-cyst formation (1–3). Approximately 20–40% of pancreatic pseudo-cysts develop in patients with chronic pancreatitis, due to chronic and progressive ductal obstruction, dilation, and disruption (1,3). Other causes include trauma, iatrogenic surgical pancreatic injury, pancreatic ductal adenocarcinoma, and very rarely hemorrhagic pancreatic pseudo-cysts associated with autoimmune pancreatitis (4–8).

Important issues to consider in the management of these lesions are the exclusion of other causes of peri- or intrapancreatic fluid collections that may complicate acute pancreatitis, requiring alternative approaches of therapeutic intervention, determination of optimal time for intervention once the diagnosis of pancreatic pseudo-cyst has been confirmed, and consideration of the optimal management approach.

WHAT IS THE DEFINITION OF A PANCREATIC PSEUDO-CYST?

Accurate definition of a pancreatic pseudo-cyst with differentiation from other pancreatic and peripancreatic fluid collections is essential for optimal management and outcome. A classification system for acute pancreatitis was published in 1993 following the International Symposium on Acute Pancreatitis in Atlanta, Georgia, in September 1992 (9,10). This was an attempt at reaching an international agreement to create a uniform set of accepted clinically based definitions for acute pancreatitis and associated local complications, including pancreatic pseudo-cysts (Level IV evidence).

Definitions of local complications of acute pancreatitis according to the Atlanta criteria (Level V evidence) (9) are as follows:

- Acute fluid collections: Occur early in the course of acute pancreatitis, are located in or near the pancreas, and always lack a wall of granulation of fibrous tissue. Spontaneous regression occurs in approximately 50% of cases. In the other 50%, an acute fluid collection progresses to a pancreatic abscess or pseudo-cyst.
- Pancreatic necrosis: Diffuse or focal area(s) of nonviable pancreatic parenchyma, typically associated with peripancreatic fat necrosis. Nonenhanced pancreatic parenchyma $>3\text{cm}$ diameter or involving $>30\%$ of the area of the pancreas is required.

- Acute pancreatic pseudo-cyst: (1) A collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, which arise as a consequence of acute pancreatitis, pancreatic trauma, or chronic pancreatitis; (2) their formation requires four or more weeks from onset of pancreatitis; (3) pseudo-cyst contents should consist of clear pancreatic fluid with no pus or necrotic debris; (4) are round or ovoid and most often sterile. In the presence of pus, the lesion is called a pancreatic abscess.
- Pancreatic abscess: Circumscribed, intra-abdominal collection of pus, usually in proximity to the pancreas, containing little or no pancreatic necrosis, which arises as a consequence of acute pancreatitis or pancreatic trauma. Usually arises ≥ 4 weeks after onset of symptoms.

However, a recent review by Bollen et al. on 447 articles retrieved using a MEDLINE literature search on studies published after 1993 on the use of the Atlanta criteria in the definition and management of acute pancreatitis, including 3 meta-analysis, 34 randomized controlled trials, 12 guidelines, and 82 reviews, suggested the existence of a large variation in the utilization and interpretation of the Atlanta definitions of local complications including pancreatic pseudo-cysts (Level II evidence) (11). Alternative or non-uniform definitions were frequently used. The authors suggested the need for a revision of the criteria (11). In 38 reviewed articles, pseudo-cysts were defined as collections containing both fluid and solid necrotic debris (11). According to Bradley, the definition of a pancreatic pseudo-cyst should be an encapsulated homogenous fluid collection without necrotic contents, and it should be carefully distinguished from a peripancreatic acute fluid collection to determine appropriate management (12). The authors concluded that treatment outcome in many published studies could not be interpreted with accuracy due to the inconsistencies in reporting techniques of distinctions between acute fluid collections and pancreatic pseudo-cysts, and acute and chronic pseudo-cysts (11).

Answer: The Atlanta classification system provides a definition for pancreatic pseudo-cyst and local complications of acute pancreatitis (Level V evidence; Grade D recommendation). However, this system has not been validated or used uniformly or consistently from 1993 to 2006 to allow accurate comparison of management outcome between centers, and has been recently criticized (Level II evidence; Grade C recommendation).

WHAT IS THE INCIDENCE OF PANCREATIC PSEUDO-CYSTS?

The true incidence of pancreatic pseudo-cysts is unknown due to inconsistencies in the application of a uniform definition, the timing of diagnosis, differing techniques of clinical monitoring, the use of varying diagnostic modalities, the use of varying clinical and radiological severity grading systems, the complexity and variety of the underlying pathology, and the wide use of multiple interventional techniques with poor reporting of treatment outcomes. Incidence rates of pseudo-cyst formation after acute pancreatitis, trauma, iatrogenic injury, and autoimmune pancreatitis have been reported in case reports, multiple case series, and review articles (Level IV evidence). Many reported case series on the incidence

and management of pseudo-cysts are limited by population heterogeneity, small patient numbers, and mixed data on patients with mild acute non-necrotizing and severe acute pancreatitis and/or the inclusion of patients with varying etiology, including acute and chronic pancreatitis. Mild and severe acute pancreatitis represent contrasting ends of a wide spectrum of disease severity with significant differences in complication and survival rates. The majority of acute fluid collections complicating acute nonnecrotizing pancreatitis will resolve spontaneously, with pseudo-cyst formation in a minority (13). The incidence of acute pancreatic pseudo-cysts is higher after severe acute pancreatitis, with higher morbidity and mortality rates related to a higher incidence of complications (14). The use of inaccurate and imprecise definitions of acute pancreatic pseudo-cysts has resulted in inaccurate representation of data. One of the most common difficulties is the differentiation of organized pancreatic and peripancreatic necrosis with associated fluid sequestration from an acute pancreatic pseudo-cyst with pancreatic necrosis (15). These clinical entities are very different in terms of treatment approach and prognosis.

Answer: The true incidence of pancreatic pseudo-cyst is unknown, due to the heterogeneity of published reports and inconsistencies in the published literature (Level IV evidence; Grade C recommendation).

WHAT IS THE INCIDENCE OF COMPLICATED PANCREATIC PSEUDO-CYSTS?

In the presence of a pancreatic pseudo-cyst, complications can arise, including pseudo-cyst infection with abscess formation; intracystic hemorrhage; rapid expansion with increasing abdominal pain; obstruction of adjacent organs, including esophagus, stomach, duodenum, jejunum, colon, biliary tree, or retroperitoneal structures; and/or rupture into an adjacent viscus, such as the stomach, duodenum, colon, or body cavity, including the peritoneal cavity, causing ascites, pleural space resulting in an effusion, bronchus, or pericardium with fistula formation (14,16–21). Pseudo-cysts may erode into an adjacent major artery, more commonly the splenic artery, resulting in a pseudo-aneurysm and/or hemorrhage. A massive gastrointestinal bleed can occur if the pseudo-aneurysm communicates with the main pancreatic duct, a condition known as hemossuccus pancreaticus. Portal and splenic vein thrombosis have been reported in patients with pancreatic pseudo-cysts with persistent inflammatory response. Although the occurrence of complications is uncommon, no accurate figures are available from the published literature on the true incidence of morbidity associated with pancreatic pseudo-cysts. Available data have been extracted from multiple case series, case reports, and review articles (Level IV evidence) (14,21–29). The incidence of complicated pseudo-cysts is higher in patients following severe acute pancreatitis, as the majority of acute fluid collections in patients with mild acute non-necrotizing pancreatitis resolve without pseudo-cyst formation (13). In a recent study by Ocampo et al., 43 (59%) of 73 patients over a 10-year period with an acute pancreatic pseudo-cyst following severe acute pancreatitis developed complications, including infection in 74%, perforation in 21%, and bleeding in 4.6% (14).

Answer: Complications of pancreatic pseudo-cysts are uncommon, however, no accurate figures of the true

incidence are available in the published literature (Level IV evidence; Grade C recommendation).

WHAT IS THE OPTIMAL TIME FOR INTERVENTION ONCE THE DIAGNOSIS OF PANCREATIC PSEUDO-CYST HAS BEEN CONFIRMED?

Once identified, the timing of intervention for pancreatic pseudo-cysts remains controversial (13,21,25,29–35). Experimental studies by Warren et al. suggested a minimum period of six weeks to allow cyst wall maturation (36). Because it is not always possible to date the onset of pseudo-cyst formation, a wait period of six weeks from the time of diagnosis has been recommended (29,37). Some authors advocate elective intervention in all patients with uncomplicated acute pancreatic pseudo-cysts greater than 6 cm in size that persist for longer than six weeks regardless of symptoms due to reduction in the possibility of spontaneous resolution and a reported increase in complications (rupture, abscess, jaundice, and hemorrhage) during extended periods of observation (14,29,34). In a series by Bradley et al., a 41% complication rate and 14% mortality rate were observed during an expectant period of observation, with 23% of the complications developing in the first six weeks (29). Others advocate a nonoperative, noninterventional approach in selected patients (21,32,35). In a series by Vitas et al., spontaneous resolution was seen in 48% of patients with asymptomatic pancreatic pseudo-cysts treated conservatively, whereas only 19 of 68 patients required elective surgery over a five-year period (35). Severe life-threatening complications developed in six patients (9%) over a mean period of 46 months. Operative intervention was more common in large pancreatic pseudo-cysts ≥ 6.9 cm diameter, however, no serious complications occurred in seven patients with pseudo-cysts ≥ 10 cm diameter treated expectantly (35). Copperman et al. also advocated expectant management of asymptomatic pseudo-cysts due to the natural history of spontaneous resolution (32). Yeo and colleagues support a conservative approach in asymptomatic patients able to tolerate oral intake, with a reported spontaneous resolution rate of 60% at one year with stability or size reduction in 40% treated nonoperatively in the absence of pseudo-cyst-related mortality (21). Again, large pseudo-cyst size predicted the need for surgical intervention, with operative drainage required in 67% of those greater than 6 cm diameter, whereas only 40% less than 6 cm diameter required operative intervention (21). Warshaw et al. defined clinical and biochemical criteria in a series of 42 patients, of whom 28 had underlying chronic pancreatitis, to guide the time of optimal drainage in patients with pancreatic pseudo-cyst (34). They observed differences in the natural history and treatment requirements dictated by etiology. Spontaneous resolution occurred in only three patients following antecedent acute pancreatitis, whereas it was not seen in any patient with chronic pancreatitis. They suggested that a pseudo-cyst is unlikely to resolve when persistent for greater than six weeks, in the presence of chronic pancreatitis, a thick cyst wall on ultrasound, and a pancreatic duct abnormality other than communication with the pseudo-cyst (34). In the setting of chronic pancreatitis, the authors concluded that internal drainage procedures should be performed at the time of diagnosis to avoid unnecessary

additional expense and potential increased complications (34). Serum levels of old amylase may help guide the optimal drainage time, indicating a mature pseudo-cyst (34).

Answer: There are no published randomized controlled trials in the literature that define the optimal time of intervention for pancreatic pseudo-cysts. Evidence from highly selected multiple case series, case reports, and review articles support an expectant approach in patients with asymptomatic pseudo-cysts following acute pancreatitis regardless of size for a minimum of six weeks after diagnosis. In the setting of chronic pancreatitis, immediate intervention is feasible and may reduce the incidence of potential complications (Level III evidence; Grade C recommendation).

WHAT ARE THE OPTIMAL IMAGING MODALITIES FOR DIAGNOSIS OF A PANCREATIC PSEUDO-CYST?

A variety of radiological techniques are used in diagnosis, monitoring, and planning of therapeutic intervention for pancreatic pseudo-cysts, including transabdominal ultrasonography, contrast-enhanced abdominal computed tomography (CECT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography. Combined radiological and endoscopic modalities include endoscopic retrograde cholangiopancreatography and endoscopic ultrasonography (EUS). Upper gastrointestinal endoscopy can be performed to plan endoscopic or surgical drainage. However, prospective data from randomized controlled trials and large patient series comparing currently available imaging modalities are lacking. CECT is the preferred and most commonly utilized modality to facilitate the accurate diagnose, define extent of disease, and plan percutaneous intervention if appropriate (38). Balthazar's CT severity index, based on combined assessments of peripancreatic inflammatory collections and degree of pancreatic necrosis, can be used to predict morbidity and mortality in patients with severe acute pancreatitis (39). However, the CT appearances cannot characterize the local complications of acute pancreatitis, and in the acute phase cannot predict the development or extent of pseudo-cyst formation. Controversies exist regarding interobserver variability in interpretation of CECT and the varying definitions used to define acute peripancreatic fluid collections, including pancreatic pseudo-cysts. A recent study performed to assess the interobserver agreement of categorizing peripancreatic collections on CECT using the Atlanta classification in patients with acute necrotizing pancreatitis who underwent surgery from 2000 to 2003, involving five radiologists from 11 hospitals, demonstrated poor concordance despite the radiologists' awareness of the clinical condition of the patient and the timing of the scan. All five agreed in only 4% of 70 cases, four of five agreed in 19%, and three agreed in 60% using terminology defined by the Atlanta criteria to define CECT findings (40). In most published series, the differentiation between an acute fluid collection and a pseudo-cyst was determined four weeks from onset of disease, however, different time periods have been described from three to eight weeks (41–44). In further publications, pseudo-cysts have been defined as collections containing fluid and necrotic debris (45–47). As previously stated, pseudo-cysts should be devoid of solid necrotic debris. Controversy also exists in correct differentiating pseudo-cysts and pancreatic

abscesses because CECT has a low sensitivity in the detection of necrotic debris in collections predominantly containing fluid and poor discriminatory ability between sterile and infected collections (15,38,48–50). Misinterpretation of CECT findings may result in instrumentation of sterile collections causing infection or a delay in appropriate intervention. MRI and EUS can more accurately detect the presence of necrotic debris and may be of additional benefit in guiding appropriate intervention (38,48,51).

Answer: There are no published randomized controlled trials in the literature to define the optimal imaging modality in the diagnosis and management of pancreatic pseudo-cysts. Evidence from multiple case series, case reports, and review articles support CECT as the imaging modality of choice. Prior to anticipated intervention, an MRI scan or EUS should be performed to exclude necrotic debris in the collection (Level III evidence; Grade C recommendation).

WHAT IS THE OPTIMAL METHOD OF THERAPEUTIC INTERVENTION?

Indications for intervention include symptomatic, large (>6 cm diameter), enlarging, and complicated pseudo-cysts, and where there is a suspicion of an underlying malignancy (3,29,31,34). Options include percutaneous external drainage; endoscopic retrograde cholangiopancreatography (ERCP) with transpapillary pancreatic duct stenting; endoscopic internal drainage; laparoscopic, laparoscopic-assisted, or open surgical internal drainage and/or resection (46,52–58). No prospective randomized trials comparing therapeutic options for pancreatic pseudo-cysts have been reported to date. Clinical decisions are based on available clinical evidence from case-control studies, case series, and isolated case reports (Level III evidence). Factors that determine the approach and timing of intervention include etiology, maturity of the cyst wall, cyst location, the presence or absence of complications, and the availability of local expertise (29,34,36,37,54). Percutaneous drainage is generally performed under CT guidance to diagnose and/or drain sepsis in infected pancreatic pseudo-cysts, or in patients with symptomatic or complicated pseudo-cysts who are too unwell to undergo a more definitive procedure (14,56). In a recent series by Ocampo et al., CT-guided percutaneous and endoscopic drainage were successful in controlling sepsis in 11 of 13 patients (85%) with severe organ failure and facilitated subsequent definitive surgical management (14,56). Open surgical drainage as an initial therapeutic option has been largely replaced by minimally invasive techniques, including endoscopic and laparoscopic approaches (52). Endoscopic drainage can be performed transmurally through the wall of the stomach or duodenum or transpapillary via the pancreatic duct (46,58,59). Transpapillary drainage is performed when the pancreatic pseudo-cyst is demonstrated to communicate with the main pancreatic duct at ERCP, or in the presence of a distal pancreatic duct stricture. Laparoscopic techniques include endogastric, transgastric, or exogastric cystgastrostomy, roux en Y, or loop cystjejunostomy (52). A review of the published literature on laparoscopic and endoscopic approaches to internal drainage of pancreatic pseudo-cysts from 1974 to 2005 was recently published by Aljarabah et al. (52). Forty-four cohort series

were identified. No randomized control or comparative studies were identified. Laparoscopic procedures were performed in 118 patients in 19 reports and endoscopic procedures in 583 patients in 25 reports. The reporting of data related to the underlying etiology, patient demographic data, pseudo-cyst size, duration of the procedure, procedural complications including estimated blood loss, and hospital stay was better in the laparoscopic group. The endoscopic approach was more widely employed with fivefold greater number of reported patients. The mean cyst diameter was significantly smaller in the endoscopic group, with a mean cyst diameter of 7 cm compared to 13 cm in the laparoscopic group. In three reports, pancreatic pseudo-cysts as small as 1.5–2 cm diameter were drained endoscopically (60–62). The success rate in achieving pseudo-cyst drainage and resolution was higher after the laparoscopic (98.3%) compared to the endoscopic (80.8%) approach. Postprocedural complications were observed in 4.2% of patients after laparoscopic versus 12% after endoscopic drainage. Two patients died after endoscopic drainage (mortality rate 0.35%) with no deaths after laparoscopic drainage. The mean follow-up period was longer at 24 months (range 0.5–70) after endoscopic than laparoscopic drainage at 13 months (range 1–59) with reported recurrence in 14.4% and 2.5%, respectively (52).

Answer: The optimal approach to pancreatic pseudo-cyst drainage remains controversial. Minimally invasive internal drainage techniques by endoscopic and laparoscopic approaches are commonly employed. These approaches are safe with minimal morbidity and mortality. Although laparoscopic drainage has a higher success rate in achieving pseudo-cyst drainage and resolution, a lower postprocedural complication rate, and a lower recurrence rate, reported follow-up periods are significantly shorter. The heterogeneity of the published reports and the lack of consistency in the reporting of data limit direct comparison between the techniques. No prospective randomized trials comparing therapeutic options for pancreatic pseudo-cysts have been reported to date (Level III evidence; Grade C recommendation).

DO DELAYS IN SURGICAL INTERVENTION AFFECT OUTCOME?

Initial interventions in the management of pancreatic pseudo-cysts are increasingly directed toward nonsurgical therapies, including percutaneous external drainage or endoscopic approaches due to the perceived benefits of reduced invasiveness and lower morbidity and mortality rates. However, these techniques can be associated with significant failure rates and complications (47,63,64). Subsequent surgical intervention is often required as a salvage procedure to treat persistent or recurrent pseudo-cysts or complications such as infection following percutaneous drainage (47,63,65). Some authors have suggested that primary nonoperative intervention with delayed surgery is associated with a higher incidence of postoperative complications, readmission, morbidity, and mortality (63,66). Rao et al. retrospectively reviewed outcome in 52 patients who underwent early surgical intervention compared to 18 who underwent delayed surgery after failed CT and endoscopic drainage (63). Perioperative morbidity was twice as

frequent in the delayed surgery group (33% versus 14%), with increased time to pancreatic pseudo-cyst resolution from the initial drainage attempt (63). In a study by Ito et al., 284 consecutive patients admitted with pancreatic pseudo-cysts over a 15.5-year period were identified retrospectively, of which 46 underwent initial operative intervention (66). Percutaneous drainage was performed in 89 patients, of whom 42 required subsequent surgical intervention for failure, and endoscopic drainage was performed in 73 patients, of whom 33 required subsequent surgical intervention for failure. There was no significant difference in patient demographics; etiology of pancreatitis; location, number, and diameter of pseudo-cysts; or morphology of the main pancreatic duct in patients treated with initial surgery versus those undergoing delayed surgery. However, the median time from diagnosis to surgery was three times longer in the delayed surgery group. The main indication

for intervention in the delayed group was pseudo-cyst infection in 43% versus 13% in the early group. The delayed surgery group had a significantly higher incidence of postoperative pancreatic complications, infectious complications, perioperative morbidity, and readmission rates. Five patients died in the postoperative period due to sepsis in two and organ failure secondary to necrotizing pancreatitis in the remainder. On univariate analysis, failure of nonsurgical intervention was associated with pseudo-cyst diameter ≥ 6 cm, main pancreatic duct stricture, two or more surgical interventional procedures, and pseudo-cyst infection (66).

Answer: Surgical intervention after failed nonoperative drainage procedures is associated with higher incidences of postoperative infection, pancreatic complications, and morbidity, mortality, and readmission rates (Level III evidence; Grade C recommendation).

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
What is the definition of a pancreatic pseudo-cyst?	1992, 2008	9, 11	2	C	Revision of the classification of complications of acute pancreatitis is required.
What is the incidence of pancreatic pseudo-cysts?	1999, 2007, 2008	13–15	4	C	The true incidence is unknown.
What is the incidence of complicated pancreatic pseudo-cysts?	1979, 1983 1990, 1992, 1995, 2001, 2007	14, 21–29	4	C	The true incidence is unknown.
What is the optimal time for intervention once the diagnosis of pancreatic pseudo-cyst has been confirmed?	1957, 1979, 1985, 1990, 1992, 2001	21, 29, 32, 34–37	3	C	Timing of intervention is determined by etiology, symptoms, and complications.
What are the optimal imaging modalities for diagnosis of a pancreatic pseudo-cyst?	2006 2007	38, 40	3	C	CECT is the imaging modality of choice. Prior to intervention, an MRI or EUS should be performed to exclude necrotic debris.
What is the optimal method of therapeutic intervention?	2007	52	3	C	Minimally invasive internal drainage by endoscopic and laparoscopic approaches are safe.
Do delays in surgical intervention affect outcome?	1993, 2007	63, 66	3	C	Surgical intervention after failed nonoperative drainage is associated with a worse outcome.

Abbreviations: CECT, contrast-enhanced computed tomography; EUS, endoscopic ultrasonography; MRI, magnetic resonance imaging.

REFERENCES

- Imrie CW, Buist LJ, Shearer MG. Importance of cause in the outcome of pancreatic pseudocysts. *Am J Surg* 1988; 156: 159–62.
- Whitcomb DC. Clinical practice. Acute pancreatitis. *N Engl J Med* 2006; 18; 354: 2142–50.
- Rosao EL, Sonnenday CJ, Lillemoe KD, et al. Pseudocysts and other complications of pancreatitis. In: Yeo CJ, ed., *Shackelford's Surgery of the Alimentary Tract*, 6th edition. Philadelphia: Saunders, 2007; 1329–57.
- Kawakami H, Kuwatani M, Shinada K, et al. Autoimmune pancreatitis associated with hemorrhagic pseudocysts: a case report and literature review. *Intern Med* 2008; 47: 603–8.
- Inagi E, Shimodan S, Amizuka H, et al. Pancreatic cancer initially presenting with a pseudocyst at the splenic flexure. *Pathol Int* 2006; 56: 558–62.
- Welsch T, Kleeff J, Esposito I, et al. Autoimmune pancreatitis associated with a large pancreatic pseudocyst. *World J Gastroenterol* 2006; 12: 5904–6.
- Lin BC, Fang JF, Wong YC, et al. Blunt pancreatic trauma and pseudocyst: management of major pancreatic duct injury. *Injury* 2007; 38: 588–93.
- Yamaguchi T, Takahashi H, Kagawa R, et al. Huge pseudo-cyst of the pancreas caused by poorly differentiated invasive ductal adenocarcinoma with osteoclast-like giant cells: report of a case. *Hepatogastroenterology* 2007; 54: 599–601.
- Bradley EL III. A clinically based classification system for acute pancreatitis. Summary of the International Symposium

- on Acute Pancreatitis, Atlanta, GA, September 11–13, 1992. *Arch Surg* 1993; 128: 586–90.
10. Bradley EL III. A clinically based classification system for acute pancreatitis. *Ann Chir* 1993; 47: 537–41.
11. Bollen TL, van Santvoort HC, Besselink MG, et al. The Atlanta classification of acute pancreatitis revisited. *Br J Surg* 2008; 95: 6–21.
12. Bradley EL III. Atlanta redux. *Pancreas* 2003; 26: 105–6.
13. Lenhart DK, Balthazar EJ. MDCT of acute mild (necrotizing) pancreatitis: abdominal complications and fate of fluid collections. *Am J Roentgenol* 2008; 190: 643–9.
14. Ocampo C, Oria A, Zandalazini H, et al. Treatment of acute pancreatic pseudocysts after severe acute pancreatitis. *J Gastrointest Surg* 2007; 11: 357–63.
15. Baron TH, Morgan DE, Vickers SM, et al. Organized pancreatic necrosis: endoscopic, radiologic, and pathologic features of a distinct clinical entity. *Pancreas* 1999; 19: 105–8.
16. Nayar MK, Leiper KL, Lombard MG. Pseudocystoesophagitis: esophagitis and stricture due to pancreatic pseudocyst. *Journal of the Pancreas* 2005; 6: 194–6.
17. Boudaya MS, Alifano M, Baccari S, et al. Hemothorax as the clinical presentation of a pancreaticopleural fistula: report of a case. *Surg Today* 2007; 37: 518–20.
18. Rigaux J, Poreddy V, Al-Kawas F. Intraperitoneal and retroperitoneal hemorrhage associated with coumadin-induced bleeding into a pancreatic pseudocyst. *Clin Gastroenterol Hepatol* 2007; 5: A32.
19. Yoon SE, Lee YH, Yoon KH, et al. Spontaneous pancreatic pseudocyst-portal vein fistula presenting with pancreatic ascites: strength of MR cholangiopancreatography. *Br J Radiol* 2008; 81: e13–e16.
20. Buelta C, Velayos B, Abril C, et al. Pancreaticobronchial fistula as the first manifestation of pancreatic pseudocysts. *Gastroenterol Hepatol* 2006; 29: 274–5.
21. Yeo CJ, Bastidas JA, Lynch-Nyhan A, et al. The natural history of pancreatic pseudocysts documented by computed tomography. *Surg Gynecol Obstet* 1990; 170: 411–17.
22. Beger HG, Rau B, Isenmann R. Prevention of severe change in acute pancreatitis: prediction and prevention. *J Hepatobiliary Pancreat Surg* 2001; 8: 140–7.
23. Ho HS, Frey CF. Gastrointestinal and pancreatic complications associated with severe pancreatitis. *Arch Surg* 1995; 130: 817–22.
24. Fedorak IJ, Ko TC, Djuricin G, et al. Secondary pancreatic infections: are they distinct clinical entities? *Surgery* 1992; 112: 824–30.
25. Kourtesis G, Wilson SE, Williams RA. The clinical significance of fluid collections in acute pancreatitis. *Am Surg* 1990; 56: 796–9.
26. Bassi C, Vesentini S, Nifosi F, et al. Pancreatic abscess and other pus-harboring collections related to pancreatitis: a review of 108 cases. *World J Surg* 1990; 14: 505–11.
27. Lumsden A, Bradley EL III. Secondary pancreatic infections. *Surg Gynecol Obstet* 1990; 170: 459–67.
28. Belinkie SA, Russell JC, Deutsch J, et al. Pancreatic pseudocyst. *Am Surg* 1983; 49: 586–90.
29. Bradley EL, Clements JL Jr, Gonzalez AC. The natural history of pancreatic pseudocysts: a unified concept of management. *Am J Surg* 1979; 137: 135–41.
30. Aghdassi AA, Mayerle J, Kraft M, et al. Pancreatic pseudocysts—when and how to treat? *HPB (Oxford)* 2006; 8: 432–41.
31. Bradley EL III, Clements LJ. Spontaneous resolution of pancreatic pseudocysts: implications for timing of operative intervention. *Am J Surg* 1975; 129: 23–8.
32. Cooperman AM. An overview of pancreatic pseudocysts: the emperor's new clothes revisited. *Surg Clin North Am* 2001; 81: 391–7, xii.
33. Ndrén-Sandberg A, Dervenis C. Pancreatic pseudocysts in the 21st century. Part I: classification, pathophysiology, anatomic considerations and treatment. *Journal of the Pancreas* 2004; 5: 8–24.
34. Warshaw AL, Rattner DW. Timing of surgical drainage for pancreatic pseudocyst. Clinical and chemical criteria. *Ann Surg* 1985; 202: 720–4.
35. Vitas GJ, Sarr MG. Selected management of pancreatic pseudocysts: operative versus expectant management. *Surgery* 1992; 111: 123–30.
36. Warren WD, Marsh WM, Mullen WH Jr. Experimental production of pseudocysts of the pancreas with preliminary observations on internal drainage. *Surg Gynaecol Obstet* 1957; 105: 385.
37. Frey CF. Pancreatic pseudocyst—operative strategy. *Ann Surg* 1978; 188: 652–62.
38. Bollen TL, van Santvoort HC, Besselink MG, et al. Update on acute pancreatitis: ultrasound, computed tomography, and magnetic resonance imaging features. *Semin Ultrasound CT MR* 2007; 28: 371–83.
39. Balthazar EJ, Robinson DL, Megibow AJ, et al. Acute pancreatitis: value of CT in establishing prognosis. *Radiology* 1990; 174: 331–6.
40. Besselink MG, van Santvoort HC, Bollen TL, et al. Describing computed tomography findings in acute necrotizing pancreatitis with the Atlanta classification: an interobserver agreement study. *Pancreas* 2006; 33: 331–5.
41. De WJ, Vogelaers D, Decruyenaere J, et al. Infectious complications of acute pancreatitis. *Acta Clin Belg* 2004; 59: 90–6.
42. Soliani P, Franzini C, Ziegler S, et al. Pancreatic pseudocysts following acute pancreatitis: risk factors influencing therapeutic outcomes. *Journal of the Pancreas* 2004; 5: 338–47.
43. Maringhini A, Uomo G, Patti R, et al. Pseudocysts in acute nonalcoholic pancreatitis: incidence and natural history. *Dig Dis Sci* 1999; 44: 1669–73.
44. Zhou ZG, Zheng YC, Shu Y, et al. Laparoscopic management of severe acute pancreatitis. *Pancreas* 2003; 27: e46–e50.
45. Ndrén-Sandberg A, Ansorge C, Eiriksson K, et al. Treatment of pancreatic pseudocysts. *Scand J Surg* 2005; 94: 165–75.
46. Kruger M, Schneider AS, Manns MP, et al. Endoscopic management of pancreatic pseudocysts or abscesses after an EUS-guided 1-step procedure for initial access. *Gastrointest Endosc* 2006; 63: 409–16.
47. Nealon WH, Walser E. Surgical management of complications associated with percutaneous and/or endoscopic management of pseudocyst of the pancreas. *Ann Surg* 2005; 241: 948–57.
48. Merkle EM, Gorich J. Imaging of acute pancreatitis. *Eur Radiol* 2002; 12: 1979–92.
49. Morgan DE, Baron TH, Smith JK, et al. Pancreatic fluid collections prior to intervention: evaluation with MR imaging compared with CT and US. *Radiology* 1997; 203: 773–8.
50. Baron TH, Morgan DE. The diagnosis and management of fluid collections associated with pancreatitis. *Am J Med* 1997; 102: 555–63.
51. Robinson PJ, Sheridan MB. Pancreatitis: computed tomography and magnetic resonance imaging. *Eur Radiol* 2000; 10: 401–8.
52. Aljarabah M, Ammori BJ. Laparoscopic and endoscopic approaches for drainage of pancreatic pseudocysts: a systematic review of published series. *Surg Endosc* 2007; 21: 1936–44.
53. Froeschle G, Meyer-Pannwitt U, Brueckner M, et al. A comparison between surgical, endoscopic and percutaneous management of pancreatic pseudocysts—long term results. *Acta Chir Belg* 1993; 93: 102–6.
54. Palanivelu C, Senthilkumar K, Madhankumar MV, et al. Management of pancreatic pseudocyst in the era of laparoscopic surgery—experience from a tertiary centre. *Surg Endosc* 2007; 21: 2262–7.

55. Pryor A, Means JR, Pappas TN. Laparoscopic distal pancreatectomy with splenic preservation. *Surg Endosc* 2007; 21: 2326–30.
56. Stiles GM, Berne TV, Thommen VD, et al. Fine needle aspiration of pancreatic fluid collections. *Am Surg* 1990; 56: 764–8.
57. Vosoghi M, Sial S, Garrett B, et al. EUS-guided pancreatic pseudocyst drainage: review and experience at Harbor-UCLA Medical Center. *MedGenMed* 2002 18; 4: 2.
58. Zein CO, Baron TH, Morgan DE. Endoscopic pancreaticoduodenostomy for treatment of pancreatic duct disconnection because of severe acute pancreatitis. *Gastrointest Endosc* 2003; 58: 130–4.
59. Cahen D, Rauws E, Fockens P, et al. Endoscopic drainage of pancreatic pseudocysts: long-term outcome and procedural factors associated with safe and successful treatment. *Endoscopy* 2005; 37: 977–83.
60. Cremer M, Deviere J, Engelholm L. Endoscopic management of cysts and pseudocysts in chronic pancreatitis: long-term follow-up after 7 years of experience. *Gastrointest Endosc* 1989; 35: 1–9.
61. Fockens P, Johnson TG, van Dullemen HM, et al. Endosonographic imaging of pancreatic pseudocysts before endoscopic transmural drainage. *Gastrointest Endosc* 1997; 46: 412–16.
62. Binmoeller KF, Seifert H, Walter A, et al. Transpapillary and transmural drainage of pancreatic pseudocysts. *Gastrointest Endosc* 1995; 42: 219–24.
63. Rao R, Fedorak I, Prinz RA. Effect of failed computed tomography-guided and endoscopic drainage on pancreatic pseudocyst management. *Surgery* 1993; 114: 843–7.
64. Bartoli E, Delcenserie R, Yzet T, et al. Endoscopic treatment of chronic pancreatitis. *Gastroenterol Clin Biol* 2005; 29: 515–21.
65. Jacobson BC, Baron TH, Adler DG, et al. ASGE guideline: the role of endoscopy in the diagnosis and the management of cystic lesions and inflammatory fluid collections of the pancreas. *Gastrointest Endosc* 2005; 61: 363–70.
66. Ito K, Perez A, Ito H, et al. Pancreatic pseudocysts: is delayed surgical intervention associated with adverse outcomes? *J Gastrointest Surg* 2007; 11: 1317–21.

Liver Abscess

Andreas G. Tzakis and Nikolaos B. Pararas

Clinical Questions		
Question	Answer	Grade of recommendation
How can liver abscess be defined?	Two types; pyogenic, caused by bacteria, and amebic, caused by <i>Entamoeba histolytica</i> .	B
Which are the epidemiologic facts for liver abscess?	Variable depending on the population and the time period. Patients with pyogenic liver abscess are more likely to be older, to be female, and to have a biliary cause and an underlying malignant disease. Amebic liver abscess (and other extraintestinal disease) is 7–10 times more common in adult men.	B
Which is the etiology of liver abscess, and which pathogens are more common?	The causes are divided into six categories, based on the route of extension of infection: biliary, portal vein, hepatic artery, direct extension, traumatic, and cryptogenic. Virtually any organism is capable of causing liver abscess.	B
Which are the symptoms of liver abscess?	Patients with an amebic liver abscess are more likely than those with a pyogenic abscess to present with pain and diarrhea and to have hepatomegaly and a tender liver on physical examination. Fever is present in most patients, occurring in approximately 90% of them with either type of liver abscess; high, spiking fevers associated with chills are seen most frequently with pyogenic hepatic abscesses.	A,B
How can the diagnosis be achieved in patients with liver abscess?	Demonstration of <i>E. histolytica</i> in the stool is still the only definitive proof of intestinal amebiasis.	B
What is the differential diagnosis for liver abscess?	A simple cyst, malignancy, and amebic abscess.	
Which are the treatment modalities for liver abscess?	For pyogenic liver abscess, usually both antibiotic therapy and drainage for successful treatment. Medical management alone gains growing interest.	A, B
What is the prognosis for the patients with liver abscess?	Mortality mainly from associated underlying disease rather than the abscess itself.	B

Intrahepatic abscess is an uncommon entity that continues to pose diagnostic and therapeutic problems. Although the majority of intra-abdominal abscesses are not localized to an organ, the liver is most commonly involved when a visceral abscess occurs.

Important questions to consider in the care of a patient with liver abscess include criteria used to select patients for surgery or medical treatment, the nature of imaging studies needed to reach the diagnosis and the delay impact this can cause, the type of intervention to be performed, the use of antibiotics, and the need to monitor patients for frequent postoperative complications. Patients with liver abscess are prone to relapse and may require subsequent drainage procedures, or the ones still having abscess cavities visible on computed tomography (CT) scan at six weeks may need longer courses of treatment. Treatment should be continued until the CT scan shows complete or near complete resolution of the abscess cavity.

HOW CAN LIVER ABSCESS BE DEFINED?

Intrahepatic abscess is an uncommon entity that continues to pose diagnostic and therapeutic problems. The two major types of liver abscesses are pyogenic, defined as those caused by bacteria, and amebic, defined as those caused by *Entamoeba histolytica*. Pyogenic hepatic abscesses have predominated in reports from medical centers in the more temperate climates. In comparison, amebic abscesses have been reported with moderate frequency from centers in the Southern United States as well as in semitropical and tropical climates. Intra-abdominal abscesses often follow an episode of peritonitis that, in turn, frequently arises from the rupture or leak of the biliary system or bowel. Although the majority of intra-abdominal abscesses are not localized to an organ, the liver is most commonly involved when a visceral abscess occurs (1).

Answer: The two major types of liver abscesses are pyogenic, caused by bacteria, and amebic, caused by *E. histolytica*. Although the majority of intra-abdominal abscesses are not localized to an organ, the liver is most commonly involved when a visceral abscess occurs. Recommendation Grade: B.

WHICH ARE THE EPIDEMIOLOGIC FACTS FOR LIVER ABSCESS?

Although ancient Greek physicians were aware of pyogenic hepatic abscess, the first description in modern times has been credited to Bright in 1835 (2). One hundred two years later, Ochsner and co-workers published their classic review documenting appendicitis as the etiologic entity in more than a third of these cases (3). Several changes have occurred since then. Since the introduction of antibiotics, pyogenic hepatic abscess secondary to appendicitis-induced pylephlebitis has become rare. Patients with pyogenic liver abscess are now more likely to be older, to be female, and to have a biliary cause and an underlying malignant disease. In addition, our understanding of the bacteriology of these abscesses improved greatly with the advent of anaerobic isolation techniques. The epidemiology of pyogenic liver abscesses is variable depending on the population studied and the time period when the study was performed. In 1938, Ochsner and associates reported that pyogenic hepatic abscesses occurred in 8 per 100,000 of admissions to the New Orleans Charity Hospital (3). In the largest case series, published in 1973, 540 cases of intra-abdominal abscess were identified during a 12-year period (1). Liver abscesses were the most common visceral abscess (48 percent) and were responsible for 13% of all intra-abdominal abscesses. In three later reports that evaluated patients seen between 1973 and 2003, the annual incidence of liver abscess was estimated at 18–20 cases per 100,000 hospital admissions (4,5) and 2.3 cases per 100,000 population (6). The incidence in the last report increased with advancing age and was significantly higher among men compared with women (3.3 versus 1.3 per 100,000). Geographic differences also seem to be significant. In a retrospective report from Taiwan, the incidence of pyogenic liver abscesses was 446 per 100,000 hospital admissions, clearly higher than series from other geographic areas (7). The most common pathogen was *Klebsiella pneumoniae*. As will be noted shortly, *K. pneumoniae*, particularly in Taiwan, may be associated with a community-acquired invasive primary liver abscess syndrome.

Amebic liver abscess (and other extraintestinal disease) is 7–10 times more common in adult men despite an equal gender distribution in children and an approximately equal sex distribution of colonic amebic disease (8,9). Although the reasons for the differences in gender distribution have not been fully explained, some possible mechanisms that have been suggested include hormonal effects (postmenopausal women have increased rates) and a potential role of alcoholic hepatocellular damage in creating a nidus for portal seeding (10). The latter is probably more important. Amebic liver abscesses can occur after travel exposures as short as four days (11). In one study, 35% of travelers with amebic liver abscess had spent less than six weeks in an endemic area (12). Most patients diagnosed with amebic

liver abscess in the United States are either from a country where amebiasis is endemic or have a relevant travel history. Conditions that affect cell-mediated immunity, such as extremes of age, pregnancy, corticosteroid therapy, malignancy, and malnutrition, may also increase the chances that *E. histolytica* infection results in invasive disease with liver involvement.

Several series documented a preponderance of pyogenic abscess among elderly patients (5,13–15), with a peak in the seventh decade. This trend toward the development of pyogenic hepatic abscess in older patients most likely reflects both an older general population and a significant shift in etiologic factors.

A male-to-female ratio of 1.8:1 among previously reported patients was calculated in 1972 by Barbour and Juniper (16). This tabulation included a 2.1:1 ratio among 877 cases collected in 1938 by Ochsner and co-workers (3). However, the striking male preponderance seen in earlier series was not present in more recent studies (3,13,17). One possible explanation for the increase in the percentage of women with pyogenic abscesses may be a shift in etiologic factors. The increased incidence of abscesses resulting from biliary infections may be responsible for this change. Compared with the dramatic change in gender incidence that has been observed since 1940, numerous studies published during this same period failed to document any racial susceptibility to pyogenic hepatic abscesses.

Answer: The epidemiology of pyogenic liver abscesses is variable depending on the population studied and the time period when the study was performed. Patients with pyogenic liver abscess are now more likely to be older, to be female, and to have a biliary cause and an underlying malignant disease. Geographic differences also seem to be significant. Amebic liver abscess (and other extraintestinal disease) is 7–10 times more common in adult men despite an equal gender distribution in children and an approximately equal sex distribution of colonic amebic disease. Recommendation Grade: B.

WHICH IS THE ETIOLOGY OF LIVER ABSCESS, AND WHICH PATHOGENS ARE MORE COMMON?

Most pyogenic liver abscesses are caused by infection in the biliary or intestinal tracts. As a result, the causes of liver abscesses have been divided into six categories, based on the route of extension of infection: (1) biliary, from ascending cholangitis; (2) portal vein, as in pylephlebitis resulting from appendicitis or diverticulitis; (3) hepatic artery, from septicemia; (4) direct extension, from a contiguous disease process; (5) traumatic, from blunt or penetrating injuries; and (6) cryptogenic, when no primary source of infection is found even after abdominal exploration of autopsy.

Among the intra-abdominal processes leading to generalized peritonitis and abscess formation, appendicitis with rupture was the most common in the past. However, biliary tract pathology is now the most common cause of pyogenic liver abscess, accounting for 40–60% of cases (5,18,19). Malignant biliary obstruction has become a more frequent cause in the past few decades (5).

Suppurative pylephlebitis, which can arise from infection within the peritoneal cavity such as diverticulitis

with rupture or infection in the female genital tract, is another potential source for bacterial seeding of the liver (20).

Hematogenous seeding is not the usual pathway for the development of liver abscesses. This is in contrast to splenic abscesses, which occur less frequently overall but more commonly arise from bacteremic spread. However, if a solitary organism, particularly a streptococcal or staphylococcal species, is isolated from a liver abscess, a distant source for hematogenous seeding should be sought. A definitive source or cause for a liver abscess may not be found even after a careful evaluation.

Animal models of intra-abdominal infection and clinical disease highlight infection in two phases: peritonitis with bacteremia usually due to aerobic Gram-negative bacilli, followed in survivors by later abscess formation (21). Although a bacteremia may accompany peritonitis, the mechanism of spread of infection to the liver is along channels within the peritoneal cavity and not via the bloodstream. The abscess phase frequently involves mixed facultative and anaerobic species.

Liver abscesses usually involve the right lobe of the liver and may occur via a number of mechanisms (6,7,22). These include contiguous spread from the gallbladder, ascending biliary infections associated with gallstones or obstruction, and penetrating or surgical wounds.

The organisms recovered from pyogenic liver abscesses are varied and often reflect the origin of the infectious process. Mixed facultative and anaerobic species are isolated most frequently. Virtually any organism is capable of causing liver abscess. The majority of liver abscesses are polymicrobial, including anaerobes. For this reason, anaerobic cultures are critical. *S. aureus*, *S. pyogenes*, *Candida* sp., *Actinomyces*, and *Yersinia* are unusual causes of liver abscesses (23–25). This highly variable microbiology is a justification for pursuing a microbiological diagnosis in virtually every case. *S. milleri* (aka *S. anginosus*) is an important cause of liver abscess. Such patients may have simultaneous metastatic infections at other locations. *K. pneumoniae* has emerged as an increasingly isolated organism in pyogenic liver abscess and can cause both primary and secondary (i.e., associated with underlying hepatobiliary disease) infection. In case series from New York and San Diego, *K. pneumoniae* was the most common cause of pyogenic hepatic abscess (18,26). In the report from New York, *K. pneumoniae* was isolated from 23 of 54 (43%) liver abscesses in which an organism was recovered (18). Underlying hepatobiliary disease was present in 43% of patients.

An invasive primary (no underlying hepatobiliary disease) liver abscess syndrome due to *K. pneumoniae* is an important community-acquired infection in Southeast Asia, particularly Taiwan, and less often in Asian and non-Asian patients in other countries. *K. pneumoniae* isolates from these primary liver abscesses have an increased number of virulence factors compared to *K. pneumoniae* isolates from secondary liver abscesses and may be associated with metastatic infection (e.g., endophthalmitis and meningitis). Many other species of organisms are reported from liver abscesses that reflect geographic differences in prevalence of certain diseases as well as common medical interventions, including chemotherapy for malignancy and stenting of the biliary tree. The following are some of the associations that have been noted.

Candida species accounted for 22% of liver abscesses in a series of patients seen between 1973 and 1993 (5). Hepatosplenic candidiasis usually occurs in patients who have received chemotherapy and presents when the neutrophil count rebounds after a neutropenic episode.

Gram-positive organisms accounted for 60% of pathogens in a report of liver abscesses in patients who underwent transarterial embolization for hepatocellular carcinoma (27).

Tuberculous liver abscess is uncommon but should be considered in patients when other organisms are not recovered (27–29).

Amebic liver abscesses should be considered in patients who are from or have traveled to an endemic area within the past six months. The clinical course and appearance may be difficult to distinguish from pyogenic liver abscesses, but some characteristic features of an amebic liver abscess include young males with a tender solitary abscess in the liver (22).

Answer: The causes of liver abscesses have been divided into six categories, based on the route of extension of infection: biliary, portal vein, hepatic artery, direct extension, traumatic, and cryptogenic. Liver abscesses usually involve the right lobe of the liver. The organisms recovered from pyogenic liver abscesses are varied and often reflect the origin of the infectious process. Mixed facultative and anaerobic species are isolated most frequently. Virtually any organism is capable of causing liver abscess. This highly variable microbiology is a justification for pursuing a microbiological diagnosis in virtually every case. Recommendation Grade: B.

WHICH ARE THE SYMPTOMS OF LIVER ABSCESS?

The major complaint of patients with an amebic liver abscess is pain, which is usually localized in the right upper quadrant (14,30,31). However, pain may also be localized to the epigastrium, or it may be generalized, pleuritic, or radiating to the right shoulder. In comparing patients with amebic and pyogenic abscesses, Conter and associates found that in addition to abdominal pain, patients with amebic abscesses were more likely to present with diarrhea, abdominal tenderness, and hepatomegaly. In comparison, patients with pyogenic abscesses were more likely to have pruritus, jaundice, septic shock, or a palpable mass at the time of presentation. Fever is present in most patients, occurring in approximately 90% (5,18,31), with either type of liver abscess, but high, spiking fevers associated with chills are seen most frequently with pyogenic hepatic abscesses. Nonspecific symptoms can also be present and they include chills (38–49%), anorexia (38%), weight loss (25–43%), nausea and vomiting (28–43%), and weakness and malaise (30%).

Patients can have symptoms and signs localized to the right upper quadrant, including pain, guarding, punch tenderness, and even rebound tenderness. This is most likely to occur in those with active disease of the biliary tract. However, the absence of right upper quadrant findings does not exclude a liver abscess. Only about one-half of patients with liver abscesses have hepatomegaly, right upper quadrant tenderness, or jaundice; thus, many have no symptoms or signs that would direct attention to the liver (32).

Fever of unknown origin may be the presenting complaint, especially in elderly patients. Thus, diagnostic studies of the right upper quadrant and the abdomen are important in the evaluation of many patients with fever of unknown origin.

Patients with amebic liver abscess usually present acutely with one to two weeks of fever (38.5–39.5°C) and right upper quadrant pain. For travelers returning from an endemic area, presentation usually occurs within 8–20 weeks (median 12 weeks) and will be within five months of their return in 95% of patients, although a longer lag (sometimes years) has been reported (12). Occasionally, patients have a more chronic presentation with months of fever, weight loss, and abdominal pain. In these patients, hepatomegaly and anemia are often associated findings.

Patients with secondary cardiac or pulmonary involvement may present with symptoms primarily due to these complications. Examination of patients with uncomplicated liver abscess will reveal hepatomegaly and point tenderness over the liver in approximately 50% of cases. Clinical jaundice occurs in less than 10% of patients (8). Occasionally, the abscess ruptures into the peritoneum, causing clinical peritonitis (2–7%) (33). Patients with amebic hepatic abscesses may also have ileocecal mass lesions that are frequently amebomas (34).

Answer: Patients with an amebic liver abscess are more likely than those with a pyogenic abscess to present with pain and diarrhea and to have hepatomegaly and a tender liver on physical examination. In comparison, patients with pyogenic abscesses are more likely to have pruritus, jaundice, septic shock, or a palpable mass at the time of presentation. However, many patients have no symptoms or signs that would direct attention to the liver. Fever is present in most patients, occurring in approximately 90% with either type of liver abscess, but high, spiking fevers associated with chills are seen most frequently with pyogenic hepatic abscesses. Recommendation Grade: A and B.

HOW CAN THE DIAGNOSIS BE ACHIEVED IN PATIENTS WITH LIVER ABSCESS?

Differentiation of an amebic liver abscess from a pyogenic hepatic abscess on clinical grounds may be impossible. Likewise, both entities may be confused with various intrahepatic neoplastic processes. Several serologic tests are available to aid in the diagnosis of amebic hepatic abscesses. However, demonstration of *E. histolytica* in the stool is still the only definitive proof of intestinal amebiasis. Based on the lack of specificity of clinical symptoms and signs as well as general laboratory abnormalities, scanning techniques are usually required to make a diagnosis of liver abscess. The diagnosis is then confirmed following aspiration and culture of the abscess material.

Laboratory Findings

Laboratory abnormalities are not specific in patients with liver abscess. An elevated serum alkaline phosphatase level is the single most common laboratory abnormality, being elevated in 67–90% of patients (5,18,32). Other tests of liver function may be normal, but one-half of patients have

elevations in serum bilirubin and aspartate aminotransferase concentrations (18,32). A number of additional laboratory findings can be seen, including leukocytosis, normochromic, normocytic anemia, and hypoalbuminemia. A chest radiograph may show a new elevation of the right hemidiaphragm, a right basilar infiltrate, or a unilateral pleural effusion that should lead to consideration of liver abscess in the differential diagnosis.

Stool Examination

The reported incidence of finding amebic cysts or trophozoites in the stool of patients with an amebic liver abscess varies considerably. Balasegaram found amebae in the stool in fewer than 15% of his 57 Malaysian patients. In comparison, Abul-Khair and associates were able to identify amebic cysts in 10 of 19 Egyptian patients (53%) with an amebic liver abscess (35). In San Jose, Maltz and Knauer found *E. histolytica* in the stool of only 8 of 44 patients (18%) with an amebic hepatic abscess (8). These varied results may be explained by the finding that identification of *E. histolytica* trophozoites or cysts requires careful handling of specimens, an experienced technician, and avoidance of interfering substances.

Microscopic examination of a fresh stool specimen or material obtained by scraping or biopsy of the rectal mucosa during sigmoidoscopy provides the best chance of identifying the motile amebic trophozoites. If an experienced technician is not readily available, the specimen may be preserved in formalin or polyvinyl alcohol. Examination of several stools may be necessary because excretion of cysts may be intermittent. The use of several stains (e.g., buffered methylene blue, trichrome, and iodine) also may assist in identification of amebae. Krogstad and associates pointed out that numerous substances, including antibiotics, antiparasitic drugs, laxatives, antacids, radiologic contrast media, enemas, and antidiarrheal drugs, may interfere with stool examination for parasites (36). These reasons explain why amebae are not found in the stools of most patients with an amebic liver abscess.

Serologic Tests

Because stools from many patients with amebic liver abscess are negative for amebae, serologic tests are particularly useful in evaluating these patients. Numerous serologic tests for amebiasis have been developed (37). These tests include indirect hemagglutination (IHA), gel diffusion precipitin (GDP), complement fixation, latex agglutination, cellulose acetate precipitin, enzyme-linked immunosorbent assay, and identification of a recombinant protein. For tests that provide titers, little correlation exists between the degree of seropositivity and the severity of infection. If results are positive, however, these tests indicate current or previous amebic infection. Therefore, these tests have the greatest use in nonendemic areas.

The IHA and GDP have been the most frequently used serologic tests. Balasegaram found that the IHA test was positive (a titer of 1:128 or greater) in 95% of 124 Malaysian patients with amebic hepatic abscess. Similarly, Cohen and Reynolds reported that the IHA was positive in 65 of 66 patients with amebic liver abscess seen at the University of Southern California (38). Adams and MacLeod

reported a positive GDP test in 94% of 400 patients tested in South Africa (33). Several investigators have reported that the IHA frequently remains positive for many years after invasive amebiasis, whereas in two-thirds of their patients, the GDP was negative in six months. The GDP test has the additional advantages that it is inexpensive and simple to perform, and it can provide information in 24–48 hours. The cellulose acetate diffusion and counter-current immunoelectrophoresis tests yield results within a few hours, but to date, experience with these tests has not been compared with that of either IHA or GDP in a large population of patients with amebic abscesses. The most recently developed test measures a 29kDa peripheral membrane protein of pathogenic *E. histolytica* (39). This test can differentiate patients with pathogenic and non-pathogenic strains and is highly specific and reasonably sensitive.

Imaging Studies

Ultrasonography and CT are the diagnostic methods of choice (40). Gallium- or indium-labeled white blood cell scans and magnetic resonance imaging can also be used for diagnosis, but these scans will not reliably distinguish an abscess from malignancy.

Radiographic Findings

Approximately two-thirds of patients with an amebic liver abscess will have an abnormal chest x-ray. The most common radiologic finding in these patients is elevation of the right hemidiaphragm. Fluoroscopy of the diaphragm also reveals decreased motion in many of these patients. Other plain radiographic findings, seen less frequently, include right pleural effusion, right lower lobe infiltrate, and hepatomegaly. Barium studies may show displacement of the stomach or colon by an enlarged liver. Cohen and Reynolds reported nonvisualization on oral cholecystography or intravenous cholangiography in 11 of 13 patients studied (38). None of these patients were vomiting, had diarrhea or acute pancreatitis, or were jaundiced. After treatment of the amebic abscess, however, six of seven patients restudied had a normal cholangiogram.

Liver Scanning

Hepatic scanning demonstrates amebic liver abscesses larger than 2cm in diameter. A review of 105 collected cases of amebic abscess in patients in whom a diagnostic liver scan was obtained revealed correct identification of the abscess in 91 patients (87%). In a 1986 analysis of 57 patients with amebic abscesses, Thompson and Glasser found that Tc-99m liver scans were 100% accurate in establishing the diagnosis (41). Another important advantage of liver scanning is that the exact number and location of abscesses can be determined; as a result, therapy can be individualized. Liver scanning is also an excellent noninvasive method of following the progress of amebic abscesses that are being treated nonoperatively. At present, Tc-99m and Ga-67 are the most widely used scans. Several investigators have reported the use of gallium scanning to differentiate amebic abscesses from pyogenic abscesses. With gallium scanning, an amebic abscess demonstrates peripheral uptake around a central cold area, whereas a

pyogenic abscess has increased uptake of element throughout the abscess. Liver scanning was the first radiographic method used in the diagnosis, localization, and follow-up of amebic abscesses, but now ultrasound and, to a lesser extent, CT are being used more frequently in the management of these patients.

Ultrasound

Several reports suggest that sonography is accurate in the diagnosis of amebic liver abscess. Thompson and Glaser reported ultrasound identification of amebic liver abscesses in 94% of their patients in Los Angeles (41), and Maltz and Knauer reported a 92% accuracy for ultrasound in 39 patients from San Jose (8). Several sonographic features of amebic liver abscesses make this diagnosis possible. The wall is smooth in two-thirds of patients, internal echoes are less dense than the surrounding normal liver in 85%, and a decrease in echoes of two-thirds or more was present in 90–95%. Thus, ultrasound is accurate and in most cases can differentiate amebic abscesses from other hepatic lesions. Sonography can determine the number, size, and location of abscesses and can be used as a guide for percutaneous aspiration. Because ultrasound is noninvasive, rapid, relatively inexpensive, and reproducible, it is also ideal for follow-up of patients with amebic abscesses, most of whom are managed nonoperatively.

CT

The great advantage of CT over ultrasound is that smaller lesions can be detected. This advantage is important in patients with multiple small (<2cm) pyogenic abscesses. However, most amebic abscesses are solitary and are of sufficient size (>2cm) to be easily detected by ultrasound. Balasegaram reported a good experience with the use of CT in a small group of patients with amebic liver abscesses. However, because of the additional expense with CT, this diagnostic modality should be reserved for patients suspected of having an amebic abscess in whom ultrasound is not diagnostic.

Answer: The diagnosis and differentiation of an amebic liver abscess from a pyogenic hepatic abscess on clinical grounds may be impossible. Likewise, both entities may be confused with various intrahepatic neoplastic processes. Several serologic tests are available to aid in the diagnosis of amebic hepatic abscesses. However, demonstration of *E. histolytica* in the stool is still the only definitive proof of intestinal amebiasis. Based on the lack of specificity of clinical symptoms and signs as well as general laboratory abnormalities, scanning techniques are usually required to make a diagnosis of liver abscess. The diagnosis is then confirmed following aspiration and culture of the abscess material. Recommendation Grade: B.

WHAT IS THE DIFFERENTIAL DIAGNOSIS FOR LIVER ABSCESS?

The differential diagnosis includes a simple cyst, malignancy, and amebic abscess. Simple cysts and malignancies are usually distinguished from liver abscess based on the appearance of the CT scan or ultrasound. Cysts do not

typically contain elements or stranding within their walls, whereas abscesses often have loculations or stranding apparent. Malignancies are usually more solid than fluid-filled and may contain calcification, although necrosis and bleeding within a tumor may sometimes be present, making it difficult to differentiate from an abscess. Amebic and pyogenic liver abscesses cannot be distinguished based on radiology; a history of travel and amebic serology can help distinguish between these two entities.

Answer: The differential diagnosis in patients with a liver mass includes a simple cyst, malignancy, and amebic abscess. Amebic and pyogenic liver abscesses cannot be distinguished based on radiology; a history of travel and amebic serology can help distinguish between these two entities.

WHAT ARE THE TREATMENT MODALITIES FOR LIVER ABSCESS?

Pyogenic liver abscess usually requires both antibiotic therapy and drainage for successful treatment, although there is growing interest in medical management alone. One group reported on 15 patients treated with medical therapy, although percutaneous aspiration for diagnosis was performed in the majority (42,43). Although this approach may be successful, patients treated without definitive drainage generally require longer courses of antibiotics. Unlike pyogenic liver abscesses, drainage of an amebic liver abscess is not usually necessary.

Drainage: There are three drainage techniques in common use: percutaneous drainage guided by imaging (with or without the placement of a catheter), surgical drainage, and drainage by endoscopic retrograde cholangiopancreatography (ERCP).

Percutaneous drainage: Percutaneous drainage guided by imaging (either ultrasonography or CT) is the preferred primary therapy as compared to surgical drainage.

Aspiration versus catheter placement: There is a debate about whether percutaneous aspiration without the placement of a catheter for continuous drainage is as effective as continuous percutaneous drainage when both are combined with antimicrobial therapy. A study of 64 consecutive patients treated with percutaneous aspiration noted a 97% success rate, although 27% required three or more aspirations and 50% needed at least two (44).

The efficacy of percutaneous aspiration was better evaluated in two randomized trials. In one, 50 patients (including 20 with amebic abscesses) were assigned to either percutaneous aspiration or percutaneous drainage (45). Only 15 of the 25 patients (60%) assigned to percutaneous aspiration were cured after one or two aspirations compared to 100% with percutaneous drainage. Although the groups were comparable in the time to resolution of the abscesses (approximately 15 weeks), the time to 50% reduction in the size of the abscess was significantly longer in the percutaneous aspiration group (11 versus 5 days).

In a later prospective, randomized trial of 64 patients seen between 1994 and 1999, there were no significant differences in clinical response rates between patients assigned to continuous catheter drainage plus antibiotics and those assigned to intermittent needle aspiration and antibiotics (46). This study suggests that both percutaneous

approaches are equally effective and safe in patients with pyogenic liver abscesses ≥ 3 cm in size.

The differing conclusions from these two studies about the best means of drainage may be related to the differences in populations studied and criteria used to define treatment failure in the aspiration groups. The first study included at least 40% of patients with amebic abscesses compared to the second study that included only patients with pyogenic abscesses. In addition, in the first study, patients in the aspiration group were defined as treatment failures if more than two aspirations were required, compared to the second study where the number of aspirations was not limited and a single aspiration was performed in 13 patients, two in 13 patients, and three or more aspirations in 6 patients.

Percutaneous versus surgical drainage: A retrospective review of 80 patients with pyogenic liver abscesses greater than 5 cm evaluated treatment outcomes in patients who underwent percutaneous versus surgical drainage (47). Overall mortality, morbidity, and time to resolution of fever did not differ between the groups. Patients receiving surgical drainage had fewer treatment failures (3 versus 10), required fewer secondary procedures (5 versus 13), and had slightly shorter hospital stays [8 (range 4–22) versus 11 (range 6–21) days]. Although morbidity did not differ between the groups (complication rates 30.5% versus 27.2% with percutaneous compared to surgical drainage, respectively), the types of complications differed. Those undergoing surgical drainage having complications of bleeding, wound infection, intra-abdominal abscess, and intestinal obstruction compared to those undergoing percutaneous drainage and having complications of peritonitis, catheter blockage, and catheter dislodgement.

Surgical drainage: Direct surgical intervention may be suitable when there appears to be no clinical response to percutaneous drainage within four to seven days.

In addition, several factors help identify patients in whom percutaneous drainage is more likely to fail and thus, surgical drainage is preferred:

- The presence of multiple, large, or loculated abscesses.
- Viscous abscess contents that tend to plug the catheter.
- Associated disease (e.g., of the biliary tract) that requires primary surgical correction.

ERCP: A report from Hong Kong described 63 patients who underwent ERCP within a median of eight days from the diagnosis of liver abscess (19). ERCP identified associated biliary tree abnormalities in 40% of the patients, some of which were amenable to endoscopic correction; the procedure detected a communication between the biliary tree and the abscess cavities in three patients. ERCP was successful in 90% of cases with no associated complication. Thus, in patients with a probable biliary source of the liver abscess, ERCP might replace surgical intervention.

Approach to drainage: The type of drainage procedure used must be individualized.

- Percutaneous aspiration with catheter placement should be performed in most patients. The catheter is usually left in place until drainage becomes minimal, typically five to seven days.

- Percutaneous aspiration without drainage can be considered in patients with small liver abscesses (e.g., <3 cm) that respond promptly to antibiotic therapy.
- Surgical drainage is recommended in patients at high risk of percutaneous drainage failure, including those requiring further surgery for the underlying cause of the abscess or with multiple, large, or loculated abscesses.

Antibiotics: No randomized controlled studies have evaluated empiric antibiotic regimens for treatment of pyogenic liver abscess. Treatment recommendations are based on the probable source of infection.

Empiric antibiotic therapy for pyogenic liver abscess should include broad-spectrum antibiotics until culture results of the abscess obtained by percutaneous aspirate or surgical drainage are available. Most patients, and all hospitalized patients, should be treated with parenteral antibiotics. Oral antibiotics can be considered for outpatients with mild, uncomplicated infection. The results of Gram stains should be considered in the selection of an empiric regimen.

- Monotherapy with a beta-lactam/beta-lactamase inhibitor, such as ampicillin-sulbactam (3g every six hours) or piperacillin/tazobactam (4.5g every six hours) or ticarcillin-clavulanate (3.1g every four hours).
- Metronidazole (500mg IV every eight hours) plus a third-generation cephalosporin, such as ceftriaxone (1g IV every 24 hours).
- Monotherapy with a carbapenem, such as imipenem (500mg every six hours) or meropenem (1g every 8 hours) or ertapenem (1g daily).
- Metronidazole (500mg IV every eight hours) plus a fluoroquinolone (ciprofloxacin 400mg IV every 12 hours or levofloxacin 500mg IV daily).

Pathogen-directed therapy: Regardless of which empiric regimen is chosen initially, therapy should be altered to reflect the organisms recovered when aspiration or drainage is performed. If more than one organism is recovered, anaerobic coverage should be continued even if anaerobes are not cultured because of the difficulty in isolating anaerobic organisms.

Duration of therapy: There are no randomized controlled studies that have evaluated the optimal duration of antibiotic therapy for pyogenic liver abscess. Treatment recommendations are based on clinical case series. The duration of therapy should be determined by the clinical response of the patient and the source and extent of infection. Patients whose abscess(es) are difficult to drain or resolve more slowly with repeat imaging often require longer courses of therapy.

The typical duration of antibiotic therapy is at least four to six weeks. Abscesses that respond well to drainage may have resolved by four weeks. Patients who require

subsequent drainage procedures or who still have abscess cavities visible on CT scan at six weeks may need longer courses of treatment. Parenteral antibiotics are often given for the first two to three weeks or until a favorable clinical response is demonstrated; the remainder of the course is completed with oral agents. The combination of metronidazole and a fluoroquinolone (ciprofloxacin or levofloxacin) is a convenient oral regimen.

Follow-up studies: Follow-up imaging is used to monitor the response to therapy, determine the duration of antibiotics, and assess the need for further aspiration. In general, treatment should be continued until the CT scan shows complete or nearly complete resolution of the abscess cavity.

Answer: Pyogenic liver abscess usually requires both antibiotic therapy and drainage for successful treatment, although there is growing interest in medical management alone. Three drainage techniques are in common use: percutaneous drainage guided by imaging (with or without the placement of a catheter), surgical drainage, or drainage by ERCP. Treatment recommendations with antibiotics are based on the probable source of infection. Empiric antibiotic therapy for pyogenic liver abscess should include broad-spectrum antibiotics until culture results of the abscess obtained by percutaneous aspirate or surgical drainage are available. Then the therapy should be altered to reflect the organisms recovered. Follow-up imaging is used to monitor the response to therapy, determine the duration of antibiotics, and assess the need for further aspiration.

WHAT IS THE PROGNOSIS FOR THE PATIENTS WITH LIVER ABSCESS?

A substantial improvement in prognosis has occurred in patients with pyogenic liver abscess since the 1950s. In different studies evaluating patients seen in different time periods, the mortality rate was 65% from 1952 to 1972 (5), 31% from 1973 to 1993 (5), 15% from 1977 to 1984 (48), and 12% from 1988 to 1999 (49). In the last study, mortality was mainly from associated underlying disease, rather than the abscess itself (49).

A retrospective series covering the decade from 1992 to 2003 described a mortality rate of only 2.5% (18). However, assessment of mortality was limited because the mean duration of follow-up after hospital discharge was 12 days, with more than one-half of patients having no documented follow-up.

Answer: A substantial improvement in prognosis has occurred in patients with pyogenic liver abscess since the 1950s and is mainly caused by associated underlying disease rather than the abscess itself. Recommendation Grade: B.

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Clinical and pathologic features of amebic and pyogenic liver abscesses and various methods of treatment	1973	1	IIb	B	Amebic abscess is treated by parenteral use of emetine and aspiration of the abscess. Pyogenic abscess is treated by adequate drainage of the purulent material without contamination of the peritoneal and pleural cavities.
Changes in the etiology, diagnosis, bacteriology, treatment, and outcome of patients with pyogenic hepatic abscesses over the past four decades	1996	5	IIb	B	Proper management remains the challenge. Appropriate systemic antibiotics and fungal agents as well as adequate surgical, percutaneous, or biliary drainage are required for the best results.
10 years of experience in the field of immunodiagnosis of this disease	1982	12	Ia	A	Together with its economic and time-saving advantages, its high sensitivity and specificity make enzyme immunoassay recommendable as a screening test. It detects substantial changes in antibody concentration during and after the acute stage of acute liver abscess, and also measures long-persisting antibodies; it is suitable for both diagnostic and epidemiological purposes.
The role of ERCP in patients with pyogenic liver abscesses.	1999	19	Ib	A	Useful in the treatment of patients with pyogenic liver abscesses.
To assess the causes of ileocecal mass in patients with amebic liver abscess postrepair	2006	34	Ib	A	Ileocecal mass is a common finding in patients with amebic liver abscess. Colonoscopy and histological examination of the target biopsies are mandatory to avoid missing a more sinister lesion. Vigilance is required for early detection
Quantitative ELISA with purified native or recombinant antigen and immunoblotting performed to determine the serological response to the 29 kDa protein	1993	39	IIb	B	The utility of a quantitative assay with defined recombinant antigen for the serodiagnosis of invasive amebiasis in nonendemic areas in conjunction with other diagnostic tools.
Determine and compare the efficacy of sonographically guided percutaneous needle aspiration and percutaneous catheter drainage in the treatment of liver abscesses	1998	45	Ia	A	Percutaneous catheter drainage is more effective than needle aspiration in the treatment of liver abscesses.
Compare the therapeutic effectiveness of continuous catheter drainage versus intermittent needle aspiration in the percutaneous treatment of pyogenic liver abscesses	2004	46	Ia	A	Intermittent needle aspiration is probably as effective as continuous catheter drainage for the treatment of pyogenic liver abscess, although further proof with a large-scale study is necessary. Due to the additional advantages of procedure simplicity, patient comfort, and reduced price, needle aspiration deserves to be considered as a first-line drainage approach.
Determine whether first-line treatment with percutaneous or surgical drainage of liver abscesses >5 cm results in better clinical outcome	2005	47	Ia	A	Surgical drainage should be considered as first-line treatment of large liver abscesses of >5 cm, providing provides better clinical outcomes than percutaneous drainage in terms of treatment success, number of secondary procedures, and hospital stay with comparable morbidity and mortality rates.

Abbreviations: ELISA, enzyme-linked immunosorbent assay; ERCP, endoscopic retrograde cholangiopancreatography.

REFERENCES

1. Altemeier WA, Culbertson WR, Fullen WD, et al. Intra-abdominal abscesses. *Am J Surg* 1973; 125: 70.
2. Bright J. Observations on jaundice. *Guys Hosp Rep* 1836; 1: 604.
3. Ochsner A, DeBakey M, Murray S. Pyogenic abscess of the liver. *Am J Surg* 1938; 40: 292.
4. Pitt HA, Zuidema GD. Factors influencing mortality in the treatment of hepatic abscess. *Surg Gynecol Obstet* 1975; 140: 228.
5. Huang CJ, Pitt HA, Lipsett PA, et al. Pyogenic hepatic abscess. *Ann Surg* 1996; 223: 600–7.
6. Kaplan GG, Gregson DB, Laupland KB. Population-based study of the epidemiology of and the risk factors for pyogenic liver abscess. *Clin Gastroenterol Hepatol* 2004; 2: 1032.
7. Chan KS, Chen CM, Cheng KC, et al. Pyogenic liver abscess: a retrospective analysis of 107 patients during a 3-year period. *Jpn J Infect Dis* 2005; 58: 366.
8. Maltz G, Knauer CM. Amebic liver abscess: a 15-year experience. *Am J Gastroenterol* 1991; 86: 704.

9. Acuna-Soto R, Maguire JH, Wirth DF. Gender distribution in asymptomatic and invasive amebiasis. *Am J Gastroenterol* 2000; 95: 1277.
10. Stanley SL Jr. Amebiasis. *Lancet* 2003; 361: 1025.
11. Aucott JN, Ravdin JI. Amebiasis and "non-pathogenic" intestinal protozoa. *Infect Dis Clin North Am* 1993; 7: 467.
12. Knobloch J, Mannweiler E. Development and persistence of antibodies to *Entamoeba histolytica* in patients with amebic liver abscess: analysis of 216 cases. *Am J Trop Med Hyg* 1983; 32: 727.
13. Branum GD, Tyson GS, Branum MA, et al. Hepatic abscess: changes in etiology, diagnosis and management. *Ann Surg* 1990; 212: 655.
14. Conter RL, Pitt HA, Tompkins RK, et al. Differentiation of pyogenic from amebic hepatic abscess. *Surg Gynecol Obstet* 1986; 162: 114.
15. Ribaud JM, Oshsner A. Intrahepatic abscess: amebic and pyogenic. *Am J Surg* 1973; 125: 570.
16. Barbour GL, Juniper K Jr. A clinical comparison of amebic and pyogenic abscess of the liver in sixty-six patients. *Ann Intern Med* 1972; 77: 629.
17. Donovan AJ, Yellin E, Ralls PW. Hepatic abscess. *World J Surg* 1991; 15: 162.
18. Rahimian J, Wilson T, Oram V, et al. Pyogenic liver abscess: recent trends in etiology and mortality. *Clin Infect Dis* 2004; 39: 1654.
19. Lam YH, Wong SK, Lee DW, et al. ERCP and pyogenic liver abscess. *Gastrointest Endosc* 1999; 50: 340.
20. Kasper DL, Zaleznik DF. Intra-abdominal infections and abscesses. In: Kasper DL, Braunwald E, Fauci AS, et al., eds., *Harrison's Principles of Internal Medicine*, 16th edition. New York: McGraw-Hill, 2005; 749.
21. Onderdonk AB, Kasper DL, Cisneros RL, et al. The capsular polysaccharide of *Bacteroides fragilis* as a virulence factor: comparison of the pathogenic potential of encapsulated and unencapsulated strains. *J Infect Dis* 1977; 136: 82.
22. Lodhi S, Sarwari AR, Muzammil M, et al. Features distinguishing amoebic from pyogenic liver abscess: a review of 577 adult cases. *Trop Med Int Health* 2004; 9: 718.
23. Sharma M, Briski LE, Khatib R. Hepatic actinomycosis: an overview of salient features and outcome of therapy. *Scand J Infect Dis* 2002; 34: 386.
24. Pulvirenti D, Aikaterini T, Neri S. Septicemia, hepatic abscess, and encephalitis due to *Yersinia enterocolitica*. *J Clin Gastroenterol* 2007; 3: 333.
25. Smith BM, Zyromski NJ, Allison DC. Community-acquired methicillin-resistant *Staphylococcus aureus* liver abscess requiring resection. *Surgery* 2007; 141: 110.
26. Lederman ER, Crum NF. Pyogenic liver abscess with a focus on *Klebsiella pneumoniae* as a primary pathogen: an emerging disease with unique clinical characteristics. *Am J Gastroenterol* 2005; 100: 322.
27. Chen C, Chen PJ, Yang PM. Clinical and microbiological features of liver abscess after transarterial embolization for hepatocellular carcinoma. *Am J Gastroenterol* 1997; 92: 257.
28. Caliskan Y, Demirturk M, Cagatay AA, et al. Isolated hepatic tuberculous abscess in a renal transplant recipient. *Transplant Proc* 2006; 38: 1341.
29. Köksal D, Köksal AS, Köklü S, et al. Primary tuberculous liver abscess: a case report and review of the literature. *South Med J* 2006; 99: 393.
30. Akgun Y, Tacyildiz IH, Celik Y. Amebic liver abscess: changing trends over 20 years. *World J Surg* 1999; 23: 102.
31. Hoffner JR, Kilagbhan T, Esekogwu VI, et al. Common presentations of amebic liver abscess. *Ann Emerg Med* 1999; 34: 351.
32. Rubin RH, Swartz MN, Malt R. Hepatic abscess: changes in clinical bacteriologic and therapeutic aspects. *Am J Med* 1974; 57: 601.
33. Adams EB, MacLeod IN. Invasive amebiasis. II. Amebic liver abscess and its complications. *Medicine (Baltimore)* 1977; 56: 315.
34. Misra SP, Misra V, Dwivedi M. Ileocecal masses in patients with amebic liver abscess: etiology and management. *World J Gastroenterol* 2006; 12: 1933.
35. Abul-Khair MH, Kenawi MM, Korashy EE, et al. Ultrasonography and amoebic liver abscesses. *Ann Surg* 1981; 193: 221.
36. Krogstad DJ, Spencer HC Jr, Healy GR. Current concepts in parasitology amebiasis. *N Engl J Med* 1978; 298: 262.
37. Shanta KS, Bhat KG, Patil CS, et al. Evaluation of laboratory techniques for diagnosis of amoebiasis. *J Commun Dis* 1998; 30: 103.
38. Cohen HG, Reynolds TB. Comparison of metronidazole and chloroquine for the treatment of amoebic liver abscess. *Gastroenterology* 1975; 69: 35.
39. Flores BM, Reed SL, Ravdin JI, et al. Serologic reactivity to purified recombinant and native 29-kilodalton peripheral membrane protein of pathogenic *Entamoeba histolytica*. *J Clin Microbiol* 1993; 31: 1403.
40. Zaleznik DF, Kasper DL. Intra-abdominal abscesses. In: Lamont JT, ed., *Gastrointestinal Infections: Diagnosis and Management*. New York: Marcel Dekker, 1997: 397.
41. Thompson JE, Glasser AJ. Amebic abscess of the liver. *J Clin Gastroenterol* 1986; 8: 550.
42. Maher JA, Reynolds TB, Yellin AE. Successful medical treatment of pyogenic liver abscess. *Gastroenterology* 1979; 77: 618.
43. Reynolds TB. Medical treatment of pyogenic liver abscess. *Ann Intern Med* 1982; 96: 373.
44. Ch YS, Hg LR, Kan PS, et al. Pyogenic liver abscess: treatment with needle aspiration. *Clin Radiol* 1997; 52: 912.
45. Rajak CL, Gupta S, Jain S, et al. Percutaneous treatment of liver abscesses: needle aspiration versus catheter drainage. *Am J Roentgenol* 1998; 170: 1035.
46. Yu SC, Ho SS, Lau WY, et al. Treatment of pyogenic liver abscess: prospective randomized comparison of catheter drainage and needle aspiration. *Hepatology* 2004; 39: 932.
47. Tan YM, Chung AY, Chow PK, et al. An appraisal of surgical and percutaneous drainage for pyogenic liver abscesses larger than 5 cm. *Ann Surg* 2005; 241: 485.
48. Bertel CK, van Heerden JA, Sheedy PF. Treatment of pyogenic hepatic abscesses: surgical vs percutaneous drainage. *Arch Surg* 1986; 121: 554.
49. Mohsen AH, Green ST, Read RC, et al. Liver abscess in adults: ten years experience in a UK centre. *QJM-Int J Med* 2002; 95: 797.

Diagnosis and Treatment of Variceal Hemorrhage due to Cirrhosis

Robert M. Esterl Jr., Greg A. Abrahamian and K. Vincent Speeg

Questions Regarding Diagnosis and Treatment of Variceal Hemorrhage		
Question	Answer	Level of evidence/Grade of recommendation
In cirrhotic patients, what is the most reliable predictor of variceal development?	Measurement of the HVPG is the preferred method to assess portal pressure and is predictive of variceal development.	Ib/A
What is the best diagnostic test to identify esophageal and gastric varices?	Upper endoscopy is the best diagnostic test to detect the presence of esophageal and gastric varices.	V/D
In cirrhotic patients who have no varices by upper endoscopy, what is the best treatment to prevent development of varices?	When screening upper endoscopy reveals no varices, β -blockers are not helpful to prevent formation of varices. Instead, these patients should undergo regular surveillance upper endoscopy.	Range from Ib/A to V/D
In cirrhotic patients who have small varices, what is the best treatment to prevent first variceal hemorrhage?	Patients with small varices—especially those with increased risk of gastrointestinal hemorrhage—should receive nonselective β -blockers to prevent growth to large varices.	IIb/C
In cirrhotic patients who have large varices, what is the best treatment to prevent first variceal hemorrhage?	Nonselective β -blockers reduce the risk of first variceal hemorrhage in patients with large varices. EBL is probably more effective than nonselective β -blockers to reduce the risk of first variceal hemorrhage in these patients, but EBL may not improve survival. EBL should be recommended when these patients have contraindications or intolerance to β -blocker therapy.	Range from Ia/A to V/D
In cirrhotic patients who have acute variceal hemorrhage, what specific resuscitative fluids should be given?	Prompt but careful resuscitation of blood loss due to acute variceal hemorrhage should occur with colloid solution to maintain hemodynamic stability and with packed red cells to maintain hemoglobin near 8 g/dl.	Ib/A
In cirrhotic patients who have acute variceal hemorrhage, what is the role of prophylactic antibiotics, if any?	Prophylactic antibiotics should begin at hospital admission for all patients who present with acute variceal hemorrhage, because they decrease bacterial infections, improve failure to control acute variceal hemorrhage, prevent recurrent variceal hemorrhage, and decrease mortality.	Ia/A
In cirrhotic patients who have acute variceal hemorrhage, what is the best treatment to control hemorrhage?	When acute variceal hemorrhage is suspected, pharmacologic intervention should begin immediately, even before variceal hemorrhage is confirmed by upper endoscopy. Upper endoscopy should be performed as soon as possible, and, if variceal hemorrhage is confirmed, endoscopic therapy (preferably with EBL) should be used to control hemorrhage. Failure to control acute variceal hemorrhage should prompt a second endoscopic attempt before considering rescue therapy with TIPSS or surgical shunt. Balloon tamponade should be considered as a temporizing measure only if definitive therapy is planned.	Range from Ia/A to IIb/B
In cirrhotic patients who recover from acute variceal hemorrhage, what is the best treatment to prevent further variceal hemorrhage?	Data support combined β -blocker and endoscopic therapy, even though a recent consensus conference recommends EBL or β -blocker + nitrate. Patients who develop recurrent variceal hemorrhage on EBL or β -blocker therapy alone should receive combined therapy. Patients who fail combined therapy should be considered for TIPSS or surgical shunt. TIPSS can be used as a bridge to transplantation, and suitable candidates should be referred to specialized liver transplant centers early.	Range from Ia/A to IV/C

Abbreviations: EBL, endoscopic band ligation; HVPG, hepatic vein pressure gradient; TIPSS, transjugular intrahepatic portosystemic shunt.

Cirrhosis is a histologic description of end-stage liver disease and is characterized by nodular regeneration and bridging fibrosis in the liver. Portal hypertension (PH) is a progressive complication of cirrhosis and is defined as a hepatic vein pressure gradient (gradient between portal and central venous pressure) of $>12\text{mmHg}$ (1). Hemorrhage from gastroesophageal varices is a common and serious complication of PH, with mortality rates as high as 50% with the initial episode (2). In this chapter we review the pathophysiology, diagnosis, and treatment of varices. We use current evidence-based articles to address primary and secondary prophylaxis of variceal hemorrhage and control of active variceal hemorrhage. Throughout we present practice guidelines for the diagnosis and treatment of variceal hemorrhage that have been developed and endorsed by the American Association for the Study of Liver Diseases and the American College of Gastroenterology and evaluated at the most recent international Baveno IV consensus conference (1,3).

PATHOPHYSIOLOGY OF PH

PH develops as a consequence of both increased resistance to portal blood flow and increased portal blood flow. Increased resistance to portal blood flow is due not only to architectural distortion in a fibrotic liver but also to intrahepatic vasoconstriction, mediated by contractile stellate cells, responding to decreased production of nitric oxide by adjacent hepatic endothelial cells. PH due to increased portal blood flow occurs as a consequence of increased splanchnic arterial flow, explained partly by decreased systemic vascular resistance and increased cardiac output seen in cirrhotic patients but also by direct splanchnic arteriolar vasodilatation mediated by multiple vasoactive agents.

IN CIRRHOTIC PATIENTS, WHAT IS THE MOST RELIABLE PREDICTOR OF VARICEAL DEVELOPMENT?

Measurement of the hepatic vein pressure gradient (HVPG) is the preferred way to assess PV pressure and is presently the most reliable predictor of variceal development (1). In this technique, a balloon catheter is advanced into the hepatic vein and is inflated to occlude a branch of the hepatic vein and measure the wedged hepatic vein pressure (WHVP). The balloon is then deflated and the free hepatic vein pressure (FHVP) is measured. The HVPG is the WHVP – FHVP. The normal HVPG is 3–5mmHg, and in PH the HVPG is $>12\text{mmHg}$ (1). The HVPG is elevated in sinusoidal causes of PH but is normal in presinusoidal causes of PH (1).

There is strong evidence that a reduction in HVPG with pharmacological intervention reduces the risk of variceal hemorrhage. Successful reduction in HVPG (“responders”) includes (1) HVPG $\leq 12\text{mmHg}$, or (2) HVPG $\geq 20\%$ from baseline regardless of final HVPG. Variceal hemorrhage does not occur when HVPG $\leq 12\text{mmHg}$ and the risk of recurrent variceal hemorrhage decreases significantly when HVPG $\geq 20\%$ from baseline. Two large meta-analyses determined that the risk of variceal hemorrhage and liver-related mortality were lower in patients who achieved HVPG reduction (5,6). Another study involving 71 cirrhotic

patients confirmed that propranolol $\pm$ isosorbide mononitrate (ISMN) significantly reduced the eight-year cumulative probability of no variceal hemorrhage to 90% in responders versus 45% in nonresponders, but there were no significant differences in liver-related mortality (7). Patients with HVPG $\geq 20\text{mmHg}$ had greater failure to control variceal hemorrhage (29% versus 83%), earlier recurrent hemorrhage, longer intensive care and hospital stays, more transfusion requirements, and worse one-year mortality (20% versus 64%) (8).

Answer: Although an invasive technique measurement of the HVPG is the preferred method to assess portal pressure and is predictive of variceal development (Ib/A). Final level of evidence/Grade of recommendation: Ib/A.

WHAT IS THE BEST DIAGNOSTIC TEST TO DETECT THE PRESENCE OF ESOPHAGEAL AND GASTRIC VARICES?

There are no satisfactory nonendoscopic indicators for the presence of varices (3). Although it is invasive, upper endoscopy is the gold standard to detect the presence of esophageal and gastric varices (1). Current consensus guidelines recommend that all patients with a new diagnosis of cirrhosis undergo screening upper endoscopy to examine for esophageal and gastric varices (1). Upper endoscopy is also the primary technique for the diagnosis and treatment of variceal hemorrhage (1).

Answer: Upper endoscopy remains the best diagnostic test to detect the presence of esophageal and gastric varices (V/D). Final level of evidence/Grade of recommendation: V/D.

IN CIRRHOTIC PATIENTS WHO HAVE NO VARICES BY UPPER ENDOSCOPY, WHAT IS THE BEST TREATMENT TO PREVENT DEVELOPMENT OF VARICES?

Without prior assessment of the presence of varices with screening upper endoscopy, there is no evidence to treat cirrhotic patients with β -blockers (3). When screening upper endoscopy demonstrates no varices, there is no evidence to treat cirrhotic patients with empiric β -blockers to prevent the formation of varices (1). In a study of 213 patients with no varices at screening upper endoscopy who were randomized to timolol (108 patients) versus placebo (105 patients), the development of varices did not differ between both groups (39% versus 40%, respectively) at a mean follow up of 54.9 months. The investigators noted that timolol not only did not prevent varices but also had more serious adverse events, including bradycardia, severe fatigue, wheezing, and syncope (timolol 18% versus placebo 6%) (9). Instead of β -blocker therapy, consensus guidelines suggest that compensated cirrhotics who have no varices on screening endoscopy should undergo surveillance upper endoscopy every two to three years; cirrhotics who develop hepatic decompensation should undergo surveillance upper endoscopy at that time and then annually to document new varices (1).

Answer: When upper endoscopy reveals no varices, data suggest that β -blockers are not helpful to prevent the formation of varices (Ib/A). Instead, these patients should

undergo regular surveillance upper endoscopy (V/D). Final level of evidence/Grade of recommendation: ranges from Ib/A to V/D.

IN CIRRHOTIC PATIENTS WHO HAVE SMALL VARICES, WHAT IS THE BEST TREATMENT TO PREVENT FIRST VARICEAL HEMORRHAGE?

Several studies suggest that compensated cirrhotics who have small varices on screening upper endoscopy should receive nonselective β -blockers to prevent growth to large varices and first variceal hemorrhage. A meta-analysis of three trials that examined nonselective β -blockers versus placebo in patients with small varices showed that the incidence of first variceal hemorrhage was low on placebo (7% over two years) and still lower on nonselective β -blockers (2% over two years), although the difference was not statistically significant (10). In another study, 161 cirrhotic patients with small varices on screening endoscopy were randomized to the nonselective β -blocker nadolol (83 patients) versus placebo (78 patients) and had surveillance upper endoscopy annually for five years (mean follow-up three years) to document growth from small to large varices. Nine (11%) patients on nadolol and 29 (37%) patients on placebo had growth from small to large varices, but there were no differences in survival. Freedom from first variceal hemorrhage was significantly higher in the nadolol group versus the placebo group (88% versus 78%), but more patients on nadolol (11%) versus placebo (1%) were removed from the trial because of adverse side effects (11).

Consensus guidelines suggest that compensated cirrhotics with small varices that have not bled should probably receive nonselective β -blockers, although survival benefit is unclear (1,3). Cirrhotics with small varices who have increased risk of gastrointestinal hemorrhage should receive nonselective β -blockers to prevent growth to larger varices (3). Compensated cirrhotics with small varices who receive β -blockers do not require repeat upper endoscopy (1). Compensated cirrhotics with small varices that have not bled and choose not to receive nonselective β -blockers should undergo surveillance upper endoscopy every two years (1). Cirrhotics with hepatic decompensation require surveillance upper endoscopy at that time then annually (1).

Answer: Patients with small varices (especially those with increased risk of gastrointestinal hemorrhage) should probably receive nonselective β -blockers to prevent growth to large varices (IIb/C). Final level of evidence/Grade of recommendation: IIb/C.

IN CIRRHOTIC PATIENTS WHO HAVE LARGE VARICES, WHAT IS THE BEST TREATMENT TO PREVENT FIRST VARICEAL HEMORRHAGE?

β -blockers

A meta-analysis of 11 trials with 1,189 cirrhotics with medium or large varices reported that β -blockers significantly reduced risk of first variceal hemorrhage versus placebo (14% versus 30%, respectively) (10). In a trial of 101 cirrhotics with large varices who received propranolol

0.15mg/kg IV followed by oral nadolol, hemodynamic responders had significantly lower risk of first variceal hemorrhage, fewer hospitalizations for decompensated cirrhosis, and lower mortality (12). A Cochrane review of cirrhotic patients with large varices demonstrated that the nonselective β -blockers propranolol and nadolol significantly reduced mortality when compared to placebo, although β -blockers significantly increased adverse side effects (13). A cost analysis that compared propranolol, sclerotherapy, and shunt surgery concluded that β -blockade was the only cost-effective therapy to prevent first variceal hemorrhage in high-risk cirrhotics with large varices (14). Abraczinskas et al. noted that prophylactic β -blockers in patients with medium to large varices should be used indefinitely, because removal of prophylactic β -blockers lead to an equal risk of first variceal hemorrhage and an increased mortality compared to an untreated population (15).

Endoscopic Band Ligation versus No Therapy

A meta-analysis of 5 trials with 601 patients who had medium or large varices reported that prophylactic endoscopic band ligation (EBL) versus no therapy significantly reduced the relative risk of first variceal hemorrhage, hemorrhage-related mortality, and all-cause mortality (16). In another abstract in which 74 patients with large varices but no history of gastrointestinal hemorrhage were randomized to EBL (36 patients) versus no therapy (38 patients), variceal hemorrhage occurred in only 1 (2.8%) patient in the EBL group and 4 (10.5%) patients in the control group, and no hemorrhage-related deaths occurred in either group (17).

In another abstract that examined EBL versus no therapy in cirrhotics with contraindications or intolerance to β -blockers, the trial was discontinued prematurely after randomization of 52 out of 214 planned patients because more variceal hemorrhage occurred than expected in the EBL group, even though mortality rates were similar. This was the first study to suggest that EBL was no better than no therapy and should be used cautiously for primary prophylaxis (18).

EBL versus Nonselective β -blockers

Twelve randomized controlled trials (RCTs) have compared EBL versus β -blockers in the prevention of first variceal hemorrhage in cirrhotics with large varices. Two of the RCTs demonstrated that EBL was superior to β -blockers, but the remaining 10 RCTs showed no significant differences between EBL and β -blockers (19). A recently published RCT demonstrated that EBL and propranolol were equally effective to decrease rates of first variceal hemorrhage (18% versus 16%, respectively) and overall mortality (28% versus 24%, respectively) (20).

Consensus guidelines recommend that when β -blockers are used, they should be adjusted upward to the maximally tolerated dose, and surveillance upper endoscopy is not necessary (1). When EBL is used, it should be repeated every one to two weeks until variceal obliteration, which usually requires two to four sessions. Surveillance upper endoscopy should occur 1–3 months after variceal obliteration and repeated every 6–12 months to screen for recurrent varices, which are again treated with EBL (1). After EBL, shallow ulcers at the base are common and sometimes bleed, so a

short course of IV pantoprazole significantly reduces the size of the ulcers (21).

A recent meta-analysis that included 8 of these 12 RCTs (596 patients total) demonstrated that EBL (285 patients) versus β -blockers (311 patients) reduced rates of first variceal hemorrhage in cirrhotics with medium and large varices by 43%; hemorrhage-related mortality and all-cause mortality were similar (22). Adverse events were significantly less frequent with EBL than β -blockers (4% versus 13%), but side effects with β -blockers (hypotension, fatigue, and shortness of breath) disappeared soon after withdrawal of the drug and did not require hospitalization. Ten of 41 patients who stopped β -blockers ultimately bled from varices, resulting in two deaths. Although less frequent, the side effects of EBL were much more severe, including ligation-induced esophageal ulcers (10 patients) and esophageal perforation (1 patient). Most of these side effects required hospitalization and blood transfusions, and they resulted in two deaths.

EBL + Nonselective β -blocker versus EBL Alone

One trial of 144 cirrhotics with high-risk varices noted that EBL + propranolol (72 patients) versus EBL alone (72 patients) were equally effective in the prevention of first variceal hemorrhage and hemorrhage-related death. The addition of propranolol, however, decreased variceal recurrence, although side effects were seen in 22% of patients, 34% of whom required drug removal (23).

Answer: Nonselective β -blockers reduce the risk of first variceal hemorrhage in patients with large varices (Ia/A). EBL is probably more effective than nonselective β -blockers to reduce the risk of first variceal hemorrhage in these patients, but it may not improve survival (Ia/A). EBL should be recommended when these patients have contraindications or intolerance to β -blocker therapy (V/D). Final level of evidence/Grade of recommendation: ranges from Ia/A to V/D.

IN CIRRHOTIC PATIENTS WHO HAVE ACUTE VARICEAL HEMORRHAGE, WHAT SPECIFIC RESUSCITATIVE FLUIDS SHOULD BE GIVEN?

Current treatment strategies for acute variceal hemorrhage have resulted in improved survival in the United States (1). A meta-analysis of 28 studies with 1,475 cirrhotic patients reported that hemorrhage-related mortality decreased from 65% to 40% between 1960 and 2000 (24). Resuscitation and management of patients with acute variceal hemorrhage should occur in the intensive care unit under the supervision of well-trained staff (19). Initial management includes airway assessment/protection and placement of large peripheral venous catheters for blood volume resuscitation (1). Replacement of blood loss should be done promptly but cautiously, often with colloid infusion to maintain hemodynamic stability and with packed red cells to maintain hemoglobin near 8g/dl (1,3). Overzealous replacement of blood can lead to increased portal pressure, causing persistent hemorrhage and greater mortality (1). Similarly, aggressive resuscitation with saline should be avoided because it can precipitate or worsen ascites, pleural effusion, or peripheral edema in cirrhotic patients (1). Transfusions of fresh frozen

plasma and platelets can be considered in patients with significant coagulopathy and thrombocytopenia, but data are limited (1,3).

Answer: Prompt but careful resuscitation of blood loss with acute variceal hemorrhage should occur with colloid to maintain hemodynamic stability and with packed cells to maintain hemoglobin near 8g/dl (Ia/A). Data regarding management of coagulopathy and thrombocytopenia are limited (V/D). Final level of evidence/Grade of recommendation: ranges from Ib/A to V/D.

IN CIRRHOTIC PATIENTS WHO HAVE ACUTE VARICEAL HEMORRHAGE, WHAT IS THE ROLE OF PROPHYLACTIC ANTIBIOTICS, IF ANY?

Cirrhotic patients with acute variceal hemorrhage are at great risk to develop bacterial infection—especially spontaneous bacterial peritonitis (SBP), which is associated with early variceal hemorrhage and greater mortality (1). A large meta-analysis of patients with acute variceal hemorrhage showed that prophylactic antibiotics significantly increased the mean percentage of patients free from all infections, bacteremia or SBP, and increased mean survival rate (25). In another study proven bacterial infection was an independent factor in failure to control acute variceal hemorrhage (26). Still another study reported that antibiotic prophylaxis prevented early recurrent hemorrhage and reduced the number of blood transfusions necessary when patients bled after initial endoscopic control (27). Prophylactic antibiotics should begin at hospital admission, and the recommended antibiotic is oral norfloxacin 400mg twice a day or IV quinolone for seven days (if patient cannot take oral medications) (1). A recent study of 100 cirrhotic patients with variceal hemorrhage demonstrated that the risk of infections was significantly less with IV ceftriaxone than oral norfloxacin (28).

Answer: Prophylactic antibiotics should begin at hospital admission for all patients who present with acute variceal hemorrhage, because they decrease bacterial infection, improve failure to control acute variceal hemorrhage, prevent recurrent variceal hemorrhage, and decrease mortality (Ia/A). Level of evidence/Grade of recommendation: Ia/A.

IN CIRRHOTIC PATIENTS WHO HAVE ACUTE VARICEAL HEMORRHAGE, WHAT IS THE BEST TREATMENT TO CONTROL HEMORRHAGE?

Pharmacological Intervention in Acute Variceal Hemorrhage

When variceal hemorrhage is suspected, pharmacological intervention should begin promptly and continue for three to five days, even before upper endoscopy confirms the diagnosis (1,3). Pharmacological intervention will control acute variceal hemorrhage in 83% of cases. A meta-analysis of 15 trials reported that sclerotherapy was equivalent to pharmacological therapy (terlipressin, somatostatin, or octreotide) but had more severe side effects, suggesting that pharmacological intervention—not sclerotherapy—should be the first-line therapy in the control of acute variceal hemorrhage (29). β -blockers should not be administered with active variceal hemorrhage, because they drop systolic

blood pressure and mask tachycardia that occurs as a normal response to blood loss (1).

Several vasoactive drugs are available for the control of acute variceal hemorrhage, including vasopressin, terlipressin, and somatostatin (and its analogs). Vasopressin is administered as a continuous infusion at 0.2–0.4 U/min and can be increased to a maximal rate of 0.8 U/min. Because vasopressin can cause cardiac, intestinal, and peripheral ischemia, it is used at the highest effective dose for only 24 continuous hours. To counteract these side effects, nitroglycerin is often used as a continuous infusion and adjusted to maintain a systolic blood pressure >90 mmHg (1).

Terlipressin, a synthetic analog of vasopressin with fewer side effects, is administered as an intermittent injection rather than a continuous infusion at an initial dose of 2 mg IV every four hours and decreased to 1 mg IV every four hours after control of hemorrhage (1). Because no other vasoactive medication reduces mortality, terlipressin should really be considered the first-line therapy in acute variceal hemorrhage, although it is currently not available in the United States (1,30).

Somatostatin and its analogs octreotide and vapreotide are very safe agents that can be administered for two to five continuous days, but only octreotide is available in the United States. Octreotide and vapreotide are administered as an initial 50 µg IV bolus followed by infusion at 50 µg/hour, whereas somatostatin is administered as an initial 250 µg IV bolus followed by infusion at 250 µg/hour (1). The conclusions of meta-analyses that examined octreotide administration for acute variceal hemorrhage are mixed. A meta-analysis of 13 trials reported that octreotide improved control of active variceal hemorrhage better than vasopressin or terlipressin, had fewer complications than vasopressin or terlipressin, and had a complication profile similar to placebo, but had no beneficial effect on mortality (31). A Cochrane review of 21 trials involving 2,588 patients noted that octreotide decreased the number of patients who failed initial control of hemorrhage and the number of blood transfusions necessary, but did not reduce the number of patients with recurrent hemorrhage or mortality rates (32). Octreotide alone may not be useful due to reported cases of tachyphylaxis, but may be much more beneficial when administered in conjunction with endoscopic therapy (1).

Endoscopic Intervention in Acute Variceal Hemorrhage

Once variceal hemorrhage is suspected and pharmacological therapy is initiated, upper endoscopy should be performed as soon as possible, usually within 12 hours from admission (1,3). If variceal hemorrhage is confirmed by upper endoscopy, endoscopic therapy should be employed to control hemorrhage (1,3). A meta-analysis of 10 trials with 404 patients reported better initial control of variceal hemorrhage with EBL versus sclerotherapy (19). One study in this meta-analysis demonstrated that although a significant increase in HVPG occurred immediately after both EBL and sclerotherapy, HVPG returned to baseline within 48 hours in the EBL group but remained elevated for the study duration (five days) in the sclerotherapy group. In the six-week follow-up period, recurrent hemorrhage was lower in the EBL group than in the sclerotherapy group, so a

persistently increased HVPG carried greater risk of recurrent hemorrhage (33). Current consensus guidelines recommend EBL as the preferred endoscopic technique to control acute variceal hemorrhage, but sclerotherapy can be used if EBL is technically difficult or not feasible (1,3).

A combination of initial pharmacological intervention followed by prompt upper endoscopy appears to be the most rational approach to control variceal hemorrhage (1,3). In a meta-analysis of 8 trials with 939 patients, this combined approach versus endoscopic therapy alone improved initial control of variceal hemorrhage and continuous five-day hemostasis, although severe adverse side effects and five-day mortality rates were equal (34). Failure of initial control of acute variceal hemorrhage with this combined approach is best managed with a second attempt of endoscopic therapy before considering rescue therapy (3).

Rescue Therapy for Acute Variceal Hemorrhage

Even though a Senstaaken-Blakemore tube controls acute variceal hemorrhage promptly, it should be used only as a temporizing measure, reserved for patients with uncontrollable hemorrhage for whom a definitive therapy (transjugular intrahepatic portosystemic shunt [TIPSS] or surgical shunt) is planned (1,3). Careful consideration should be exercised before placement of the Senstaaken-Blakemore tube because its use is associated with significant complications (aspiration, tube migration, esophageal necrosis, and perforation) that carry a 20% mortality rate (1).

Shunt Therapy

Because a surgical shunt reduces HVPG promptly, it has proven efficacy in limited retrospective trials for patients with acute variceal hemorrhage who fail combined pharmacological and endoscopic treatment (1). In 400 unselected patients followed over three decades, Orloff performed urgent side-to-side portocaval shunts and reported immediate and permanent control of variceal hemorrhage in 99% of patients and shunt thrombosis in only 0.5% of patients. Survival rates in the most recent cohort of 220 patients at 30 days, 5 years, 10 years, and 15 years were 85%, 78%, 71%, and 57%, respectively, and hepatic encephalopathy occurred in only 8% of patients (35). Urgent portocaval shunt is not widely accepted or used for control of acute variceal hemorrhage, and this surgical approach needs validation in large prospective randomized trials (1).

There are limited trials describing the use of emergent TIPSS for the control of acute variceal bleeding in patients who fail combined pharmacological and endoscopic intervention (1). One study compared emergent TIPSS in 11 patients who failed endoscopic treatment versus elective TIPSS in 22 patients who were stable after initial control of variceal hemorrhage. Although hemorrhage was controlled by emergent TIPSS in 10/11 patients, early recurrent hemorrhage (≤two weeks) and TIPSS occlusion occurred more frequently after emergent than elective TIPSS, but hepatic encephalopathy and mortality were similar in both groups (36). In another study of 100 consecutive patients with refractory or recurrent variceal hemorrhage, Sahagun et al. reported that emergent TIPSS placement controlled all cases of refractory hemorrhage (37). Another trial of 181 patients with acute or recurrent variceal hemorrhage reported a 51.4% mortality rate within 30 days after TIPSS placement,

and subgroup analysis showed an even higher mortality rate in patients with emergent TIPSS placement, so the indications for emergent TIPSS placement must be delineated clearly (38). Larger prospective randomized trials must be performed before emergent TIPSS can be firmly recommended for control of acute variceal hemorrhage (1).

Liver Transplantation

Liver transplantation is not a feasible rescue therapy for acute variceal hemorrhage due to lack of regular supply of donor organs. Liver transplantation is sometimes necessary for patients who develop hepatic decompensation after an operative shunt for refractory variceal hemorrhage (39).

Answer: When acute variceal hemorrhage is suspected, pharmacological intervention should begin immediately, even before variceal hemorrhage is confirmed by upper endoscopy (Ib/A). Upper endoscopy should be performed as soon as possible (Ia/A), and, if variceal hemorrhage is confirmed, endoscopic therapy preferably with EBL should be used to control hemorrhage (Ib/A). This combined approach of initial pharmacological intervention followed by prompt upper endoscopy appears to be the most rational approach to control variceal hemorrhage, although data are limited (Ia/A). Failure to control acute variceal hemorrhage should prompt a second endoscopic attempt before considering rescue therapy with TIPSS or surgical shunt (IIb/B). Balloon tamponade should be considered as a temporizing measure only if definitive therapy is planned (IIb/B). There is no role for liver transplantation in acute variceal hemorrhage due to lack of regular supply of donor organs. Final level of evidence/Grade of recommendation: ranges from Ia/A to Ib/B.

IN CIRRHOTIC PATIENTS WHO RECOVER FROM ACUTE VARICEAL HEMORRHAGE, WHAT IS THE BEST TREATMENT TO PREVENT FURTHER VARICEAL HEMORRHAGE?

Patients who recover from variceal hemorrhage should receive secondary prophylaxis to prevent recurrent hemorrhage (1). Patients who required rescue therapy with TIPSS or surgical shunt do not need secondary prophylaxis (1). If suitable candidates otherwise, all of these patients should be referred to liver transplant centers early (1).

β -blockers

A meta-analysis of 26 studies involving 983 patients showed that nonselective β -blockers reduced rates of recurrent hemorrhage to 37–57% with mortality rates of 13–39% (40). The combination of nonselective β -blockers + ISMN may be more effective in the prevention of recurrent hemorrhage, but the combination carries greater side effects and has no beneficial effect on mortality, so most patients usually take nonselective β -blockers only (1,41).

EBL versus Sclerotherapy

EBL was shown long ago to be superior to sclerotherapy in the prevention of recurrent hemorrhage (1). A meta-analysis of 18 studies involving 836 patients demonstrated

that the rate of recurrent hemorrhage after EBL was 20–43% (median 32%) with mortality rates of 19–34% (median 27%), whereas a meta-analysis of 54 studies involving 2,347 patients showed that the rate of recurrent hemorrhage after sclerotherapy was 34–53% (median 44%) with mortality rates of 18–36% (median 27%) (40).

EBL versus EBL + Sclerotherapy

Two large meta-analyses have compared EBL alone versus EBL + sclerotherapy (combined therapy) in the prevention of recurrent hemorrhage. In both studies there was no significant difference between EBL alone versus combined therapy in the risk of recurrent hemorrhage, the number of endoscopic sessions to achieve variceal obliteration, and mortality, but the combined therapy had greater risk of esophageal stricture. Therefore, combined therapy offers no advantage over EBL alone in the prevention of recurrent hemorrhage (42,43).

β -blockers versus EBL

Three randomized studies that compared optimal pharmacological therapy (nonselective β -blockers + nitrates) versus EBL in the prevention of recurrent hemorrhage showed mixed results (1). One study randomized EBL (72 patients) versus nadolol + ISMN (72 patients) and noted significantly higher rates of recurrent hemorrhage (49% versus 33%) and more severe adverse events in the EBL group. Recurrent hemorrhage and one-year mortality were significantly lower for patients who achieved targeted hemodynamic response over those who did not (44). Another study randomized EBL (60 patients) versus nadolol + ISMN (61 patients) and noted that recurrent hemorrhage was significantly lower in the EBL group (20% versus 42%), but both groups had similar complications and mortality rates (45). A third study randomized EBL (51 patients) versus propranolol + ISMN (51 patients) and noted similar recurrent hemorrhage rates at one year (53.8% versus 43.7%) (46).

Combination of EBL and β -blockers

Combined endoscopic and pharmacological therapy is probably the most rational approach to prevent recurrent hemorrhage, although data are limited (1,3). One study randomized EBL alone (62 patients) versus triple therapy (EBL, sulcralfate, and nadolol) (60 patients) and reported that the EBL alone group had significantly greater rates of variceal recurrence (50% versus 26%) and recurrent hemorrhage (29% versus 12%) (47). Another study randomized EBL alone (37 patients) versus EBL + nadolol (43 patients) and noted significantly more recurrent variceal hemorrhage in the EBL alone group (38% versus 14%). The probability of recurrent hemorrhage at one year was lower in the combined group versus the EBL alone group (54% versus 77%), although mortality rates were similar (48). Outcomes from these two trials supported combined endoscopic and pharmacological therapy for the prevention of recurrent variceal hemorrhage, even though a recent consensus conference recommended EBL or combined pharmacological therapy (β -blocker + nitrate) for secondary prophylaxis (1,3). Patients who develop recurrent variceal hemorrhage on EBL or β -blocker therapy alone should receive combined therapy (1). Patients who fail combined endoscopic and

pharmacological therapy should be considered for TIPSS or surgical shunts (1,3).

TIPSS versus EBL

Two large meta-analyses noted that TIPSS prevented recurrent variceal hemorrhage better than endoscopic therapy, but TIPSS carried a greater risk of encephalopathy with no survival benefit (49,50). Another large trial that randomized high risk cirrhotics to TIPSS (47 patients) versus optimal pharmacological therapy (propranolol + ISMN) (44 patients) noted similar outcomes, but reported that the cost was double for TIPSS-treated patients (51). These data suggest that although TIPSS prevents recurrent variceal hemorrhage effectively, it should be used as rescue therapy for patients who have failed combined endoscopic and pharmacological treatment (1,3).

TIPSS versus Surgical Shunt

For child A/B patients with recurrent variceal hemorrhage who failed combined endoscopic and pharmacological therapy, one study noted that TIPSS and distal splenorenal shunt (DSRS) had similar rates of hemorrhage (TIPSS 10.5%, DSRS 5.5%), encephalopathy (TIPSS 50%, DSRS 50%), and survival at two and five years (TIPSS 88% and 61%, DSRS 81% and 62%, respectively). The development of ascites, need for transplant, quality of life, and cost were similar in both groups. Stenosis, thrombosis, and need for reintervention were significantly greater in the TIPSS group versus the DSRS group (52). In another study which randomized patients to polytetrafluoroethylene-covered stents (39 patients) versus usual stents (41 patients), the use of covered stents significantly decreased rates of TIPSS dysfunction, thereby decreasing rates of recurrent hemorrhage (53). Because both TIPSS and DSRS have equivalent outcomes in regard to recurrent hemorrhage in child A/B patients, the option really depends on center-specific expertise and the ability to monitor shunts and intervene when appropriate (1). In poor operative candidates, TIPSS is the only realistic option although TIPSS surveillance is mandatory. Finally TIPSS can be used as a bridge to liver transplantation (3).

Answer: For cirrhotic patients who recover from acute variceal hemorrhage, data support a combination of β -blocker and endoscopic therapy (Ib/B), even though a recent consensus conference recommended EBL or combined pharmacological therapy (β -blocker + nitrate) (Ia/A). Patients who develop recurrent variceal hemorrhage on EBL or β -blocker therapy alone should receive combined therapy (Ib/B). Patients who fail combined therapy should be considered for TIPSS or surgical shunt (IIb/B). TIPSS can be used as a bridge to transplantation (IV/C), and suitable candidates should be referred to specialized liver transplant centers early (IIb/B). Final level of evidence/Grade of recommendation: ranges from Ia/A to IV/C.

CONCLUSION

Results from evidence-based protocols have clearly changed the treatment of variceal hemorrhage. HVPG measurement has become the most reliable predictor of variceal development, and screening upper endoscopy

remains the best tool to detect esophageal and gastric varices. No medical therapy is available to prevent the formation of varices, but nonselective β -blockers and EBL are equivalent therapies to prevent first variceal hemorrhage in patients with medium or large varices. Acute variceal hemorrhage requires prompt but careful resuscitation; overzealous resuscitation can lead to persistent variceal hemorrhage. Antibiotic therapy is critical to prevent bacterial infections in patients with acute variceal hemorrhage. A combination of immediate pharmacological therapy followed by prompt endoscopic therapy appears to be the most reasonable approach for acute variceal hemorrhage. For patients who fail optimal medical therapy for acute variceal hemorrhage, rescue techniques (Senstaaken-Blakemore tube placement, TIPSS, and surgical shunts) can be carefully considered. Combined pharmacological and endoscopic therapy appears to be the most effective approach in the prevention of recurrent variceal hemorrhage, and TIPSS and operative shunts are reserved for patients who fail combined therapy. TIPSS can be used as a bridge to liver transplantation, and suitable patients should be referred to specialized liver transplant centers early (1,3).

REFERENCES

1. Garcia-Tsao G, Sanyal AJ, Grace ND, et al. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007; 46: 922–38.
2. Qureshi W, Adler DG, Davila R, et al. ASGE Guideline: the role of endoscopy in the management of variceal hemorrhage, updated July 2005. *Gastrointest Endosc* 2005; 62: 651–5.
3. de Franchis R. Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 2005; 43: 167–76.
4. Wolf DC. Cirrhosis. eMedicine. Available from <http://emedicine.medscape.com/article/185856-overview>. Accessed April 2, 2009.
5. Albillos A, Banares R, Gonzalez M, et al. Value of the hepatic venous pressure gradient to monitor drug therapy for portal hypertension: a meta-analysis. *Am J Gastroenterol* 2007; 102: 1116–26.
6. D'Amico G, Garcia-Pagan JC, Luca A, et al. Hepatic vein pressure gradient reduction and prevention of variceal bleeding in cirrhosis: a systematic review. *Gastroenterology* 2006; 131: 1611–24.
7. Turnes J, Garcia-Pagan JC, Abraldes JG, et al. Pharmacological reduction of portal pressure and long-term risk of first variceal bleeding in patients with cirrhosis. *Am J Gastroenterol* 2006; 101: 506–12.
8. Moitinho E, Escorsell A, Bandi JC, et al. Prognostic value of early measurements of portal pressure in acute variceal bleeding. *Gastroenterology* 1999; 117: 626–31.
9. Groszmann RJ, Garcia-Tsao G, Bosch J, et al. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. *N Engl J Med* 2005; 353: 2254–61.
10. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. *Semin Liver Dis* 1999; 19: 475–505.
11. Merkel C, Marin R, Angeli P, et al. A placebo-controlled clinical trial of nadolol in the prophylaxis of growth of small esophageal varices in cirrhosis. *Gastroenterology* 2004; 127: 476–84.

12. Aracil C, Lopez-Balaguer J, Monfort D, et al. Hemodynamic response to beta-blockers and prediction of clinical efficacy in the primary prophylaxis of variceal bleeding in patients with cirrhosis. *Hepatology* 2003; 38(S4): 296A.
13. Chen W, Nikolova D, Fredericksen S, et al. Beta-blockers reduce mortality in cirrhotic patients with oesophageal varices who have never bled. *J Hepatol* 2004; 40(Suppl 1): 67.
14. Teran JC, Imperiale TF, Mullen KD, et al. Primary prophylaxis of variceal bleeding in cirrhosis: a cost-effectiveness analysis. *Gastroenterology* 1997; 112: 473–82.
15. Abraczinskas DR, Ookubo R, Grace ND, et al. Propranolol for the prevention of first esophageal variceal hemorrhage: a lifetime commitment? *Hepatology* 2001; 34: 1096–102.
16. Imperiale TF, Chalasani N. A meta-analysis of endoscopic variceal ligation for primary prophylaxis of esophageal variceal bleeding. *Hepatology* 2001; 33: 802–7.
17. Omar M, Attia M, Mostafa I. Prophylactic band ligation of large esophageal varices. *J Hepatol* 2000; 32(S2): 73.
18. Triantos C, Vlachogiannakos J, Armonis A, et al. Is prophylactic banding always safe? Randomized controlled trial for the prevention of first variceal bleeding in cirrhotic patients with contraindications or intolerance to beta-blockers. *J Hepatol* 2004; 40(S1): 73.
19. Garcia-Pagan JC, Bosch J. Endoscopic band ligation in the treatment of portal hypertension. *Nat Clin Pract Gastroenterol Hepatol* 2005; 2: 526–35.
20. Lay CS, Tsai YT, Lee FY, et al. Endoscopic variceal ligation versus propranolol in prophylaxis of first variceal bleeding in patients with cirrhosis. *J Gastroenterol Hepatol* 2006; 21: 413–19.
21. Shaheen NJ, Stuart E, Schmitz SM, et al. Pantoprazole reduces the size of postbanding ulcers after variceal band ligation: a randomized, controlled trial. *Hepatology* 2005; 41: 588–94.
22. Khuroo MS, Khuroo NS, Farahat KL, et al. Meta-analysis: endoscopic variceal ligation for primary prophylaxis of oesophageal variceal bleeding. *Aliment Pharmacol Ther* 2005; 21: 347–61.
23. Sarin SK, Wadhawan M, Agarwal SR, et al. Endoscopic variceal ligation plus propranolol versus endoscopic variceal ligation alone in primary prophylaxis of variceal bleeding. *Am J Gastroenterol* 2005; 100: 797–804.
24. McCormick PA, O'Keefe C. Improving prognosis following a first variceal haemorrhage over four decades. *Gut* 2001; 49: 682–5.
25. Bernard B, Grange JD, Khac EN, et al. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. *Hepatology* 1999; 29: 1655–61.
26. Goulis J, Armonis A, Patch D, et al. Bacterial infection is independently associated with failure to control bleeding in cirrhotic patients with gastrointestinal hemorrhage. *Hepatology* 1998; 27: 1207–12.
27. Hou MC, Lin HC, Liu TT, et al. Antibiotic prophylaxis after endoscopic therapy prevents rebleeding in acute variceal hemorrhage: a randomized trial. *Hepatology* 2004; 39: 746–53.
28. Fernandez J, Ruiz del Arbol L, Gomez C, et al. Norfloxacin vs ceftriaxone in the prophylaxis of infections in patients with advanced cirrhosis and hemorrhage. *Gastroenterology* 2006; 131: 1049–56.
29. D'Amico G, Pietrosi G, Tarantino I, et al. Emergency sclerotherapy versus vasoactive drugs for variceal bleeding in cirrhosis: a Cochrane meta-analysis. *Gastroenterology* 2003; 124: 1277–91.
30. Ioannou G, Doust J, Rockey DC. Terlipressin for acute esophageal variceal hemorrhage. *Cochrane Database Syst Rev* 2001; CD002147.
31. Corley DA, Cello JP, Adkisson W, et al. Octreotide for acute esophageal variceal bleeding: A meta-analysis. *Gastroenterology* 2001; 120: 946–54.
32. Gotzsche PC, Hrobjartsson A. Somatostatin analogues for acute bleeding oesophageal varices. *Cochrane Database Syst Rev* 2008; CD000193.
33. Avgerinos A, Armonis A, Stefanidis G, et al. Sustained rise of portal pressure after sclerotherapy, but not band ligation, in acute variceal bleeding in cirrhosis. *Hepatology* 2004; 39: 1623–30.
34. Banares R, Albillos A, Rincon D, et al. Endoscopic treatment versus endoscopic plus pharmacological treatment for acute variceal bleeding: a meta-analysis. *Hepatology* 2002; 35: 609–15.
35. Orloff MJ, Orloff MS, Orloff SL, et al. Three decades of experience with emergency portacaval shunt for acutely bleeding esophageal varices in 400 unselected patients with cirrhosis of the liver. *J Am Coll Surg* 1995; 180: 257–72.
36. Gerbes AL, Gulberg V, Wiggershauser T, et al. Transjugular intrahepatic portosystemic shunt (TIPS) for variceal bleeding in portal hypertension: comparison of emergency and elective interventions. *Dig Dis Sci* 1998; 43: 2463–9.
37. Sahagun G, Benner KG, Saxon R, et al. Outcome of 100 patients after transjugular intrahepatic portosystemic shunt for variceal hemorrhage. *Am J Gastroenterol* 1997; 92: 1444–52.
38. Domagk D, Patch D, Dick R, et al. Transjugular intrahepatic portosystemic shunt in the treatment of portal hypertension using memotherm stents: a prospective multicenter study. *Cardiovasc Intervent Radiol* 2002; 25: 506–12.
39. Orloff MJ, Orloff MS, Girard B, et al. When is liver transplant indicated in cirrhosis with bleeding varices? *Transplant Proc* 2001; 33: 1366.
40. Bosch J, Garcia-Pagan JC. Prevention of variceal rebleeding. *Lancet* 2003; 361: 952–4.
41. Gournay J, Masliah C, Martin T, et al. Isosorbide mononitrate and propranolol compared with propranolol alone for the prevention of variceal rebleeding. *Hepatology* 2000; 31: 1239–45.
42. Singh P, Pooran N, Indaram A, et al. Combined ligation and sclerotherapy versus ligation alone for secondary prophylaxis of esophageal variceal bleeding: a meta-analysis. *Am J Gastroenterol* 2002; 97: 623–9.
43. Karsan HA, Morton SC, Shekelle PG, et al. Combination endoscopic band ligation and sclerotherapy compared with endoscopic band ligation alone for the secondary prophylaxis of esophageal variceal hemorrhage: a meta-analysis. *Dig Dis Sci* 2005; 50: 399–406.
44. Villanueva C, Minana J, Ortiz J, et al. Endoscopic ligation compared with combined treatment with nadolol and isosorbide mononitrate to prevent recurrent variceal bleeding. *N Engl J Med* 2001; 345: 647–55.
45. Lo GH, Chen WC, Chen MH, et al. Banding ligation versus nadolol and isosorbide mononitrate for the prevention of esophageal variceal rebleeding. *Gastroenterology* 2002; 123: 728–34.
46. Patch D, Sabin CA, Goulis J, et al. A randomized, controlled trial of medical therapy versus endoscopic ligation for the prevention of variceal rebleeding in patients with cirrhosis. *Gastroenterology* 2002; 123: 1013–19.
47. Lo GH, Lai KH, Cheng JS, et al. Endoscopic variceal ligation plus nadolol and sucralfate compared with ligation alone for the prevention of variceal rebleeding: a prospective, randomized trial. *Hepatology* 2000; 32: 461–5.
48. de la Pena J, Brullet E, Sanchez-Hernandez E, et al. Variceal ligation plus nadolol compared with ligation for prophylaxis of variceal rebleeding: a multicenter trial. *Hepatology* 2005; 41: 572–8.
49. Papatheodoridis GV, Goulis J, Leandro G, et al. Transjugular intrahepatic portosystemic shunt compared with endoscopic treatment for prevention of variceal rebleeding: a meta-analysis. *Hepatology* 1999; 30: 612–22.

50. Luca A, D'Amico G, La Galla R, et al. TIPS for prevention of recurrent bleeding in patients with cirrhosis: meta-analysis of randomized clinical trials. *Radiology* 1999; 212: 411–21.
51. Escorsell A, Banares R, Garcia-Pagan JC, et al. TIPS versus drug therapy in preventing variceal rebleeding in advanced cirrhosis: a randomized controlled trial. *Hepatology* 2002; 35: 385–92.
52. Henderson JM, Boyer TD, Kutner MH, et al. Distal splenorenal shunt versus transjugular intrahepatic portal systematic shunt for variceal bleeding: a randomized trial. *Gastroenterology* 2006; 130: 1643–51.
53. Bureau C, Garcia-Pagan JC, Otal P, et al. Improved clinical outcome using polytetrafluoroethylene-coated stents for TIPS: results of a randomized study. *Gastroenterology* 2004; 126: 469–75.

Gangrene of the Foot

Maureen K. Sheehan

Gangrene of the Foot: Question Summary

Question	Answer	Grade of recommendation
What imaging or testing is best?	ABI and TBI for screening MRA, CTA, duplex for operative planning.	B
Is cardiac work-up necessary?	No. Maximize medical management.	A, C
Is endovascular or open revascularization best?	Endovascular first approach is reasonable in most patients.	B
Is primary amputation best for some patients?	Yes, in select patients.	C

Abbreviations: ABI, ankle-brachial index; CTA, computed tomography angiography; MRA, magnetic resonance arteriography; TBI, toe-brachial index.

Gangrene of the lower extremity most frequently occurs in the toes and is a result of inadequate perfusion. Gangrene can be either wet, in which there is liquefaction of tissue secondary to bacterial infection, or dry, which is comprised of desiccated dead tissue. The incidence of gangrene is not well known. However, epidemiologic information for critical limb ischemia (CLI), of which gangrene is a subset, although still limited, is more available. In Italy a seven-year prospective study estimated the rate of CLI as 450–650 cases per million people per year (1). A national survey in Great Britain and Ireland reported an incidence of 4,000 patients per million population per year (2).

WHAT VASCULAR TESTING OR IMAGING IS BEST FOR PATIENTS WITH GANGRENE?

Patients who present with gangrene require evaluation of the peripheral arterial system to assess if the problem is microvascular in nature, that is, disease at the arteriolar level, or macrovascular due to atherosclerosis of larger vessels. If evaluation determines the gangrene is due to microvascular disease, either nonoperative management with aggressive wound care or a limited amputation (i.e., toe or transmetatarsal amputation) is generally sufficient and the amputation site should heal without vascular operative intervention. However, if testing demonstrates significant peripheral arterial disease involving the iliac, femoral, popliteal, or infrageniculate vessels, then revascularization is usually required for the tissue and/or amputation site to heal.

Multiple modalities exist for evaluation of the arterial system. Ankle-brachial index (ABI) can demonstrate decrease blood flow to an extremity as well as severity of disease. However, the ABI can be unreliable in patients with diabetes who are more likely to have medial calcinosis, which may cause the arteries to be stiff and noncompliant.

The vessel may then be either noncompressible or give a falsely elevated pressure, leading to a normal ABI despite presence of severe disease. Toe-brachial indices (TBIs) are frequently more useful in such patients except in the face of gangrene of the toe or significant isolated microvascular disease, in which case the TBI is not reflective of the blood flow of the entire leg. Whereas they can determine whether peripheral arterial disease is present, neither ABIs nor TBIs localize the disease. As such, ABIs and TBIs are best used as screening tests to evaluate for the presence of significant atherosclerotic disease. Pulse volume recordings (PVRs) can assist in localizing disease but cannot specifically isolate or visualize the disease. To determine which intervention may be best for a patient additional testing modalities such as duplex, computed tomography angiography (CTA), or magnetic resonance arteriography (MRA) need to be employed for better visualization of the disease.

Duplex ultrasound with Doppler provides visualization of the vessel as well as the flow through the vessel, demonstrating the stenosis or occlusion. Based on flow velocity criteria, duplex scanning can determine if a vessel is disease free, has less than 50% stenosis, or has more than 50% stenosis, which is the criteria used to ascertain if intervention is warranted. Although many physicians still use the duplex as a screening tool, others have reported using it as the definitive test by which intervention is determined or performed (3). Duplex ultrasonography has the advantage of being noninvasive and not requiring contrast.

Both CTA and MRA require contrast injection for vessel visualization. Compared to CTA, MRA has the advantage of not requiring iodinated contrast. Therefore it is felt to be less nephrotoxic than CTA, however, more recent reports of nephrogenic systemic fibrosis have resulted in recommendations that gadolinium not be used in patients with a glomerular filtration rate (GFR) of 30 ml/min/1.73 m².

Hingorani et al. (4) compared MRA and duplex angiography (DA) with contrast angiography (CA) for visualization of lower extremity arterial tree prior to and for planning of revascularization in 61 patients (64 procedures). The indication in the majority (90%) of these patients was CLI (gangrene 43%, ischemic ulcer 28%, rest pain 19%). Accuracy was assessed by arterial segments (iliac, femoropopliteal, tibial). Of the 192 arterial segments, 17% were unable to be fully assessed with DA, whereas with MRA, only 7% were unable to be fully assessed. Between CA and DA, discordance was found in iliac, femoropopliteal, and tibial segments 0%, 7%, and 14% of the time, respectively, and between CA and MRA discordance was 10%, 26%, and 42%. When including nonvisualized segments as false negatives, accuracy of MRA was 84%, 90%, and 65% for aortoiliac, femoropopliteal, and tibial segments, respectively, whereas for DA accuracies were 81%, 75%, and 43%, respectively. The authors concluded that although neither testing modality may completely replace contrast angiography, either can be used as preoperative imaging tools (Level IIb).

Heijenbroek-Kal et al. (5) performed a meta-analysis of the use of multi-detector CTA for assessing lower extremity arterial disease. Seventy studies were initially identified, of which 12 were included in the meta-analysis and resulted in the evaluation of 9,541 arterial segments in 436 patients. To detect a stenosis of >50%, the pooled sensitivity and specificity were 92% [95% confidence interval (CI) 89–95%] and 93% (95% CI 91–95%), respectively. The indication for testing was claudication in the majority of patients (75%), nonetheless the meta-analysis showed that CTA is an accurate test to evaluate the lower extremity for significant arterial disease (Level IIa).

A similar meta-analysis was performed by Koelemay et al. (6) examining the role of MRA for detecting lower extremity arterial disease. Pooled analysis demonstrated that MRA is highly accurate in diagnosing >50% stenosis or occlusion of arteries in the lower extremity (Level IIa).

Recommendation: Patients with gangrene need initial screening for presence of peripheral arterial disease with ABIs, TBIs, and/or PVRs. If peripheral arterial disease is present, additional testing modalities are necessary to visualize disease and plan for intervention. MRA, CTA, or duplex examination can all give adequate visualization. Because all are technician-dependent, which modality is used may depend on resources available to the individual physician (Grade B).

IS PREOPERATIVE CARDIAC WORK-UP INDICATED IN PATIENTS REQUIRING OPERATIVE INTERVENTION FOR GANGRENE?

Patients with gangrene or any form of CLI are at higher risk of limb loss than patients with intermittent claudication. Therefore, expedient revascularization is warranted, especially in the face of gangrene. However, these patients are at higher risk of coronary arterial disease and thus may benefit the most from cardiac evaluation. The Coronary Artery Revascularization Prophylaxis trial (7) randomized patients with aortic aneurysms, claudication, or CLI and significant coronary artery disease to coronary revascularization prior to vascular surgery or no coronary revascularization

prior to vascular surgery. No statistical difference was demonstrated in 30-day or long-term mortality or perioperative myocardial infarct (Level Ib). Subsequent data analysis looking only at patients with peripheral occlusive disease (8) found among patients with CLI, there was no difference in mortality or incidence of myocardial infarction during the perioperative period or in follow-up regardless of coronary revascularization status (Level Ib).

The American College of Cardiology and American Heart Association guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery (9) recommend preoperative resting 12-lead electrocardiogram in patients undergoing vascular surgery procedures. Noninvasive stress testing is reasonable in patients undergoing vascular surgery if they have three or more clinical risk factors for coronary disease and have a functional capacity of less than 4 metabolic equivalents if the results will change management. However, usefulness of preoperative coronary revascularization in high-risk ischemic patient with an abnormal dobutamine stress echo is not well established (Level IV).

Recommendation: Patients requiring surgical intervention for gangrene do not require an extensive cardiac work-up because preoperative coronary revascularization does not improve morbidity and mortality in these patients. Patients with coronary artery disease should be medically maximized (Grades A, C).

ARE PATIENTS WITH GANGRENE BEST SERVED WITH AN ENDOVASCULAR OR AN OPEN APPROACH?

Endovascular procedures allow for a minimally invasive approach and reduced hospitalization for patients with peripheral arterial disease. As such, many surgeons have embraced an “endovascular first” approach to peripheral arterial disease in which the first attempt at revascularization is by endovascular means; if that is not technically successful, they proceed to an open approach.

The BASIL trial (10) randomized 452 patients with severe ischemia due to infrainguinal disease to surgery first versus percutaneous transluminal angioplasty (PTA) first approach. The endpoints were amputation of trial leg above the ankle or death. Perioperative mortality for surgery versus angioplasty was 5% versus 3%, respectively, and was not statistically significant. However, there was a significant difference in morbidity rate between the two groups with surgery arm having a higher rate of morbidity (57% versus 41%). The higher morbidity was mostly attributed to infections, wound complications, and cardiovascular complications. At 12 months, 56% of surgery patients were alive with an intact leg versus 50% of angioplasty patients, which was not significantly different. The surgery cohort did have a decreased incidence of reintervention compared to the angioplasty arm. There was no significant difference in one- or three-year survival between the groups. All patients in the endovascular arm underwent only angioplasty without stenting (Level Ib).

In another multicenter randomized prospective study, Wolf et al. (11) randomized 263 patients with claudication or rest pain to surgery or PTA, again with no differences found between the two groups after a median follow-up of four years (Level Ib).

Neither of these studies examined the results of PTA when combined with stent placement, which may improve patency of the intervention. Examination of PTA alone versus PTA with stenting has generally been performed in the femoropopliteal segment, including patients with both claudication as well as CLI. Schillinger et al. (12) looked at the benefit of stent versus PTA alone in the superficial femoral artery (SFA) of patients with symptomatic peripheral arterial disease (PAD). At 24 months, after adjusting for confounders in an intention-to-treat analysis, they found a reduced restenosis rate in those undergoing stent placement as compared to PTA alone (adjusted risk ratio 0.52, 95% CI 0.24–0.93). Of the 46 patients who underwent stent placement, 4 had critical limb ischemia (one rest pain, three ulcers), and 6 of 52 who underwent PTA had CLI as an indication (two rest pain, four ulcers) (Level Ib).

Sabeti et al. (13) examined quality of life (QOL) as assessed by the SF 36 preoperatively and immediately in the postoperative period and at 3, 6, and 12 months in the same group of patients. QOL was improved in both groups. When analyzed by intention to treat, there was no difference in QOL, however, a statistically significant difference in QOL favoring stenting was noted when analyzed by treatment received (Level IIb).

Cejna et al. (14), in a multicenter prospective randomized study, looked at PTA versus Palmaz stent placement in the superficial femoral artery of 154 limbs, 46 of which had rest pain or tissue loss. Primary success rate was higher after stent placement, but at one year there was no difference in angiographic or clinical/hemodynamic success between the groups (Level Ib).

Dick et al. (15) in a prospective cohort study examined 383 consecutive patients with CLI stratifying for presence or absence of diabetes undergoing either an endovascular first or surgical first revascularization. When compared with patients undergoing only medical therapy, they found that patients with CLI regardless of diabetes status can benefit from revascularization, either endovascular or open, but that multiple interventions may be required in those with diabetes (Level IIb).

Overall success rates including patencies and limb salvage frequently hinge on location of disease treated with larger vessels (such as iliac or femoral), faring better than infrageniculate, as well as the length of the lesion, with shorter lesions faring better than longer. Romiti et al. (16) performed a meta-analysis of infrapopliteal angioplasty for CLI examining 30 studies. Pooled estimate of primary patency of $77.4\% \pm 4.1\%$ and $48.6\% \pm 18.0\%$ at 1 and 36 months, respectively, and secondary patency $83.3\% \pm 1.4\%$ and $62.9\% \pm 11.0\%$. These results were compared to a recent meta-analysis of popliteal to distal bypass grafts for CLI (17). Although the pooled estimates for primary and secondary patency were better for bypass, the limb salvage rates were comparable for PTA and bypass at 1 ($93.4\% \pm 2.3\%$ versus $95.1\% \pm 1.2\%$) and 36 months ($82.4\% \pm 3.4\%$ versus $82.3\% \pm 3.0\%$) (Level IIb).

Recommendation: Although some studies may demonstrate lower patency rates for endovascular revascularization than for bypass, limb salvage rates appear equivalent between the two. Endovascular revascularization has the benefit of decreased morbidity and increased patient satisfaction. Therefore endovascular revascularization is an acceptable first-line approach in patients with gangrene (Grade B).

ARE SOME PATIENTS WITH GANGRENE BEST SERVED WITH AMPUTATION RATHER THAN AN ATTEMPT AT LIMB SALVAGE?

Patients with gangrene have decreased life expectancy compared to patients with PAD who present with claudication. Additionally the patients may have significant comorbidities, which increase their morbidity and mortality following intervention (as compared to patients with claudication) as well as limit their ambulation. Taylor et al. (18) in a retrospective review of five-year functional outcomes of 1,000 patients noted that 76% of patients were independently ambulatory and 81.3% maintained independent living status. However, five-year survival was 41.9% (Level IIc).

Additionally, revascularization, even when successful, does not guarantee a successful limb salvage. Nicoloff et al. (19) followed 112 consecutive patients undergoing surgery for CLI for five to seven years and found that only 14% had an ideal outcome (complete wound healing, no complications, relief of symptoms) (Level IIc).

Similarly, Taylor et al. (20) reviewed 331 patients undergoing bypass for ischemic tissue loss and evaluated them for clinical success, which was defined as graft patency to point of wound healing, limb salvage for one year, maintenance of ambulatory status for one year, and survival for 6 months. As such, clinical success was achieved in only 44.4% of patients despite higher graft patencies and limb salvage rates (Level IIc).

Taylor et al. (21) retrospectively reviewed 314 patients with CLI who were unsuitable for open repair and subsequently underwent either primary amputation ($n = 183$) or complex PTA for limb salvage ($n = 131$). The PTA group had lower rates of ambulatory failure [hazards ratio (HR) 0.44; $p = 0.0002$] and lower rates of living status deterioration (HR, 0.53; $p = 0.0245$). However, the effects appeared short-lived, and beyond one year the treatments appeared equivalent. One unanticipated result was that PTA was the only independent predictor of mortality (HR, 1.62; $p = 0.0064$). Although the reason for the survival differences is unknown it was postulated that the continued burden of chronic illness may contribute to the increased mortality. They concluded that regardless, PTA should be used selectively in this group of individuals, and limb amputation may sometimes be the better treatment option (Level IIc).

Recommendation: Patients with severe comorbidities, limited preoperative functioning, large wounds, or limited capacity to regain function in the postoperative period may best be served by primary amputation (Grade C).

REFERENCES

1. Catalano M. Epidemiology of critical limb ischaemia: North Italian data. *Eur J Med* 1993; 2: 11–14.
2. Critical limb ischaemia: management and outcome. Report of a national survey. The vascular surgical society of Great Britain and Ireland. *Eur J Vasc Endovasc Surg* 1995; 10: 108–13.
3. Ascher E, Hingorani A, Markevich N, et al. Role of duplex arteriography as the sole preoperative imaging modality prior to lower extremity revascularization surgery in diabetic and renal patients. *Ann Vasc Surg* 2004; 18: 433–9.

4. Hingorani A, Ascher E, Markevich N, et al. Magnetic resonance angiography versus duplex arteriography in patients undergoing lower extremity revascularization: which is the best replacement for contrast arteriography? *J Vasc Surg* 2004; 39: 717–22.
5. Heijenbrok-Kal MH, Kock MC, Hunink MG. Lower extremity arterial disease: multidetector CT angiography meta-analysis. *Radiology* 2007; 245: 433–9.
6. Koelemay MJ, Lijmer JG, Stoker J, et al. Magnetic resonance angiography for the evaluation of lower extremity arterial disease: a meta-analysis. *JAMA* 2001; 285: 1338–45.
7. McFall EO, Ward HB, Moritz TE, et al. Coronary-artery revascularization before elective major vascular surgery. *N Eng J Med* 2004; 351: 2795–804.
8. Raghunathan A, Rapp JH, Littooy F, et al. Postoperative outcomes for patients undergoing elective revascularization for critical limb ischemia and intermittent claudication: a subanalysis of the Coronary Artery Revascularization Prophylaxis (CARP) trial. *J Vasc Surg* 2006; 43: 1175–82.
9. Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): Developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *Circulation* 2007; 116: e418–e499.
10. Adam DJ, Beard JD, Cleveland T, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* 2005; 366: 1925–34.
11. Wolf GL, Wilson SE, Cross AP, et al. Surgery or balloon angioplasty for peripheral vascular disease: a randomized clinical trial. Principal investigators and their Associates of Veterans Administration Cooperative Study Number 199. *J Vasc Intervent Radiol* 1993; 4: 639–48.
12. Schillinger M, Sabeti S, Dick P, et al. Sustained benefit at 2 years of primary femoropopliteal stenting compared with balloon angioplasty with optional stenting. *Circulation* 2007; 115: 2745–9.
13. Sabeti S, Czerwenka-Wenkstetten A, Dick P, et al. Quality of life after balloon angioplasty versus stent implantation in the superficial femoral artery: findings from a randomized controlled trial. *J Endovasc Ther* 2007; 14: 431–7.
14. Cejna M, Thurnher S, Illiasch H, et al. PTA versus Palmaz stent placement in femoropopliteal artery obstructions: a multicenter prospective randomized study. *J Vasc Intervent Radiol* 2001; 12: 23–31.
15. Dick F, Diehm N, Galimanis A, et al. Surgical or endovascular revascularization in patients with critical limb ischemia: influence of diabetes mellitus on clinical outcome. *J Vasc Surg* 2007; 45: 751–61.
16. Romiti M, Albers M, Brochado-Neto FC, et al. Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia. *J Vasc Surg* 2008; 47: 975–81.e1.
17. Albers M, Romiti M, Brochado-Neto FC, et al. Meta-analysis of popliteal-to-distal vein bypass grafts for critical ischemia. *J Vasc Surg* 2006; 43: 498–503.
18. Taylor SM, Kalbaugh CA, Blackhurst DW, et al. Determinants of functional outcome after revascularization for critical limb ischemia: an analysis of 1000 consecutive vascular interventions. *J Vasc Surg* 2006; 44: 747–55; discussion 55–6.
19. Nicoloff AD, Taylor LM Jr., McLafferty RB, et al. Patient recovery after infrainguinal bypass grafting for limb salvage. *J Vasc Surg* 1998; 27: 256–63; discussion 64–6.
20. Taylor SM, Cull DL, Kalbaugh CA, et al. Critical analysis of clinical success after surgical bypass for lower-extremity ischemic tissue loss using a standardized definition combining multiple parameters: a new paradigm of outcomes assessment. *J Am Coll Surg* 2007; 204: 831–8; discussion 838–9.
21. Taylor SM, Kalbaugh CA, Blackhurst DW, et al. A comparison of percutaneous transluminal angioplasty versus amputation for critical limb ischemia in patients unsuitable for open surgery. *J Vasc Surg* 2007; 45: 304–10; discussion 310–11.

Acute Arterial Embolus

Ryan T. Hagino

Clinical Questions		
Question	Answer	Grade of recommendation
Can embolic ischemia be distinguished from thrombotic ischemia based on clinical findings alone?	Yes, but expect a subgroup that defies accurate diagnosis.	C
Is perioperative anticoagulation necessary in treatment of acute limb ischemia?	No conclusive evidence is available to support administration or withholding of anticoagulation.	C
Should initial thrombolysis be performed over surgical revascularization?	No. Selected patients receiving thrombolysis may avoid surgical intervention or undergo a procedure of decreased magnitude, but higher risks of bleeding, embolization, and stroke are expected.	B

Peripheral artery embolism to an extremity is associated with considerable risk for limb loss and death. Even with aggressive intervention, limb loss rates range from 5% to 40% (1–5). Mortality has been high, approaching 25% (3). Although progression of ischemia to irreversible cellular damage, membrane failure, and cellular death in an affected extremity is a large contributor to morbidity and mortality, patients suffering from acute peripheral embolic events represent a uniquely medically compromised group. These often elderly patients present with a cardiogenic source for the arterial emboli, most notably from a fibrillating left atrium (2). This is followed closely by myocardial mural thrombus occurring within the first two weeks of myocardial infarction.

Presentation is characterized by the classic five P's of acute limb ischemia: pain, paresthesia, pallor, paralysis, and pulselessness. The presence or all of these characteristics is not essential in establishing the diagnosis, but some are manifestations of ischemia severity. For instance, ischemia involving neural tissue will result in a spectrum of symptoms from paresthesias to motor dysfunction. Sensory manifestations occur early as the small-caliber nerve fibers are more susceptible to ischemia. Therefore, early ischemic symptoms include pain, paresthesias, and loss of proprioception. Persistent, progressive, or profound ischemia will result in loss of gross sensation and eventually motor function. The loss of motor function is a precursor to irreversible tissue loss; paralysis is a grave sign of motor neural dysfunction combined with muscle death and compartment swelling. The absolute elapsed time following initiation of ischemia is less important than an evaluation for viability (4). Rapid initiation of anticoagulation to prevent

thrombus propagation combined with early revascularization for severely ischemic yet salvageable extremities is recommended (6,7). The ischemic limb can be stratified into viable, threatened, and irreversible clinical categories (8). Using these criteria, reports suggest that 45% of limbs present as viable, 45% threatened, and 10% as suffering from irreversible ischemia (6).

In addition, historical and physical exam characteristics of the P's may aid in defining the etiology of a particular event. Although the drama associated with acute limb ischemia is profound, distinguishing between an acute thrombosis superimposed on preexisting atherosclerotic plaque or peripheral aneurysm compared with an acute embolic event obstructing a relatively healthy artery can be difficult (5). This distinction is important because it may lead to the application of further diagnostic testing or method of restoring blood flow. For instance, balloon embolectomy may easily extract an intact embolus lodged in a relatively disease-free arterial bifurcation; thrombotic events are in situ occurrences involving diseased vessels: intrinsic atherosclerotic critical stenoses and peripheral aneurysms.

IS IT POSSIBLE TO DIAGNOSE AN EMBOLIC VERSUS THROMBOTIC ETIOLOGY TO ACUTE LIMB ISCHEMIA BASED ON HISTORY AND PHYSICAL EXAMINATION?

Although no studies specifically address clinical distinction between these two entities, several retrospective reviews of consecutive patient cohorts presenting with acute limb ischemia and one prospective study do provide some insight into diagnosis.

Jivegard and colleagues performed a retrospective review of patients treated with surgical embolectomy for acute limb ischemia (3). These patients had a preoperative diagnosis of acute arterial embolism, and the surgical therapy was embolism extraction. They sought to define a group of patients misdiagnosed with arterial embolism who actually suffered from acute thrombosis. Diagnosis of arterial embolus was made if an embolic source was established (atrial fibrillation or recent myocardial infarction), the event was of sudden onset, and the patient was without prior history of underlying chronic arterial insufficiency (intermittent claudication). The main clinical criteria for diagnosis of arterial thrombosis include an absence of cardiovascular source for an embolism, rapid (not sudden) onset of symptoms with less than seven days' duration, and a history of symptomatic peripheral artery disease. Based on these criteria, 25% of the cohort had been misdiagnosed with an embolic etiology for their ischemia (Level IV). The same authors examined a more contemporary cohort of 87 consecutive patients and found 26% of patients had an etiology of acute limb ischemia that could not be determined (embolic versus thrombotic) (2) (Level IIb).

Using surgical findings and/or angiographic findings to confirm the clinical diagnosis of embolic versus thrombotic occlusion, Cambria and Abbott noted the diagnosis of embolism was incorrect in 17% of their patients (9). The only clinical finding distinguishing the two groups was the presence of atrial fibrillation among embolism patients. Interestingly, only 40% of thrombotic patients actually had antecedent symptoms of chronic arterial insufficiency prior to their acute event (Level IIb).

McPhail et al.'s one-year prospective examination of patients treated for acute limb ischemia based the diagnosis of etiology on clinical exam alone; embolism: demonstration of potential source and sudden onset of symptoms; thrombosis: prior chronic arterial insufficiency, more gradual onset, and the absence of an embolic source. The initial diagnosis of embolism was incorrect (as determined on surgical exploration, angiography or necropsy) in 9%. However, no discernible impact on outcomes was seen because of misdiagnosis (1) (Level IIb).

Answer: Yes, it is possible to distinguish between acute limb ischemia secondary to an embolus versus a thrombotic cause based on clinical criteria alone. However, there remains a significant minority in whom the etiology defies diagnosis and requires additional testing or exploration (Grade C recommendation).

The therapeutic choices for treatment of acute arterial ischemia due to embolism include observation, primary amputation, surgical revascularization, or a combination percutaneous intra-arterial thrombolysis and surgical revascularization. It is generally accepted that anticoagulation is a primary component of any treatment regime (6,7).

IS PERIOPERATIVE ANTICOAGULATION A NECESSITY IN TREATMENT OF ACUTE LIMB ISCHEMIA?

Anticoagulation is accepted as an important treatment for prevention of propagation of thrombus following acute arterial occlusion from any cause. The concept is simple. Stasis created by the primary occlusive event will lead to thrombosis and gradual loss of collateral flow through this

advancing secondary occlusive process. This concept is largely based on expert opinion (6,7) (Level V). However, several investigators have suggested the surgical treatment of acute limb ischemia can be delayed if sufficient anticoagulation is administered with acceptable results provided the limb is without evidence of impending muscle loss (1,2,4,5,9). This strategy seeks to avoid the profound systemic metabolic consequences following immediate revascularization of an ischemic limb. Though attractive, this strategy is not possible in many patients because of the severity of ischemia, with up to 50% of patients requiring immediate revascularization (2).

One single-center review compared results of patients receiving anticoagulants prior to, during, and after surgical revascularization with those undergoing revascularization without anticoagulants (10). They omitted all patients who received only temporary anticoagulation or those in whom the use of anticoagulants could not be determined. Patients who received adequate anticoagulation were twice as likely to have a "good result," defined as amputation free survival at four months. However, no differences were seen in hospital death between the groups, but the anticoagulated patients suffered more bleeding complications ($p < 0.05$). There was no difference in 36-month recurrence rates of thromboembolism between the two groups (Level IV).

A prospective, randomized, multicenter trial was conducted involving 188 patients with acute limb ischemia randomized to anticoagulation or no anticoagulation in conjunction with thromboembolectomy. Perioperative anticoagulation with heparin was transitioned to warfarin therapy. Results were evaluated at 30 days. No significant differences were noted in amputation free survival, mortality, or reoperation at 30 days (11) (Level IIb).

Answer: No definitive evidence exists for the use of perioperative anticoagulation in treatment of acute limb ischemia. In the absence of this definitive evidence, consensus panels recommend perioperative anticoagulation (6,7) (Grade C).

SHOULD PERCUTANEOUS CATHETER DIRECTED INTRA-ARTERIAL THROMBOLYSIS BE INITIAL TREATMENT FOR ACUTE ARTERIAL EMBOLISM OVER SURGICAL REVASCLARIZATION?

Percutaneous thrombolytic therapy involves placement of a catheter regionally or, more appropriately, within the arterial occlusion and infusing a thrombolytic agent directly into the thrombus. This is distinct from systemic intravenous thrombolysis. Catheter directed intra-arterial therapy is associated with fewer hemorrhagic complications and better clot lysis when compared with systemic intravenous therapy (12). Theoretic advantages of thrombolytic therapy over surgery include the ability to clear a thrombus from smaller vessels inaccessible to traditional embolectomy catheters, a more gradual reperfusion, and the ability to unmask underlying pathology following lysis of acute thrombus. Disadvantages include increased time for reperfusion, expense, intensive hospital resource utilization, hemorrhage, and distal embolization.

Much of the literature regarding use of thrombolytic therapy for limb ischemia is confounded by small numbers, nonstandardized endpoints or treatment protocols, poor

follow-up, and diverse patient populations, including both acute and chronic ischemia, graft occlusions, and mixtures of thrombotic/embolic or indeterminate events. The actual reported numbers of patients treated specifically for embolic acute ischemia with thrombolysis is small. A recent systematic review found only 27 patients treated with thrombolytic therapy gleaned from larger, unfiltered cohorts (13). Although limb salvage was a gratifying 100% at 6–12 months and mortality was nil, selection bias clearly plays a role in choice of therapy. There is general belief that embolic material, particularly that originating from the heart, is more organized, is more fibrous, and may be more resistant to thrombolytic therapy than in situ thrombus (6).

Several randomized prospective trials have been conducted comparing percutaneous thrombolytic therapy with surgical therapy. However, a mixture of nonstandardized endpoints and patient populations makes analysis difficult. One large study excluded all patients suffering from an embolic source of ischemia from randomization (14). Smaller, single-center trials comparing the two treatment modalities for the collective group of patients suffering from acute limb ischemia of any cause found no differences in limb salvage (15,16) (Level IIb).

The largest randomized, multicenter prospective trial compared thrombolysis or peripheral arterial surgery in patients presenting with <two weeks of acute ischemia. Phase I noted no difference in one-year mortality or amputation-free survival between the two groups. Following thrombolysis, 46% of the patients avoided some form of surgical revascularization (17) (Level IIb). The larger second phase of the study randomized 548 patients (18). The primary endpoint of amputation-free survival was no different between the two groups (but subject to wide confidence intervals). Twenty-three percent of patients receiving initial thrombolytic therapy did not require a secondary revascularization procedure during the initial hospitalization. Over the ensuing six months, 31.5% of the thrombolysis

patients required only a percutaneous revascularization procedure. At six months, 40% of the same patients required some form of open surgical intervention. Bleeding complications were significantly higher in the thrombolysis group. Though the majority of ischemic limbs were suffered from thrombotic causes, there were no differences seen between limbs treated for thrombotic etiology compared with embolic causes. The authors concluded that reduced the need for open surgical revascularization, but this may be at the expense of statistically higher rates of bleeding associated with thrombolytic therapy (Level IIb).

A recent Cochrane Database meta-analysis summarized five major randomized trials encompassing 1,283 patients addressing this question. There was no difference in the primary endpoint of amputation-free survival at 1, 6, and 12 months following initial thrombolysis versus surgical therapy, nor was a difference seen in the secondary endpoint of death. The initial thrombolysis group underwent secondary interventions of lesser severity than the surgical treatment arm [odds ratio (OR) 5.37; 95% confidence interval (CI) 3.99 to 7.22]. However, initial thrombolysis was associated with an increased risk of secondary complications of major hemorrhage at 30 days (OR 2.8; 95% CI 1.7 to 4.6), stroke at 30 days (OR 6.41; 95% CI 1.57 to 26.2), and distal embolization (OR 8.35; 95% CI 4.47 to 15.58) (19) (Level Ia).

Answer: Intra-arterial catheter-directed thrombolysis as initial therapy for acute limb ischemia is no better than surgical therapy in achieving limb salvage or reducing mortality. However, in select patients, successful thrombolysis may reduce the need for additional surgical revascularization, supplanting open surgery with percutaneous intervention. This comes with an associated higher risk of major hemorrhage, distal embolization, and stroke. Therefore, most agree that thrombolysis should be considered an adjunct to care, and it is rarely used as a stand-alone modality of treatment (7). The treatment of acute embolic ischemia is all extrapolation from broader cohorts (Grade B).

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings	Comments
Diagnosis of embolism	1983	1	Ib	C	Diagnosis is possible in almost 90% of patients, but 10% will defy diagnosis.	Prospective consecutive cohort diagnosed on predetermined clinical criteria.
Perioperative anticoagulation	1986	10	IV	C	Anticoagulation is associated with improved early results, but this benefit is lost at 36-month follow-up.	Retrospective review with many patients excluded because of temporary anticoagulation regimes.
Perioperative anticoagulation	1991	11	IIb	C	No differences in amputation free survival, mortality, or reoperation is seen at 30 days.	Randomized, multicenter intent-to-treat trial with very short follow-up.
Thrombolysis as initial therapy	1994	15	IIb	B	No differences in amputation free survival, but magnitude of subsequent revascularization lower with thrombolysis.	Single-center randomized trial including a diverse group of patients.
Thrombolysis as initial therapy	1992	16	IIb	B	No difference in limb salvage.	Very small, single-center randomized trial utilizing a nonstandard treatment thrombolysis protocol.

(Continued)

Levels of Evidence (Continued)

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings	Comments
Thrombolysis as initial therapy	1996	17	IIb	B	No difference between groups, but 46% of thrombolytic patients did not require surgery.	Phase I study designed to examine optimal thrombolysis treatment regime.
Thrombolysis as initial therapy	1998	18	IIb	B	No difference seen between groups.	Multicenter randomized trial with wide confidence intervals on the primary endpoint of amputation free survival.
Thrombolysis as initial therapy	2008	19	Ia	B	No difference seen between groups.	Meta-analysis of five randomized trials, but inclusive of diverse cohorts of patients.

REFERENCES

- McPhail N, Fratesi SJ, Barger GG, et al. Management of acute thromboembolic limb ischemia. *Surgery* 1983; 93: 381–5.
- Jivegard L, Arfvidsson B, Holm J, et al. Selective conservative and routine early operative treatment in acute limb ischemia. *Br J Surg* 1987; 74: 798–801.
- Jivegard L, Holm J, Schersten T. The outcome in arterial thrombosis misdiagnosed as arterial embolism. *Acta Chir Scand* 1986; 152: 251–6.
- Dale W. Differential management of acute peripheral arterial ischemia. *J Vasc Surg* 1984; 1: 269–78.
- Blaisdell F, Steele M, Allen RE. Management of acute lower extremity arterial ischemia due to embolism and thrombosis. *Surgery* 1978; 84: 822–34.
- Norgren LHW, Dormandy JA, Nehler MR, et al. Inter-societal consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg* 2007; 45: S1–S67.
- Clagett GPM, Jackson MR, Lip GYH, et al. Antithrombotic therapy in peripheral arterial occlusive disease: The seventh ACCP Conference on antithrombotic and thrombolytic therapy. *Chest* 2004; 126: 609–26.
- Rutherford R, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg* 1997; 26: 517–38.
- Cambria R, Abbott WM. Acute arterial thrombosis of the lower extremity. *Arch Surg* 1984; 119: 784–7.
- Jivegard LHJ, Schersten T. Arterial thromboembolism—should anticoagulants be administered? *Acta Chir Scand* 1986; 152: 493–7.
- Jivegard L, Holm J, Bergqvist D, et al. Acute lower limb ischemia: failure of anticoagulant treatment to improve one-month results of arterial thromboembolism. A prospective randomized multi-center study. *Surgery* 1991; 109: 610–16.
- Berridge D, Gregson RHS, Hopkinson BR, et al. Randomized trial of intra-arterial recombinant tissue plasminogen activator, intravenous recombinant tissue plasminogen activator and intra-arterial streptokinase in peripheral arterial thrombolysis. *Br J Surg* 1991; 78: 988–95.
- Diffin D, Kandarpa K. Assessment of peripheral intraarterial thrombolysis versus surgical revascularization in acute lower-limb ischemia: a review of limb-salvage and mortality statistics. *J Vasc Inv Rad* 1996; 7: 57–63.
- Results of a prospective randomized trial evaluating surgery versus thrombolysis for ischemia of the lower extremity. The STILE Trial. *Ann Surg* 1994; 220: 251–68.
- Ouriel K, Shortell CK, DeWeese JA, et al. A comparison of thrombolytic therapy with operative revascularization in the initial treatment of acute peripheral arterial ischemia. *J Vasc Surg* 1994; 19: 1021–30.
- Nilsson L, Albrechtsson U, Jonung T, et al. Surgical treatment versus thrombolysis in acute arterial occlusion: a randomised controlled study. *Eur J Vasc Surg* 1992; 6: 189–93.
- Ouriel K, Veith FJ, Sasahara AA, et al. Thrombolysis or peripheral arterial surgery: phase I results. *J Vasc Surg* 1996; 23: 64–73.
- Ouriel K, Veith FJ, Sasahara AA, et al. A comparison of recombinant urokinase with vascular surgery as initial treatment for acute arterial occlusion of the legs. *N Engl J Med* 1998; 338: 1105–11.
- Berridge DC, Kessel D, Robertson I. The Cochrane Database of Systematic Reviews: surgery versus thrombolysis for initial management of acute limb ischemia. *Cochrane Library* 2008; 2.

Ruptured Abdominal Aortic Aneurysm

Boulos Toursarkissian

Clinical Questions		
Question	Answer	Grade of recommendation
What are the optimal resuscitation goals?	Low-grade hypotension is acceptable.	C
What are the preferred resuscitation fluids?	Blood products are preferred.	B
Should a CT scan be obtained in patients with suspected rAAA?	Yes, except in most extreme cases.	B
Can EVAR be used in patients with rAAA?	Yes.	B
What can be done to avoid paraplegia and/or ischemic colitis?	Try to maintain flow to at least one hypogastric artery.	B
Abbreviations: CT, computed tomography; EVAR, endovascular repair; rAAA, ruptured abdominal aortic aneurysm.		

A ruptured abdominal aortic aneurysm (rAAA) is a serious, life-threatening surgical emergency. It ranks among the top 15 leading causes of death in the United States, despite many advances in anesthesia and critical care medicine.

Important questions to consider in the care of a patient with a rAAA include preoperative resuscitation goals and methods, criteria used to select patients for surgery (i.e., survival prediction), the nature of imaging studies needed before surgical intervention and the delay impact this can cause, the type of intervention to be performed, the use of anticoagulants intraoperatively, and the need to monitor patients for frequent postoperative complications. Patients with rAAA are prone to the development of complications, including ischemic colitis, paraplegia from spinal cord ischemia, renal failure, peripheral atheroembolic complications, and abdominal compartment syndrome.

WHAT ARE THE OPTIMAL RESUSCITATION GOALS AND METHODS TO BE USED IN PATIENTS WITH RUPTURED ANEURYSMS?

As far as resuscitation goals and measures go, only expert opinions are available in the literature (Level V evidence). Many experts suggest that it is acceptable to tolerate a systolic blood pressure under 100mmHg and as low as 70mmHg, as long as adequate mentation is maintained (Grade C recommendation). This is mostly an extrapolation from trauma literature. The rationale presented is that a higher blood pressure may exacerbate the tendency for retroperitoneal hemorrhage and may convert what was

otherwise a contained rupture into a free intraperitoneal rupture. The subject has not been submitted to rigorous studies, although it seems intuitive to recommend that overt hypertension be avoided (1,2).

The nature of the fluids to be used for resuscitation purposes in the perioperative period in patients with rAAA has been the subject of at least one prospective cohort study (Level IIb evidence). In this Danish study, 55 patients with rAAA were proactively administered fresh frozen plasma and platelets concentrates immediately when the diagnosis of rAAA was suspected (3). Thirty-day survival improved to 66% as compared to a 44% survival for the 93 patients treated by conventional means in the preceding two-year period. All patients in the study group were treated with open aneurysm surgery. From this study, as well as other data on the resuscitation of massively injured trauma patients (4), an aggressive approach toward the use of blood products appears justifiable (Grade B recommendation).

Answer: Moderate hypotension is acceptable, and blood products should be used early (Grade C and B recommendations).

CAN MORTALITY FROM RAAA BE PREDICTED?

Mortality after repair of rAAA remains high. A factor that has been associated with increasing mortality in a number of studies is advanced age, especially when comparing patients over the age of 80 years to younger individuals (Level IIIb evidence). However, an age cut-off beyond which survival is unlikely has never been identified, and

survival rates over 50% have been reported in octogenarians (5). Therefore, age alone cannot be used as a contraindication to attempting surgical repair of a rAAA (Grade B recommendation).

There is no single preoperative parameter to indicate whether a patient with a rAAA will survive a surgical attempt to repair the rAAA. Many models have been developed to help predict mortality and survival. The Glasgow aneurysm score is equal to the age in years, plus 17 points for the presence of shock, plus 7 points for a prior myocardial infarction or ongoing angina, plus 10 points for any prior stroke or transient ischemic attack, plus 14 points for renal insufficiency (6). A retrospective nationwide survey in Finland (7) found the Glasgow score to predict mortality, with a score greater than 98 associated with an 80% postoperative mortality (Level IIIb evidence). The Hardman index is another such model and gives one point for each of age greater than 76 years, creatinine over 190 $\mu\text{mol/L}$, hemoglobin less than 9 g/dl, myocardial ischemia on electrocardiogram, and a history of loss of consciousness after arrival in hospital (8). The presence 3 or more points was reported as uniformly fatal in one study (9). Both the Glasgow score and the Hardman index have been reported as poor predictors of survival in at least one retrospective study from Scotland (10). It appears, therefore, that there currently are no scores to allow reliable prediction of mortality (Grade B recommendation).

Whereas preoperative predictors of survival may be poor, there are formulas that use postoperative data to predict short-term mortality. For instance, in patients who are alive after 48 hours from surgery, the SOFA (sequential organ failure assessment) score has been shown to be predictive of mortality. The SOFA score evaluates respiratory, coagulation, hepatic, cardiovascular, renal, and neurologic function, with each assigned a value from 0 to 4 (11). In one a retrospective study (12), a 48-hour SOFA score greater than 11 predicted mortality with a 93% specificity (Level IIIb evidence).

Answer: Neither age nor any of the available formulas are accurate enough to allow mortality prediction (Grade B recommendation).

DO DELAYS IN REACHING AN OPERATING ROOM AFFECT OUTCOMES?

Controversy continues as to whether delays in reaching an operating room affect the ultimate mortality of patients with rAAA. Studies have been published with completely conflicting results (1–15). All these studies, however, are retrospective cohort studies (Level III evidence). Many but not all exclude patients who do not survive until hospital arrival, thereby creating a clear selection bias. It appears rather intuitive to try to minimize any delays in accessing an operating room, given the overall risks and benefits ratios (Grade B recommendation).

The question of delay in getting to surgery has become particularly relevant with the increasing use of endovascular repair (EVAR) for treating rAAA (see following discussion). To allow proper EVAR planning, a computed tomography (CT) scan of the abdomen and pelvis is usually needed. With spiral CT units, the time needed for an abdomen scan is considerably short. In a study of

time-to-death in patients with rAAA not operated on, 87.5% of patients admitted to hospital with rAAA died after more than two hours of admission (16), with most of those not treated aggressively. It appears therefore reasonable to consider a CT angiogram scan of the abdomen and pelvis in all except the most unstable patients (Grade B recommendation).

The other reason delays may be important has to do with the possible need to regionalize the care of patients with rAAAs. Increasing data are showing that high-volume surgeons with subspecialty training may produce better results for rAAA patients (17) (Level IIb evidence). Other data suggest that large centers that are able to more rapidly mobilize large resources may produce better outcomes for rAAA (18). Transfer of patients to such high-volume centers and surgeons may be time-consuming. Is that preferable to treatment in a local low-volume hospital? A clear-cut answer to this question is not available.

Answer: The data is controversial. Getting a CT scan is reasonable in the majority of cases (Grade B recommendation).

IS ENDOVASCULAR REPAIR PREFERRED IN PATIENTS WITH RAAA?

A rAAA is usually a fatal condition unless treated surgically. There are two major choices of surgical intervention: open repair and stent graft placement or EVAR. The EVAR1 trial compared open repair to EVAR in patients undergoing elective repair of a nonruptured AAA (19). The group undergoing EVAR had a lower early mortality and fewer complications. Given this finding, and given the fact that open repair for rAAA has continued to have a high mortality, the question has arisen as to whether EVAR should be preferred over open repair for patients presenting with rAAA.

To date, no randomized controlled trial has been carried out to help answer this question. A large number of retrospective and prospective cohort studies have been published on the subject. None of these studies are randomized, and in many but not all cases, patients who are very unstable are treated with open surgery (Level IIb evidence).

Nevertheless, from a review of these studies, a number of points can be made. Even with devices versatile enough for emergency cases, slightly less than half of patients with rAAA have anatomy amenable to EVAR; this proportion is less compared to patients with nonruptured AAA (20). There is also a trend toward accepting less than optimal anatomy for EVAR in patients with rAAA (21). No long-term follow-up exists on patients having undergone EVAR for rAAA (21). Despite this, the proportion of patients with rAAA being treated with EVAR is increasing in the United States (22). Many of the studies published to date have shown improved mortality for EVAR as opposed to open repair in patients with rAAAs, whereas others have shown no difference. Most, however, show that in patients who can undergo EVAR, the morbidity, blood loss, and intensive care unit length of stay are decreased. Many of the studies also indicate that emergency EVAR may be more technically challenging and may require the use of adjunctive techniques, such a temporary aortic

occlusion with balloons or an aortomonoiliac graft with the placement of a contralateral iliac occluder along with a femorofemoral bypass graft.

We can conclude that EVAR for rAAA is a viable therapeutic option when offered by an experienced surgeon in a center familiar with elective EVAR therapy and with quick access to a variety of stent graft sizes. To date, no data exist to support or refute its preferred use over open repair (Grade B recommendation).

Answer: Endovascular repair is an acceptable treatment method, but not necessarily superior to open repair (Grade B recommendation).

SHOULD ANTICOAGULATION BE USED INTRAOPERATIVELY?

Heparin anticoagulation prior to aortic clamping is routinely done in elective AAA surgery. Patients with rAAAs may have already lost a large amount of blood and may be coagulopathic and hypothermic. It seems therefore reasonable to avoid full anticoagulation in those cases. No prospective or retrospective data on the subject have been published, and only expert opinion is available (Level V evidence). The decision to use anticoagulants must be individualized based on patient factors.

In patients who develop coagulopathy intraoperatively, the use of abdominal packing is a surgical option. There is only one retrospective series of 23 patients identified from a prospective surgical data base (Level III evidence). Survival was achieved in 48% of the patients packed, but there was a high 22% incidence of early or late infectious complications (23). Use of packing should therefore be very selective (Grade C recommendation).

Intraoperative hypothermia has been shown to be correlated with increased mortality in a retrospective review of 100 consecutive patients treated for rAAA at one institution (24) (Level IIb evidence). Therefore, every effort should be made to avoid hypothermia starting in the preoperative period (Grade B recommendation). The room should be warmed, blankets used, and fluids and gas administered should be heated.

The final issue relates to the level of aortic clamping for cases done via an open approach. Again, no prospective or retrospective data on the subject have been published, and only expert opinion is available (Level V evidence). Infrarenal clamping appears desirable when possible, because it avoids renal and mesenteric ischemia. However, this is often not possible because a large hematoma with a large rAAA may obscure the planes and mandate a supraceliac clamp.

Answer: No data are available. Decision must be individualized. Hypothermia should be avoided (Grade C recommendation).

CAN PARAPLEGIA BE AVOIDED?

Spinal cord ischemia has been associated with shock, embolization, interruption of flow to the artery of Adamkiewicz, and interruption of flow to the hypogastric arteries. An incidence of up to 11.5% was noted in a retrospective study of 35 patients with endovascular repair for ruptured aneurysm (25); a statistical association was noted with occlusion of one or more hypogastric arteries by the stent graft (Level III evidence). It therefore seems prudent to try to maintain flow to at least one hypogastric artery during stent graft placement for rAAA (recommendation Grade B).

Answer: Not always. Try to maintain flow to at least one hypogastric artery (Grade B recommendation).

SHOULD SIGMOIDOSCOPY BE PERFORMED ROUTINELY IN THE POSTOP PERIOD?

Ischemic colitis after repair of rAAA is a common occurrence. It may be related to hypotension, embolization, or interruption of flow to the hypogastric arteries. Endoscopically verified ischemic colitis after open surgery for rAAA may be as frequent as 42% of cases (26). After EVAR for rAAA, the incidence has been reported at 23% (27). Even patients with evidence of transmural ischemia may fail to show laboratory anomalies early on. Retrospective data does suggest that early detection of ischemic colitis may be associated with decreased mortality (Level III evidence). As a consequence, many surgeons advocate routine flexible sigmoidoscopy at 24 hours after surgery for rAAA (recommendation Grade C).

Answer: Ischemic colitis is frequent enough that sigmoidoscopy should be performed at the least clinical suspicion (Grade C recommendation).

SHOULD PATIENTS BE MONITORED FOR ABDOMINAL COMPARTMENT SYNDROME?

Abdominal compartment syndrome (ACS) can affect as many as 20% of patients after EVAR for rAAA. In retrospective series, a number of risk factors for ACS have been identified to include coagulopathy, massive transfusion requirements, and the need for an aortic occlusion balloon because of ongoing hypotension (28). Similar risk factors for the development of ACS after open repair of rAAA have also been reported (Level IIb evidence). Early recognition (via bladder pressure monitoring) of ACS and aggressive treatment appear to result in decreased mortality and appear therefore reasonable (recommendation Grade B).

Answer: ACS is frequent enough that bladder monitoring should be considered (Grade B recommendation).

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Choice of fluids for resuscitation	2007	3	IIb	B	Early administration of blood products may be beneficial.
Imaging prior to treatment	2004	16	IIb	B	Spiral CT scanning is a reasonable test in most patients.
Repair technique	2007	21	IIb	B	EVAR is an acceptable alternative to open repair.
Ischemic colitis post-rAAA repair	2007	27	IIb	B	Ischemic colitis is frequent, and vigilance is required for early detection.

Abbreviations: CT, computed tomography; EVAR, endovascular repair; rAAA, ruptured abdominal aortic aneurysm.

REFERENCES

- Castelli P, Caronno R, Piffaretti G, et al. Ruptured abdominal aortic aneurysm: endovascular treatment. *Abdom Imaging* 2005; 30: 263–9.
- Piffaretti G, Caronno R, Tozzi M, et al. Endovascular versus open repair of ruptured abdominal aortic aneurysms. *Expert Rev Cardiovasc Ther* 2006; 4: 839–52.
- Johansson PI, Stensballe J, Rosenberg I, et al. Proactive administration of platelets and plasma for patients with a ruptured abdominal aortic aneurysm: evaluating a change in transfusion practice. *Transfusion* 2007; 47: 593–8.
- Cinat ME, Wallace WC, Nastanski F, et al. Improved survival following massive transfusion in patients who have undergone trauma. *Arch Surg* 1999; 134: 964–70.
- Chiesa R, Setacci C, Tshomba Y, et al. Ruptured abdominal aortic aneurysm in the elderly patient. *Acta Chir Belg* 2006; 106: 508–16.
- Samy AK, Murray G, MacBain G. Glasgow aneurysm score. *Cardiovasc Surg* 1994; 2: 41–4.
- Korhonen SJ, Ylonen K, Biancari F, et al. Glasgow aneurysm score as a predictor of immediate outcome after surgery for ruptured abdominal aortic aneurysm. *Br J Surg* 2004; 91: 1449–52.
- Hardman DT, Fisher CM, Patel MI, et al. Ruptured abdominal aortic aneurysms: who should be offered surgery? *J Vasc Surg* 1996; 23: 123–9.
- Prance SE, Wilson YG, Cosgrove CM, et al. Ruptured abdominal aortic aneurysms: selecting patients for surgery. *Eur J Vasc Endovasc Surg* 1999; 17: 129–32.
- Tambyraja AL, Fraser SCA, Murie JA, et al. Validity of the Glasgow aneurysm score and the Hardman index in predicting outcome after ruptured abdominal aortic aneurysm repair. *Br J Surg* 2005; 92: 570–3.
- Kniemayer HW, Kessler T, Reber PU, et al. Treatment of ruptured abdominal aortic aneurysm, a permanent challenge or a waste of resources? Prediction of outcome using a multi-organ-dysfunction score. *Eur J Vasc Endovasc Surg* 2000; 19: 190–6.
- Laukontaus SJ, Lepantalo M, Hynninen M, et al. Prediction of survival after 48 hours of intensive care following open surgical repair of ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2005; 30: 509–15.
- DeSouza VC, Strachan DP. Relationship between travel time to the nearest hospital and survival from ruptured abdominal aortic aneurysms: record linkage study. *J Pub Health* 2005.
- Hames H, Forbes TL, Harris JR, et al. The effect of patient transfer on outcomes after rupture of an abdominal aortic aneurysm. *Can J Surg* 2007; 50: 43–7.
- Salhab M, Farmer J, Osman I. Impact of delay on survival of patients with a ruptured abdominal aortic aneurysm. *Vascular* 2006; 14: 38–42.
- Lloyd GM, Bown MJ, Norwood MGA, et al. Feasibility of preoperative computer tomography in patients with ruptured abdominal aortic aneurysm: a time-to-death study in patients without operation. *J Vasc Surg* 2004; 39: 788–91.
- Dueck AD, Kucey DS, Johnston KW, et al. Survival after ruptured abdominal aortic aneurysm: effect of patient, surgeon and hospital factors. *J Vasc Surg* 2004; 39: 1253–60.
- Utter GH, Maier RV, Rivara FP, et al. Outcomes after ruptured abdominal aortic aneurysms: the halo effect of trauma center designation. *J Am Coll Surg* 2006; 203: 498–505.
- EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomized controlled trial. *Lancet* 2005; 365: 2187–92.
- Hoornweg LL, Wisselink W, Vahl A, et al. The Amsterdam acute aneurysm trial: suitability and application rate for endovascular repair of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2007; 33: 679–83.
- Dillon M, Cardwell C, Blair PH, et al. Endovascular treatment for ruptured abdominal aortic aneurysm. *Cochrane Collection* 2007.
- Greco G, Egorova N, Anderson PL, et al. Outcomes of endovascular treatment of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2006; 43: 453–9.
- Adam DJ, Fitridge RA, Raptis S. Intra-abdominal packing for uncontrollable haemorrhage during ruptured abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 2005; 30: 516–19.
- Janczyk RJ, Howells GA, Blar HA, et al. Hypothermia is an independent predictor of mortality in ruptured abdominal aortic aneurysms. *Vasc Endovasc Surg* 2004; 38: 37–42.
- Peppelenbosch N, Cuypers PWM, Vahl AC, et al. Emergency endovascular treatment for ruptured abdominal aortic aneurysm and the risk of spinal cord ischemia. *J Vasc Surg* 2005; 42: 608–14.
- Champagne BJ, Darling RC, Daneshmand M, et al. Outcome of aggressive surveillance colonoscopy in ruptured abdominal aortic aneurysm. *J Vasc Surg* 2004; 39: 792–6.
- Champagne BJ, Lee EC, Valerian B, et al. Incidence of colonic ischemia after repair of ruptured abdominal aortic aneurysm with endograft. *J Am Coll Surg* 2007; 204: 597–602.
- Mehta M, Darling RC, Roddy SP, et al. Factors associated with abdominal compartment syndrome complicating endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2005; 42: 1047–51.

Acute Aortic Dissection

V. Seenu Reddy

Clinical Questions		
Question	Answer	Grade of recommendation
What are the two basic categories of aortic dissection?	Ascending (type A), descending (type B)	N/A
What is the optimal imaging modality for aortic dissections?	CT scanning with and without contrast using multidetector array technology; MRI and TEE may be useful adjuncts	A
When is further or different modality of imaging indicated?		
Should D-dimer levels be measured?	Yes	A
What is the appropriate role and timing of operative intervention for each type of AAD?	Immediate open surgery for type A; initial med Rx for type B	A
What is the role of blood pressure management during the acute and subacute phase of the injury? What is the role of long-term blood pressure management?	Beta-blocker is crucial for early management, lifelong blood pressure monitoring and treatment is necessary	A
What is the role of endovascular stent graft repair for type B dissections? What are the data?	Limited role for stent graft repair and no long-term data	C
What follow-up is required post-stent graft placement?	Serial CTs of the treated aorta for at least 5 years	A
Abbreviations: AAD, acute aortic dissection; CT, computed tomography; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography.		

Acute aortic dissection (AAD) is a medical and often a surgical emergency. AAD has an approximate incidence of 3.5/100,000 persons annually in the United States. It is five times more common in males than females and has a peak incidence in the fifth and sixth decades of life. Over 60% of the time, aortic dissections involve the ascending aorta, and the remainder of cases involve primarily the descending thoracic and abdominal aorta. Although treatment has evolved over the past several decades, numerous controversies remain. Our most recent and complete knowledge about AAD comes from the multicenter International Registry of Acute Aortic Dissection, which has more than 1,700 patients from 22 institutions dating back to 1996 (1–3).

Although the general approach has been surgical management for AAD of the proximal or ascending aorta and medical management for the descending aorta, newer modalities of treatment have led to changes in overall therapy. Some of the critical issues to consider when treating AAD are understanding the classification system and its relevance, considering which AADs should be managed medically or surgically, what modality of imaging should be employed, what the role of blood pressure therapy is in AAD, and the role endovascular therapy may play in the current era (4).

WHAT ARE THE TWO BASIC CATEGORIES OF AORTIC DISSECTION? WHAT OTHER CLASSIFICATION SYSTEMS ARE USED?

As imaging modalities have multiplied and their resolution improved, a multitude of aortic pathologies have been uncovered and given descriptions. Some of these entities include aortic intramural hematoma and penetrating aortic ulcer, as well as the catch-all diagnosis of acute aortic syndrome. Specifically defined, an AAD is a disruption of the layers of the arterial wall of the aorta. It is typically defined by a breach of the intimal layer with extension and disruption of the media of the vessel wall. A dissection is complex in that it may form a spiral tear as it extends distally and proximally. Rarely is the tear or disruption linear, and it may involve several reentry points between true and false lumens. If the adventitial layer is disrupted, then the AAD is essentially a rupture and may freely extravasate blood into the chest or abdomen.

By accepted definition, AADs are those that are detected less than 14 days from time of the onset of symptoms. Those that are diagnosed more than 14 days are often called *sub-acute* if detected prior to two months from symptoms or *chronic* if greater than two months from symptom onset.

The three basic types of nomenclature that exist include the DeBakey classification, the Stanford classification, and the anatomical classification (5). The DeBakey system divides AADs into three discrete categories based on location of the dissection and location of the intimal tear. DeBakey type I AADs involve the proximal or ascending aorta and the descending aorta. The type II AAD involves only the ascending aorta without involvement of the arch or brachiocephalic vessels. Type III under the DeBakey schema describe AADs that are limited to the descending aorta alone and are further subdivided into IIIa that is limited to the descending thoracic aorta distal to the subclavian or IIIb, limited to the infradiaphragmatic aorta.

The other major system of classification was developed at Stanford University Medical Center and is a simplified grouping of type A involving a dissection in the ascending aorta and any other portion of the aorta and type B being limited to a dissection in the aorta distal to the take-off of the left subclavian. The Stanford type A includes the DeBakey types I and II, and the type B includes DeBakey types IIIa and IIIb (6).

A system that might be more accurate and plainly descriptive relies on anatomic specificity. An example would be separating AADs into those that involve the ascending aorta (that portion from the aortic valve to the level of the innominate artery), the transverse or arch aorta (that portion encompassing the innominate, left carotid, and left subclavian origins) and the descending aorta. The descending aortic dissections could then be further divided into descending thoracic aortic dissections and thoracoabdominal dissections for those that traverse the diaphragm and involve the visceral vessels. This system would allow clear description of both the location of the intimal tear and the extension of the dissection.

Answer: There are three major schema for classifying AADs. The most widely used are the DeBakey and Stanford classifications. The Stanford classification is the most widely used. Stanford type A dissections involve the ascending aorta, and type B dissections are limited to the aorta distal to the subclavian origin.

One area of clarification regards the often misused terminology of dissecting aneurysm. As aneurysms of the aorta enlarge, the risk of dissection of their walls increases logarithmically. Conversely, the dissected wall of an aorta can undergo aneurysmal degeneration over time, and most enlarge at a rate of several millimeters per year. Thus, although many dissections occur in portions of aorta that have other disease processes, such as atherosclerosis, aneurysmal disease, or medial necrosis, the most appropriate description is AAD for the immediately defined event.

DO D-DIMER LEVEL MEASUREMENTS HAVE A ROLE IN DIAGNOSING AADS?

Biomarkers are useful for making the diagnosis of a variety of medical and surgical problems, such as myocardial infarction and acute pancreatitis. Several studies have examined whether the measurement of serum levels of D-dimer, an end product derived from plasmin-mediated degradation of cross-linked fibrin clots, has a role in the acute diagnosis of AAD. The European Society of Cardiology

recommends the measurement of D-dimer levels as part of the evaluation of AAD (7,8). Current studies appear to corroborate the utility of the measurement of D-dimer levels and to use a cut-off value of 0.1 mcg/ml to achieve 100% sensitivity or 0.5 mcg/ml to achieve a negative predictive value of 99%. Consideration should be given, however, to the fact that there are different assay types for the measurement of D-dimer levels, and different cut-off values will result in variation in the sensitivity and negative predictive value in patients with suspected AAD. Furthermore, although a negative D-dimer value may be useful in ruling out the presence of AAD, especially when there is an equivocal presentation or low level of suspicion, a positive D-dimer value is insufficient to confirm the diagnosis (9–11).

Answer: The use of serum D-dimer levels in the acute care setting to help evaluate patients with suspected AAD is recommended. The presence of elevated levels of D-dimer does not confirm the diagnosis but should prompt careful and thorough evaluation for AAD or other serious conditions (Grade A recommendation).

WHAT IS THE OPTIMAL IMAGING MODALITY FOR AORTIC DISSECTIONS? WHEN IS FURTHER OR DIFFERENT MODALITY OF IMAGING INDICATED?

Early and accurate diagnosis of AAD is critical. A high degree of clinical suspicion combined with careful symptom interrogation often provide the diagnosis, which can then be confirmed with imaging. The most common symptom reported is pain, often described as a shearing, tearing, or ripping in nature with a location that is often interscapular or paraspinous. Pain is present in the vast majority of AADs, with only 4% of patients denying symptoms (3).

Electrocardiogram-gated, multidetector row computed tomography (CT) imaging, with and without the use of an intravenous contrast agent, is the mainstay of radiological evaluation of the patient with a suspected AAD (12). A CT of the chest, abdomen, and pelvis can rapidly (less than 30 seconds acquisition time) and accurately provide imaging of the entire aorta from the level of the aortic valve to the femoral vessels. The primary finding is that of two lumens or channels with blood, as opposed to one distinct channel, and the visualization of the intimal or medial flap. CT with contrast will also allow for understanding the location and extent of the dissection. A non-contrast CT scan often provides important information about calcification in the walls of the aorta and whether intramural hematoma is present or thrombosis of the false lumen has occurred (13). Appropriate renal protective strategies should be employed for patients who have suspected or known diminution of their renal function. Hydration and alkalinization of the patient's urine are thought to be the most effective strategies to reduce the nephrotoxicity of most intravenous iodinated contrast agents.

The accuracy of multidetector CT with contrast for the detection of aortic dissection was 100% in several studies. In terms of locating the entry tear, CT has a 82% sensitivity and a 100% specificity. For defining involvement of the cephalic or visceral branch vessels, the sensitivity and specificity are 95% and 100%, respectively. Several other

studies report nearly 100% sensitivity and specificity for CT scanning to detect aortic dissections.

Magnetic resonance imaging (MRI) is an alternative modality that is used when traditional contrast agents cannot be administered due to renal insufficiency or allergies. Gadolinium, the contrast agent used for most MRI, has been implicated in a many-fold increase in nephrogenic systemic fibrosis and has to be avoided in patients with chronic renal insufficiency. Furthermore, MRI is associated with longer image acquisition times (up to 30 minutes) and is often not readily available in many outlying medical centers, especially during off hours. MRI has been noted to have between 95% and 100% sensitivity and 94% and 98% specificity for the detection of aortic dissection (14).

Invasive imaging, such as contrast aortography, is almost obsolete for the acute diagnosis of AAD, although it was the previous gold standard. Catheterization and angiography is sometimes useful in operative planning, such as the imaging of coronary arteries or the assessment of visceral vessel patency and run-off. In this regard, intravascular ultrasound has proven to be a useful adjunct for intraoperative imaging and in better defining and identifying the true and false lumens of vessels.

Transesophageal echocardiography (TEE) is an invaluable resource when discrepancy exists regarding the diagnosis or if clarification is needed to understand whether an AAD involves the ascending aorta. Given that type A dissections necessitate immediate surgery, the confirmation of a true flap or dissection in the ascending aorta by TEE is mandatory if there is any doubt or equivocation on the CT images. Although its utility is limited in the descending thoracic aorta, and despite the modality being much more operator-dependent than CT or MRI, TEE can often clearly define the origin of the dissection as either distal or proximal to the subclavian artery and definitively reveal whether the ascending aorta is involved.

Plain chest x-rays, although suggestive, are not diagnostic and do not provide the necessary detail for the diagnosis of either type A or type B acute aortic dissections. Findings on chest x-ray of a widened mediastinum, tracheal deviation, obscured or altered aortic contours, or the noted displacement of a nasogastric tube in the thoracic portion should all prompt further, more specific diagnostic imaging modalities (15,16).

Answer: CT of the chest, abdomen and pelvis, both with and without intravenous contrast enhancement is the mainstay of imaging for AADs. MRI, intravascular ultrasound, and TEE are all adjunctive imaging modalities that can be used to supplement and substantiate imaging data from the CT scan. Coronal and sagittal reconstructions are often useful additions to the traditional axial images obtained via CT (Grade A recommendation).

WHAT IS THE APPROPRIATE ROLE AND TIMING OF OPERATIVE INTERVENTION FOR EACH TYPE OF AAD?

Mortality with an AAD of the proximal or ascending aorta is extremely high. Many cases result in death at the time of the dissection due to acute compromise of the coronary arteries or of the aortic valve. Of the patients that survive to hospital admission, mortality is thought to be approximately 1–2% per hour (17).

The primary indication for surgery of AAD involving the ascending aorta is the very presence of the dissection. Ascending aortic dissections present the greatest danger for sudden death given the high likelihood of further proximal extension into the left, right, or both main coronary arteries. In addition, ascending AADs can also result in acute aortic valvular insufficiency or pericardial tamponade, both of which can be fatal. Thus, urgent operative intervention via a median sternotomy with cardiopulmonary bypass and hypothermia is the standard of care (3).

The key indications for surgery for type B AAD are free or contained rupture, rapid expansion of the dissected portion of artery or diameter greater than 5.5 cm, malperfusion syndrome involving a critical vessel, and intractable pain. Rupture and malperfusion with AAD of the descending thoracic aorta represent the highest mortality and are the most common reasons for urgent early intervention.

The timing of surgery for type A AAD is as soon as an operating team and cardiopulmonary bypass support can be mobilized. The surgeon should be prepared to address issues with the aortic valve, the coronary arteries, and the cephalic vessels at the time of surgery. Appropriate availability of artificial valves or aortic homografts must be considered, and the possibility for the need for coronary bypass grafting should be noted.

Surgery for Type B dissections usually can be delayed unless rupture is evident on imaging studies. The indications for intervention in the chronic setting are a total aortic diameter (both lumens and any thrombus) of greater than 55mm or expansion of greater than 5mm in a six-month period. Malperfusion syndromes that result in compromised renal or abdominal visceral flows may require endovascular or open repair techniques. Dynamic obstruction of the true vessel lumen from the intimal flap or static obstruction via false lumen thrombosis can cause malperfusion to the end organ and mandates surgical or interventional radiological therapy (18).

In general, most studies have supported the medical management of distal aortic dissections in the acute setting. This includes careful management of blood pressure with the avoidance of either hyper- or hypotension to minimize risks of extending or enlarging the dissection as well as avoiding hypoperfusion to end organs. In addition, aggressive pain management and evaluation of any neurological compromise necessitating spinal drainage are important adjuncts to medical therapy. Finally, lower limb ischemia and abdominal visceral ischemia should be monitored for in the acute setting and may mandate emergency surgical intervention such as femoral-femoral bypass or mesenteric vessel bypass. Surgery for type B dissections should ideally be performed at centers with experience and advanced techniques for spinal protection, cerebral and visceral perfusion, and sensory-evoked potential monitoring to minimize risk of stroke and paraplegia (19).

Answer: AADs of the ascending or proximal aorta are true surgical emergencies and mandate immediate operative intervention with cardiopulmonary bypass. AADs of the descending thoracic aorta are generally treated medically unless complications or sequelae mandate surgical or interventional radiological intervention (Grade A recommendation).

WHAT IS THE ROLE OF BLOOD PRESSURE MANAGEMENT DURING THE ACUTE AND SUBACUTE PHASES OF THE INJURY? WHAT IS THE ROLE OF LONG-TERM BLOOD PRESSURE MANAGEMENT?

Blood pressure management is the sine qua non of treatments for AAD. Appropriate, early, and judicious regulation of blood pressure in the patient with an AAD can decrease early mortality and ameliorate symptoms of both pain and malperfusion. The importance of early initiation of beta-blockade cannot be overemphasized. By reducing both the absolute pressure as well as diminishing the change in pressure over any time interval (dP/dT), beta-blockade plays an important role in preventing extension of the dissection and possibly reducing flow in the false lumen. Adjuncts to beta-blocker therapy include the use of a variety of agents such as nitrates and calcium channel blockers. In general, angiotensin-converting enzyme inhibitors and alpha-blocking agents have been avoided in the acute settings due to either concerns of renal compromise or sudden decrements in blood pressure.

In the longer term management of blood pressure, a variety of agents may be required, and it is usually mandatory for these patients to have the supervision of a specialist, such as a cardiologist or nephrologist, to aid in the management of blood pressure. It is not unusual for patients with aortic dissections to require multidrug therapy combining beta-blockade with a host of other medications to achieve sustainable blood pressure control. Optimal blood pressure control also requires these patients to initiate home monitoring system for blood pressure checks and medication timing. Lifelong blood pressure therapy is mandatory in patients with aortic dissection and along with careful follow-up, imaging plays an important role in the long-term management of these patients.

Answer: In the acute setting, beta-blockade is the mainstay of therapy with additional vasoactive agents used as needed. In the long-term management of these patients, beta-blockade along with second or third drug therapy is often needed with specialist supervision and home blood pressure monitoring (Grade A recommendation).

WHAT IS THE ROLE OF ENDOVASCULAR STENT GRAFT REPAIR FOR TYPE B DISSECTIONS. WHAT ARE THE DATA?

Stent graft repair of the aorta was first introduced for aneurysms of the abdominal aorta in the early 1990s. Randomized trials reported in the *New England Journal of Medicine* further prompted the development and role of endovascular repair (EVAR) of other aortic pathologies and more proximal regions of the aorta (21). Meta-analysis in 2006 documents the technical success that is achievable with an endovascular approach to both acute and chronic type B dissections. In 609 patients with type B dissections, technical procedural success was documented in 98.2% with an in-hospital conversion to open surgery required in only 2.3%. There was a relatively low 5.2% in-hospital mortality noted and a very low rate of paralysis of 0.8% noted when compared to open series that report up to 25% mortality and 10–15% paraplegia rates. In addition, false lumen

thrombosis occurred in over 75% of patients, and a two-year survival of 88.8% was noted in the endovascularly treated patient (22).

The role of stent grafting appears to be its effectiveness in sealing the proximal tear and promoting thrombosis of the false lumen. Due to the complex nature of most dissections and the presence of numerous reentry points, EVAR may not be completely effective in preventing continued flow in the false lumen, pressurization of the false lumen, and subsequent aneurismal degeneration of the aorta with continued risk for expansion and rupture. In the ideal treatment, all areas of intimal disruption would be sealed off, thereby permitting flow only in the true lumen. In realistic terms, with current-generation devices, this is not yet practical. In addition, other studies have documented substantial rate of endoleaks, 11% at 30 days and 6% at one year, that occur. Furthermore, aortic expansion occurs in up to 13% of patients at two years, and stent graft fracture rates in earlier generation devices was as high as 14%.

The Investigation of Stent Grafts in type B dissections trial was conducted in Europe. In 136 patients, EVAR was added to maximal medical therapy to determine if all-cause mortality at one year could be ameliorated. The trial was limited to patients with AADs (dissections that are treated within 52 weeks of diagnosis and without false lumen thrombosis). Early results seem to show significant mortality in patients undergoing EVAR (20,21).

In general, stent grafts should be avoided in treating patients with known connective tissue disorders, such as Marfan syndrome, because the tissue abnormality exists in all portions of the aorta. In addition, given the unknown long-term results with EVAR, using this as a treatment modality in younger patients should be guided by careful risk stratification, extensive discussion with the patient and family, and counseling regarding the need for lifetime follow-up. Stent grafts may have a role in treating patients at high risk for open repair, those in whom previous treatment with open repair provides landing zones with synthetic material, or those in whom debranching procedures are possible to allow treatment of the arch and descending aorta in a combined manner. Preparation to deal with known complications of EVAR such as proximal extension of the dissection, arm ischemia, stroke, endograft migration or collapse, endoleaks, and paralysis is essential in centers performing these procedures (22–24).

Answer: Stent graft repair for dissections of the descending aorta should be approached with caution. It is contraindicated in the presence of known connective tissue disorders. EVAR may have a role in patients at too high a risk for open surgery or for whom a debranching procedure may allow treatment of the arch and descending aorta in a combined approach (Grade C recommendation).

WHAT FOLLOW-UP IS NECESSARY POST-ENDOVASCULAR STENT GRAFT REPAIR?

Endovascular repair via the deployment of stent grafts are being more widely employed in the surgical management of aortic dissections. The relative scarcity of long-term data, especially since there has been such a continuous and rapid

evolution of devices, mandates that patients treated with this type of surgical therapy have regular and dedicated follow-up with radiological imaging and clinical correlation.

In general, most centers are obtaining a completion angiogram at the time of stent graft deployment, as well as a follow-up CT at either 24 to 48 hours or prior to discharge. A CT scan is then obtained usually at one month, three months, and six months postoperatively. Further imaging and the imaging interval can be determined or guided by the type and extent of dissection treated, the region and extent of aorta covered, and the noted or expected changes in status that are being monitored. If a complete thrombosis of a false lumen and a decrease in aortic size are noted, it would be reasonable to lengthen the follow-up interval. Conversely, if there is continued patency of the false lumen or if there is continued aneurismal degeneration of the stent graft-treated portion of the aorta, then closer follow-up intervals might be warranted. In addition, with the advent of devices that allow the monitoring of endolumenal wall tension or pressure, these might become the standard of care for long-term management of these patients (24).

Current studies and data do not exist regarding the long-term outcome or efficacy of stent graft/endovascular based therapies for aortic dissections. Patients and families should be counseled that mandatory periodic follow-up with CT scans employing the use of intravenous contrast will be necessary for all current generation devices.

Of note, follow-up is needed even after repair of type A dissections if there is residual dissection of the arch and descending thoracic aorta. This portion of the aorta should be evaluated by scheduled CT scans or MRI to measure any aneurismal degeneration of the dissected region or for change in the true and false lumens or extent of the dissection (12).

Answer: Close follow-up with CT scanning should be employed following stent graft repair of aortic dissections. There are no long-term data regarding the efficacy of stent graft repair for AAD, and patients should be advised that lifetime follow-up may be necessary with this therapeutic modality. There are numerous reports in the literature of differing modalities of stent graft failures, including stent graft fracture, endoleaks, and graft migration (Grade A recommendation).

Levels of Evidence

Question	Answer	Level of evidence	Ref.
What are the two basic categories of aortic dissection?	Ascending (type A), descending (type B)	N/A	4
What is the optimal imaging modality for aortic dissections? When is further or different modality of imaging indicated?	CT scanning with and without contrast using multidetector array technology; MRI and TEE may be useful adjuncts	II	12, 15, 16
Should D-dimer levels be measured?	Yes	II	7-11
What is the appropriate role and timing of operative intervention for each type of AAD?	Immediate open surgery for type A; initial med Rx for type B	II	1-3, 17-19
What is the role of blood pressure management during the acute and subacute phase of the injury? What is the role of long-term blood pressure management?	Beta-blocker is crucial for early management, lifelong blood pressure monitoring and treatment is necessary	II	13, 17, 19
What is the role of endovascular stent graft repair for type B dissections? What are the data?	Limited role for stent-graft repair and no long-term data	II	20-23
What follow-up is required post-stent graft placement?	Serial CTs of the treated aorta for at least 5 years	II	21-22

Abbreviations: AAD, acute aortic dissection; CT, computed tomography; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography.

REFERENCES

- Trimarchi S, Nienaber CA, Rampoldi V, et al.; IRAD investigators. Role and results of surgery in acute type B aortic dissection: Insights from the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2006; 114(1 Suppl): I357-I3564.
- Tsai TT, Evangelista A, Nienaber CA, et al. International Registry of Acute Aortic Dissection (IRAD). Long-term survival in patients presenting with type A acute aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2006; 114(1 Suppl): I350-I356.
- Hagan PG, Nienaber DA, Isselbacher EM, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. *JAMA* 2000; 283: 897-903.
- Cohn LH, ed. *Cardiac Surgery in the Adult*, 3rd edition. New York: McGraw-Hill, 1195-308.
- Erbel R, Alfonso F, Boileau C, et al. Task Force on Aortic Dissection, Eur Soc. of Cardiology, diagnosis and management of aortic dissection. *Eur Heart J* 2001; 22: 1642-81.
- Lansman SL, McCullough JN, Nguyen KH, et al. Subtypes of acute aortic dissection. *Ann Thorac Surg* 1999; 67: 1975-8; discussion 1979-80.
- Eggebrecht H, Naber CK, Bruch C, et al. Value of plasma fibrin D-dimers for detection of acute aortic dissection. *J Am Coll Cardiol* 2004; 44: 804-9.
- Pepe G, Giusti B, Yacoub M, et al. An expanding role of biomarkers in acute aortic syndromes. *Clin Cardiol* 2006; 29: 432-3.
- Ohlmann P, Faure A, Morel O, et al. Diagnostic and prognostic value of circulating D-dimers in patients with acute aortic dissection. *Crit Care Med* 2006; 34: 1358-64.
- Marrill KA. Serum D-dimer is a sensitive test for the detection of acute aortic dissection: a pooled meta-analysis. *Ann Emerg Med* 2007; 14: S129.

11. Sodeck G, Domanotvits H, Schillinger M, et al. D-dimer in ruling out acute aortic dissection: a systematic review and prospective cohort study. *Eur Heart J* 2007; 28: 2067–75.
12. Chughtai A, Kazerooni E. CT and MRI of acute thoracic cardiovascular emergencies. *Crit Care Clin* 2007; 23: 835–53.
13. Wong DR, Lemaire SA, Coselli JS. Managing dissections of the thoracic aorta. *Am Surg* 2008; 74: 364–80.
14. Jagannath AS, Sos TA, Lockhart SH, et al. Aortic dissection: a statistical analysis of the usefulness of plain chest radiographic findings. *Am J Roentgenol* 1986; 147: 1123–6.
15. Hayter RG, Rhea JT, Small A, et al. Suspected aortic dissection and other aortic disorders: Multi-detector row CT in 373 cases in the emergency setting. *Radiology* 2006; 238: 841–52.
16. Sommer T, Fehske W, Holzknecht N, et al. Aortic dissection: a comparative study of diagnosis with spiral CT, multiplanar TEE and MR imaging. *Radiology* 1996; 199: 347–52.
17. Kamalakannan D, Rosman HS, Eagle KA. Acute aortic dissection. *Crit Care Clin* 2007; 23: 779–800.
18. Mehta RH, Suzuki T, Hagan PG, et al. Predicting death in patients with acute type A aortic dissection. *Circulation* 2002; 105: 200–6.
19. Umana JP, Lai DT, Mitchell RS, et al. Is medical therapy still the optimal treatment strategy for patients with acute Type B aortic dissections? *J Thorac Cardiovasc Surg* 2002; 124: 896–910.
20. Nienaber CA, Zannetti S, Barbieri B, et al. Investigation of stent grafts in patients with Type B aortic dissection: design of the INSTEAD trial. *Am Heart J* 2005; 149: 592–9.
21. Dake MD, Kato N, Mitchell RS, et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. *New Engl J Med* 1999; 340: 1546–52.
22. Eggebrecht H, Nienaber CA, Neuhauser M, et al. Endovascular stent-graft placement in aortic dissection: A meta-analysis. *Eur Heart J* 2006; 27: 489–98.
23. Atkins MD Jr., Black JH III, Cambria RP. Aortic dissection: perspectives in the era of stent-graft repair. *J Vasc Surg* 2006; 43(Suppl A): 30A–43A.
24. Criado FJ, Abul-Khoudoud OR, Domer GS, et al. Endovascular repair of the thoracic aorta: Lesions learned. *Ann Thor Surg* 2005; 80: 857–63.

Deep Venous Thrombosis

Paula K. Shireman

Summary of Clinical Questions		
Question	Answer	Grade
What is the best initial treatment for venous thromboembolism?	LMWH is the preferred initial treatment for DVT compared to unfractionated heparin in most patients.	A
Is home therapy for venous thromboembolism safe and effective compared to inpatient care?	Home therapy for DVT with LMWH is safe and cost-effective in carefully chosen patients.	A
What is the optimal oral starting dose of vitamin K antagonists?	There is no consensus on the optimal starting dose of warfarin. Clinicians should consider patient-specific factors for determining a warfarin dose. Patients at low risk for bleeding may safely tolerate a 10 mg loading dose.	B
What is the optimal length of oral vitamin K antagonist treatment for DVT?	Extended therapy with vitamin K antagonists is warranted to prevent recurrent venous thromboembolism. Risks of bleeding versus recurrence of venous thromboembolism for individual patients may alter the optimal duration of therapy.	A
	DVT associated with a transient event maybe effectively treated with 3 months of vitamin K antagonists.	B
Does catheter-directed thrombolysis decrease DVT recurrences and incidence of post-thrombotic syndrome?	Though catheter-directed thrombolysis results in increased venous patency and decreased incidence of post-thrombotic syndrome, bleeding complications limit the routine use of this technology.	B
Do compression stockings reduce the long-term complication of post-thrombotic syndrome?	Graded compression stockings reduce the incidence of post-thrombotic syndrome when used early after the diagnosis of DVT.	A
Abbreviations: DVT, deep venous thrombosis; LMWH, low molecular weight heparin.		

Deep venous thrombosis (DVT) is a major health problem with an annual incidence of 0.5–1 per 1,000 (1). The main short-term complication of DVT is pulmonary embolism, and the long-term complication of the post-thrombotic syndrome can occur in as many as 50% of patients despite treatment (2). Multiple evidence-based reviews of the diagnosis and treatment of DVT have recently been published (3–5) as well as practice guidelines (6–8). This chapter reviews several aspects of DVT treatment. Although pulmonary embolism is discussed in Chapter 70, many studies combine both disease entities. As such, some of the questions address the broader topics of both DVT and pulmonary embolism; collectively referred to as venous thromboembolism.

WHAT IS THE BEST INITIAL TREATMENT FOR VENOUS THROMBOEMBOLISM?

Traditionally, DVT has been treated with intravenous, unfractionated heparin until a therapeutic level of oral anticoagulation can be achieved with vitamin K antagonists. However, frequent lab tests with adjustment of the unfractionated

heparin dose are necessary due to variable clinical effects. On the other hand, the effects of low molecular weight heparins (LMWHs) are more predictable and do not require routine lab testing (9). Multiple randomized controlled trials have been performed comparing the efficacy and safety of unfractionated heparin versus LMWH and have been summarized in evidence-based reviews (3,4,7, 9,10) and society-sponsored practice guidelines (6,7).

A Cochrane review (10) performed an analysis of 22 randomized trials (11–32) with a total of 8,867 patients. The primary outcome of recurrence of symptomatic venous thromboembolism using the pooled data revealed a statistically significant reduction using LMWH during the initial treatment [odds ratio (OR) 0.68; 95% confidence interval (CI) 0.48–0.97] and at the end of follow-up (OR 0.68; 95% CI 0.55–0.84) compared to unfractionated heparin. Secondary outcomes of reduction in major hemorrhage during the initial treatment (OR 0.57; 95% CI 0.39–0.83) and lower overall mortality at the end of follow-up (OR 0.76; 95% CI 0.62–0.92) also favored the LMWH group.

LMWH has the advantages of providing predictable anticoagulation levels in patients using weight-adjusted

dosing without laboratory monitoring in most patients. However, clinical situations such as renal failure or pregnancy may require dose adjustment using plasma anti-Xa levels (7).

Recommendation: LMWH is the preferred initial treatment for DVT compared to unfractionated heparin in most patients. Level of evidence: Ia. Grade of recommendation: A.

IS HOME THERAPY FOR VENOUS THROMBOEMBOLISM SAFE AND EFFECTIVE COMPARED TO INPATIENT CARE?

Multiple trials have been performed comparing the safety of DVT treatment at home with LMWH compared to hospitalization and treatment with unfractionated heparin or LMWH; these trials have been summarized in several evidence-based reviews (4,7,33,34). A Cochrane review (34) performed an analysis of six randomized controlled trials (24,25,35–38) with 1,708 participants. Venous thromboembolism recurrence was significantly lower in the LMWH patients treated at home [relative risk (fixed) 0.6; 95% CI 0.42–0.90] compared to hospitalized patients. In addition, patients treated at home exhibited lower mortality and fewer major bleeding complications but were more likely to have minor bleeding complications compared to patients treated in the hospital; however, these differences were not statistically significant. Home therapy was also deemed to be cost-effective and preferred by patients.

Study limitations to home versus inpatient treatment of DVT include differences in the treatments studied, such as using unfractionated heparin in the hospital but LMWH for home treatment (4,33,34). Furthermore, strict criteria for patients considered for home treatment were used and may affect the generalizability of the studies to patients seen in clinical practice (33,34).

Recommendation: Home therapy for DVT with LMWH is safe and cost-effective in carefully chosen patients. Level of evidence: Ib. Grade of recommendation: A.

WHAT IS THE OPTIMAL ORAL STARTING DOSE OF VITAMIN K ANTAGONISTS?

Three prospective, randomized trials (39–41) compared starting doses of 5 or 10 mg warfarin therapy. These trials have been previously reviewed (7,42), and guidelines for the initial dosing of vitamin K antagonists have been published by several societies (7,43). Vitamin K–dependent clotting factors have circulating half-lives ranging from 6–60 hours. Because factor II has the longest circulating half-life of 60 hours, the full anticoagulant effect of vitamin K antagonists, such as warfarin, maybe delayed by a week or more. Furthermore, initiation of vitamin K antagonist therapy can result in a transient hypercoagulable state due to the circulating half-lives of 6 and 42 hours for the anticoagulant protein C and protein S, respectively. Thus, unfractionated heparin or LMWH therapy is initiated and maintained for several days until oral vitamin K antagonist therapy is therapeutic, as measured by an international normalized ratio (INR) with values generally between 2 and 3 (42).

Two small trials randomized 49 patients (41) and 53 patients (40) to receive an initial dose of 5 or 10 mg

warfarin and measured the time necessary for warfarin therapy to become therapeutic. Harrison et al. (41) determined that at 36 hours, significantly more patients were therapeutic in the 10 mg group (44% versus 8%, $p = 0.005$) compared to the 5 mg group. In contrast, Crowther et al. (40) determined that significantly more patients in the 5 mg group exhibited a therapeutic INR on days 1–5 of therapy (66% versus 24%, $p < 0.003$) compared to the 10 mg group. The 10 mg group in both studies exhibited an increased risk of excessive anticoagulation (40,41), and there was a faster rate of decrease in protein C levels in the first 36 hours of treatment with the 10 mg group (41), leading the authors to speculate that the 5 mg warfarin dose maybe less likely to induce a hypercoagulable state. Both studies recommended using a 5 mg dose for initiation of warfarin therapy.

The third trial by Kovacs et al. (39) randomized 210 patients to receive 5 or 10 mg initial doses of warfarin; the study was powered to detect a 0.5-day difference in time necessary to reach a therapeutic INR. Patients receiving 10 mg warfarin achieved a therapeutic INR 1.4 days faster than patients receiving 5 mg (4.2 ± 1.1 versus 5.6 ± 1.4 days, mean $\pm$ standard deviation, $p < 0.001$) with no significant increase in excessive anticoagulation. However, this study excluded patients at high risk for bleeding.

Recommendation: There is no consensus on the optimal starting dose of warfarin. Clinicians should consider patient-specific factors for determining a warfarin dose. Patients at low risk for bleeding may safely tolerate a 10 mg loading dose if appropriate nomograms are strictly followed. Level of evidence: IIb. Grade of recommendation: B.

WHAT IS THE OPTIMAL LENGTH OF ORAL VITAMIN K ANTAGONIST TREATMENT FOR DVT?

Multiple trials have evaluated the duration of therapy with vitamin K antagonists on venous thromboembolism; these trials have been summarized in several evidence-based reviews (4,7,44) and society-sponsored practice guidelines (6,7). A Cochrane review (44) performed an analysis of eight randomized trials (45–52) with a total of 2,994 patients. Reduction in the risk of recurrent venous thromboembolism occurred during prolonged treatment with vitamin K antagonists (OR 0.18; 95% CI 0.13–0.26) as well as a substantial increased risk in bleeding complications during the entire study period (OR 2.61; 95% CI 1.48–4.61). Risk of recurrent venous thromboembolism was decreased with vitamin K antagonists for as long as the treatment was used, but the risk of recurrent venous thromboembolism decreased over time. Furthermore, the risk of major bleeding remained as long as vitamin K antagonist therapy was continued. Thus, the authors concluded that the efficacy of vitamin K antagonist therapy decreased over time and the optimal duration of therapy would vary between different groups of patients dependent on balancing risk/benefit profiles (44).

Segal et al. (4) identified 10 trials (45–54) that included 4,240 patients that used objective radiologic documentation of venous thromboembolism and used INR to monitor vitamin K antagonist therapy. Durations of vitamin K antagonist therapy were evaluated in multiple trials. Only one randomized blinded trial (48) compared

one versus three months of therapy for DVT associated with a transient event, such as surgery. Treatment for one month resulted in increased rates of recurrent venous thromboembolism with similar bleeding complications compared to three months of therapy. The trial was stopped for slow patient accrual and was only able to randomize 165 patients of the estimated 390 needed to provide conclusive results.

Recommendation: Extended therapy with vitamin K antagonists is warranted to prevent recurrent venous thromboembolism. Risks of bleeding versus recurrence of venous thromboembolism for individual patients may alter the optimal duration of therapy. Level of evidence: Ia. Grade of recommendation: A. DVT associated with a transient event maybe effectively treated with three months of vitamin K antagonists. Level of evidence: IIb. Grade of recommendation: B.

DOES CATHETER-DIRECTED THROMBOLYSIS DECREASE DVT RECURRENCES AND INCIDENCE OF POST-THROMBOTIC SYNDROME?

The goal of catheter-directed thrombolysis is to rapidly remove thrombus, thereby potentially preserving venous valvular function and reducing the incidence and severity of post-thrombotic syndrome. Detailed evidence-based evaluations of catheter-directed thrombolysis for DVT treatment have recently been performed (4,7,55). One randomized trial evaluated catheter-directed thrombolysis compared to intravenous unfractionated heparin, both groups subsequently received six months of vitamin K antagonist therapy (56). Patients were evaluated six months after the initial treatment; the venous patency rate was significantly higher in the catheter-directed thrombolysis group (72% versus 12%) and the incidence of venous reflux was significantly decreased (11% versus 41%) compared to the unfractionated heparin group.

Segal et al. (4) reviewed 14 observational trials of catheter-directed thrombolysis that used a variety of lytic agents (57–70). The range of complete thrombus lysis in the studies ranged from 31% to 92%. Only five studies reported long-term results (60–62,64,69) with general agreement between the studies that catheter-directed thrombolysis resulted in increased vein patency and venous valvular competency with a decreased incidence of post-thrombotic syndrome. The rates of minor bleeding ranged from 0% to 25% and the rates of major bleeding ranged from 0% to 13% with one fatal intracranial hemorrhage occurring (4).

Although bleeding complications continue to limit the general use of catheter-directed thrombolysis, the incidence of bleeding complications have been reduced over time with the advent of more strict selection criteria (55). Several devices are currently in use that combine chemical lysis with mechanical or ultrasound energy clot removal [recently reviewed by McLafferty (71)]; however, no randomized trials exist with these devices.

Recommendation: Though catheter-directed thrombolysis results in increased venous patency and decreased incidence of post-thrombotic syndrome, bleeding complications limit the routine use of this technology. Level of evidence: IIb. Grade of recommendation: B.

DO COMPRESSION STOCKINGS REDUCE THE LONG-TERM COMPLICATION OF POST-THROMBOTIC SYNDROME?

Three randomized trials (2,72,73), all with nearly five years of follow-up, have assessed the efficacy of compression stockings for the prevention of post-thrombotic syndrome. Two larger trials randomized patients to graduated compression stockings with an ankle pressure of 30–40 mmHg versus no intervention. Patients initiated stocking treatment shortly after DVT diagnosis and continued to wear stockings for two years compared to no stockings. Both trials demonstrated a reduction in post-thrombotic syndrome in the compression stocking group. Brandjes et al. (2) randomized 194 patients and observed a decreased incidence of both mild to moderate (20% versus 47%) as well as severe (11% versus 23%) post-thrombotic syndrome in the custom-fit stocking group versus no stocking group. Pradoni et al. (73) randomized 180 patients and observed a cumulative two-year incidence of post-thrombotic syndrome of 24% in the over-the-counter stocking group and 49% in the control group. Furthermore, the incidence of severe post-thrombotic syndrome was also significantly reduced (3% versus 11%) in the stocking versus control group, respectively. A third trial (72) randomized 47 patients to compression stockings versus placebo stockings one year after the diagnosis of DVT; this study did not show a benefit from using compression stockings.

Recommendation: Graded compression stockings reduce the incidence of post-thrombotic syndrome when used early after the diagnosis of DVT. Both custom-fit (2) and over-the-counter (73) stockings provide benefit. Level of evidence: Ia. Grade of Recommendation: A.

REFERENCES

1. Fowkes FJ, Price JF, Fowkes FG. Incidence of diagnosed deep vein thrombosis in the general population: systematic review. *Eur J Vasc Endovasc Surg* 2003; 25: 1–5.
2. Brandjes DP, Buller HR, Heijboer H, et al. Randomised trial of effect of compression stockings in patients with symptomatic proximal-vein thrombosis. *Lancet* 1997; 349: 759–62.
3. Segal JB, Eng J, Jenckes MW, et al. Diagnosis and treatment of deep venous thrombosis and pulmonary embolism. *Evid Rep Technol Assess (Summ)* 2003; 68: 1–6.
4. Segal JB, Streiff MB, Hofmann LV, et al. Management of venous thromboembolism: a systematic review for a practice guideline. *Ann Intern Med* 2007; 146: 211–22.
5. Segal JB, Eng J, Tamariz LJ, et al. Review of the evidence on diagnosis of deep venous thrombosis and pulmonary embolism. *Ann Fam Med* 2007; 5: 63–73.
6. Snow V, Qaseem A, Barry P, et al. Management of venous thromboembolism: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med* 2007; 146: 204–10.
7. Buller HR, Agnelli G, Hull RD, et al. Antithrombotic therapy for venous thromboembolic disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126(3 Suppl): 401S–28S.
8. Qaseem A, Snow V, Barry P, et al. Current diagnosis of venous thromboembolism in primary care: a clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians. *Ann Intern Med* 2007; 146: 454–8.
9. Krishnan JA, Segal JB, Streiff MB, et al. Treatment of venous thromboembolism with low-molecular-weight heparin: a

- synthesis of the evidence published in systematic literature reviews. *Respir Med* 2004; 98: 376–86.
10. van Dongen CJ, van den Belt AG, Prins MH, et al. Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for venous thromboembolism. *Cochrane Database Syst Rev* 2004; 4: CD001100.
 11. Belcaro G, Nicolaidis AN, Cesarone MR, et al. Comparison of low-molecular-weight heparin, administered primarily at home, with unfractionated heparin, administered in hospital, and subcutaneous heparin, administered at home for deep-vein thrombosis. *Angiology* 1999; 50: 781–7.
 12. Goldhaber SZ, Morrison RB, Diran LL, et al. Abbreviated hospitalization for deep venous thrombosis with the use of ardeparin. *Arch Intern Med* 1998; 158: 2325–8.
 13. Breddin HK, Hach-Wunderle V, Nakov R, et al. Effects of a low-molecular-weight heparin on thrombus regression and recurrent thromboembolism in patients with deep-vein thrombosis. *N Engl J Med* 2001; 344: 626–31.
 14. Kirchmaier CM, Wolf H, Schafer H, et al. Efficacy of a low molecular weight heparin administered intravenously or subcutaneously in comparison with intravenous unfractionated heparin in the treatment of deep venous thrombosis. *Certoparin-Study Group. Int Angiol* 1998; 17: 135–45.
 15. The Columbus Investigators. Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. *N Engl J Med* 1997; 337: 657–62.
 16. Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *Prevention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. N Engl J Med* 1998; 338: 409–15.
 17. Simonneau G, Charbonnier B, Decousus H, et al. Subcutaneous low-molecular-weight heparin compared with continuous intravenous unfractionated heparin in the treatment of proximal deep vein thrombosis. *Arch Intern Med* 1993; 153: 1541–6.
 18. Faivre R, Neuhaert Y, Kieffer Y, et al. A new treatment of deep venous thrombosis: low molecular weight heparin fractions. *Randomized study. Presse Med* 1988; 17: 197–200.
 19. Fiessinger JN, Lopez-Fernandez M, Gatterer E, et al. Once-daily subcutaneous dalteparin, a low molecular weight heparin, for the initial treatment of acute deep vein thrombosis. *Thromb Haemost* 1996; 76: 195–9.
 20. Findik S, Erkan ML, Selcuk MB, et al. Low-molecular-weight heparin versus unfractionated heparin in the treatment of patients with acute pulmonary thromboembolism. *Respiration* 2002; 69: 440–4.
 21. Harenberg J, Schmidt JA, Koppenhagen K, et al. Fixed-dose, body weight-independent subcutaneous LMW heparin versus adjusted dose unfractionated intravenous heparin in the initial treatment of proximal venous thrombosis. *EASTERN Investigators. Thromb Haemost* 2000; 83: 652–6.
 22. Riess H, Koppenhagen K, Tolle A, et al. Fixed-dose, body weight-independent subcutaneous low molecular weight heparin certoparin compared with adjusted-dose intravenous unfractionated heparin in patients with proximal deep venous thrombosis. *Thromb Haemost* 2003; 90: 252–9.
 23. Hull RD, Raskob GE, Pineo GF, et al. Subcutaneous low-molecular-weight heparin compared with continuous intravenous heparin in the treatment of proximal-vein thrombosis. *N Engl J Med* 1992; 326: 975–82.
 24. Koopman MM, Prandoni P, Piovella F, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. *The Tasman Study Group. N Engl J Med* 1996; 334: 682–7.
 25. Levine M, Gent M, Hirsh J, et al. A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. *N Engl J Med* 1996; 334: 677–81.
 26. Lindmarker P, Holmstrom M, Granqvist S, et al. Comparison of once-daily subcutaneous Fragmin with continuous intravenous unfractionated heparin in the treatment of deep vein thrombosis. *Thromb Haemost* 1994; 72: 186–90.
 27. Lopaciuk S, Meissner AJ, Filipiecki S, et al. Subcutaneous low molecular weight heparin versus subcutaneous unfractionated heparin in the treatment of deep vein thrombosis: a Polish multicenter trial. *Thromb Haemost* 1992; 68: 14–18.
 28. Luomanmaki K, Grankvist S, Hallert C, et al. A multicentre comparison of once-daily subcutaneous dalteparin (low molecular weight heparin) and continuous intravenous heparin in the treatment of deep vein thrombosis. *J Intern Med* 1996; 240: 85–92.
 29. Merli G, Spiro TE, Olsson CG, et al. Subcutaneous enoxaparin once or twice daily compared with intravenous unfractionated heparin for treatment of venous thromboembolic disease. *Ann Intern Med* 2001; 134: 191–202.
 30. Ninet J, Bachet P, Prandoni P, et al. A randomized trial of subcutaneous low molecular weight heparin (CY216) compared with intravenous unfractionated heparin in the treatment of deep vein thrombosis. *Thromb Haemost* 1991; 65: 251–6.
 31. Prandoni P, Lensing AW, Buller HR, et al. Comparison of subcutaneous low-molecular-weight heparin with intravenous standard heparin in proximal deep-vein thrombosis. *Lancet* 1992; 339: 441–5.
 32. Simonneau G, Sors H, Charbonnier B, et al. A comparison of low-molecular-weight heparin with unfractionated heparin for acute pulmonary embolism. *The THESEE Study Group. Tinzaparine ou Heparine Standard: Evaluations dans l'Embolie Pulmonaire. N Engl J Med* 1997; 337: 663–9.
 33. Segal JB, Bolger DT, Jenckes MW, et al. Outpatient therapy with low molecular weight heparin for the treatment of venous thromboembolism: a review of efficacy, safety, and costs. *Am J Med* 2003; 115: 298–308.
 34. Othieno R, Abu Affan M, Okpo E. Home versus in-patient treatment for deep vein thrombosis. *Cochrane Database Syst Rev* 2007; 3: CD003076.
 35. Boccalon H, Elias A, Chale JJ, et al. Clinical outcome and cost of hospital vs home treatment of proximal deep vein thrombosis with a low-molecular-weight heparin: the Vascular Midi-Pyrenees study. *Arch Intern Med* 2000; 160: 1769–73.
 36. Daskalopoulos ME, Daskalopoulou SS, Tzortzis E, et al. Long-term treatment of deep venous thrombosis with a low molecular weight heparin (tinzaparin): a prospective randomized trial. *Eur J Vasc Endovasc Surg* 2005; 29: 638–50.
 37. Chong BH, Brighton TA, Baker RI, et al. Once-daily enoxaparin in the outpatient setting versus unfractionated heparin in hospital for the treatment of symptomatic deep-vein thrombosis. *J Thromb Thrombolysis* 2005; 19: 173–81.
 38. Ramacciotti E, Araujo GR, Lastoria S, et al. An open-label, comparative study of the efficacy and safety of once-daily dose of enoxaparin versus unfractionated heparin in the treatment of proximal lower limb deep-vein thrombosis. *Thromb Res* 2004; 114: 149–53.
 39. Kovacs MJ, Rodger M, Anderson DR, et al. Comparison of 10-mg and 5-mg warfarin initiation nomograms together with low-molecular-weight heparin for outpatient treatment of acute venous thromboembolism. *A randomized, double-blind, controlled trial. Ann Intern Med* 2003; 138: 714–19.
 40. Crowther MA, Ginsberg JB, Kearon C, et al. A randomized trial comparing 5-mg and 10-mg warfarin loading doses. *Arch Intern Med* 1999; 159: 46–8.
 41. Harrison L, Johnston M, Massicotte MP, et al. Comparison of 5-mg and 10-mg loading doses in initiation of warfarin therapy. *Ann Intern Med* 1997; 126: 133–6.

42. Eckhoff CD, Didomenico RJ, Shapiro NL. Initiating warfarin therapy: 5 mg versus 10 mg. *Ann Pharmacother* 2004; 38: 2115–21.
43. Hirsh J, Fuster V, Ansell J, et al. American Heart Association/American College of Cardiology Foundation guide to warfarin therapy. *J Am Coll Cardiol* 2003; 41: 1633–52.
44. Hutten BA, Prins MH. Duration of treatment with vitamin K antagonists in symptomatic venous thromboembolism. *Cochrane Database Syst Rev* 2006; 1: CD001367.
45. Agnelli G, Prandoni P, Becattini C, et al. Extended oral anticoagulant therapy after a first episode of pulmonary embolism. *Ann Intern Med* 2003; 139: 19–25.
46. Agnelli G, Prandoni P, Santamaria MG, et al. Three months versus one year of oral anticoagulant therapy for idiopathic deep venous thrombosis. Warfarin Optimal Duration Italian Trial Investigators. *N Engl J Med* 2001; 345: 165–9.
47. Kearon C, Gent M, Hirsh J, et al. A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. *N Engl J Med* 1999; 340: 901–7.
48. Kearon C, Ginsberg JS, Anderson DR, et al. Comparison of 1 month with 3 months of anticoagulation for a first episode of venous thromboembolism associated with a transient risk factor. *J Thromb Haemost* 2004; 2: 743–9.
49. Levine MN, Hirsh J, Gent M, et al. Optimal duration of oral anticoagulant therapy: a randomized trial comparing four weeks with three months of warfarin in patients with proximal deep vein thrombosis. *Thromb Haemost* 1995; 74: 606–11.
50. Pinede L, Ninet J, Duhaut P, et al. Comparison of 3 and 6 months of oral anticoagulant therapy after a first episode of proximal deep vein thrombosis or pulmonary embolism and comparison of 6 and 12 weeks of therapy after isolated calf deep vein thrombosis. *Circulation* 2001; 103: 2453–60.
51. Schulman S, Granqvist S, Holmstrom M, et al. The duration of oral anticoagulant therapy after a second episode of venous thromboembolism. The Duration of Anticoagulation Trial Study Group. *N Engl J Med* 1997; 336: 393–8.
52. Schulman S, Rhedin AS, Lindmarker P, et al. A comparison of six weeks with six months of oral anticoagulant therapy after a first episode of venous thromboembolism. Duration of Anticoagulation Trial Study Group. *N Engl J Med* 1995; 332: 1661–5.
53. Ridker PM, Goldhaber SZ, Danielson E, et al. Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism. *N Engl J Med* 2003; 348: 1425–34.
54. Kearon C, Ginsberg JS, Kovacs MJ, et al. Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. *N Engl J Med* 2003; 349: 631–9.
55. Watson LI, Armon MP. Thrombolysis for acute deep vein thrombosis. *Cochrane Database Syst Rev* 2004; 4: CD002783.
56. Elsharawy M, Elzayat E. Early results of thrombolysis vs anticoagulation in iliofemoral venous thrombosis. A randomised clinical trial. *Eur J Vasc Endovasc Surg* 2002; 24: 209–14.
57. Acharya G, Singh K, Hansen JB, et al. Catheter-directed thrombolysis for the management of postpartum deep venous thrombosis. *Acta Obstet Gynecol Scand* 2005; 84: 155–8.
58. Castaneda F, Li R, Young K, et al. Catheter-directed thrombolysis in deep venous thrombosis with use of reteplase: immediate results and complications from a pilot study. *J Vasc Interv Radiol* 2002; 13: 577–80.
59. Grunwald MR, Hofmann LV. Comparison of urokinase, alteplase, and reteplase for catheter-directed thrombolysis of deep venous thrombosis. *J Vasc Interv Radiol* 2004; 15: 347–52.
60. Laiho MK, Oinonen A, Sugano N, et al. Preservation of venous valve function after catheter-directed and systemic thrombolysis for deep venous thrombosis. *Eur J Vasc Endovasc Surg* 2004; 28: 39–396.
61. Mewissen MW, Seabrook GR, Meissner MH, et al. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. *Radiology* 1999; 211: 39–49.
62. Ogawa T, Hoshino S, Midorikawa H, et al. Intermittent pneumatic compression of the foot and calf improves the outcome of catheter-directed thrombolysis using low-dose urokinase in patients with acute proximal venous thrombosis of the leg. *J Vasc Surg* 2005; 42: 940–4.
63. Raju S, Fountain T, McPherson SH. Catheter-directed thrombolysis for deep venous thrombosis. *J Miss State Med Assoc* 1998; 39: 81–4.
64. Sillesen H, Just S, Jorgensen M, et al. Catheter directed thrombolysis for treatment of ilio-femoral deep venous thrombosis is durable, preserves venous valve function and may prevent chronic venous insufficiency. *Eur J Vasc Endovasc Surg* 2005; 30: 556–62.
65. Sugimoto K, Hofmann LV, Razavi MK, et al. The safety, efficacy, and pharmacoeconomics of low-dose alteplase compared with urokinase for catheter-directed thrombolysis of arterial and venous occlusions. *J Vasc Surg* 2003; 37: 512–17.
66. Razavi MK, Wong H, Kee ST, et al. Initial clinical results of tenecteplase (TNK) in catheter-directed thrombolytic therapy. *J Endovasc Ther* 2002; 9: 593–8.
67. Horne MK III, Mayo DJ, Cannon RO III, et al. Intracat recombinant tissue plasminogen activator in the treatment of deep venous thrombosis of the lower and upper extremities. *Am J Med* 2000; 108: 251–5.
68. Ouriel K, Katzen B, Mewissen M, et al. Reteplase in the treatment of peripheral arterial and venous occlusions: a pilot study. *J Vasc Interv Radiol* 2000; 11: 849–54.
69. Bjarnason H, Kruse JR, Asinger DA, et al. Iliofemoral deep venous thrombosis: safety and efficacy outcome during 5 years of catheter-directed thrombolytic therapy. *J Vasc Interv Radiol* 1997; 8: 405–18.
70. Semba CP, Dake MD. Iliofemoral deep venous thrombosis: aggressive therapy with catheter-directed thrombolysis. *Radiology* 1994; 191: 487–94.
71. McLafferty RB. Endovascular management of deep venous thrombosis. *Perspect Vasc Surg Endovasc Ther* 2008; 20: 87–91.
72. Ginsberg JS, Hirsh J, Julian J, et al. Prevention and treatment of postphlebotic syndrome: results of a 3-part study. *Arch Intern Med* 2001; 161: 2105–9.
73. Prandoni P, Lensing AW, Prins MH, et al. Below-knee elastic compression stockings to prevent the post-thrombotic syndrome: a randomized, controlled trial. *Ann Intern Med* 2004; 141: 249–56.

Pulmonary Embolism

George C. Velmahos

Clinical Questions		
Question	Answer	Grade of recommendation
Who is at risk for PE?	Patients with spinal injuries, older age, major surgery or trauma, previous history of thromboembolism, and cancer.	B
What is the optimal diagnostic test for PE?	CT angiography	A
Are heparin and compression devices adequate for PE prophylaxis?	The effectiveness of heparin and compression devices in trauma and emergency surgery patients is unclear. LMWH seems to perform better than UFH.	B
Is PE and mortality from PE reduced by IVC filters?	The effectiveness of IVC filters in reducing PE and mortality from PE in trauma and emergency surgery patients is unclear.	C
Is LMWH as safe and effective as UFH for the treatment of PE?	Yes	A
Abbreviations: CT, computed tomography; IVC, inferior vena cava; LMWH, low-molecular weight heparin; PE, pulmonary embolism; UFH, unfractionated heparin.		

INTRODUCTION

Pulmonary embolism (PE) is a national health problem, claiming over 50,000 lives in the United States. PE has been found in 32% of surgical patients who had autopsy, and in about half of these cases PE was thought to be the causing or contributing factor for death (1). Although the sample of patients in that study was not representative of the entire surgical population and was subject to variable thromboprophylactic practices, the high figures indicate the importance of the problem. Currently, the PE rates are estimated to be overall lower but vary significantly (0.3–30%) due to the inconsistent screening and diagnosis among centers. The exact percentage of fatal PE is unknown for the same reasons.

The pathogenesis of PE is based on the theory of clot dislodgment from a lower extremity or pelvic deep venous thrombosis (DVT). Neck and upper extremity veins contribute on occasions. However, there is a consistent disconnect in the literature between DVT and PE. Although one would expect that a lower extremity or pelvic DVT would be found on patients with PE, this is infrequently the case. In the past, this discrepancy was explained by the inaccuracy of available diagnostic methods to detect DVT, particularly of pelvic origin. With the development of CT venography and high-definition ultrasonography, this is no longer the case. These tests evaluate accurately the pelvic and proximal extremity veins and frequently fail to discover DVT associated with an existing PE. Therefore, the original theory of PE pathogenesis may be incorrect. It is possible that PE does not always originate from peripheral

veins but may be formed de novo in the pulmonary circulation (2).

There are more unknowns than standards in PE. The optimal diagnosis, prevention, and treatment are under constant debate.

WHO IS AT RISK FOR PE?

The classic Virchow's triad places the surgical patient at risk for PE, but the exact level of risk that allows intelligent risk-to-benefit calculations and decisions about the administration of potentially harmful thromboprophylaxis is unknown. Multiple risk factors have been suggested: obesity, immobility, cancer, major abdominal or pelvic operations, trauma, oral contraceptives, increasing age, previous thromboembolism, pregnancy and postpartum period, smoking, coagulation abnormalities, and acute medical illness, including heart, renal, and respiratory failure. There is poor evidence documenting the impact of each of these risk factors on the pathogenesis of PE, and contradictory studies are common. For example, it is unknown which exact level of obesity, exact duration and level of immobility, exact age, type and stage of cancer, or severity of medical illness predisposes a patient for PE. A systematic review and meta-analysis of the existing literature among trauma patients underscores precisely this inconsistency (3). Although gender, head injuries, spinal fractures, spinal cord injuries, long-bone fractures, and pelvic fractures were examined as possible risk factors among studies of trauma

patients, only spinal fractures and spinal cord injuries were found on pooled analysis to affect the incidence of venous thromboembolism (Level IIb evidence). The study also found that the likelihood of venous thromboembolism increases with older age and higher Injury Severity Score (ISS); the threshold at which the rate of the outcome increases significantly could not be determined by the available literature.

The seventh ACCP conference created a stratification of risk according to the presence of risk factors (4). This stratification makes clinical sense but is based on variable levels of evidence (typically Level III) and therefore should be considered with caution. Patients younger than 40 years, no other risk factors, and minor surgery are at low risk for PE. Patients at moderate risk have only one of the following: age 40–60 years, major surgery, or a major preexisting risk factor. Patients at high risk are those who are either older than 60 years or older than 40 years but with major surgery and a major preexisting risk factor present. At the highest risk are patients who are older than 40 years of age *and* have major surgery *and* one of the following: previous thromboembolic event or cancer or hypercoagulable condition, major trauma, spinal injury, hip/knee arthroplasty, hip surgery. Major surgery was considered as a thoracic or abdominal operation under general anesthesia lasting over 30 minutes. The authors calculated a risk of 2–4% for PE and 0.4–1% for fatal PE in patients at high risk and 4–10% for PE and 0.5–5% for fatal PE in patients at the highest risk.

Answer: There is inconsistent evidence about the exact risk factors that predispose to PE. It seems that major trauma—particularly spinal injuries—older age, major surgery, previous history of thromboembolism, and cancer increase the risk. The effect of other factors, such as immobility, obesity, and medical illness is ill-defined (Grade B recommendation).

WHAT IS THE OPTIMAL DIAGNOSTIC TEST FOR PE?

The ventilation-perfusion (V-P) scan and pulmonary angiography (PA) have been the main tests for diagnosis of PE for more than 20 years. The Prospective Investigation of Pulmonary Embolism Diagnosis study (5) showed that V-P scan is 96% sensitive when the index of clinical suspicion is high. However, 75% of the patients belong to the intermediate category in which V-P scan is less sensitive. PA may remain the standard of reference, but it is invasive and requires significant time spent in the angiography suite, a major setback for critically ill patients.

Over the past 10 years, computed tomographic pulmonary angiography (CTPA) has evolved to become the preferred diagnostic method for PE in surgical patients. In a meta-analysis of the diagnostic performance of CTPA and V-P scan, Hayashino et al. (6) examined 12 studies from 1985 to 2003, which were selected according to the following three criteria: (a) the tests were performed for the diagnosis of acute PE, (b) PA was used as the standard of reference, and (c) absolute numbers of true positive, true negative, false positive, and false negative findings were given. Based on these studies, a random effects model found CTPA to have 86% sensitivity [95% confidence interval (CI): 80.2–92.1%] and 93.7% specificity (95% CI 91.1–96.3%). V-P scan was found to have low sensitivity (39%) and high specificity (97.1%) with high probability threshold but high

sensitivity (98.3%) and low specificity (4.8%) with normal threshold. The authors concluded that although V-P scan and CTPA have similar diagnostic ability for patients with a high probability for PE, CTPA has higher discriminatory power than V-P scan for patients with normal and nearly normal probability (Level Ib evidence).

In another systematic review of the literature, Quiroz et al. (7) examined the clinical validity of a negative CTPA for suspected pulmonary embolism. Of particular concern was the alleged low sensitivity of CTPA for peripheral PE. To calculate the overall negative likelihood ratio of PE after a negative or inconclusive CTPA, the authors included PE, which was confirmed by another diagnostic test within three months of CTPA. Fifteen studies with a total population of 3,500 patients were included from 1994 to 2002. Single-slice, multidetector, and electron-beam scanners were used in the different studies. The negative predictive value of a normal CTPA was 99.7% (95% CI 98.7–99.5%) and the negative likelihood ratio of a PE after a normal CTPA was 0.7 (95% CI 0.05–0.11). There was no difference in the risk of PE based on the different type of CT scanner. The authors concluded that the clinical validity of CTPA to rule out PE is similar to that reported for conventional PA (Level Ib evidence). This study shows that even if the diagnosis of peripheral PE is the principal limitation of CTPA, undiagnosed peripheral PE (which can exist in as many as 30% of “normal” CTPA) is usually not clinically significant and does not cause subsequent clinically detectable PE or death from PE.

Finally, a meta-analysis of different diagnostic strategies for PE by Roy et al. (8) included 48 articles of 1,012 patients examined from 1990 to 2003. The study attempted to determine the clinical application of each test according to pretest clinical probability. In patients with a high pretest probability, a high-probability V-P scan, a positive CTPA, and a positive lower extremity venous ultrasound were associated with a higher than 85% post-test probability of PE. In patients with an intermediate or low pretest probability, a normal or nearly normal V-P scan, a normal CTPA in combination with normal lower extremity venous ultrasound, and a D-dimer concentration of less than 500 µg/L measured by quantitative enzyme-linked immunosorbent assay was associated with a less than 5% post-test probability of PE. CTPA alone, magnetic resonance angiography, a low-probability V-P scan, and a quantitative latex or hemoagglutination D-dimer test could only exclude PE in patients with low pretest probability. The authors concluded that the accuracy of the different tests vary significantly and according to the pretest clinical probability for PE (Level II evidence).

Answer: CTPA is convenient, safe, and accurate for the diagnosis of clinically significant PE. It is the preferred diagnostic method for most emergency surgery and trauma patients (Grade A recommendation).

IS HEPARIN AND COMPRESSION DEVICES ADEQUATE FOR PE PROPHYLAXIS?

The use of low-dose unfractionated heparin (UFH), usually administered subcutaneously, for prevention of PE was established in the mid-1970s by the seminal study of Kakkar et al. (9). That study included only elective surgery patients; emergency surgery and trauma patients were excluded. Despite this fact, thromboprophylaxis by UFH became

common practice for all surgical patients. An overview of randomized trials of general, orthopedic, and urologic surgery patients concluded that UFH reduced symptomatic PE rates from 2% to 1.3% and fatal PE rates from 0.8% to 0.3%, but the risk of perioperative bleeding increased from 3.8% to 5.9% (10). However, the evidence about UFH in trauma is controversial, and evidence in emergency non-traumatic general surgery patients simply does not exist. Low molecular weight heparin (LMWH), also administered subcutaneously, has shown increased stability and bio-availability compared to UFH, benefits possibly associated with improved effectiveness and safety. There are multiple randomized studies and meta-analyses in general surgery patients documenting equivalence or superiority of LMWH over UFH (11,12), but again, this evidence is only modestly applicable to the emergency surgery population because the majority of included patients had elective operations.

Sequential compression devices (SCDs) have been used extensively based on the assumption that they promote blood flow, simulating muscle function, and trigger the release of fibrinolytic agents from the vascular endothelium. The evidence on their effectiveness is also questionable, and at least two studies document poor compliance (13,14). This could be the ultimate drawback for their use, as it gives the physician a false sense of security, while the patient receives no benefit from the prescribed treatment.

There are a number of noncontrolled studies and a few prospective randomized trials in trauma patients. Knudson et al. produced three randomized trials (Level Ic evidence). In 1992 the authors randomized 113 trauma patients to UFH or SCD and found no significant difference in thromboembolic complications (five patients with DVT, four with PE, and three with DVT and PE) between the two groups (15). In 1994, the authors compared patients receiving UFH, SCD, or no treatment and found similar DVT rates in the three groups, except for a mild advantage of SCD over no treatment in neurosurgical patients (16). There were only two documented PEs, one in an SCD patient and one in a patient who received no thromboprophylaxis. In 1996 they randomized 181 patients to LMWH or SCD and failed to find any significant difference in DVT (17). There were no documented cases of PE in any of the randomized groups.

In a study of LMWH against SCD in head and spinal trauma, 60 patients were randomized to LMWH and 60 to SCD (18). The incidence of PE was not different between the two groups, 7% in the LMWH group and 3% in the SCD group. This high incidence of PE could indicate a poor thromboprophylactic effect of LMWH and SCD (Level Ic evidence). In another randomized study, spinal cord injury patients received either UFH with SCD or LMWH and showed no difference in proximal DVT or PE rates (19). The total number of thromboembolic events was very high and almost identical in the two groups (65.5% for LMWH and 63.3% for UFH with SCD, $p = 0.81$), again placing in doubt the effectiveness of these regimens (Level Ic evidence).

Probably, the two best-designed randomized trials in trauma patients examined LMWH versus SCD (20) or LMWH versus UFH (21). In both, DVT and not PE (or total thromboembolic events) was the principal outcome. In the study by Ginzburg et al. (20) the DVT rates were similar between LMWH and SCD. There was one PE in each group. There was no difference in thromboembolic events when a subanalysis of patients with ISS higher than 19 was

undertaken. The rate of bleeding was not different, either (Level Ib evidence). In the study by Geerts et al. (21), LMWH was associated with lower DVT rates compared to UFH. There was only one patient with documented PE (a high-probability V-P scan), and he belonged to the LMWH group. The rate of major bleeding was not different (0.6% versus 2.9%, $p = 0.12$), but of the six documented episodes, one was in the UFH group and five were in the LMWH group (Level Ib evidence). Two systematic reviews of the existing evidence in trauma confirmed the low level of evidence that exists about UFH, SCD, and LMWH and the uncertainty about their exact profile of effectiveness and safety (22,23) (Level Ib evidence).

Answer: Although general surgery patients with elective operations seem to benefit from the current thromboprophylactic methods, the effectiveness of UFH, LMWH, and SCD in emergency surgery and trauma patients remains uncertain. An individual risk-to-benefit assessment should be made for each such patient at risk of PE. LMWH is probably more effective than UFH or SCD (Grade B recommendation).

IS PE AND MORTALITY FROM PE REDUCED BY IVC FILTERS?

The effectiveness of inferior vena cava (IVC) filters relies on their ability to capture clots originating from lower extremity or pelvic veins. Three scenarios may hamper this ability. First, a misplaced or tilted filter may not function adequately. A tilt of as little as 10° in relationship to the IVC axis has been reported to compromise optimal function (24). Second, the capture of a primary clot at the apex of the filter may force blood circulation toward the periphery of the vessel, and recurrent clots to escape in this way. Third, clots may originate from upper extremity or neck veins (25) or possibly form *de novo* in the pulmonary circulation (2), in which case a device in the IVC is obviously of no use. One can argue that a filter is never used therapeutically, because its effect never involves a PE that has already occurred but only the embolus that may follow. The use of IVC filters in patients with “breakthrough” PE (occurring while the patient is fully anticoagulated) or with primary PE and inability to anticoagulate is well accepted. Other criteria are more controversial and include (a) a contraindication for prophylactic anticoagulation in the presence of high risk for PE, (b) added prophylaxis in patients at very high risk for PE even if prophylactic anticoagulation is feasible, and (c) added prophylaxis in patients who have already sustained a significant PE and are therapeutically anticoagulated but would be at risk of death, if a breakthrough PE occurred (26) (Level IIIb evidence).

Currently, retrievable filters have replaced temporary filters for most indications. Unless it is deemed that a filter needs to remain in place for life, as may happen with spinal cord injury patients or very old patients with significant comorbidities, most trauma and emergency surgery patients have only a finite period of risk and therefore do not need a permanent device. Unfortunately, a multicenter study (27) has shown that only 19% of these filters are being removed; therefore, most are left permanently, even if not designed for this purpose (Level IIIa evidence).

There is not a single prospective randomized study on the use of IVC filters in trauma and emergency surgery

patients. Decousous et al. (28) randomized a mixed population of 200 predominantly medical patients with DVT into IVC filter versus no filter. After a two-year follow-up, those with filters had a significant decrease in PE but a significant increase in DVT. There was no difference in mortality. When this population was followed-up for 8 years (29) the results remained unchanged: the IVC filter group had a lower incidence of PE (6.2% vs. 15.1%, $p = 0.008$), higher incidence of DVT (35.7% vs. 27.5%, $p=0.042$), and no difference in mortality compared to the no filter group (Level Ib evidence). Studies of trauma patients have failed to consistently prove that the insertion of vena cava filters resulted in a decrease of PE or death from PE (30–32) (Level IIIb evidence).

IVC filters are not complication free. Morbidity related to access (bleeding, thrombosis, arterial damage), catheter advancement (vessel damage), contrast material (anaphylaxis, renal failure), and the filter itself (vessel wall perforation, migration, IVC thrombosis, DVT, misplacement) is detected in approximately 4–7% of the cases, although the variability in rates among studies is great (26) (Level IIIa evidence). A new class of complications is now related to the removal of retrievable filters, including all of the foregoing problems as well as dislodgement of clot captured by the filter, damage of the IVC wall, and inability to retrieve.

Answer: There is no convincing evidence that in emergency surgery and trauma patients IVC filters reduce the incidence of PE and mortality from PE. Use of IVC filters should be made based on an individual patient-by-patient risk-to-benefit analysis (Grade C recommendation).

IS LMWH AS SAFE AND EFFECTIVE AS UFH FOR THE TREATMENT OF PE?

Dose-adjusted intravenous UFH is used for the treatment of PE. However, subcutaneous LMWH at therapeutic doses presents significant benefits over UFH, because monitoring is not required and treatment can be self-administered at home. There are multiple randomized studies in the literature, and all of them include either exclusively or predominantly medical patients. Therefore, the evidence on emergency surgery and trauma patients is poor. A meta-analysis of 12 randomized studies (33) found that LMWH was associated with a nonsignificant decrease of symptomatic PE (1.7% versus 2.3%) and asymptomatic PE (1.2% versus 3.2%), while offering a nonsignificant advantage in decreasing bleeding (1.3% versus 2.1%), compared to UFH (Level Ia evidence). The authors concluded that LMWH was at least as safe and effective as UFH for the initial treatment of PE. It is expected that in emergency surgery and trauma patients the rates of the outcomes—specifically of bleeding—may be different, but there is little reason to believe that the equivalence between the two groups will not be maintained. However, concerns about the inability to reverse LMWH effectively by protamine if a high-risk patient were to bleed, may still create discomfort in consistently using LMWH over UFH.

Answer: LMWH is as safe and effective as UFH for the treatment of PE. It may be the preferred treatment in patients at lower risk of bleeding, based on the convenience of outpatient self-administration and no need for monitoring (Grade A recommendation).

Evidence-Based Table

Ref.	Design	Intervention	Description	Results
15	RCT	Duplex within 24 hours of admission and every 5 days. Prophylaxis by SCD or UFH or nothing.	113 patients included. 76 randomized to SCD and 37 to UFH.	VT developed in 12 (5 DVT, 4 PE, 3 both); 9 SCD and 3 UFH. Risk factor for DVT was spinal trauma.
16	RCT	Duplex within 24 hours of admission and then every 5–7 days. Prophylaxis by SCD or UFH or nothing.	Division in three groups and randomization within each group. Group I: UFH or SCD or nothing, group II: UFH or nothing, group III: SCD or nothing	255 patients; 15 developed DVT, unclear PE. No difference in group I (2.3% UFH, 14.2% SCD, 3.2% nothing) and group II (5.5% UFH, 8% nothing). Lower DVT in group III (0% SCD, 14.7% nothing).
17	RCT	Duplex on admission and every 5–7 days. Prophylaxis by LMWH, SCD, AVF.	487 patients included, 372 analyzed. 202 stratified to the heparin group and randomized to LMWH (120) or SCD (61)/AVF (21). 170 stratified to the no heparin group and received SCD/AVF.	DVT in 9 (2.4%) and PE in 1. In randomized patients 1 LMWH and 2 SCD patients had DVT. The other 6 DVTs were in the nonrandomized group.
20	RCT	Duplex within 24 hours of admission and weekly after that.	294 moderately and 148 severely injured patients randomized separately into LMWH and SCD.	DVT in 2.7% of SCD and 0.5% of LMWH ($p = 0.12$). PE in 1 patient per group.
21	RCT	Venography 10–14 days after admission. Prophylaxis by UFH or LMWH.	265 included; 136 randomized to UFH and 129 to LMWH.	DVT (44% UFH, 31% LMWH, $p = 0.014$). Proximal DVT (15% UFH, 6% LMWH, $p = 0.012$). 1 PE in LMWH.
28	RCT	V-P scan, and if necessary, PA	400 randomized: 200 to filter and 200 to no filter.	At day 12, PE developed in 1.1% of filters and 4.8% of no filters ($p = 0.03$). At 2 years 20.8% filter and 11.6% no filter patients had recurrent DVT ($p = 0.02$).

Note: The intervention described refers to DVT. No study except 28 had a protocolized routine intervention for PE.

Abbreviations: AVF, arteriovenous foot pumps; DVT, deep venous thrombosis; LMWH, low molecular weight heparin; PA, pulmonary angiography; PE, pulmonary embolism; RCT, randomized controlled study; SCD, sequential compression device; UFH, unfractionated heparin; V-P, ventilation perfusion.

REFERENCES

1. Lindblad B, Eriksson A, Bergqvist D. Autopsy-verified pulmonary embolism in a surgical department. Analysis of the period from 1951 to 1988. *Br J Surg* 1991; 78: 849–52.
2. Velmahos GC, Spaniolas K, Tabbara M, et al. The relationship of pulmonary embolism and deep venous thrombosis in trauma. Are they really related? *Arch Surg*, in press.
3. Velmahos GC, Kern J, Chan LS, et al. Prevention of venous thromboembolism after injury: an evidence-based report—part II: analysis of risk factors and evaluation of the role of vena caval filters. *J Trauma* 2000; 49: 140–4.
4. Geerts WH, Pineo GF, Heit HA, et al. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004; 126(3 Suppl): 338S–400S.
5. The PIOPED Investigators. Value of the ventilation/perfusion scan in the diagnosis of pulmonary embolism: results of the prospective investigation for pulmonary embolism diagnosis (PIOPED). *JAMA* 1990; 263: 2753–9.
6. Hayashino Y, Goto M, Noguchi Y, et al. Ventilation-perfusion scanning and helical CT in suspected pulmonary embolism: meta-analysis of diagnostic performance. *Radiology* 2005; 234: 740–8.
7. Quiroz R, Kucher N, Zou KH, et al. Clinical validity of a negative computed tomography scan in patients with suspected pulmonary embolism. A systematic review. *JAMA* 2005; 293: 2012–17.
8. Roy PM, Colombet I, Durieux P, et al. Systematic review and meta-analysis of strategies for the diagnosis of suspected pulmonary embolism. *Br Med J* 2005; 331: 1–9.
9. Kakkar VV, Corrigan TP, Fossard DP, et al. Prevention of fatal postoperative pulmonary embolism by low doses of heparin. An international multicentre trial. *Lancet* 1975; 2: 45–51.
10. Collins R, Scrimgeour A, Yusuf S, et al. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med* 1988; 318: 1162–73.
11. Koch A, Bouges S, Ziegler S, et al. Low molecular weight heparin and unfractionated heparin in thrombosis prophylaxis after major surgical intervention: update of previous meta-analyses. *Br J Surg* 1997; 84: 750–9.
12. Mismetti P, Laporte S, Darmon JY, et al. Meta-analysis of low molecular weight heparin for the prevention of venous thromboembolism in general surgery. *Br J Surg* 2001; 88: 913–30.
13. Cornwell EE, Chang D, Velmahos G, et al. Compliance with sequential compression device prophylaxis in at-risk trauma patients: a prospective analysis. *Am Surg* 2002; 68: 470–3.
14. Comerota AJ, Katz ML, White JV. Why does prophylaxis with external pneumatic compression for deep vein thrombosis fail? *Am J Surg* 1994; 164: 265–8.
15. Knudson MM, Collins JA, Goodman SB, et al. Thromboembolism following multiple trauma. *J Trauma* 1992; 32: 2–11.
16. Knudson MM, Lewis FR, Clinton A, et al. Prevention of venous thromboembolism in trauma patients. *J Trauma* 1994; 37: 480–7.
17. Knudson MM, Morabito D, Paiement GD, et al. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. *J Trauma* 1996; 41: 446–59.
18. Kurtoglou M, Yanar H, Bilsel Y, et al. Venous thromboembolism prophylaxis after head and spinal trauma: intermittent pneumatic compression devices versus low molecular weight heparin. *World J Surg* 2004; 28: 807–11.
19. Merli G. Spinal Cord Injury Thromboprophylaxis Investigators. Prevention of venous thromboembolism in the acute treatment phase after spinal cord injury: a randomized, multicenter trial comparing low-dose heparin plus intermittent pneumatic compression with enoxaparin. *J Trauma* 2003; 54: 1116–26.
20. Ginzburg E, Cohn SM, Lopez K, et al. Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma. *Br J Surg* 2003; 90: 1338–44.
21. Geerts WH, Jay RM, Code KI, et al. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med* 1996; 335: 701–7.
22. Velmahos GC, Kern J, Chan LS, et al. Prevention of venous thromboembolism after injury: an evidence-based report—part I: Analysis of risk factors and evaluation of the role of vena caval filters. *J Trauma* 2000; 49: 132–8.
23. Rogers FB, Cipolle MD, Velmahos GC, et al. Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice management guidelines work group. *J Trauma* 2002; 53: 142–64.
24. Rogers FB, Stringberg G, Shackford GR, et al. Five-year follow-up of prophylactic vena cava filters in high-risk trauma patients. *Arch Surg* 1998; 133: 406–11.
25. Hingorani A, Ascher E, Lorenson E, et al. Upper extremity deep venous thrombosis and its impact on morbidity and mortality rates in a hospital-based population. *J Vasc Surg* 1997; 26: 853–60.
26. Martin MJ, Salim A. Vena cava filters in surgery and trauma. *Surg Clin N Am* 2007; 87: 1229–52.
27. Karmy-Jones R, Jurkovich G, Velmahos GC, et al. Practice patterns and outcomes after retrievable vena cava filters in trauma patients: a AAST multicenter study. *J Trauma* 2007; 62: 17–25.
28. Decousous A, Leizorovicz S, Parent F, et al., for the PREPIC study group. A clinical trial of vena cava filters in the prevention of pulmonary embolism in patients with deep vein thrombosis. *N Engl J Med* 1998; 338: 409–15.
29. The PREPIC study group. Eight year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism.
30. Antevil JL, Sise MJ, Sack DI, et al. Retrievable vena cava filters for preventing pulmonary embolism in trauma patients: A cautionary tale. *J Trauma* 2006; 60: 35–40.
31. Rogers FB, Shackford SR, Ricci MA, Wilson JT, Parsons S. Routine prophylactic vena cava filter insertion in severely injured trauma patients decreases the incidence of pulmonary embolism. *J Am Coll Surg* 1995; 180: 641–7.
32. McMurtry AL, Owings JT, Anderson JT, et al. Increased use of prophylactic vena cava filters in trauma patients failed to decrease overall incidence of pulmonary embolism. *J Am Coll Surg* 1999; 189: 314–20.
33. Quinlan DJ, McQuillan AM, Eikelbloom JW. Low-molecular-weight heparin compared with intravenous unfractionated heparin for treatment of pulmonary embolism. *Ann Intern Med* 2004; 140: 175–83.

Necrotizing Soft Tissue Infections

Mark D. Sawyer

Clinical Questions		
Question	Answer	Grade
What is the standard for diagnosis in NSTIs?	Clinical; confirmation by open biopsy.	C
What is the best approach to initial resection?	As complete as the patient will tolerate.	C
Should hyperbaric oxygen be part of the standard treatment for NSTIs?	No. More rigorous trials are needed.	C
Should intravenous immunoglobulin be part of the standard treatment for NSTIs?	No; although it may be helpful, it has not been proven to improve outcomes.	C
Abbreviations: NSTI, necrotizing soft tissue infection.		

INTRODUCTION AND DEFINITIONS

Necrotizing soft tissue infections (NSTIs) are a subject that would seem to lend itself poorly to a textbook of evidence-based surgery. Such uncommon and highly lethal disease processes make quality large, prospective, randomized trials extremely difficult to design and implement. Further complicating the picture is that a large proportion of current practice is by necessity based on individual observations and deductions concerning the disease, which, as one might expect, can engender strong biases and suspicions that at times seem to be in inverse proportion to available evidence. Thus, an evidence-based discussion of questions concerning necrotizing soft tissue infections may have more the appearance of a photographic negative—deciding which tentative conclusions are probably not justified because there is no quality evidence to support them, rather than raising to the fore those conclusions best supported by solid statistical evidence. This also points out the need for a larger, cooperative effort to glean more substantial evidence from the thousand or so cases per year (5) that occur.

Although necrotizing soft tissue infections comprise a wide variety of clinical scenarios as reflected by the bewildering array of terms utilized in the literature, a simple division—predominantly fascial versus predominantly muscular involvement—categorizes these infections reasonably well both in terms of their behavior and a pragmatic approach to empiric treatment (7,8). Although anyone may be affected, the immunocompromised and debilitated—most commonly those with advancing age and diabetes mellitus—are disproportionately represented both in terms of acquiring the disease and in suffering poorer outcomes.

NECROTIZING FASCIITIS

The Disease

Necrotizing fasciitis is an infection involving the investing fascia of muscle, primarily the superficial layer, and may secondarily involve a modest amount of juxtaposed fat and muscle. It has a predilection for the immunocompromised, in which it is more morbid and lethal as well. Originally described as a streptococcal or streptococcal-predominant infectious process (1,2), it is usually a polymicrobial infection, although monomicrobial forms of the disease (*Vibrio*, *Pseudomonas*, *Klebsiella*, and others) exist as well. Studies carefully culturing the tissues may show a mix of Gram-positive, Gram-negative, and anaerobic bacteria, as well as candidal species in some.

Necrotizing fasciitis has been described as a rapidly progressive process, but some patients may describe a relatively indolent period prior to seeking medical attention, with subsequent decompensation giving the outward appearance of rapid progression (3,4).

Diagnosis

Open biopsy of suspected tissues has been the standard of care for diagnosis, although radiographic studies such as computed tomography (CT) scans can provide useful data regarding the location and extent of disease.

Mainstay Therapy

There are two cornerstones of initial therapy: expeditious and complete debridement and broad-spectrum antimicrobial therapy. Immediate initiation of empiric broad-spectrum

antimicrobial therapy based on an anti-*Streptococcal* component is key; awaiting culture or even Gram stain data to guide therapy would constitute an unnecessary and potentially dangerous delay. With one study using careful culture techniques showing *Candida* species in a majority of patients and the dangers of superinfection following potent broad-spectrum antimicrobial therapy, many would advocate empiric therapy with an antifungal agent as well.

The other unequivocal cornerstone of therapy is expeditious and complete excision of the infected and necrotic fascia to prevent further progression and begin the healing process, although there is some controversy regarding whether a staged approach versus a “complete” initial resection is superior. Regardless of initial philosophy, returning to the operating room for second-look procedures to at least assess if not complete the resection process is ubiquitous. Necrotizing fasciitis is a progressive disease, and ensuring that progression has been halted is mandatory. Though excision and debridement can be debilitating and disfiguring, completeness is essential to halt the progression of disease and maximize survival. Following the initial phase, a prolonged healing convalescent phase is usual in survivors, with care of open wounds that may constitute a large percentage of the patient’s body surface area. In addition to standard techniques for dressing and closing such wounds, newer technologies, such as vacuum-assisted wound closure devices, may be helpful.

Supplemental Therapy

There are a number of therapies that have been used in NSTIs to try and improve outcome, such as hyperbaric oxygen and immunoglobulin therapy. The rationale for the former had its genesis in the treatment of anaerobic NSTIs, such as clostridial necrotizing myositis, and the latter as an attempt to improve treatment of aggressive streptococcal infections and their complications, such as streptococcal toxic shock syndrome. Although theoretically attractive, neither has definitively proven itself as a mainstay of treatment in NSTIs.

NECROTIZING MYOSITIS

The most common eponyms for necrotizing muscle infections are gas gangrene, clostridial/streptococcal myonecrosis, and necrotizing myositis. The lattermost term is simple, descriptive, and alliteratively associates the disease process with its fascial cousin. The infection infects, spreads, and necroses entire muscle compartments with celerity; it is rapidly progressive and in contradistinction to necrotizing fasciitis has no recognized indolent variants. Pragmatically, this means that exceptionally aggressive surgery, such as proximal amputation, may be required to gain control of the disease process before the patient succumbs, which may occur within hours of presentation. In further contradistinction to necrotizing fasciitis, necrotizing myositis is usually a monomicrobial infection, most commonly a toxin-producing *Clostridium* or *Streptococcus* species.

IS OPEN BIOPSY STILL THE STANDARD FOR DIAGNOSIS OF NSTI, OR HAS IT BEEN SUPPLANTED BY RADIOGRAPHIC STUDIES?

The standard of diagnosis in NSTIs is clinical diagnosis, confirmed by open biopsy with frozen section (7–9), but imaging modalities—particularly CT and magnetic resonance imaging (MRI)—have developed ever finer resolution and sophistication in the software. However, although the CT characteristics of NSTIs are well delineated, they may not be specific, as exemplified by elements such as fascial thickening and edema without asymmetry. Other more specific findings, such as gas within soft tissues, are not ubiquitous, and therefore, their absence does not rule out the disease (10,11). MRI findings have been found to be perhaps even more nonspecific; one author found the MRI findings similar between necrotizing fasciitis, dermatomyositis, and post-traumatic muscle injury (12). If it does not delay definitive surgical therapy, CT may help in planning a thorough surgical intervention by showing the extent of disease, but it should not be relied on to rule in or out the diagnosis of NSTI.

Answer: The standard for diagnosis in NSTI is clinical; confirmation by open biopsy. Grade of recommendation: C.

WHICH IS A BETTER APPROACH TO INITIAL RESECTION IN NSTI, STAGED OR “COMPLETE?”

There has been little in the literature to suggest a standardized approach to NSTI. Certainly, the objective is to remove all necrotic and infected tissue as quickly as possible. Whether this may be achieved in one operative intervention, however, depends heavily on the patient’s ability to tolerate extended, aggressive resection. Regardless of whether the first procedure is considered complete, nearly all patients will require at least one second-look procedure to ensure a lack of disease progression. Recently, Wong et al. advocated a standardized approach to resection, involving a complete resection in the first procedure, with second-look operations to follow (23). Though the approach seems sensible in those who will tolerate their complete approach to the initial procedure, it is not on the basis of randomized data but the authors’ considered approach to the problem.

Answer: As complete an approach as the patient will tolerate. Grade of recommendation: C.

IS THERE CONVINCING EVIDENCE FOR THE USE OF HYPERBARIC OXYGEN THERAPY IN THE TREATMENT OF NSTIS?

Hyperbaric oxygen (HBO) therapy was originally devised as a way to treat decompression sickness after deep underwater diving (the bends). At many atmospheres of depth, more nitrogen is solubilized in the bloodstream, and too-rapid ascent results in nitrogen desolubilizing out of the bloodstream as bubbles, which then cause gas emboli. The use of hyperbaric oxygen is currently unregulated, and usage ranges from legitimate and proven (treating decompression sickness) to therapeutic and experimental use in

medicine such as carbon monoxide poisoning and NSTIs, to “oxygen bar”-like operations hawking sessions for their purported general health benefits.

HBO therapy is a theoretically attractive potential therapy for NSTIs, using oxygen as a direct toxin to combat anaerobic bacteria (9,21). What comparative studies exist are generally not randomized, and controls may be historical. One recent comparative but nonrandomized study in a small number of patients showed a shorter length of treatment when using HBO (18). Most studies of NSTIs are observational in nature (16,17,20,22); there are synergistic factors that make randomized controlled trials in NSTIs difficult to complete. The first is the rarity of the infections. It can take a single center decades to accrue a few dozen cases, making adequate statistical analysis difficult as well as weakening any conclusions by virtue of the rapid general advances made in medicine over such a long period of time—the longer the study, the less comparable the first patients entered into such a study are to the last. The second factor is the zeal and evangelism that proponents of HBO therapy for NSTIs maintain despite any solid statistical evidence to support its use in these infections. Some have gone so far as to say that randomized controlled trials of its use are unethical because (in their minds) it is so clearly beneficial. This attitude may be compounded by the long time between patients; in fact, there are studies spanning decades that use the “pre-hyperbaric chamber” era as a historical control for the “post-hyperbaric chamber” era. A further bias is clearly risked by the purchase of these expensive chambers; having spent millions of dollars for one such, two questions must be asked: (1) would such an expensive piece of equipment have been purchased if it was not thought to be efficacious a priori, and (2) having made the investment, how objective can one be regarding its supposed benefits in the absence of the objective evidence of a randomized controlled trial? The strength with which its use is championed by its supporters is at odds with the literature, as it is bereft of any solid objective evidence supporting its use as a standard component of therapy.

Answer: No, HBO should not be part of the standard treatment for NSTIs. More rigorous trials are needed. Grade of recommendation: C.

IS IMMUNOGLOBULIN THERAPY PART OF STANDARD CARE FOR NSTIS?

Because streptococcal species have been strongly implicated in NSTIs since their initial description, and immunoglobulin has been used in the treatment of *Streptococcus pyogenes* (group A streptococcus) and streptococcal toxic shock syndrome, it is reasonable to examine whether immunoglobulin therapy has any salutary effect on NSTIs (13). Immunoglobulin therapy has been used in an attempt to improve survival in cases of streptococcal toxic shock syndrome (14,15). Although case reports and observational studies have been encouraging, the efficacy of gamma globulin in streptococcal toxic shock syndrome has not been confirmed by randomized studies.

Answer: No. Although intravenous immunoglobulin treatment may be helpful, it has not been proven to improve outcomes. Grade of recommendation: C.

CONCLUSIONS

NSTIs are uncommon, highly lethal diseases requiring rapid diagnosis and treatment to achieve optimal outcomes. With only a thousand or so cases a year across the United States, however, prospective randomized trials are difficult, and in the case of a single institution near impossible. With agreement on the basics of therapy—aggressive surgical debridement and broad-spectrum antimicrobials—the important questions presently involve secondary therapies, which at best remain unproven. To obtain quality data for questions such as the use of HBO and polyclonal immunoglobulin administration, multicenter studies will almost certainly be required to obtain a level of evidence sufficient to recommend their use with confidence. Until such time, the care of patients with these difficult infections will remain more dogmatic than definitive, as much supposition as science.

REFERENCES

1. Meleny FL. Hemolytic streptococcus gangrene. *Arch Surg* 1924; 9: 317–64.
2. Wilson B. Necrotizing fasciitis. *Am Surg* 1952; 18: 416.
3. Wong CH, Tan SH. Subacute necrotizing fasciitis. *Lancet* 2004; 364: 1376.
4. Wong CH, Wang YS. What is subacute necrotizing fasciitis? A proposed clinical diagnostic criteria. *J Infection* 2006; 52: 415–19.
5. Eke N. Fournier's gangrene: a review of 1726 cases. *Br J Surg* 2000; 87: 718–28.
6. Cainzos M, Gonzalez-Rodriguez FJ. Necrotizing soft tissue infections. *Curr Opin Crit Care* 2007; 13: 433–9.
7. Sawyer MD, Dunn DL. Deep soft tissue infections. *Curr Opin Infect Dis* 1991; 4: 649–54.
8. Dunn DL, Sawyer MD. Deep soft-tissue infections. *Curr Opin Infect Dis* 1990; 3: 691–6.
9. Stamenkovic I, Lew PD. Early Recognition of potentially fatal necrotizing fasciitis: the use of frozen section biopsy. *N Engl J Med* 1984; 310: 1689–93.
10. Majeski JA, Majeski E. Necrotizing fasciitis: improved survival with early recognition by tissue biopsy and aggressive surgical treatment. *South Med J* 1997; 90: 1065–8.
11. Wong CH, Wang YS. The diagnosis of necrotizing fasciitis. *Curr Opin Infect Dis* 2005; 18: 101–6.
12. Levenson RB, Singh AK, Novelline RA. Fournier gangrene: role of imaging. *Radiographics* 2008; 28: 519–28.
13. Wysoki MG, Santora TA, Sha RM, et al. Necrotizing fasciitis: CT characteristics. *Radiology* 1997; 203: 859–63.
14. Arslan A, Pierre-Jerome C, Borthne A. Necrotizing fasciitis: unreliable MRI findings in the preoperative diagnosis. *Eur J Radiol* 2000; 36: 139–43.
15. Stevens DL. Streptococcal toxic shock syndrome associated with necrotizing fasciitis. *Ann Rev Med* 2000; 51: 271–88.
16. Barry W, Hudgins L, Donta S, et al. Intravenous immunoglobulin therapy for toxic shock syndrome. *JAMA* 1992; 267: 3315–16.
17. Kaul R, McGeer A, Norrby-Teglund A, et al. Intravenous immunoglobulin therapy for streptococcal toxic shock syndrome—a comparative observational study. *Clin Infect Dis* 1999; 28: 800–7.
18. Jallali N, Withey MS, Butler PE. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. *Am J Surg* 2005; 189: 462–6.
19. Kaide CG, Khandelwal S. Hyperbaric oxygen: applications in infectious disease. *Emerg Med Clin N Amer* 2008; 26: 571–95.

20. Sugihara A, Watanabe H, Oohashi M, et al. The effect of hyperbaric oxygen therapy on the bout of treatment for soft tissue infections. *J Infect* 2004; 48: 330–3.
21. Korhonen K. Hyperbaric oxygen therapy in acute necrotizing infections with special reference to the effects on tissue gas tensions. A clinical and experimental study. *Ann Chirurg Gynaecol Suppl* 2000; 214: 3–36.
22. Korhonen K, Klossner J, Hirn M, et al. Management of clostridial gas gangrene and the role of hyperbaric oxygen. *Ann Chirurg Gynaec* 1999; 88: 139–42.
23. Korhonen K, Him M, Miinkoski J. Hyperbaric oxygen in the treatment of Fournier's gangrene. *Eur J Surg* 1998; 164: 251–5.
24. Korhonen K, Kuttala K, Niinkoski J. Tissue gas tensions in patients with necrotizing fasciitis and healthy controls during treatment with hyperbaric oxygen: a clinical study. *Eur J Surg* 2000; 166: 530–4.
25. Wong CH, Yam AKT, Tan ABH, et al. Approach to debridement in necrotizing fasciitis. *Am J Surg* 2008; 196: e19–e24.

Incarcerated Hernias

Steven Schwaitzberg

Key Issues in the Management of Incarcerated Hernias			
Question	Answer	Grade of recommendation	Level of evidence
What are the appropriate physical examination and imaging evaluations necessary to diagnose incarcerated hernia?	Physical examination is acceptable for diagnosis of most incarcerated hernias. CT imaging or ultrasound are acceptable adjunctive modalities in specific clinical scenarios.	C C	V IV
What are the technical considerations for treating incarcerated hernia that influence choice of repair?	Laparoscopic and open repairs with mesh are acceptable forms of hernia repair in the presence of incarceration. Experience with laparoscopic technique influences outcome.	B B	IIB IIB
What are the repair options in the face of GI contamination or infection?	The use of biologic/synthetic prostheses are well documented for use in contaminated/infected hernias. Higher complication rates are expected.	B	IIIB, IV IIIB
What are the characteristics of incarceration/strangulation that impact mortality/morbidity?	Mortality correlates with severity scoring in general; however, delay in treatment and the need for bowel resection have additional implications for subsequent mortality.		IIB, IIIB
What are the most effective intraoperative evaluation tools to assess bowel viability?	Objective techniques are superior to clinical evaluation. Laser Doppler flowmetry may be most sensitive technique; however, Doppler ultrasound and/or fluorescein dye are more readily available. Laparoscopy transabdominally or through the hernia sac is useful technique for assessing intestinal viability in selected cases.	B C	IIB, IIIB IV
Should hernias be repaired to prevent incarceration and strangulation?	Authors continue to cite the need for elective hernia repair to avoid morbidity and mortality. Watchful waiting of its small hernias in healthy patients can be recommended.	B	IB, IIB, IIIB
Abbreviations: CT, computed tomography; GI, gastrointestinal.			

Incarcerated hernia is one of the more common emergencies for the general surgeon. There are several important questions to consider when dealing with this entity. Emergent imaging has become ubiquitous and seems to replace physical examination in an increasing number of settings. In addition, hernia repair has evolved over the past decade with several new options and paradigms to consider. Certain dilemmas remain unchanged, such as determining the viability of incarcerated intestine. Finally the age-old dilemma of what to do when the incarcerated hernia turns out to be the strangulated hernia with contamination remains a formidable challenge.

WHAT ARE THE APPROPRIATE PHYSICAL EXAMINATION AND IMAGING EVALUATIONS NECESSARY TO DIAGNOSE INCARCERATED HERNIA?

There are no randomized trials in the literature comparing physical examination alone to imaging in securing the diagnosis of incarcerated abdominal wall hernia. There are, however, numerous case reports and short retrospective series that offered testimonial benefit to the use of computed tomography (CT) or ultrasound (US) in the diagnosis of abdominal wall incarcerated hernia (1,2) (Level IV evidence). Imaging appeared to be of the greatest benefit in three

categories: obese patients, spigelian hernias, and obturator hernias (3–7). (Level IV evidence) (Grade C recommendation). The vast majority of inguinal and ventral hernias appear to be diagnosed clinically (Level V evidence). There is no evidence that a diagnosis made on physical exam requires imaging confirmation (Grade C recommendation).

Answer: Physical examination is an acceptable modality for the diagnosis of most incarcerated hernias. CT imaging or ultrasound are acceptable adjunctive modalities in specific clinical scenarios where the diagnosis is difficult to ascertain or in doubt (Grades C and B recommendations).

WHAT ARE THE TECHNICAL CONSIDERATIONS FOR TREATING INCARCERATED HERNIA THAT INFLUENCE CHOICE OF REPAIR?

Prior to the mid-1980s, the choices for repair of elective and emergent hernia repairs was simple. Primary tissue repairs were exclusively performed. The introduction of the first polypropylene mesh then expanded polytetrafluoroethylene change the face of elective hernia repairs almost completely by the mid-1990s. The use of mesh for elective hernia repairs is well established now (8–11) (Level IV evidence). Laparoscopic repairs were added to the elective hernia repair options in the early 1990s, and all use some form of prosthesis. It was inevitable that these options would be considered for urgent/emergent repairs as well. Unfortunately, there are very few prospective trials performed to determine optimal repair of incarcerated hernias (12–14) (Level IIB evidence). Cohort sizes ranged from 21 to 60 patients. The conclusions from these three trials would seem to indicate that a tension-free Lichtenstein repair is superior to a primary open repair; however, a laparoscopic preperitoneal repair may be superior to either when repairing an incarcerated hernia (Grade C recommendation). Operator experience will influence outcome in laparoscopic repairs (15) (Level IIB evidence). In addition to these prospective trials, there are a number of retrospective series and case reports indicating success repairing inguinal, femoral, and ventral hernias with Lichtenstein repairs, transabdominal laparoscopic repairs (TAP), and totally extraperitoneal laparoscopic repairs (TEP) (16–20) (Level IV evidence). These studies indicate use of polypropylene synthetic mesh in incarcerated (nonstrangulated) hernias appears acceptable and concerns of translocation leading to clinical infection appear unwarranted (Grade B recommendation).

Answer: Laparoscopic and open repairs with mesh are acceptable forms of hernia repair in the presence of incarceration with or without strangulation. Experience with laparoscopic technique influences outcome (Grade B recommendation).

WHAT ARE THE REPAIR OPTIONS IN THE FACE OF GI CONTAMINATION OR INFECTION?

The challenge of repairing and abdominal wall defects in the face of significant gastrointestinal (GI) contamination or infection is formidable. Primary tissue repair avoids foreign body–based infections recurrences common. Retrospective studies support the use of polypropylene mesh in selected contaminated settings (21–23) (Level IIIB and IV evidence).

The use of biologic prosthesis has become popular despite the fact that there are no long-term or randomized outcome studies concerning the use of biologic prosthesis, such as acellular dermis or reconstituted collagen, in the contaminated or infected setting. Retrospective reviews suggest clearly imperfect but acceptable results in grossly contaminated fields with modest complication rates (infection, hernia, and reoperation) considering the magnitude of the clinical problem (24–30) (Level IIIB and IV evidence). Absorbable mesh should be discouraged because hernia development is nearly inevitable (31,32) (Level IIIB evidence).

Answer: The use of biologic and synthetic prostheses are well documented in retrospective studies for use in contaminated and infected hernias. Higher complication rates are expected when compared to elective hernia repair including recurrence and reoperation (Grade C recommendation).

WHAT ARE THE CHARACTERISTICS OF INCARCERATION/STRANGULATION THAT IMPACT MORTALITY AND MORBIDITY?

General features of risk stratification have been well worked out for emergency surgery. APACHE classification assigns increasing risk for derangements of physiology, laboratory parameters, age greater than 55, and emergent surgery (33) (Level IIB evidence). The increased mortality noted in the large Swedish prospectively recorded database of nearly 108,000 hernia repairs clearly highlight the increased risk for emergent surgery (34) (Level IIB evidence). Other retrospective series have confirmed this as well. These series generally agree that increased mortality is most significantly influenced by the need for bowel resection, long duration of symptoms, delay to hospitalization, concomitant illness, and high American Society of Anesthesiologists scores (35–38) (Level IIIB evidence). Worsened outcomes associated with femoral hernias, which are more common in women (39) were attributed to higher risk of bowel resection in these patients (40–42) (Level IIB and IIIB evidence).

Answer: Mortality correlates with severity scoring in general; however, delay in treatment and the need for bowel resection have additional implications for subsequent mortality.

WHAT ARE THE MOST EFFECTIVE INTRAOPERATIVE EVALUATION TOOLS TO ASSESS BOWEL VIABILITY?

Every abdominal surgeon has been faced with the need to evaluate abnormally appearing bowel to determine its viability. In addition there are circumstances where the reduction of an incarcerated hernia leaves a question of bowel viability unanswered. The surgical myth that “strangulated bowel will not reduce” has been disproven on many occasions. A number of techniques have been offered to assess intestinal viability, currently in trial. Most comparative studies were performed in preclinical settings. The most commonly evaluated modalities were clinical assessment, Doppler ultrasound, fluorescein dye administration, myoelectric activity, surface pulse oximetry, and noncontact laser Doppler blood flow assessment (43–53) (Level IIB and IIIB evidence). Preclinical comparative assessments show mixed results when comparing pulse oximetry,

Doppler ultrasound, and fluorescein that are superior to clinical judgment alone. Laser Doppler may be superior when compared to fluorescein and pulse oximetry (45). In addition, nonrandomized prospective evaluation of laser Doppler flowmetry demonstrated excellent predictive assessment when compared to clinical assessment (54,55) (Level IIIB evidence).

Multiple accounts of the utility of laparoscopy or hernioscopy report clinical utility when assessing bowel liability in those cases where intestinal reduction occurs prior to clinical evaluation of intestinal viability (56–60) (Level IIIB evidence).

Answer: Objective techniques are superior to clinical evaluation alone when assessing intestinal ischemia. Laser Doppler flowmetry may be the most sensitive technique; however, Doppler ultrasound and/or fluorescein dye are likely to be more readily available. (Grade B recommendation). Laparoscopy either transabdominally or through the hernia sac has emerged as a useful technique for assessing intestinal viability after reduction of the incarcerated mass in selected cases where bowel viability is in doubt (Grade C recommendation).

SHOULD HERNIAS BE REPAIRED TO PREVENT INCARCERATION AND STRANGULATION?

Many authors recommend elective repair of inguinal hernia as a strategy to prevent complications and poorer outcomes associated with emergent repairs for incarcerated or strangulated hernias, particularly in elderly patients (42,61,62) (Level IIB and IIIB evidence). These studies show that approximately 5% of the hernia repairs reviewed were performed emergently. These cases were the source of most of the significant morbidity and mortality in the population studied. Comorbidities contributed significantly to poor outcome in the emergent setting 63. Elective hernia repair even in the very elderly population is safe, particularly when performed under local anesthesia (62,64) (Level IIIB evidence). This traditional approach of repairing inguinal hernias as they are discovered to prevent these complications has been challenged. The prospective Veterans Administration multicenter trial of immediate tension-free repair versus “watchful waiting” demonstrated a less than 1% risk of catastrophic event related to observation and study population (65) (Level IB evidence). The limitations of this study include the fact that about 30% of the patients screened refuse to participate in the trial, the follow-up was only two years, sicker patients were excluded, and then about half the patients’ hernias were detectable on cough impulse examination. This latter finding indicates a large proportion of very small, if actually real, hernias were included in the study. Nonetheless, this remains one of the best attempts to understand the natural history of modern hernias within the context of the severe limitations. Thus watchful waiting appears safe and healthy patients with very small hernias until longer term follow-up and a greater understanding of the types of hernias that go on to incarcerate is accomplished (Grade B recommendation).

Answer: Authors continue to cite the need for elective repair of hernias to avoid morbidity and mortality in outcome studies of hernia repairs. Watchful waiting of its

small hernias in healthy patients can be recommended (Grade B recommendation).

REFERENCES

1. Chen SC, Lee CC, Liu YP, et al. Ultrasound may decrease the emergency surgery rate of incarcerated inguinal hernia. *Scand J Gastroenterol* 2005; 40: 721–4.
2. Ramseyer L, Abernethy EA III, McCune EA, et al. The role of CT in the diagnosis of small bowel obstruction: a case and literature review. *J Okla State Med Assoc* 1998; 91: 103–6.
3. Buljavec M, Grgurevic I, Lackovic Z, et al. Duplex ultrasonography in diagnosis of spigelian hernia with incarcerated jejunal loop. *Acta Med Croatica* 2001; 55: 225–7.
4. van der Linden FM, Puylaert JB, De Vries BC. Ultrasound diagnosis of incarcerated obturator hernia. *Eur J Surg* 1995; 161: 531–2.
5. Losanoff JE, Kjossev KT. Incarcerated Spigelian hernia in morbidly obese patients: The role of intraoperative ultrasonography for hernia localization. *Obes Surg* 1997; 7: 211–14.
6. Avaro JP, Biance N, Savoie PH, et al. Incarcerated obturator hernia: Early diagnostic using helical computed tomography. *Hernia* 2008; 12: 199–200.
7. Rodriguez-Hermosa JL, Codina-Cazador A, Maroto-Genover A, et al. Obturator hernia: clinical analysis of 16 cases and algorithm for its diagnosis and treatment. *Hernia* 2008; 12: 289–97.
8. Mathes SJ, Steinwald PM, Foster RD, et al. Complex abdominal wall reconstruction: a comparison of flap and mesh closure. *Ann Surg* 2000; 232: 586–96.
9. Luijendijk RW, Hop WC, van den Tol MP, et al. A comparison of suture repair with mesh repair for incisional hernia. *N Engl J Med* 2000; 343: 392–8.
10. Amid PK, Shulman AG, Lichtenstein IL. An analytic comparison of laparoscopic hernia repair with open “tension-free” hernioplasty. *Int Surg* 1995; 80: 9–17.
11. Klaristfeld DD, Mahoney E, Iannitti DA. Minimally invasive tension-free inguinal hernia repair. *Surg Technol Int* 2005; 14: 157–63.
12. Karatepe O, Adas G, Battal M, et al. The comparison of preperitoneal and Lichtenstein repair for incarcerated groin hernias: a prospective randomized study. *Int J Surg* 2008.
13. Derici H, Unalp HR, Nazli O, et al. Prosthetic repair of incarcerated inguinal hernias: Is it a reliable method? *Langenbecks Arch Surg* 2008.
14. Abdel-Baki NA, Bessa SS, Abdel-Razek AH. Comparison of prosthetic mesh repair and tissue repair in the emergency management of incarcerated para-umbilical hernia: a prospective randomized study. *Hernia* 2007; 11: 163–7.
15. Neumayer L, Giobbie-Hurder A, Jonasson O, et al. Open mesh versus laparoscopic mesh repair of inguinal hernia. *N Engl J Med* 2004; 350: 1819–27.
16. Landau O, Kyzer S. Emergent laparoscopic repair of incarcerated incisional and ventral hernia. *Surg Endosc* 2004; 18: 1374–6.
17. Lohsiriwat V, Sridermma W, Akaraviputh T, et al. Surgical outcomes of Lichtenstein tension-free hernioplasty for acutely incarcerated inguinal hernia. *Surg Today* 2007; 37: 212–14.
18. Ferzli G, Shapiro K, Chaudry G, et al. Laparoscopic extraperitoneal approach to acutely incarcerated inguinal hernia. *Surg Endosc* 2004; 18: 228–31.
19. Wysocki A, Pozniczek M, Krzywon J, et al. Lichtenstein repair for incarcerated groin hernias. *Eur J Surg* 2002; 168: 452–54.
20. Yau KK, Siu WT, Cheung YS, et al. Laparoscopic management of acutely incarcerated femoral hernia. *J Laparoendosc Adv Surg Tech A* 2007; 17: 759–62.
21. Antonopoulos IM, Nahas WC, Mazzucchi E, et al. Is polypropylene mesh safe and effective for repairing infected

- incisional hernia in renal transplant recipients? *Urology* 2005; 66: 874–7.
22. Bleichrodt RP, Simmermacher RK, van der Lei B, et al. Expanded polytetrafluoroethylene patch versus polypropylene mesh for the repair of contaminated defects of the abdominal wall. *Surg Gynecol Obstet* 1993; 176: 18–24.
23. Kelly ME, Behrman SW. The safety and efficacy of prosthetic hernia repair in clean-contaminated and contaminated wounds. *Am Surg* 2002; 68: 524–8; discussion 528–9.
24. Bellows CF, Albo D, Berger DH, et al. Abdominal wall repair using human acellular dermis. *Am J Surg* 2007; 194: 192–8.
25. Bachman S, Ramshaw B. Prosthetic material in ventral hernia repair: How do I choose? *Surg Clin North Am* 2008; 88: 101–12, ix.
26. Catena F, La Donna M, Gagliardi S, et al. Use of prosthetic mesh in complicated incisional hernias. *Minerva Chir* 2002; 57: 363–9.
27. Diaz JJ Jr., Guy J, Berkes MB, et al. Acellular dermal allograft for ventral hernia repair in the compromised surgical field. *Am Surg* 2006; 72: 1181–7; discussion 1187–8.
28. Gupta A, Zahriya K, Mullens PL, et al. Ventral herniorrhaphy: experience with two different biosynthetic mesh materials, Surgisis and Alloderm. *Hernia* 2006; 10: 419–25.
29. Kim H, Bruen K, Vargo D. Acellular dermal matrix in the management of high-risk abdominal wall defects. *Am J Surg* 2006; 192: 705–9.
30. Patton JH Jr., Berry S, Kralovich KA. Use of human acellular dermal matrix in complex and contaminated abdominal wall reconstructions. *Am J Surg* 2007; 193: 360–3; discussion 363.
31. Dayton MT, Buchele BA, Shirazi SS, et al. Use of an absorbable mesh to repair contaminated abdominal-wall defects. *Arch Surg* 1986; 121: 954–60.
32. Greene MA, Mullins RJ, Malangoni MA, et al. Laparotomy wound closure with absorbable polyglycolic acid mesh. *Surg Gynecol Obstet* 1993; 176: 213–18.
33. Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest* 1991; 100: 1619–36.
34. Nilsson E, Haapaniemi S, Gruber G, et al. Methods of repair and risk for reoperation in Swedish hernia surgery from 1992 to 1996. *Br J Surg* 1998; 85: 1686–91.
35. Kulah B, Kulacoglu IH, Oruc MT, et al. Presentation and outcome of incarcerated external hernias in adults. *Am J Surg* 2001; 181: 101–4.
36. Ashirov AA, Malevannyi AV. Immediate results of treating strangulated hernias. *Vestn Khir Im I I Grek* 1986; 136: 37–41.
37. Kurt N, Oncel M, Ozkan Z, et al. Risk and outcome of bowel resection in patients with incarcerated groin hernias: Retrospective study. *World J Surg* 2003; 27: 741–3.
38. Alvarez-Perez JA, Baldonado-Cernuda RF, Garcia-Bear I, et al. Presentation and outcome of incarcerated external hernias in adults. *Cir Esp* 2005; 77: 40–5.
39. Heydorn WH, Velanovich V. A five-year U.S. Army experience with 36,250 abdominal hernia repairs. *Am Surg* 1990; 56: 596–600.
40. Corder AP. The diagnosis of femoral hernia. *Postgrad Med J* 1992; 68: 26–8.
41. Koch A, Edwards A, Haapaniemi S, et al. Prospective evaluation of 6895 groin hernia repairs in women. *Br J Surg* 2005; 92: 1553–8.
42. Nilsson H, Stylianidis G, Haapamaki M, et al. Mortality after groin hernia surgery. *Ann Surg* 2007; 245: 656–60.
43. Johansson K, Ahn H, Kjellstrom C, et al. Laser Doppler flowmetry in experimental mesenteric vascular occlusion. *Int J Microcirc Clin Exp* 1989; 8: 183–90.
44. Orland PJ, Cazi GA, Semmlow JL, et al. Determination of small bowel viability using quantitative myoelectric and color analysis. *J Surg Res* 1993; 55: 581–7.
45. Ando M, Ito M, Nihei Z, et al. Assessment of intestinal viability using a non-contact laser tissue blood flowmeter. *Am J Surg* 2000; 180: 176–80.
46. Holmes NJ, Cazi G, Reddell MT, et al. Intraoperative assessment of bowel viability. *J Invest Surg* 1993; 6: 211–21.
47. Horgan PG, Gorey TF. Operative assessment of intestinal viability. *Surg Clin North Am* 1992; 72: 143–55.
48. Shah SD, Andersen CA. Prediction of small bowel viability using Doppler ultrasound. Clinical and experimental evaluation. *Ann Surg* 1981; 194: 97–9.
49. Bergman RT, Gloviczki P, Welch TJ, et al. The role of intravenous fluorescein in the detection of colon ischemia during aortic reconstruction. *Ann Vasc Surg* 1992; 6: 74–9.
50. Erikoglu M, Kaynak A, Beyatli EA, et al. Intraoperative determination of intestinal viability: a comparison with transresorral pulse oximetry and histopathological examination. *J Surg Res* 2005; 128: 66–9.
51. Freeman DE, Gentile DG, Richardson DW, et al. Comparison of clinical judgment, Doppler ultrasound, and fluorescein fluorescence as methods for predicting intestinal viability in the pony. *Am J Vet Res* 1988; 49: 895–900.
52. Tollefson DF, Wright DJ, Reddy DJ, et al. Intraoperative determination of intestinal viability by pulse oximetry. *Ann Vasc Surg* 1995; 9: 357–60.
53. Wright CB, Hobson RW II. Prediction of intestinal viability using Doppler ultrasound techniques. *Am J Surg* 1975; 129: 642–5.
54. Redaelli CA, Schilling MK, Carrel TP. Intraoperative assessment of intestinal viability by laser Doppler flowmetry for surgery of ruptured abdominal aortic aneurysms. *World J Surg* 1998; 22: 283–9.
55. Redaelli CA, Schilling MK, Buchler MW. Intraoperative laser Doppler flowmetry: a predictor of ischemic injury in acute mesenteric infarction. *Dig Surg* 1998; 15: 55–9.
56. Lavonius MI, Ovaska J. Laparoscopy in the evaluation of the incarcerated mass in groin hernia. *Surg Endosc* 2000; 14: 488–9.
57. Al-Naami MY, Al-Shawi JS. The use of laparoscopy to assess viability of slipped content in incarcerated inguinal hernia: a case report. *Surg Laparosc Endosc Percutan Tech* 2003; 13: 292–4.
58. Guvenc BH, Tugay M. Laparoscopic evaluation in incarcerated groin hernia following spontaneous reduction. *Ulus Travma Acil Cerrahi Derg* 2003; 9: 143–4.
59. Lin E, Wear K, Tiszenkel HI. Planned reduction of incarcerated groin hernias with hernia sac laparoscopy. *Surg Endosc* 2002; 16: 936–8.
60. Morris-Stiff G, Hassn A. Hernioscopy: a useful technique for the evaluation of incarcerated hernias that retract under anaesthesia. *Hernia* 2008; 12: 133–5.
61. Nehme AE. Groin hernias in elderly patients. Management and prognosis. *Am J Surg* 1983; 146: 257–60.
62. Alvarez Perez JA, Baldonado RF, Bear IG, et al. Emergency hernia repairs in elderly patients. *Int Surg* 2003; 88: 231–7.
63. Kulah B, Duzgun AP, Moran M, et al. Emergency hernia repairs in elderly patients. *Am J Surg* 2001; 182: 455–9.
64. Rigberg D, Cole M, Hiyama D, et al. Surgery in the nineties. *Am Surg* 2000; 66: 813–16.
65. Fitzgibbons RJ Jr., Giobbie-Hurder A, Gibbs JO, et al. Watchful waiting vs repair of inguinal hernia in minimally symptomatic men: a randomized clinical trial. *JAMA* 2006; 295: 285–92.

Surgical Endocrine Emergencies

Christopher Busken, Rebecca Coefield, Robert Kelly and Steven Brower

A surgeon is never called to operate acutely on a patient's endocrine abnormality that has led to a crisis, but a thorough understanding of the causes and treatments of these crises is important in the comprehensive treatment of these patients. The topics to be covered in this chapter are central diabetes insipidus, carcinoid crisis, hypertensive crisis secondary to pheochromocytoma, adrenal crisis, and thyroid storm.

CENTRAL DIABETES INSIPIDUS

Central diabetes insipidus (CDI) is a lack or decrease of secretion of the hypothalamic polypeptide antidiuretic hormone (ADH), also known as arginine vasopressin, from the posterior pituitary gland. Normally, hypovolemia or increased serum osmolality causes ADH secretion, which in turn regulates distal renal tubule permeability, causing water retention. Therefore, lack of ADH is manifest by polyuria. A urine specific gravity of 1.005 or less and a urine osmolality less than 200 mOsm/kg is the hallmark of diabetes insipidus. Plasma osmolality is usually >290 (2,3,5). In the acute trauma setting with severe traumatic brain injury (TBI), polyuria can lead to severe dehydration and hypotension, requiring aggressive resuscitation.

What Are the Causes of CDI?

CDI is most commonly related to TBI, brain tumors, brain surgery, or idiopathic origin but can also be related to thoracic spinal injury (1). TBI, tumors, or brain surgery involving the hypothalamic osmoreceptors, supraoptic or paraventricular nuclei, or the supraopticohypophyseal tract are likely to cause CDI (2). Posterior pituitary injury can also cause CDI, but it is usually transient as the hypothalamus secretes ADH directly into the bloodstream after injury (2).

Answer: CDI is most commonly related to TBI, brain tumors, brain surgery, or idiopathic origin but can also be related to thoracic spinal injury. Posterior pituitary injury can also cause CDI. Recommendation Grade: C.

What Is the Optimal Treatment of CDI?

Treatment of CDI involves replacing the lacking ADH with a synthetic analog, in the form of DDAVP or vasopressin, in the IV, SQ, intranasal, or oral forms (1–5). Recommendation Grade: B. Because this is a replacement of the body's natural substance, studies of form of deliverance and

dosage have been performed (3), but no other treatments are studied.

CARCINOID CRISIS

Carcinoid syndrome is a syndrome associated with carcinoid tumors, usually metastatic to the liver (90%), caused by the secretion of polypeptides, biogenic amines, and prostaglandins, of which the most significant are serotonin, histamine, tachykinins, kallikrein, and prostaglandins. The main symptoms involved are diarrhea and flushing, but it can also cause include venous telangiectasia, bronchospasm, cardiac valvular lesions, pellagra, and muscle wasting. Carcinoid crisis describes episodes of extreme hypotension, flushing, bronchoconstriction, arrhythmias, and even death, which corresponds to the palpation of the tumor (directly or externally), at the time of anesthesia induction or at the time of embolization of the hepatic artery in metastatic disease. Carcinoid crises have also been described with bronchoscopy and laser removal with bronchiogenic carcinoid.

What Is the Optimal Treatment of Carcinoid Crisis?

The treatment of carcinoid crisis is with octreotide 300 mcg or 50–150 mcg/hour drip and volume support (6). The hypotension associated with this crisis is refractory to typical treatments, including vasopressors, and may actually exacerbate bronchoconstriction and hypotension. Prevention of carcinoid crisis with perioperative octreotide is key when removal or manipulation of the tumor is anticipated. After the discovery of successful treatment of carcinoid crises with octreotide, studies for dosages and forms have been done, but no other alternative studies have been performed.

Answer: The treatment of carcinoid crisis is with octreotide 300 mcg or 50–150 mcg/hour drip and volume support. Recommendation Grade: B.

THYROID STORM

Thyroid storm is an entity characterized by severe hyperthyroidism. Multiple etiologies exist, and care of the surgical patient can precipitate this disease. Thyroid storm can have a high mortality (9,10), and knowledge of this entity can provide the physician with valuable tools to assist the care for the patient. Questions to be addressed in this section include diagnosis, medical management, and surgical management.

Level of Evidence							
Author	Ref.	Year	Level of evidence	Groups	Design	Median follow-up	Endpoint
Lam, et al.	3	1996	IIb	Previously controlled patients with DI with compared to themselves with oral medication	Prospective nonrandomized trial	Acute, 7 days	Acute, urine output and osmols, plasma osmols, DDAVP levels
Kinney, et al.	6	2001	IIb	Those who received perioperative octreotide and those who did not receive octreotide	Retrospective chart review	Chronic, 4 weeks and 3-month intervals	Chronic, 24 hour urine output, DDAVP levels
Garland, et al.	7	2003	Ib	Sandostatin vs naive octreotide administration	RCT	23 months	Death and other adverse outcomes
Witte	9	2000	Ib	Bilateral subtotal, total unilateral with subtotal contralateral, total thyroidectomy	RCT	NR	Symptom control
Palit	10	2000	IIb		Meta-analysis		TSH-R-Ab, size of postoperative remnant, difference in Graves' ophthalmopathy, complications
Lenders	19	2002	IIa	Confirmed patients with and without pheochromocytoma	Retrospective cohort study	NR	Recurrence, remnant size, complications, mortality
Bhatia	23	2005	IIa	Evaluated patients with and without tumors via MIBG versus CT/MRI	Retrospective analysis	NR	Sensitivities and specificities of biochemical markers for pheochromocytoma
Prys-Roberts	27	2002	IIa	Comparison of phenoxybenzamine versus doxazosin	Prospective sequential study	NR	Sensitivity o f MIBG versus CT/MRI scans for the detection of adrenal and extra-adrenal tumors
Kocak	28	2002	IIb	Compared an α -blocker to other blood pressure meds	Retrospective cohort study	NR	Efficacy and safety of doxazosin compared to the standard treatment
Tiberio	29	2008	Ib	Comparison of laproscopic versus open adrenalectomy for pheochromocytoma	Prospective randomized analysis	NR	Blood pressure control
Mark	32	2008		Recommendations concerning corticosteroid insufficiency	Consensus statement from an international task force	NR	Operative time, hypertensive episodes, and long-term follow-up
Annane	33	2006	IIb	Comparison of serum cortisol levels in septic and nonseptic patients	Consecutive cohort study	NR	NA
Briegel	35	1999	Ia	Comparison between septic patients who received stress-dosed steroids versus placebo	Randomized, prospective, double blinded	NR	Baseline cortisol level, free cortisol level, and Δ cortisol level after stimulation
Time to wean from vasopressors							
Abbreviations: CT, computed tomography; DDAVP, ; DI, diabetes insipidus; MIBG, metaiodobenzylguanidine; MRI, magnetic resonance imaging; NA, not available; NR, not reported; RCT, randomized controlled trial; TSH, thyroid stimulating hormone.							

Abbreviations: CT, computed tomography; DDAVP, ; DI, diabetes insipidus; MIBG, metaiodobenzylguanidine; MRI, magnetic resonance imaging; NA, not available; NR, not reported; RCT, randomized controlled trial; TSH, thyroid stimulating hormone.

How Is the Diagnosis of Thyroid Storm Made?

The initial diagnosis of hyperthyroidism is usually made on the basis of thyroid function tests in addition to a detailed history and physical exam. In thyroid storm, serum total and free triiodothyronine (T_3) levels are elevated. In addition, thyroid stimulating hormone (TSH) is generally depressed. However, the differentiation between thyroid storm and simple thyrotoxicosis is not easily made. In 1993, Burch and Wartofsky (9), developed a point system that describes the likelihood of a patient's signs and symptoms of being caused by thyroid storm.

Answer: The initial diagnosis of hyperthyroidism is usually made on the basis of thyroid function tests in addition to a detailed history and physical exam. Specifically, serum total and free T_3 levels are elevated while TSH is depressed. Recommendation Grade: None.

What Is the Medical Management of Thyroid Storm?

The management of thyroid storm is primarily medical in nature. There are numerous drug combinations, each addressing different aspects of the disease process. Antithyroid drugs (propylthiouracil and methimazole) are widely used in the United States. These are used to inhibit new formation of thyroid hormone. There have been studies over 10 years old that have explored different administration routes for both of propylthiouracil and methimazole; however, no study has compared the efficacy of these drugs to each other. Thus, no recommendation can be made as to the superiority of one over the other (11).

Another treatment for thyroid storm is iodine therapy. This is used to decrease the amount of thyroid hormone that is released. Lugol's solution is classically described to be given no earlier than 30 minutes after initiation of antithyroid drug administration. However, there is little evidence to support this statement.

β -adrenergic blockade is also classically described in the treatment of hypertension, tachycardia, and other adrenergic symptoms associated with thyroid storm (12). Depending on the specific clinical situation, propranolol, esmolol, atenolol, metoprolol, or nadolol is used. In thyroid storm, drug metabolism is increased, which might lead to increased dosing requirements, necessitating using increased doses of pharmaceuticals. Many of these drugs have differing administration routes, which is helpful for tailoring therapy to the individual situation (13).

Management of anticoagulation in the setting of thyroid storm-induced atrial fibrillation has also been studied. There are no studies within the past decade that contribute any knowledge on this subject. We are left with the *Chest* guidelines stating that anticoagulation should be initiated on the presence of other stroke risk factors (14).

Other treatments include lithium, reserpine, guanethidine, cholestyramine, plasmapheresis, charcoal hemoperfusion, and plasma exchange. The studies that have examined their indications, and effects are either greater than 10 years old or deal with thyrotoxicosis.

Antipyretics (excluding salicylates) to decrease fever are often used to decrease fever. External cooling measures including alcohol sponges, ice packs, or cooling blankets are used as well. Fluid resuscitation is a mainstay of treatment. It is also of high importance to determine the inciting event

causing the thyroid storm and initiate appropriate treatment. Preoperative management for emergent surgery in the setting of thyroid storm consists of the following goals: lowering thyroid hormone levels, decreasing hormone release, and successful management of peripheral manifestations of high levels of thyroid hormone.

Answer: The management of thyroid storm is primarily medical. The many drug combinations address different aspects of the disease process. Recommendation Grade: None.

What Is the Surgical Management for Thyroid Storm?

Although the mainstay of treatment for thyroid storm is medical management, there are still indications for surgical management. These include toxic multinodular goiter, very large goiters, patients with ophthalmopathy, children, pregnant women, women desiring pregnancy within one year of treatment, or severe allergies to the aforementioned medications (14,15). Currently, there is not enough evidence to guide the extent of resection for thyroid storm. The inciting event determines the ensuing resection. There is conflicting evidence with regard to total versus subtotal thyroidectomy for resolution of Graves' ophthalmopathy. Witte et al. in a randomized controlled trial found that subtotal thyroidectomy was preferred, whereas a meta-analysis by Palit et al. in 2000 recommended a total thyroidectomy for patients with severe disease, whereas in patients with milder disease a subtotal thyroidectomy could be performed (17,18).

Answer: Indications for surgical management include toxic multinodular goiter, very large goiters, patients with ophthalmopathy, children, pregnant women, women desiring pregnancy within a year of treatment, or severe allergies to medications. Recommendation Grade: None.

PHEOCHROMOCYTOMA

Pheochromocytoma is an uncommon tumor of neuroendocrine origin found in approximately 1–2% of the general population. Commonly located within the adrenal gland, extra-adrenal tumors are not infrequent and when encountered are commonly seen in the neck, mediastinum, abdomen, pelvis, or organ of Zuckerkandl. With a peak incidence between the fourth and fifth decade, pheochromocytomas are associated with carriers of MEN2A and MEN2B seen in families with a RET gene mutation. Historically, this tumor has been known as the "10% tumor" because it tends to be 10% bilateral, 10% familial, 10% malignant, 10% extra-adrenal, and 10% found in the pediatric population. However, scientific evidence would suggest that the 10% rule is a generalization with findings demonstrating at least 25% of tumors arising ectopically (23).

What Signs and Symptoms Are Found in Patients with a Pheochromocytoma Tumor?

Associated with the triad of headaches, palpitations, and diaphoresis, uncommon presentations of the tumor are not infrequent. Other symptoms, such as anxiety, dizziness, syncope, or flushing, may also be attributed to the tumor

and concern for the diagnosis should be elicited (6). When hypertension is absent from the symptomatology experienced by the patient, the likelihood of diagnosing this tumor remains low, and further evaluation is necessary. Approximately 0.1% of all hypertensive patients are found to have a curable form of high blood pressure with the etiology stemming from this neuroendocrine tumor (20).

Answer: Associated with the triad of headaches, palpitations, and diaphoresis; other symptoms may include anxiety, dizziness, syncope, or flushing. Recommendation Grade: None.

What Steps Are Involved in Making the Diagnosis of Pheochromocytoma?

When suspected, work-up for the tumor normally begins by testing for fractionated metanephrines and catecholamines. This is done by obtaining 24-hour urinary excretion and measuring for urinary vanillyl mandelic acid (VMA) and metanephrines. Interestingly, except for tumors arising from the organ of Zuckerlandl, all extra-adrenal pheochromocytomas secrete only norepinephrine due to lacking the enzyme phenylethanolamine N-methyltransferase, which metabolizes norepinephrine to epinephrine. However, recent trends to diagnose pheochromocytomas are shifting more toward obtaining plasma metanephrines and chromagranin A levels with reported sensitivities approaching 100% as described by Lenders et al. This multicenter cohort study evaluated approximately 1,000 patients with predisposing factors related to the neuroendocrine tumor. Biochemical tests were then performed on this group comparing plasma and urinary catecholamines against plasma concentrations of free metanephrines and normetanephrines. Plasma free metanephrines demonstrated the highest sensitivity for detecting the tumor, and urinary VMA showed the highest specificity (19).

With the advent of computed tomography (CT) scans approximately half of all adrenal masses are diagnosed incidentally. One university study found that 23% of all pheochromocytomas in this institution were found on work-up for trauma-related injuries (21). Though CT scans remain a popular choice for assessing an adrenal mass, noncontrasted studies should be advocated when concern for a pheochromocytoma is suspected secondary to the risk of precipitating a contrast-induced hypertensive crisis. Although not as commonly used, magnetic resonance imaging with T2-weighted imaging is the modality of choice for assessing this tumor with reported sensitivities and specificities approaching almost 100% (22). Although not as sensitive iodine-131-radiolabeled metaiodobenzylguanidine (MIBG) scans are useful to detect ectopically located tumors. MIBG is taken up by the tumor and concentrated, thus giving a discernible appearance from surrounding tissue, which is useful in not only analyzing the primary tumor but also evaluating metastatic foci. Tumor detection was lower for extra-adrenal (58%) versus adrenal (85%) pheochromocytomas with an overall sensitivity of 75% in the study by Bhatia et al. (23).

Answer: Work-up for the tumor normally begins by testing for fractionated metanephrines and catecholamines. Recommendation Grade: B.

How Is the Treatment of this Disease Instituted?

Once diagnosed, treatment begins with appropriate preoperative management. Initial management is directed at controlling the sudden release of catecholamines during induction of anesthesia and surgical intervention. Non-selective α -blockers, such as phenoxybenzamine (POB) may be dosed over a period of two weeks. The dose is increased until the patient begins experiencing orthostatic hypotension and reflex tachycardia. (26) Unfortunately, even with adequate α -receptor blockade, complete prevention of hypertensive events are seldom guaranteed, and further medical management is required at the time of surgery.

Selective postsynaptic α_1 -receptor antagonists have since been introduced as an attempt to limit the undesired postoperative effects of POB. These drugs display a more selective effect on presynaptic receptors in combination with a shorter half-life, which theoretically reduces the incidence of reflex tachycardia and overall duration of postoperative hypotension (27). In a recent prospective sequential study, prazosin and doxazosin were evaluated against POB and found to have the same overall efficacy in controlling operative hypertension without a significant difference in the postoperative course with regard to blood pressure and volume replacement in certain studies (28).

β -blockers are also used as an adjunct to α -blockade in patients with tachycardia and/or arrhythmias. The early addition of β -blockade may lead to unopposed α stimulation, leading to excessive hypertension and even congestive heart failure. Preventive measures such as adequate volume expansion and hydration reduce this overall risk. Furthermore, volume repletion helps circumvent postoperative hypotension once unopposed α stimulation has been ceased on removal of the tumor.

Answer: Initial management is directed at controlling the sudden release of catecholamines during induction of anesthesia and surgical intervention. Recommendation Grade: B.

What Approach Is Best Suited for Removal of Pheochromocytoma?

Historically the first surgery for pheochromocytoma occurred in 1926 by Roux. Since then, tremendous advancements in technique have occurred, including the use of laparoscopic techniques for tumor removal. However, with the advent of laparoscopic surgery, attention has been focused on using a minimally invasive technique for operative intervention. With this technique, safety concerns have been expressed over the establishment of pneumoperitoneum and the hemodynamic effects exerted in patients with an existing catecholamine-secreting tumor. Comparisons have been made between the laparoscopic versus open techniques, and studies have demonstrated that in an experienced surgeon's hands, the laparoscopic technique minimizes manipulation of the tumor, decreases blood loss, and shortens hospital stay without displaying a significant difference in intraoperative hypertension or operative length (29). Further analysis has been conducted to guide a surgeon's decision making on when to convert from laparoscopic to the open technique. Factors such as extensive tumor invasion, concomitant open procedures, or tumors greater than 6 cm in size render themselves more favorable to an open approach (30,31).

Answer: Laparoscopic techniques have been shown to minimize manipulation of the tumor, decrease blood loss, and shorten hospital stay without displaying a significant difference in intraoperative hypertension or operative length. Factors such as extensive tumor invasion, concomitant open procedures or for tumors greater than 6cm in size render themselves more favorable to an open approach. Recommendation Grade: B.

ADRENAL CRISIS

The adrenal gland may be divided into the cortex, which produces steroid hormones, and the medulla, which is responsible for the secretion of catecholamines. Although each part functions independently of the other, they both play a vital role in homeostasis. When this gland dysfunctions, the consequences may be severe and even mortal. This dysfunction may be seen in critically ill patients, and through testing it has become more evident that adrenal insufficiency is occurring at a higher rate than initially thought. Adrenal crisis in the critical ill is believed to be caused by an exaggerated inflammatory response, tissue resistance to corticosteroids, and an intrinsic adrenal gland deficiency (32).

What Signs and Symptoms Are Found in Patients with Adrenal Insufficiency?

Adrenal crisis may be induced in many pathological states. Specifically seen in states of shock with hypotension, patients with critical illness are often diagnosed with adrenal insufficiency. Other symptoms seen in adrenal insufficiency include nausea, vomiting, abdominal pain, fever, or lethargy. The clinician should also be aware of electrolyte abnormalities, specifically hyponatremia with hyperkalemia. The diagnosis should be suspected in all septic patients unresponsive to fluids and vasopressors.

Answer: Symptoms seen in adrenal insufficiency include nausea, vomiting, abdominal pain, fever, or lethargy and states of shock with hypotension. Recommendation Grade: None.

What Is the Appropriate Work-up Concerning a Patient with Suspected Adrenal Insufficiency?

An article by Marik et al. outlined via a consensus statement the diagnostic parameters for the etiology of patients in shock as being multifactorial. The paper defined adrenal insufficiency as a total cortisol level <10 or a Δ total serum cortisol of $<9\mu\text{g/dl}$ after adrenocorticotrophic hormone (250mcg) challenge (32). These guidelines are supported by a prospective cohort study in which a septic and nonseptic arm were evaluated with an overnight metyrapone stimulation. The paper also demonstrated that when the baseline cortisol level was greater than 43mcg/dl or when the Δ cortisol was greater than or equal to 16.8mcg/dl , then the diagnosis of adrenal insufficiency was unlikely (33).

Further studies have been designed to evaluate differences between the use of low-dose stimulant testing with 1 mcg versus the conventional 250mcg when testing for adrenal insufficiency. A specific article by Siraux et al.

evaluated the response in critically ill patients to both test and found the low-dose test delineated out a group of patients in septic shock who had adrenal insufficiency that would have been missed by the high-dose group. The study also confirmed that the basal or maximal cortisol levels in both tests were not independent predictors of survival (34).

Answer: The diagnostic parameters for the etiology of patients in shock are multifactorial. Recommendation Grade: B.

What Is the Optimal Treatment in Patients with Adrenal Failure?

Patients in septic shock who are diagnosed with adrenal insufficiency are commonly treated with hydrocortisone. A prospective, randomized, double-blinded, single-center study compared two groups of septic patients on vasopressors with one arm receiving hydrocortisone and the other receiving normal saline. The study was limited by its small power in regard to evaluating overall mortality outcomes; however, the trial did demonstrate earlier vasopressors independence in the hydrocortisone-receiving arm (35). Furthermore, steroids should always be tapered prior complete cessation. Thus, in patients with confirmed adrenal insufficiency or found to be unresponsive to vasopressors, a trial of corticosteroids should be instituted.

Answer: A trial of corticosteroids should be instituted. Recommendation Grade: B.

REFERENCES

1. Kuzeyli, Kayhan MD, et al. Diabetes insipidus secondary to penetrating spinal cord trauma: case report and literature review. *Spine* 2001; 26: E510-E511.
2. Maghnie M, Cosi G, Genovese E, et al. Central diabetes insipidus in children and young adults. *N Engl J Med* 2000; 343: 998.
3. Lam SL, et al. Pharmacokinetics, pharmacodynamics, long-term efficacy and safety of oral 1-deamino-8-d-arginine vasopressin in adult patients with central diabetes insipidus. *Br J Clin Pharmacol* 1996; 42: 379-85.
4. Singer I, Oster JR, Fishman LM. The management of diabetes insipidus in adults. *Arch Int Med* 1997; 157: 1293-301.
5. Richardson DW, Robinson AG. Desmopressin. *Ann Intern Med* 1985; 103: 228-39.
6. Kinney MAO, Warner ME, Nagorney DM, et al. Perianesthetic risks and outcomes of abdominal surgery for metastatic carcinoid tumours+. *Br J Anaesth* 2001; 87: 447-52.
7. Garland J, et al. Sandostatin LAR (long-acting octreotide acetate) for malignant carcinoid syndrome: a 3-year experience. *Alim Pharmacol Ther* 2003; 17: 437-44.
8. Marsh M, et al. Carcinoid crisis during anesthesia: successful treatment with a somatostatin analogue. *Anesthesiology* 1987; 66: 89-91.
9. Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. *Endocrinol Metab Clin North Am* 1993; 22: 263-77.
10. Nayak B, Burman K. Thyrotoxicosis and thyroid storm. *Endocrinol Metab Clin North Am* 2006; 35: 663-86.
11. Cooper DS. Antithyroid drugs. *N Engl J Med* 2005; 352: 905-17.
12. Goldberg PA, Inzucchi SE. Critical issues in endocrinology. *Clin Chest Med* 2003; 24: 583-606.
13. Klein I, Ojamaa K. Thyrotoxicosis and the heart. *Endocrinol Metab Clin North Am* 1998; 27: 51-61.

14. Singer DE, Albers DW, Dalen JE. Antithrombotic therapy in atrial fibrillation: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004; 126: 429–56.
15. Boger MS, Perrier ND. Advantages and disadvantages of surgical therapy and optimal extent of thyroidectomy for the treatment of hyperthyroidism. *Surg Clin N Am* 2004; 84: 849–74.
16. Alsanea O, Clark O. Treatment of Grave's disease: the advantages of surgery. *Endocrinol Metab Clin North Am* 2000; 29: 321–35.
17. Witte J, Goretzki P, Dotzenrath C, et al. Surgery for Graves' disease: total versus subtotal thyroidectomy: results of a prospective randomized trial. *World J Surg* 2000; 24: 1303–11.
18. Palit T, Miller C, Miltenburg D. The efficacy of thyroidectomy for Graves' disease: a meta-analysis. *J Surg Res* 2000; 90: 161–5.
19. Lenders JW, Pacak K, Walther MM, et al. Biochemical diagnosis of pheochromocytoma: which is best? *JAMA* 2002; 287: 1427.
20. Beard CM, Sheps SG, Kurland LT, et al. Occurrence of pheochromocytoma in Rochester, Minnesota, 1950 through 1979. *Mayo Clinic* 1983; 58: 802–4.
21. Kirshtein B, Pagliarello G, et al. Incidence of pheochromocytomas in trauma patients during the management of unrelated illness: a retrospective review. *Int J Surg* 2007; 5: 332–5.
22. Mayo-Smith WW, Boland G, Noto RB, et al. State-of-the-art adrenal imaging. *Radiographics* 2001; 21: 995–1012.
23. Bhatia KS, Ismail MM, Sahdev A, et al. (123)I-metaiodobenzylguanidine (MIBG) scintigraphy for the detection of adrenal and extra-adrenal pheochromocytomas: CT and MRI correlation. *Clin Endocrinol (Oxf)*. 2008; 69: 181–8.
24. Madani R, Al-Hashmi M, et al. Ectopic pheochromocytoma: Does the rule of tens apply? *World J Surg* 2007; 849–54; erratum: *World J Surg* 2008; 32: 334.
25. Safwat AS, Bissada NK, et al. The clinical spectrum of pheochromocytoma: analysis of 115 patients. *BJU Int* 2008.
26. Kinney MA, Narr BJ, Warner MA. Perioperative management of pheochromocytoma. *J Cardiothor Vasc Anesth* 2002; 16: 359–69.
27. Prys-Roberts C, Farndon JR. Efficacy and safety of doxazosin for perioperative management of patients with pheochromocytoma. *World J Surg* 2002; 26: 1037–42.
28. Kocak S, Aydinoglu S, et al. Alpha blockade in preoperative preparation of patients with pheochromocytomas. *Int Surg* 2002; 87: 191–4.
29. Tiberio GA, Baiocchi GL, et al. Prospective randomized comparison of laparoscopic versus open adrenalectomy for sporadic pheochromocytoma. *Surg Endosc* 2008.
30. Phitayakom R, McHenry CR. Laparoscopic and selective open resection for adrenal and extraadrenal neuroendocrine tumors. *Am Surg* 2008; 74: 37–42.
31. Benetrem DJ, Pappas SG, et al. Contemporary surgical management of pheochromocytoma. *Am J Surg* 2002 Dec; 184: 621–4.
32. Mark PE, Pastores SM, et al. Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: consensus statements from an international task force by the American College of Critical Care Medicine. *Crit Care Med* 2008.
33. Annane D, Maxime V, et al. Diagnosis of adrenal insufficiency in severe sepsis and septic shock. *Am J Respir Crit Care Med* 2006; 174: 1319–26.
34. Siraux V, DeBacker D, et al. Relative adrenal insufficiency in patients with septic shock: Comparison of low-dose and conventional corticotropin tests. *Crit Care Med* 2005; 33: 2688–9.
35. Briegel J, Frost H, et al. Stress doses of hydrocortisone reverse hyperdynamic septic shock: a prospective, randomized, double-blind, single-center study. *Crit Care Med* 1999; 27: 723–4.

Evidence-Based Surgery: Bacteremia

Sapooria Manshahi and Greg J. Beilman

Clinical Questions		
Question	Answer	Grade of recommendation
What is the protocol for diagnosis of bacteremia?	Blood cultures remain the gold standard. Multiple PCR methods can be used as an adjunct.	B
What is the best way to diagnose catheter-related bacteremia when the catheter is removed?	We recommend a semiquantitative or preferentially quantitative culture of the catheter segment in addition to two blood cultures obtained percutaneously from a peripheral vein and from a suspected intravascular device.	B
What is the significance of empiric therapy in the patient with bacteremia?	Early administration of effective empiric antimicrobial treatment leads to a decrease in the mortality rate, duration of hospital stay, and hospital costs.	B
How can we prevent the occurrence of catheter-related bloodstream infections?	Recommended preventive strategies with the strongest supportive evidence are:	B
	- Education and training of health care providers	A
	- Maximal sterile barrier precaution	A
	- Use of a 2% chlorhexidine preparation for skin antisepsis	A
	- Use of antiseptic/antibiotic impregnated catheter if rate of infection is high despite adherence to other strategies	A
Abbreviations: PCR, polymerase chain reaction.		

INTRODUCTION

Bacteremia, the presence of bacteria in the bloodstream, was recognized more than a century ago. It was first described by Libman in 1897 (1). Bacteremia accounts for approximately 5–15% of all health care–associated infections and remains a major cause of morbidity and mortality (2,3). Case fatality rates are high ranging from 10% to 60% (2). In addition to being an important cause of death, bloodstream infections lead to prolonged length of hospitalizations and higher cost of care (3–5). The incidence rates of bacteremia have increased since the 1980s (6). Bacteremia is classified as community-acquired, health care–associated, and hospital-acquired (7). Bacteremia can be further classified as primary or secondary. Primary bacteremia is a documented bloodstream infection without a known source. In the presence of an indwelling catheter, a primary bacteremia is considered a catheter-related bloodstream infection (2). These device-related nosocomial bloodstream infections have increased eightfold over the past decades.

In the 1970s, Gram-negative aerobic organisms were most frequently isolated from patients with nosocomial bloodstream infections. However, over the past decades, Gram-positive organisms have become the predominant cause of bloodstream infections (3,4,8). In the adult U.S.

population, the incidence for Gram-positive bacteremia is currently reported as 133 cases per 100,000 person-years for men and about half that for women (9).

In this chapter, we review the literature concerning the diagnosis, management, and prevention of hospital-acquired bloodstream infections and provide recommendations as supported by the current level of evidence.

WHAT IS THE PROTOCOL FOR DIAGNOSIS OF BACTEREMIA?

Bloodstream infections are a common and serious problem with a high mortality rate (10,11). Numerous studies have demonstrated that a delay in empiric antibiotic treatment is associated with an increase in this already high mortality rate. In turn, the initiation of appropriate and effective treatment is dependent on an accurate diagnosis established in a timely fashion. More rapid diagnosis of bacteremia allows for a more expeditious implementation of appropriate antimicrobial treatment and reduces morbidity and mortality (1).

Blood cultures are the current cornerstone for detection of bloodstream infections (12). A blood culture is defined as a specimen of blood obtained from a single venipuncture or intravascular access device. Over the past 30 years,

numerous changes have been made to blood culture media and systems with the goal of improving sensitivity and speed of diagnosis (13). We reviewed the literature to assess how many blood cultures are necessary. Until the 1990s, the recommendation was to obtain two to three blood cultures. However, Cockerill and colleagues performed an observational study at the Mayo Clinic and found that two blood cultures detected only 80% of blood stream infections, three detected 96% of blood stream infections, and four cultures were necessary to detect 100% of bloodstream infections (14).

These findings were confirmed in another retrospective observational study performed by Lee et al. They analyzed their data to determine the cumulative sensitivity of blood cultures obtained sequentially during a 24-hour time period. The results of their study demonstrated that two blood cultures in a 24-hour period will detect approximately 90% of blood stream infections. They further concluded that to achieve a greater than 99% detection rate, as many as four blood cultures may be necessary. They further observed that *Staphylococcus aureus* was the most likely microorganism to be detected with the initial blood culture, and *Pseudomonas aeruginosa* and *Candida albicans* are the least likely bloodstream pathogens to be detected with the initial blood culture (13).

The next question we asked was the relevance of the routine use of the anaerobic blood culture bottle. Classically, two bottles are collected routinely, an aerobic and an anaerobic bottle. However, Murray et al. conducted a retrospective review and demonstrated that the frequency of obligate anaerobic bacteremia has declined significantly, and with the exception of obligate anaerobic bacteria, many organisms grow preferentially in aerobic bottles (15). Based on these results, the routine use of two aerobic blood cultures with selective use of anaerobic bottles has been proposed in the literature. Grohs and colleagues performed a retrospective study on blood cultures focusing on the relevance of routine use of the anaerobic bottle and demonstrated that 13.5% of patients with a positive blood culture had a positive anaerobic bottle in the absence in any positive aerobic bottle and two-thirds of these grew with non-obligate anaerobes. Furthermore, they demonstrated that in 64% of the blood cultures growing *Enterobacter*, the anaerobic bottles detected growth earlier than the corresponding aerobic bottle. They concluded that in their institution the use of anaerobic bottle is still relevant (12).

Despite remaining the cornerstone for diagnosis of bacteremia, blood cultures have certain limitations: delay in diagnosis, poor sensitivity for slow-growing and fastidious organisms, and decrease in sensitivity when blood samples are taken after the start of antimicrobial therapy (1,16). New diagnostic techniques are necessary to increase the sensitivity and specificity, decrease turnaround time, and reduce inhibitory effects of antibiotics on the detection of pathogens.

One of the most promising developments is the direct detection of bacteria in whole blood with multiplex polymerase chain reaction (PCR) assays. Louie et al. performed a prospective cohort study to test multiplex PCR for simultaneous detection of multiple organisms in bloodstream infections (17). Two hundred adult patients at risk of bloodstream infections had blood samples collected for PCR and blood culture. When PCR assay results were compared to

blood culture results, PCR detected bacteria and fungi in 45 cases compared to 37 detected by blood cultures. More than 68% of PCR results were confirmed by blood, urine, and catheter cultures. PCR did not detect *Enterococcus faecalis* in five blood culture-confirmed cases. In conclusion, multiplex PCR detected bacteria and fungi that were not found by blood culture, and blood culture identified organisms that were not detected by PCR. A major limitation of all molecular techniques is the lack of simultaneous provision of the antimicrobial susceptibility pattern (19). Despite limitations of both methods, PCR may serve as an adjunct to blood culture to improve speed and sensitivity of detection of organisms in the case of bacteremia.

Recommendation: Despite the lack of Level I evidence precluding Grade A recommendations, blood cultures remain the gold standard for diagnosis of bloodstream infections. Until the advent of further microarray-based techniques, multiplex PCR methods may be used as an adjunct to blood cultures (Grade B recommendation). Based on the currently available data, the number of blood cultures drawn and the use of anaerobic blood culture bottles should be left at the discretion of the clinician.

WHAT IS THE BEST WAY TO DIAGNOSE CATHETER-RELATED BACTEREMIA WHEN THE CATHETER IS REMOVED?

A significant number of bloodstream infections are related to intravascular catheters. An estimated 250,000–500,000 episodes of catheter-related bloodstream infections occur in the United States annually (17). A variety of diagnostic tests have been developed for diagnosis of catheter-related bloodstream infections. They can be categorized as methods that necessitate intravascular device removal and those that do not.

Guidelines from the Infectious Disease Society of America (IDSA) recommend paired cultures of blood drawn through the IV catheter and percutaneously as well as quantitative or semi-quantitative cultures of catheters (18). In a retrospective cohort study, Desjardin and colleagues looked at a cohort of 185 hospitalized patients retrospectively to determine the sensitivity, specificity, and positive and negative predictive values of cultures done with blood obtained through a central venous catheter compared with a peripheral venipuncture. Of the 551 paired cultures, 85% were catheter negative/venipuncture negative, 6% were catheter positive/venipuncture positive, 3% were catheter negative/venipuncture positive, and 6% were catheter positive/venipuncture negative. For catheter draw compared with peripheral venipuncture, sensitivity was 89% and 78%, specificity was 95% and 97%, PPV was 63% and 73%, and NPV was 99% and 98%, respectively. It was concluded that culture of blood drawn through either the central catheter or peripheral vein shared excellent negative predictive value. However, culture of blood from an indwelling central venous catheter had a low positive predictive value compared to a peripheral venipuncture. Therefore, a positive result from a central venous catheter blood draw requires clinical interpretation and may require further confirmatory study (19).

Semi-quantitative (roll plate method) or quantitative (vortex or sonication methods) catheter culture techniques are the most reliable diagnostic methodologies. This is due to greater specificity in identification of catheter-related

infections compared to qualitative cultures, in which contamination can result in a false positive culture.

In a recent prospective observational study, Sherertz and colleagues removed 248 triple-lumen catheters from patients in an intensive care unit (ICU). Catheter tips and subcutaneous segments were cultured by both the sonication and roll plate methods. One hundred ninety-one of these catheters had flush cultures performed. The results demonstrated that sonication of the subcutaneous segment was the most sensitive at detecting colonization (58%) followed by sonication of the catheter tip (53%). The greater sensitivity of the sonication method may be secondary to an improved ability to access catheter lumen colonization, an area difficult to sample with the roll plate method. They concluded that sonication was the most sensitive method (80%) followed by the roll plate method (60%) and the flush culture (40–50%) (20).

Safdar and colleagues performed a meta-analysis reviewing the literature addressing diagnostic methods requiring removal of the intravascular device. In their analysis of six studies, they came to the conclusion that qualitative culture of the catheter segment has poor specificity but high sensitivity and was found to be the least accurate of the tests studied. Their analysis of 19 studies of semi-quantitative catheter segment culture demonstrated an overall sensitivity of 85% and specificity of 82%. The positive predictive value was low in the setting of low prevalence of catheter-related bloodstream infections. They analyzed 14 studies of quantitative catheter segment cultures demonstrating an overall sensitivity of 83% and specificity of 87%, making it the most accurate test of catheter segment culture followed by semi-quantitative culture. From the results of their meta-analysis, the authors concluded that with short-term intravascular devices, quantitative or semi-quantitative culture of the catheter combined with two blood cultures, one drawn percutaneously from a peripheral vein and one through the catheter, will allow accurate diagnosis of catheter-related bloodstream infections (17).

Recommendation: Intravascular device-related bloodstream infections are common and associated with a high mortality and morbidity. Clinical findings alone are unreliable for diagnosing catheter-related bloodstream infections. In the presence of symptoms of infection at the device insertion site and/or high suspicion for bacteremia and sepsis, removal of the catheter is recommended. We recommend a semi-quantitative or preferably quantitative culture of the catheter segment in addition to two blood cultures obtained percutaneously from a peripheral vein and from the suspected intravascular device (Grade B recommendation).

WHAT IS THE SIGNIFICANCE OF EMPIRIC THERAPY IN THE PATIENT WITH BACTEREMIA?

Empiric therapy is defined as the initiation of an antimicrobial regimen in a patient with suspected infection before the type of infecting organism has been identified (25). The administration of appropriate antibiotics in a timely manner is crucial to improving outcome. Empiric therapy has been shown to be a predictor of mortality in numerous analyses.

In a large prospective cohort study, Leibovici and colleagues reported mortality rates of 20% compared to 34% in patients receiving appropriate (n = 2,158) versus

inappropriate (n = 1,255) antibiotic therapy (p = 0.0001). Furthermore, hospital stay of survivors who were given appropriate empirical treatment was shorter than in those given inappropriate treatment. They concluded that appropriate empirical antibiotic treatment was associated with a significant reduction in fatality in patients with bloodstream infections (21).

Ibrahim et al. performed a cohort study, prospectively evaluating 492 patients. They established that 29.9% of these patients received inadequate antimicrobial treatment for their bacteremia. The hospital mortality of these patients was statistically greater than the hospital mortality rate of patients with bloodstream infections who received adequate treatment (62% versus 28%, respectively, p = 0.001). Independent risk factors for inappropriate antimicrobial therapy were bloodstream infection with *Candida* species, prior antibiotic administration during the same hospitalization, low serum albumin concentration, and increasing central venous catheter duration (5).

Micek and colleagues performed a retrospective cohort analysis of 355 patients with *P. aeruginosa* bloodstream infection and established that hospital mortality was statistically greater for patients receiving inappropriate initial antimicrobial treatment compared to appropriate initial treatment (30.7% versus 17.8%, p = 0.018). Multiple logistic regression analysis identified inappropriate initial antimicrobial treatment as an independent predictor for hospital mortality (22).

To decrease mortality, length of hospital stay, and cost, appropriate and effective empiric therapy should be initiated in a timely fashion. To achieve this goal in the face of increasing antimicrobial resistance, it is necessary to follow hospital and, if possible, unit-specific pathogen type and sensitivity and resistance patterns of these pathogens causing bloodstream infections. Another key to proper antibiotic selection is the patient's history of previous antibiotic therapy.

It is important to achieve a balance between the need for effective empiric antibiotic treatment and the potential risk of predisposing the patient to subsequent emergence of antibiotic-resistant infections. This goal may be achieved by early administration of effective antimicrobial treatment to patients with suspected bloodstream infections. With the availability of culture results, the antimicrobial regimen should then be rapidly tailored or discontinued.

Recommendation: The timely administration of effective empiric antimicrobial treatment in patients with suspected bloodstream infection leads to a decrease in the mortality rate, duration of hospital stay, and hospital costs. The choices in empiric antimicrobial agents should be based on knowledge of local distribution of pathogens and their resistance patterns, as well as the cause of bloodstream infection and recent administration of antimicrobial agents. This recommendation is based on the results of observational studies, as randomized control trials and withholding of treatment would not have been ethical (Grade B recommendation).

WHEN CAN I SAFELY STOP ANTIBIOTICS FOR TREATMENT OF BACTEREMIA?

There have been no randomized prospective clinical trials to guide prescribing practices in treating patients with bacteremia. Great variability exists in the treatment duration for bloodstream infections in the critically ill patient.

To have a better understanding of differences in current prescribing practices, Corona and colleagues performed a large-scale international survey by sending questionnaires to national and international intensive care societies. As expected, the responses from 254 ICUs in 34 countries revealed a wide variation in the duration of antibiotic treatment for bacteremia, ranging from short courses (≤ 5 days) of a restricted-spectrum antibiotic to long courses (≥ 10 days) of broad-spectrum antibiotics. The survey results further revealed that the greater the involvement of infectious disease specialists and/or microbiologists, the shorter the duration of therapy ($p < 0.0001$) (24).

Corona and colleagues' routine practice in their ICU at University College London Hospitals is to use short course monotherapy (five to six days) for bloodstream infections unless there was deep-seated infection present. The authors carried out a prospective observational study to assess their management policy by monitoring clinical response and relapse rate. From 84 bacteremic patients in the ICU, a total of 78 with bloodstream infections were treated with short-course monotherapy. The results demonstrated a death rate of 23.8% directly related to bloodstream infection and a satisfactory clinical response of 72%. The incidence of ICU-acquired resistant Gram-negative bacteremias (6.5%) and fungemias (3%) were low. They further observed that none of the patients discharged from the ICU developed a bacteremic relapse. They concluded that short-course antibiotic monotherapy strategy provides a satisfactory clinical response, low relapse rate, and no long-term infectious complications (25). One of the limitations of this study was that a small number of patients were involved.

In their guidelines for the management of intravascular catheter-related bloodstream infections, Mermel and colleagues state that patients with catheter-related bacteremias are to be separated into those with complicated and uncomplicated infections. They describe complicated infections as those bacteremias associated with endocarditis, osteomyelitis, possible metastatic seeding, and septic thrombosis. They recommend 10–14 days of antimicrobial therapy in uncomplicated cases of bacteremia, excluding bloodstream infections with coagulase-negative staphylococci, in which case they recommend only 5–7 days of antibiotic treatment. They further recommend four to six weeks of antibiotic therapy for complicated cases of bacteremia and in cases of persistent bacteremia or fungemia after catheter removal. In the presence of osteomyelitis, their recommendation is six to eight weeks of antimicrobial therapy. The authors state that there are no compelling data to support their specific recommendations (18).

Recommendation: Taking into consideration the cause of bacteremia and types of pathogens involved, clinicians should strive for the shortest course of antimicrobial treatment of bloodstream infections, finding a balance between successful eradication of the infecting microorganism and low relapse rate and avoidance of drug toxicity, fungemia, and development of antimicrobial resistance. Unless in the presence of complicated bloodstream infections requiring a prolonged course of antimicrobial treatment, antibiotic therapy should be stopped with the resolution of bacteremia-related clinical findings and improvement in related organ dysfunction. There is an urgent need for a large-scale randomized control trial to guide us in terms of optimal

duration of antimicrobial treatment of bloodstream infections (Grade D recommendation).

HOW CAN WE PREVENT THE OCCURRENCE OF CATHETER-RELATED BLOODSTREAM INFECTIONS?

According to the National Nosocomial Infection Surveillance (NNIS) system of the Centers for Disease Control and Prevention (CDC), the median rate of catheter-related bloodstream infections in ICUs ranges from 1.8 to 5.2 per 1,000 catheter-days (26). Many of these infections are preventable. However, measures to reduce the infections are not uniformly implemented.

O'Grady and colleagues reviewed laboratory-based studies, controlled clinical trials, prospective interventional trials, and epidemiologic investigations with the goal of updating existing evidence-based guidelines to promote strategies to prevent catheter-related bloodstream infections. They concluded that the recommended preventive strategies with the strongest supportive evidence are education and training of health care providers who insert and maintain catheters, maximal sterile barrier precautions during central venous catheter insertion, use of a 2% chlorhexidine preparation for skin antisepsis, no routine replacement of central venous catheters for prevention of infection, and use of antiseptic/antibiotic impregnated short-term central venous catheters if the rate of infection is high despite adherence to the other strategies (26).

Education-based programs are now recommended as a first line measure in the CDC guidelines for the prevention of catheter-related bloodstream infections (26). Egginman and colleagues performed a prospective cohort study to evaluate the input of an education program on catheter-related bloodstream infection rates in an 18-bed medical ICU before and after training of nurses and physicians. A total of 3,538 patients were followed. After training, they found an overall reduction rate of 75% in the occurrence of bacteremia over six years ($p < 0.0001$) (27,28).

Berenholtz et al. performed a prospective cohort study in a surgical ICU to determine whether a multifaceted systems intervention would eliminate catheter-related bloodstream infections. A quality improvement team implemented five interventions: educating the staff, creating a catheter insertion cart, asking providers daily whether catheters could be removed, implementing a checklist to ensure adherence to evidence-based guidelines for preventing catheter-related bloodstream infections, and empowering nurses to stop the catheter insertion procedure if a violation of the guidelines was observed. During the intervention time, the catheter-related bacteremia rate in the study ICU decreased from 11.3 per 1,000 catheter-days to 0 per 1,000 catheter-days. They concluded that multifaceted interventions that helped ensure adherence with evidence-based infection control guidelines nearly eliminate catheter-related bloodstream infections in their ICU (29,30).

Coopersmith and colleagues performed a pre- and postintervention observational study to evaluate the effect of an education program on decreasing catheter-related bloodstream infections in the surgical ICU. This education program was primarily directed toward registered nurses. Seventy-four primary bloodstream infections occurred in the 18 months before the intervention. After implementation

of the education module, the authors observed a 66% decrease in the rate of bloodstream infections. They concluded that educational programs can lead to a significant decrease in cost, morbidity, and mortality attributable to central venous catheterization (30,31).

Use of maximal barrier precautions during insertion of central venous catheters is a central part of the interventions to reduce the rate of catheter-related bloodstream infections and has been shown to be cost-effective (2). The only randomized trial comparing maximal sterile barriers (MSBs) with less stringent precautions was conducted by Raad et al. This prospective trial randomized 343 ambulatory oncology patients to MSB or standard precautions during central venous catheterization. The patients were followed for three months or until catheter removal. The MSB group had significantly fewer episodes of both catheter colonization (Relative Risk = 0.32, $p = 0.04$) and catheter-related bloodstream infections (RR = 0.16, $p = 0.06$). These patients were ambulatory oncology patients, and extrapolation of these findings to other types of patients should be done cautiously (32,33).

Hun and colleagues performed a cost-effectiveness analysis to determine the effective of MSB on reducing catheter-related bloodstream infections. They concluded that use of MSBs lowered cost and decreased the incidence of these infections from 5.3% to 2.8% (34).

Rigorous cleansing and disinfection of the central venous catheter insertion site with aqueous or chlorhexidine 2% has been shown to be effective in preventing central venous catheter colonization (2). Chaikunapruk and colleagues performed a meta-analysis of randomized controlled trials comparing chlorhexidine gluconate with povidone-iodine solution for catheter site care. Eight studies involving a total of 4,143 catheters met the inclusion criteria. They concluded that chlorhexidine gluconate reduced the risk for catheter-related bloodstream infections by 49% (35).

Juan-Torres and Harbarth in their overview of recent advances in prevention of primary bacteremia mention that surveillance of catheter-related bloodstream infections, monitoring rates, and reporting results to personnel are important to ensure the quality of catheter insertion and care (2). Zuscovitch et al. evaluated trends in the rates of

catheter-associated primary bloodstream infections in 84 German ICUs participating in a surveillance system. Their study showed a decrease from 2.1 to 1.5 primary bloodstream infections per 1,000 central venous catheter-days, with an overall relative reduction of 29% during the two-year observation period (37).

There is also evidence to support bundles of different measures to help decrease bacteremia rates. Pronovost and colleagues conducted a collaborative cohort studying 108 ICUs. The study intervention consisted of five evidence-based procedures: hand washing, using full barrier precautions during insertion of central venous catheters, cleaning skin with chlorhexidine, avoiding femoral site if possible, and removing unnecessary catheters. The mean rate per 1,000 catheter-days decreased from 7.7 at baseline to 1.4 at 16–18 months of follow-up ($p < 0.002$). The authors demonstrated a large and sustained reduction (66%) in rates of catheter-related bloodstream infections (38).

The efficacy of antibiotic-coated catheters has been demonstrated in many clinical trials (2). A meta-analysis by Veenstra demonstrated that central venous catheters impregnated with a combination of chlorhexidine and silver sulfadiazine appears to be effective in reducing the incidence of both catheter colonization and catheter-related bloodstream infections in patients at high risk for these infections (39). Catheters coated with silver alone and silver/platinum/carbon have no clinical proof of efficacy on infection rates contrary to devices coated with chlorhexidine/silver sulfadiazine or monocycline/rifampin (2).

Recommendation: Intravascular device-related bloodstream infections have become largely preventable. Detailed guidelines have been provided on catheter insertion and maintenance on basis of identified risk factors. The recommended preventive strategies with strongest supportive evidence are education and training of health care providers who insert and maintain catheters (Grade B recommendation), MSB precautions during catheter insertion (Grade A recommendation), use of a 2% chlorhexidine preparation for skin antisepsis (Grade A recommendation), and use of antiseptic/antibiotic-impregnated short-term central venous catheters if rate of infection is high despite adherence to other strategies (Grade A recommendation).

Level of Evidence

Subject	Year	Ref.#	Level of evidence	Strength of recommendation	Findings
Diagnosis of bacteremia	2007	13	Ib	B	Blood cultures remain the gold standard of diagnosis.
	2004	14	Ib		
Diagnosis of catheter-related bacteremia when catheter is removed	2005	17	Ib	B	Two blood cultures obtained percutaneously from a peripheral vein and a suspected catheter in addition to a semiquantitative or quantitative culture of the catheter.
	1999	19	Ic		
	1997	20	Ic		
Empiric therapy of bacteremia	2000	5	IIb	B	Early administration of effective empiric antibiotic therapy leads to a decrease in mortality rate, duration of hospital stay, and hospital costs.
	1998	21	IIb		
	2005	22	IIb		
Prevention of catheter-related bloodstream infections	2000	27	IIb	B	Recommended preventive strategies with strongest supportive evidence are:
	2002	31	IIb	A	- education and training
	1994	33	Ib	A	- maximal sterile barrier precautions
	2002	35	Ia	A	- use of 2% chlorhexidine preparation
	1999	39	Ia		- use of antiseptic/antibiotic impregnated-catheters if infection rate remains high despite adherence to other strategies
		2	Ib		
	2007				

REFERENCES

- Peters R, van Agtmael M, Danner S, et al. New developments in the diagnosis of bloodstream infections. *Lancet Infect Dis* 2004; 4: 751–60.
- Juan-Torres A, Harbarth S. Prevention of primary bacteraemia. *Int J Antimicrob Agents* 2007; 30S: S80–S87.
- Wisplinghoff H, Bischoff T, Tallent S, et al. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clin Infect Dis* 2004; 39: 309–17.
- Taylor G, Buchanan-Chell M, Kirkland T, et al. Long term trends in the occurrence of nosocomial blood stream infection. *Can J Infect Dis* 2000; 11: 29–33.
- Ibrahim E, Sherman G, Ward S, et al. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest* 2000; 118: 146–55.
- Khayr W, CarMichael M, Dubanowich C, et al. Bacteremia in veterans administration nursing home patients. *Am J Ther* 2004; 11: 251–7.
- Shorr A, Tabak Y, Killian A, et al. Healthcare-associated bloodstream infection: a distinct entity? Insights from a large U.S. database. *Crit Care Med* 2006; 34: 2588–95.
- Laupland K, Zygun D, Davies H, et al. Population-based assessment of intensive care unit-acquired bloodstream infections in adults: Incidence, risk factors, and associated mortality rate. *Crit Care Med* 2002; 30: 2462–7.
- Uckay I, Harbarth S, Pittet D, et al. Management of gram-positive bacteraemia. *Curr Opin Infect Dis* 2007; 20: 561–7.
- Minton J, Clayton J, Sandoe J, et al. Improving early management of bloodstream infection: A quality improvement project. *Br Med J* 2008; 336: 3,440–3.
- Nakamura T, Takahashi O, Matsui K, et al. Clinical prediction rules for bacteremia and in-hospital death based on clinical data at the time of blood withdrawal for culture: An evaluation of their development and use. *J Eval Clin Pract* 2005; 12: 692–703.
- Grohs P, Mainardi JL, Podglajen I, et al. Relevance of routine use of the anaerobic blood culture bottle. *J Clin Microbiol* 2007; 45: 2711–15.
- Lee A, Mirrett S, Reller B, et al. Detection of bloodstream infections in adults: how many blood cultures are needed? *J Clin Microbiol* 2007; 45: 3546–8.
- Cockerill FR, Wilson JW, Vetter EA, et al. Optimal testing parameters for blood cultures. *Clin Infect Dis* 2005; 40: 202–3.
- Murray PR, Traynor P, Hopson D. Critical assessment of blood culture techniques: Analysis of recovery of obligate and facultative anaerobes, strict aerobic bacteria, and fungi in aerobic and anaerobic blood culture bottles. *J Clin Microbiol* 1992; 30: 1462–8.
- Louie RF, Tang Z, Albertson TE, et al. Multiplex polymerase chain reaction detection enhancement of bacteremia and fungemia. *Crit Care Med* 2008; 36: 1487–92.
- Safdar N, Fine JP, Maki DG, et al. Meta-analysis: Methods for diagnosing intravascular device-related bloodstream infection. *Ann Intern Med* 2005; 142: 451–66.
- Mermel LA, Farr BM, Sherertz RJ, et al. Guidelines for the management of intravascular catheter-related infections. *Clin Infect Dis* 2001; 32: 1249–72.
- DesJardin JA, Falagas ME, Ruthazer R, et al. Clinical utility of blood cultures drawn from indwelling central venous catheters in hospitalized patients with cancer. *Ann Intern Med* 1999; 131: 614–47.
- Sherertz RJ, Heard SO, Raad II. Diagnosis of triple lumen catheter infection: Comparison of roll plate, sonication, and flushing methodologies. *J Clin Microbiol* 1997; 35: 641–6.
- Leibovici L, Shraga I, Drucker M, et al. The benefit of appropriate empirical antibiotic treatment in patients with bloodstream infection. *J Int Med* 1998; 244: 379–86.
- Micek ST, Lloyd AE, Ritchie DJ, et al. *Pseudomonas aeruginosa* bloodstream infection: Importance of appropriate initial antimicrobial treatment. *Antimicrob Agents Chemother* 2005; 49: 1306–11.
- Zaragoza R, Artero A, Camarena JJ, et al. The influence of inadequate empirical antimicrobial treatment on patients with bloodstream infections in an intensive care unit. *Clin Microbiol Infect* 2003; 9: 412–18.
- Corona A, Bertolini G, Ricotta AM, et al. Variability of treatment duration for bacteraemia in the critically ill: A multinational survey. *J Antimicrob Chemother* 2003; 52: 849–52.
- Corona A, Wilson APR, Grassi M, et al. Short-course monotherapy strategy for treating bacteremia in the critically ill. *Minerva Anestesiol* 2006; 72: 841–57.
- O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 2002; 23: 759–69.
- Eggimann P, Harbarth S, Constantin MN, et al. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet* 2000; 355: 1864–8.
- Eggimann P, Hugonnet S, Sax H, et al. Long-term reduction of vascular access-associated bloodstream infection. *Ann Intern Med* 2005; 142: 875–6.
- Berenholtz S, Pronovost P, Lipsett P, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004; 32: 2014–20.
- Gastmeier P, Geffers C. Prevention of catheter-related bloodstream infections: analysis of studies published between 2002 and 2005. *J Hosp Infect* 2006; 64: 326–35.
- Coopersmith C, Rebmann T, Zack J, et al. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. *Crit Care Med* 2002; 30: 59–64.
- Hu KK, Lipsky BA, Veenstra DL, et al. Using maximal sterile barriers to prevent central venous catheter-related infection: a systematic evidence-based review. *Am J Infect Control* 2004; 32: 142–6.
- Raad II, Hohn DC, Gilbreath BJ, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994; 15: 231–8.
- Hu KK, Veenstra DL, Lipsky BA, et al. Use of maximal sterile barriers during central venous catheter insertion: clinical and economic outcomes. *Clin Infect Dis* 2004; 39: 1441–5.
- Chaiyakunapruk N, Veenstra DL, Lipsky BA, et al. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002; 136: 792–801.
- Deshpande K, Hatem C, Ulrich H, et al. The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Crit Care Med* 2005; 33: 13–20.
- Zuschneid I, Schwab F, Geffers C, et al. Reducing central venous catheter-associated primary bloodstream infections in intensive care units is possible: data from the German nosocomial infection surveillance system. *Infect Control Hosp Epidemiol* 2003; 24: 501–5.
- Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006; 355: 2725–32.
- Veenstra DL, Saint S, Saha S, et al. Efficacy of antiseptic-impregnated central venous catheters in preventing catheter-related bloodstream infection. *JAMA* 1999; 281: 261–7.

Prevention of Central Venous Catheter Infections

J. Matthias Walz and Stephen O. Heard

Strategies to Reduce Catheter Infections		
Question	Answer	Grade
What is the best method and site to insert intravascular catheters?	Use of the subclavian site, chlorhexidine skin prep solutions, and maximum barrier precautions.	B, A, A
Is education useful in preventing CRBSI?	Education programs reduce the risk of CRBSI.	B
What other behavioral interventions are helpful in preventing or reducing CRBSI?	Multimodal intervention programs that encompass education and process reduce the incidence of CRBSI.	B
How long should catheters remain <i>in situ</i> ?	Catheters should not be changed on a scheduled basis but should be removed when no longer needed, when they are suspected of causing infection, or when they are not functional.	B
Should anti-infective catheters be used?	Anti-infective catheters should be used if the rate of CRBSI remains high despite the use of best practices to prevent CRBSI.	A
Do anti-infective catheters promote antibiotic resistance?	Anti-infective catheters do not promote antibiotic resistance.	B
Abbreviations: CRBSI, catheter-related bloodstream infection.		

Despite improvements in the prevention of catheter-related bloodstream infection (CRBSI) in the past decade, they still remain a significant problem. Approximately 250,000 cases of CRBSI occur per year in U.S. hospitals, and 80,000 of these cases occur in the intensive care unit (ICU) (1). Although the attributable mortality associated with CRBSI remains a matter of debate, the morbidity is high and the economic costs are profound (1). Consequently, it is very important to prevent CRBSI. Over the past 20 years, there has been a plethora of investigations examining ways to prevent CRBSI. In this chapter, we review and grade the evidence for a variety of strategies to prevent central venous catheter infection.

WHAT IS THE BEST METHOD AND SITE TO INSERT INTRAVASCULAR CATHETERS?

A significant amount of research has focused on these issues. A number of randomized prospective trials and observational studies support the notion that use of the femoral insertion site is associated with a higher risk of catheter colonization and CRBSI compared to the jugular and subclavian sites. Merrer et al. (2) randomized ICU patients to receive either a femoral or subclavian central venous catheter (CVC). At the time of removal, catheters were cultured using a quantitative broth dilution technique. The authors found that the femoral catheters had a much

higher rate of significant colonization compared to the CVCs in the subclavian position. Furthermore, there was a trend toward a higher rate of CRBSI in the femoral catheter group. The majority of (but not all) prospective observational studies have corroborated these findings (3,4). The subclavian site of insertion appears to be associated with a lower risk of colonization (if not infection) compared to the internal jugular site. In a prospective observational study, Nagashima et al. observed a twofold increase in CRBSI when catheters were inserted in the internal jugular vein compared to the subclavian vein (3). Randomized, prospective studies evaluating the effectiveness of anti-infective catheters have shown that the subclavian insertion site is associated with the lowest rate of significant catheter colonization (5,6). Thus, the preponderance of data supports the use of the subclavian site for catheter insertion.

Skin antisepsis is an important component of preparation for catheter insertion and maintenance. Many studies have compared a variety of skin antiseptics, most notably 10% povidone-iodine, 70% isopropyl alcohol, and 2% aqueous chlorhexidine, and the majority of them have demonstrated that the aqueous or alcoholic chlorhexidine solutions are superior in reducing significant catheter colonization. In a meta-analysis of eight randomized controlled trials evaluating the effectiveness of chlorhexidine solutions compared to povidone-iodine solutions in preventing significant catheter colonization and CRBSI, Chaiyukaunlapruk et al. (7)

found that the chlorhexidine solutions were the superior skin antiseptic agents. In a follow-up study, the authors found that the use of a chlorhexidine skin prep resulted in an economic savings of \$113 per catheter (8).

Maintenance of sterility during insertion of the catheter is extremely important in preventing catheter infection. Most clinicians in the 1980s and early 1990s wore only sterile gloves and used a small drape when inserting CVCs. In a randomized, controlled trial in cancer patients undergoing central venous catheterization, Raad et al. demonstrated conclusively that the use of maximum barrier precautions reduces the incidence of CRBSI (9). Other observational studies have supported these findings (10).

Recommendations: The subclavian site is the preferred site for catheter insertion (Grade B). An aqueous or alcoholic chlorhexidine solution is the preferred skin antiseptic prior to catheter insertion and during catheter maintenance (Grade A). Maximum barrier precautions (cap, mask, sterile gown and gloves, and a sterile drape that completely covers the patient) should be used during catheter insertion (Grade A).

IS EDUCATION USEFUL IN PREVENTING CRBSI?

Studies have demonstrated that catheterization by less experienced providers is associated with a higher risk of infection (11). The presumption around these observations was that it was the *technical skill* of the provider performing the task rather than the *knowledge* about basic infection control practices that was important in the development of infection. Sherertz et al. demonstrated that an education program that consisted of a didactic program and a “hands-on” demonstration of insertion of both arterial and central venous catheters and offered to beginning PGY-1 physicians resulted in a steady and significant reduction in catheter-related and primary bloodstream infections (per 1,000 patient days) over time. Other investigators have expanded the scope of infection control and best practices education. Coopersmith et al. (12) and Warren et al. (13) have used a focused educational initiative that includes not only interns but also ICU nurses, residents, and attending physicians. The educational aspect consisted of a 10-page self-study module with a pre- and post-test. When the educational program was implemented, a sustained reduction in CRBSI was documented in both surgical and medical ICUs. Similar educational programs have achieved success in nonteaching, community hospitals (14).

Recommendations: An education program for all staff including nurses, physicians, and physician extenders will reduce the risk of CRBSI (Grade B).

WHAT OTHER BEHAVIORAL INTERVENTIONS ARE HELPFUL IN PREVENTING OR REDUCING CRBSI?

Although educational programs are helpful in reducing CRBSI, compliance to the principles enumerated in the initiatives may wane over time. Eighteen months after initiation of an education program, Coopersmith et al. (15) audited the compliance in their surgical ICU with the best practice principles to reduce CRBSI. They discovered that hand hygiene before catheter insertion was poor: only 17%

of providers washed their hands prior catheter insertion, and a large sterile drape was used only in 50% of insertions. Subsequently, they posted pictures of every step of catheter insertion (aimed at physicians) and maintenance (aimed at nurses) at the bedside, throughout the ICU, and in the orientation manuals of the residents. In addition to the previously mentioned written educational modules, yearly lectures were given to the nurses and monthly lectures to the residents as they rotated into the ICU. Despite these interventions, hand hygiene before catheter insertion increased to only 30%, and use of a large sterile drape during the procedure increased to 80%. The authors observed an insignificant reduction in rates of CRBSI, from 3.4/1,000 catheter-days to 2.8/1,000 catheter-days. This study highlights the difficulty with adherence to best practice principles.

In contrast, Berenholtz et al. (16) used a somewhat different intervention model to prevent CRBSI. Their intervention consisted of five parts: (1) a Web-based education program (preinsertion hand hygiene, use of chlorhexidine skin preparation, full barrier precautions during insertion, the use of the subclavian vein as the preferred insertion site, maintenance of sterile field during catheter placement, and the proper care of the catheter after placement) and test that all physicians or physician extenders were required to take before they could insert CVCs; (2) creation of a CVC insertion cart where all necessary equipment and supplies were readily available; (3) use of a daily checklist during patient rounds where the need for central venous catheterization was questioned; (4) use of a checklist by the bedside nurse during insertion of a CVC to ensure compliance to best practices; and (5) empowering nurses to stop procedures if the guidelines were not followed. The control ICU was one in which only an institutional educational initiative was used to increase provider awareness about evidence-based infection control practices for catheter insertion and maintenance. The authors found that their program resulted in sustained reductions in CRBSI.

The results of Berenholtz and colleagues have been replicated in other studies. Most recently, Pronovost et al. (17) demonstrated that an interventional program very similar to the one described by Berenholtz et al. and applied to 108 ICUs in the state of Michigan resulted in a sustained reduction in CRBSI for up to 18 months. Incidence rate ratios of CRBSI decreased continuously from 0.62 at the 0–3 -month time interval to 0.34 at the 16–18-month interval.

Recommendations: Use of “catheter bundles” or multimodal interventional programs will reduce the incidence of CRBSI (Grade B).

HOW LONG SHOULD CATHETERS REMAIN IN SITU?

Numerous observational studies have demonstrated that the risk of significant catheter colonization or CRBSI increases with the duration of catheterization. These data led to the hypothesis that scheduled changes of catheters, either by insertion at a new site or changing over a guidewire, would reduce the risk of infection. Small, relatively underpowered studies (18–20) of CVCs, peripheral arterial catheters, and pulmonary artery catheters demonstrated that routine changes irrespective of method did not result

in a reduction of infection. Cook et al. (21) performed a meta-analysis of 12 prospective randomized trials evaluating this question and determined that scheduled changes were associated with a higher risk of catheter colonization. Furthermore, there was a trend toward a higher risk of CRBSI when guidewire exchange was used. Based on these data, scheduled changes of CVCs cannot be recommended, and guidewire exchanges should be avoided unless the risk for mechanical complications associated with the insertion of CVC at a new site exceeds the risk of infectious complications associated with a guidewire change.

Recommendations: Catheters should not be routinely changed. If the catheter needs to be changed, a new insertion site should be used (Grade B).

SHOULD ANTI-INFECTIVE CATHETERS BE USED?

Three commercial anti-infective catheters are available with different protective coatings or impregnated materials: (1) chlorhexidine and silver sulfadiazine (CH-SS); (2) minocycline-rifampin (MR); and (3) silver in a carbon/platinum (SPC) matrix.

Raad et al. (22) and Darouiche et al. (23) compared the MR catheters to uncoated catheters and first-generation CH-SS, respectively, and demonstrated a significant reduction in CRBSI in the MR catheter group.

A second-generation CH-SS catheter has subsequently been introduced with more chlorhexidine present on the catheter surface as well as coating of the catheter lumen. Recent large, randomized controlled trials comparing second-generation CH-SS catheters to uncoated catheters have failed to demonstrate any efficacy in reducing CRBSI (24,25).

Several recent randomized controlled trials (5,26,27) have evaluated the effectiveness of the SPC catheter against uncoated catheters. In general, catheter colonization is significantly reduced when the SPC catheters are used. In one study, the rate of CRBSI was significantly reduced when the anti-infective catheter was used (26). One large prospective randomized study (28) has been performed that compared the SPC catheter to the MR catheter. There was a trend toward reduced colonization in the MR catheter group, but overall there was no difference in the rate of CRBSI between the two groups.

Because focused education and behavior modification programs reduce the risk of CRBSI, the use of anti-infective catheters may be ineffective in ICUs where the rate of CRBSI is low. Many of the negative randomized, prospective controlled trials cited used best practices during the conduct of the study. Such practices may explain why no difference was noted in CRBSI rates. Further support for this notion comes from an observational study by Schuerer et al. (29) where they examined CRBSI rates before and after the introduction of second-generation CH-SS catheters in their ICU. An education program to reduce the risk of CRBSI was in place during the entire study. The authors found that there was no significant difference in CRBSI between the control period when uncoated catheters were used (3.3/1,000 catheter-days) and the intervention period when the anti-infective catheters were used (2.1/1,000 catheter-days).

Recommendations: In summary, the anti-infective catheters appear to be efficacious in preventing significant catheter colonization, which is often used as a proxy for efficacy. In ICUs where the rate of CRBSI is high, they also reduce the risk of CRBSI (Grade A).

DO ANTI-INFECTIVE CATHETERS PROMOTE ANTIBIOTIC RESISTANCE?

With the availability of anti-infective catheters, fears about the development of antiseptic or antibiotic resistance when these catheters are used (particularly the antimicrobial-impregnated catheters) persist. However, the preponderance of data suggests that resistance to either antiseptic or antibiotic combinations does not occur. For the CH-SS catheters, randomized prospective trials (24,25,30) and observational studies suggest that these catheters do not promote antiseptic resistance. Furthermore, following a cluster of coagulase-negative Staphylococcus (CNS) CRBSIs after the introduction of CH-SS CVCs, Rosato et al. (31) did not observe any resistance of the CNS isolates to the antiseptic combination *in vitro*.

In vitro studies of the MR catheters suggest that bacterial resistance does not develop (32,33), but small increases in the minimum inhibitory concentration of the bacterial combination may occur with *S. epidermidis* (34). Randomized controlled trials have not demonstrated the development of bacterial resistance to minocycline or rifampin (22,23). One prospective observational study demonstrated that when the catheter was introduced in an ICU, there was a significant decrease in nosocomial and multidrug-resistant bacteremias. Last, in a retrospective cohort study of the use of the MR catheter in patients hospitalized for leukemia or bone marrow transplantation, Chatzinikolaou et al. (35) demonstrated no change in the susceptibility patterns of staphylococci to either antibiotic over a four-year period when compared to a baseline time period.

Recommendations: The use of anti-infective catheters does not promote bacterial resistance to either CH-SS or MR (Grade B).

REFERENCES

1. Raad I, Hanna H, Maki D. Intravascular catheter-related infections: Advances in diagnosis, prevention, and management. *Lancet Infect Dis* 2007; 7: 645–57.
2. Merrer J, De Jonghe B, Golliot F, et al. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA* 2001; 286: 700–7.
3. Nagashima G, Kikuchi T, Tsuyuzaki H, et al. To reduce catheter-related bloodstream infections: is the subclavian route better than the jugular route for central venous catheterization? *J Infect Chemother* 2006; 12: 363–5.
4. Deshpande KS, Hatem C, Ulrich HL, et al. The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Crit Care Med* 2005; 33: 13–20; discussion 234–5.
5. Moretti EW, Ofstead CL, Kristy RM, et al. Impact of central venous catheter type and methods on catheter-related colonization and bacteraemia. *J Hosp Infect* 2005; 61: 139–45.

6. Heard SO, Wagle M, Vijayakumar E, et al. Influence of triple-lumen central venous catheters coated with chlorhexidine and silver sulfadiazine on the incidence of catheter-related bacteremia. *Arch Intern Med* 1998; 158: 81–7.
7. Chaiyakunapruk N, Veenstra DL, Lipsky BA, et al. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002; 136: 792–801.
8. Chaiyakunapruk N, Veenstra DL, Lipsky BA, et al. Vascular catheter site care: The clinical and economic benefits of chlorhexidine gluconate compared with povidone iodine. *Clin Infect Dis* 2003; 37: 764–71.
9. Raad II, Hohn DC, Gilbreath BJ, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994; 15: 231–8.
10. Carrer S, Bocchi A, Bortolotti M, et al. Effect of different sterile barrier precautions and central venous catheter dressing on the skin colonization around the insertion site. *Minerva Anestesiol* 2005; 71: 197–206.
11. Armstrong CW, Mayhall CG, Miller KB, et al. Prospective study of catheter replacement and other risk factors for infection of hyperalimentation catheters. *J Infect Dis* 1986; 154: 808–16.
12. Cooper DJ, Myles PS, McDermott FT, et al. Prehospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trial. *JAMA* 2004; 291: 1350–7.
13. Warren DKM, Zack JER, Cox MJM, et al. An educational intervention to prevent catheter-associated bloodstream infections in a nonteaching, community medical center. *Crit Care Med* 2003; 31: 1959–63.
14. Warren DK, Zack JE, Elward AM, et al. Nosocomial primary bloodstream infections in intensive care unit patients in a nonteaching community medical center: a 21-month prospective study. *Clin Infect Dis* 2001; 33: 1329–35.
15. Coopersmith CM, Zack JE, Ward MR, et al. The impact of bedside behavior on catheter-related bacteremia in the intensive care unit. *Arch Surg* 2004; 139: 131–6.
16. Berenholtz SM, Pronovost PJ, Lipsett PA, et al. Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004; 32: 2014–20.
17. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006; 355: 2725–32.
18. Powell C, Kudsk KA, Kulich PA, et al. Effect of frequent guidewire changes on triple-lumen catheter sepsis. *J Parenter Enteral Nutr* 1988; 12: 462–4.
19. Eyer S, Brummitt C, Crossley K, et al. Catheter-related sepsis: prospective, randomized study of three methods of long-term catheter maintenance. *Crit Care Med* 1990; 18: 1073–9.
20. Cobb DK, High KP, Sawyer RG, et al. A controlled trial of scheduled replacement of central venous and pulmonary-artery catheters. *N Engl J Med* 1992; 327: 1062–8.
21. Cook D, Randolph A, Kernerman P, et al. Central venous catheter replacement strategies: a systematic review of the literature. *Crit Care Med* 1997; 25: 1417–24.
22. Raad I, Darouiche R, Dupuis J, et al. Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections. A randomized, double-blind trial. The Texas Medical Center Catheter Study Group. *Ann Intern Med* 1997; 127: 267–74.
23. Darouiche RO, Raad II, Heard SO, et al. A comparison of two antimicrobial-impregnated central venous catheters. Catheter Study Group. *N Engl J Med* 1999; 340: 1–8.
24. Brun-Buisson C, Doyon F, Sollet JP, et al. Prevention of intravascular catheter-related infection with newer chlorhexidine-silver sulfadiazine-coated catheters: a randomized controlled trial. *Intensive Care Med* 2004; 30: 837–43.
25. Rupp ME, Lisco SJ, Lipsett PA, et al. Effect of a second-generation venous catheter impregnated with chlorhexidine and silver sulfadiazine on central catheter-related infections: a randomized, controlled trial. *Ann Intern Med* 2005; 143: 570–80.
26. Corral L, Nolla-Salas M, Ibanez-Nolla J, et al. A prospective, randomized study in critically ill patients using the Oligon Vantex catheter. *J Hosp Infect* 2003; 55: 212–19.
27. Ranucci M, Isgro G, Giomarelli PP, et al. Impact of oligon central venous catheters on catheter colonization and catheter-related bloodstream infection. *Crit Care Med* 2003; 31: 52–9.
28. Fraenkel D, Rickard C, Thomas P, et al. A prospective, randomized trial of rifampicin-minocycline-coated and silver-platinum-carbon-impregnated central venous catheters. *Crit Care Med* 2006; 34: 668–75.
29. Schuerer DJ, Zack JE, Thomas J, et al. Effect of chlorhexidine/silver sulfadiazine-impregnated central venous catheters in an intensive care unit with a low blood stream infection rate after implementation of an educational program: a before-after trial. *Surg Infect (Larchmt)* 2007; 8: 445–54.
30. Maki DG, Stolz SM, Wheeler S, et al. Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. A randomized, controlled trial. *Ann Intern Med* 1997; 127: 257–66.
31. Rosato AE, Tallent SM, Edmond MB, et al. Susceptibility of coagulase-negative staphylococcal nosocomial bloodstream isolates to the chlorhexidine/silver sulfadiazine-impregnated central venous catheter. *Am J Infect Control* 2004; 32: 486–38.
32. Aslam S, Darouiche RO. Prolonged bacterial exposure to minocycline/rifampicin-impregnated vascular catheters does not affect antimicrobial activity of catheters. *J Antimicrob Chemother* 2007; 60: 148–51.
33. Munson EL, Heard SO, Doern GV. In vitro exposure of bacteria to antimicrobial impregnated-central venous catheters does not directly lead to the emergence of antimicrobial resistance. *Chest* 2004; 126: 1628–35.
34. Sampath LA, Tambe SM, Modak SM. In vitro and in vivo efficacy of catheters impregnated with antiseptics or antibiotics: evaluation of the risk of bacterial resistance to the antimicrobials in the catheters. *Infect Control Hosp Epidemiol* 2001; 22: 640–6.
35. Chatzinikolaou I, Hanna H, Graviss L, et al. Clinical experience with minocycline and rifampin-impregnated central venous catheters in bone marrow transplantation recipients: efficacy and low risk of developing staphylococcal resistance. *Infect Control Hosp Epidemiol* 2003; 24: 961–3.

Ventilator-Associated Pneumonia

Aaron M. Fields

Clinical Questions		
Question	Answer	Grade of recommendation
Are invasive methods better for diagnosing VAP?	Invasive methods of diagnosing VAP are no better than noninvasive methods and are much less expensive.	A
What are the modifiable risk factors for VAP?	The use of closed suction systems, ETT with subglottic suctioning ports, PUC and silver coating, new water bath-type humidifiers, and the semi-recumbent position all decrease the rates of VAP.	A
How should antibiotics be used to treat VAP?	Empiric coverage should be broad and nearly always includes more than one drug. Studies have not demonstrated any advantage to double-covering any microbe after speciation including <i>Pseudomonas</i> . Vancomycin is as effective as linezolid. Antibiotics should be given for no more than 8 days.	A
Does timing of tracheotomy change outcomes in patients with VAP?	Yes, early tracheostomy should be performed.	B
What is the epidemiology of VAP?	Rates of VAP are between 20% and 71% with wide variability based on patient population. Rates of VAP increase as time of intubation accumulates.	B
What is the best method to assess and tailor treatment for VAP?	Antibiotics can be stopped when clinical signs of infection have resolved.	B
Abbreviations: ETT, endotracheal tube; PUC, polyurethane cuff; VAP, ventilator-associated pneumonia.		

ARE INVASIVE METHODS BETTER FOR DIAGNOSING VENTILATOR-ASSOCIATED PNEUMONIA?

The concept that tracheal aspirate is as good as bronchoalveolar lavage (BAL) is not new. In 1998, Sanchez-Nieto and colleagues (1) performed a pilot study of 51 patients. They were randomized to invasive or noninvasive groups. The invasive group received a bronchoscopy with protected brush specimen collection and BAL plus tracheal aspirate. The noninvasive group received only tracheal aspirate. In this small, single-center study, the authors found no difference in mortality, length of mechanical ventilation, or stay in the intensive care unit (ICU). In their conclusion, they called for larger trials.

In 2000, three studies were published that responded to this call. Sole Violan et al. (2) randomized 91 patients at a single institution to either invasive or noninvasive diagnosis of ventilator-associated pneumonia (VAP). The patients in the invasive group received bronchoscopy with either a protected brush or BAL. Tracheal aspiration was performed in the noninvasive group. Once again, they found no difference in mortality, length of mechanical ventilation, or length of stay in the ICU.

Ruiz and colleagues (3) randomized 76 patients at a single center to invasive or noninvasive groups. There was no difference in length of mechanical ventilation or ICU stay. They were also unable to show a difference in 30-day mortality. They were able to show a statistical difference in cost: ~US\$30 for noninvasive, and ~US\$370 for invasive testing ($p < 0.0001$).

In contrast, Fagon et al. (4) were able to demonstrate outcome differences between invasive and noninvasive techniques. Theirs was a multicenter trial that enrolled 413 patients. At 28 days, there was no difference in organ failure, length of mechanical ventilation, length of ICU stay, or mortality. They were able to show more antibiotic-free days in the invasive group.

Finally, in 2006 the Canadian Critical Care Trials Group (5) performed a randomized controlled trial in which they obtained samples for the diagnosis of VAP using either noninvasive tracheal aspirate or BAL. This large study of 740 patients was performed at 28 institutions. There were no differences in the primary outcome, which was 28-day mortality. Additionally, there were no differences in targeted therapy, days alive without antibiotics, or length of ICU or hospital stay.

Answer: invasive methods of diagnosing VAP are no better than noninvasive methods and are much less expensive. Grade of recommendation: A.

WHAT ARE THE MODIFIABLE RISK FACTORS FOR VAP?

The use of closed versus open suctioning systems has been identified as a potentially modifiable risk factor for developing VAP. Several studies have examined their use. In 2005, Lorente et al. (6) randomized 443 patients to open suction versus closed suction changed daily. They showed no difference in incidence of VAP but a higher cost associated with the closed system. The same group in 2006 (7) showed that in patients intubated longer than four days and their systems changed only when clinically indicated, the closed loop systems became less expensive, although, they were still unable to change the incidence of VAP.

Topeli et al. (8) conducted a randomized controlled trial examining the use of closed versus open systems in 78 patients. Though they found increased rates of colonization of ventilator tubing in the closed suction group, there was no difference in mortality, rate of VAP, length of ICU stay, or length of hospital stay. Other smaller studies have reached the same conclusions (9,10).

Recommendation: Closed suction systems should be used in all intubated patients. Multiple small studies failed to find a difference in rates of VAP using a closed suction system. However, over time, these systems are less expensive and expose health care workers to fewer secretions. Closed loop systems should not be changed daily.

Endotracheal Tube Attributes

Continuous subglottic suctioning was shown to decrease the incidence of all types of VAP by Vallés and colleagues (11) in a randomized controlled trial of 190 patients [relative risk (RR) 1.98, $p < 0.03$]. Mahul et al. (12) conducted a two by two randomized study using endotracheal tube (ETT) with and without subglottic suctioning, and patients were randomized to antacids or sucralfate. They were able to show a statistically significant reduction in pneumonia (29.1% versus 12.8%, $p < 0.05$). Additionally, the pneumonia that occurred in the subglottic suctioning group was much later than in the regular ETT group (8 days versus 16 days). The use of sucralfate versus antacids failed to show any difference in rates of VAP. Kollef et al. (13) showed that using continuous subglottic secretions in cardiac patients did not change the rate of VAP, but did decrease the incidence of early VAP.

Subglottic suction was shown to be offer statistically significant protection in 150 general ICU intubated patients by Smulders et al. (14) (RR 0.22, $p = 0.014$). Mortality, length of ICU stay, length of hospital stay, length of mechanical ventilation were all not statistically changed by the use of the subglottic suctioning device.

Metz and colleagues (15) investigated whether lavage of the pharynx and the subglottic area decreased the rates of VAP. They found that large-volume pharyngeal lavage reduced the bacterial counts briefly in the subglottic area but led to a slightly higher incidence of VAP. Lavage of the subglottic area offered no advantage over simple suctioning of the subglottic port.

Lorente (16) randomized 280 patients to receive a standard ETT or a tube with both a polyurethane cuff

(PUC) and a subglottic suctioning channel that was placed to suction intermittently. They showed a statistically significant decrease in the development of both early and late VAP [hazardous ratio (HR) 3.3, $p < 0.001$]. Unfortunately, at the time of this writing, this type of tube is not available in the United States. However, standard ETT with a PUC is available and was used by Poelaert and colleagues (17) in a small randomized study of 134 patients. They were able to show a statistically significant protective effect using the PUC ETT.

Silver-coated ETT tubes were shown to reduce bacterial colonization and burden in intubated patients in a pilot study by Rello and colleagues in 2006 (18). Further studies are needed to elucidate whether this has effects on VAP and other outcome measurements.

Recommendation: ETT with subglottic suctioning ports reduce the incidence of VAP and should be used in anyone anticipated needing invasive ventilation for >48 hours.

Heat and Moisture-inducing Devices

Gases entering the nose are warmed and humidified before reaching the lungs. Endotracheal intubation removes this protective barrier. Attempts to overcome the drying effects of the tubes have included heat and moisture exchangers (HMEs), and heated water baths, which include a wire in the circuit to prevent condensation. Both are efficacious in preventing tracheal mucosa and desiccation. Multiple studies have examined if either are associated with an increased risk of VAP. Most recently, Boots et al. (19) showed that the rate of VAP was the same for both types of heater/moisturizer systems. Three hundred eighty-one patients were randomized to either hot water bath with circuit wires or HME with viral and bacterial filters. There was no difference in rates of VAP in the groups. HMEs were shown to have a higher resistance over time. Other studies have failed to show a difference in VAP rates (20–24).

Lorente et al. in 2006 (25) showed that a modern hot water bath was protective for VAP when compared to HME. They acknowledged the fact that their findings were contradictory to previous studies showing no difference in HME and the hot water bath. They attributed this to the fact that the hot water bath they used was able to deliver higher partial pressures of water and the ability to refill its reservoir without opening it.

Recommendation: Newer water bath humidifiers should be used whenever possible. However, HMEs are a suitable alternative.

Semi-Recumbent Position

The semi-recumbent position received considerable attention after a study by Drakulovic and colleagues (26) was stopped early due to an early clinically and statistically significant decrease in VAP rates among patients in the semi-recumbent position. The rate decreased from 11/47 (23%) to 2/39 (5%) where $p = 0.018$. Some critics of this study felt that supine position was not the standard of care at the time. In answer to these questions, van Nieuwenhoven et al. (27) randomized 221 patients to standard of care (which turned out to be 10°) versus treatment, which was 45°. They were unable to achieve 45°, and succeeded in only able to reach 28° in the treatment group. However, no differences were found between the groups.

Recommendation: Avoid the supine position in intubated patients. It may not be possible to achieve 45° elevation, but some elevation should be attempted.

Answer: The use of closed suction systems, ETT with subglottic suctioning ports, PUC and silver coating, new water bath-type humidifiers, and the semi-recumbent position all decrease the rates of VAP. Grade of recommendation: A

HOW SHOULD ANTIBIOTICS BE USED TO TREAT VAP?

Empiric coverage is defined as antibiotic coverage for VAP prior to having culture results. Only one randomized study was found regarding empiric versus late antibiotic coverage. The 2003 study by Baker et al. (28) randomized 98 trauma patients to empiric coverage or beginning antibiotic coverage after having invasively obtained samples (BAL). They found a trend toward decreased hospital costs associated with late antibiotic usage.

Alvarez-Lerma (29) conducted a prospective nonrandomized observational study of 16,872 ICU patients. They found that mortality was 24.7% in those whose initial coverage was inadequate, but only 16.2% in those who received adequate empiric antibiotic coverage for VAP ($p = 0.034$).

Luna et al. (30) performed an observational study using BAL to diagnose VAP. When patients had received appropriate antibiotics early in their VAP course (i.e., before bronchoscopy), their mortality was 37%. However, if this therapy was inadequate, their mortality was 91% ($p < 0.001$).

Another nonrandomized trial examining the timing of antibiotics was performed by Iregui et al. (31). They showed that mortality from VAP was significantly increased if appropriate antibiotics were given more than 24 hours after diagnostic criteria were met [odds ratio (OR) 7.68, $p < 0.001$].

Mortality benefit may be attributed to prescribing antibiotic coverage to which the pathogen is sensitive. Kollef and Ward (32) performed a cohort study using mini-BAL. They showed that VAP due to a pathogen resistant to the empiric antibiotics led to an increased mortality (OR 3.28, $p < 0.006$).

Similar findings were demonstrated in trauma patients by Mueller et al. (33). Many of their patients had multiple instances of VAP. They demonstrated that mortality increased as the number of times that each patient received inadequate empiric coverage. Mortality increased from 3.6% for no episodes, 8.8% for one episode, and 45% for more than one episode ($p < 0.001$).

In 2008, Heyland et al. (34) showed in a subgroup of patients who had *Pseudomonas* randomized to either monotherapy with meropenem or dual coverage with meropenem plus ciprofloxacin that those with double empiric coverage had a higher rate of adequate initial coverage (18.8% versus 84.2%, $p < 0.001$).

Recommendations: When clinical diagnosis of VAP is met, broad-spectrum antibiotics (multiple) should be given without delay. Attempts to elucidate speciation and sensitivity should be made as soon as possible.

Double Coverage?

Damas et al. (35) showed that in patients diagnosed with pneumonia who were given adequate empiric coverage with

a single agent, there was no benefit to other antibiotics for double coverage or synergy.

Rubinstein et al. (36) prospectively randomized patients with many types of infections, including *Pseudomonas*, to either ceftazidime monotherapy or ceftriaxone/tobramycin. Those with *Pseudomonas* had the same mortality despite monotherapy. There was no increased incidence of resistance or superinfection in those treated with a single agent.

Recommendation: After speciation and sensitivities are proven, antibiotics should be tailored and monotherapy should be continued.

Linezolid versus Vancomycin for MRSA Pneumonia

Rubinstein and colleagues (37) conducted a prospective randomized controlled trial comparing linezolid and vancomycin for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia. Although there was a trend toward linezolid causing increased cure rates, no statistically significant differences were found between the two groups.

Wunderink et al. (38) conducted an additional RCT using the same agents in patients with pneumonia. Again, no statistically significant differences were found in the two groups. There were also no differences in drug-related adverse events between the two groups.

Most recently, Kohno et al. (39) evaluated the use of these two agents in a randomized controlled trial in patients with several types of MRSA infections. They found no statistically significant differences in clinical outcomes. They did find that diagnoses of thrombocytopenia were less in patients treated with linezolid.

Recommendation: Unless there is a concern for thrombocytopenia, vancomycin should be the empiric and treatment of choice for MRSA pneumonia.

Length of Treatment

Chastre et al. (40) compared 8 days versus 15 days of treatment with antibiotics for pneumonia. There was no difference in mortality between the groups, including those with *Pseudomonas*. They found a higher incidence of recurrence in those with *Pseudomonas* and less total antibiotic use in those treated for eight days. Finally, they found decreased incidence of resistance in the group treated for eight days.

Answer: Empiric coverage should be broad and nearly always includes more than one drug. Studies have not demonstrated any advantage to double covering any microbe after speciation including *Pseudomonas*. Vancomycin is as effective as linezolid. Antibiotics should be given for no more than eight days. Grade of recommendation: A.

DOES TIMING OF TRACHEOTOMY CHANGE OUTCOMES IN PATIENTS WITH VAP?

Rumbak et al. (41) conducted a prospective, randomized, multicenter, controlled trial evaluating the timing of percutaneous tracheotomy versus long-term endotracheal intubation in 120 patients. The patient population was limited to those anticipated needing longer than 14 days of mechanical ventilation. Patients randomized to early tracheotomy had the procedure performed during the first

48 hours of their intubation. They found that mortality, pneumonia, and accidental extubation were all reduced in the early tracheotomy group. Length of ICU stay and mechanical ventilation were also reduced. Finally, damage to the mouth and larynx were significantly less in the early tracheotomy group. Lower mortality rates were attributed to fewer diagnoses of pneumonia and less need for sedation.

In contrast, Boudierka et al. (42) found that in head-injured patients, no difference in frequency of pneumonia or mortality. They did, however, find a shorter length of mechanical ventilation in the early tracheostomy group. This study included only 62 patients at a single center.

Several other studies were examined but were felt to offer little evidence in support or rebuttal of early tracheostomy. In 1990, Rodriguez et al. (43) showed that tracheostomy had a low morbidity and mortality. Sugerman et al. (44) designed an elegant multicenter trial assessing the effects of early versus late tracheostomy in ICU patients. However, of the 157 patients entered, only 14 late tracheostomy patients completed the study. It seems they were unable to eliminate physician bias. They were able to show low morbidity and mortality associated with tracheostomy. Saffle and colleagues (45) randomized 44 patients over approximately five years and showed no differences between early and late tracheostomy. However, the early tracheostomy group had larger full-thickness burns, potentially confounding the results.

Recommendation: In centers that frequently perform percutaneous tracheostomies, patients expected to be intubated longer than 14 days should have early tracheostomy due to a possible decrease in mortality and low risk of the procedure.

Answer: Yes, early tracheostomy should be performed. Grade of recommendation: B.

WHAT IS THE EPIDEMIOLOGY OF VAP?

Hedrick et al. (46) performed a retrospective analysis of rates of VAP in trauma and nontrauma ICU patients. They found VAP in 71% of trauma admissions and 29% in nontrauma admissions. Da Silva et al. (47) found a VAP rate of 20.7% in patients intubated for longer than 48 hours. The overall rate of VAP was 21.6 episodes per 1,000 days of mechanical ventilation with a mortality rate of 71% while in the ICU and 80% during the hospital stay.

Answer: Rates of VAP are between 20% and 71% with wide variability based on patient population. Rates of VAP increase as time of intubation accumulates. Grade of recommendation: B.

WHAT IS THE BEST METHOD TO ASSESS AND TAILOR TREATMENT FOR VAP?

Micek et al. (48) conducted a randomized controlled trial in which patients were assigned to a control group or an antibiotic discontinuation policy. Those placed in the discontinuation group had their antibiotics stopped when clinical findings indicated that the suspicion of pneumonia was resolved. To meet these criteria, patients had to show noninfectious etiology for their infiltrates plus resolution of symptoms of active infection, such as decreasing temperature, decreasing white blood cell count, reassuring chest radiographs, absence of purulent sputum, and P/F >250. Statistically significantly shorter duration of antibiotic usage was found ($p = 0.001$). Secondary episodes of VAP, mortality, and length of ICU stay were similar between the groups.

Answer: Antibiotics can be stopped when clinical signs of infection have resolved. Grade of recommendation:

Levels of Evidence

Subject	Year	Ref.	Level of evidence	Strength of recommendation	Findings
Invasive or noninvasive methods of VAP diagnosis	2006	5	Ia	A	Invasive methods of VAP diagnosis do not change outcomes.
Closed circuit suctioning	2004	8	Ib	A	Closed circuit suctioning devices should be used and only changed on a clinical basis.
ETT with subglottic suctioning	1992	12	Ia	A	ETT with subglottic suctioning decreases the rates of VAP.
Double antibiotic coverage for VAP	1995	36	Ia	A	Monotherapy is as good as double coverage for VAP treatment.

Abbreviations: ETT, endotracheal tube; VAP, ventilator-associated pneumonia.

REFERENCES

- Sanchez-Nieto JM, Torres A, Garcia-Cordoba F, et al. Impact of invasive and noninvasive quantitative culture sampling on outcome of ventilator-associated pneumonia: a pilot study. *Am J Resp Crit Care Med* 1998; 157: 371–6.
- Solé Violán J, Fernández JA, Benítez AB, et al. Impact of quantitative invasive diagnostic techniques in the management and outcome of mechanically ventilated patients with suspected pneumonia. *Crit Care Med* 2000; 28: 2737–41.
- Ruiz M, Torres A, Ewig S, et al. Noninvasive versus invasive microbial investigation in ventilator-associated pneumonia: evaluation of outcome. *Am J Resp Crit Care Med* 2000; 162: 119–25.
- Fagon JY, Chastre J, Wolff M, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. *Ann Intern Med* 2000; 132: 621–30.
- A randomized trial of diagnostic techniques for ventilator-associated pneumonia. *N Eng J Med* 2006; 355: 2619–30.

6. Lorente L, Lecuona Ma, Martín MM, et al. Ventilator-associated pneumonia using a closed versus an open tracheal suction system. *Crit Care Med* 2005; 33: 115–19.
7. Lorente L, Lecuona Ma, Jiménez A, et al. Tracheal suction by closed system without daily change versus open system. *Int Care Med* 2006; 32: 538–44.
8. Topeli A, Harmanci A, Cetinkaya Y, et al. Comparison of the effect of closed versus open endotracheal suction systems on the development of ventilator-associated pneumonia. *J Hosp Infect* 2004; 58: 14–19.
9. Deppe SA, Kelly JW, Thoi LL, et al. Incidence of colonization, nosocomial pneumonia, and mortality in critically ill patients using a Trach Care closed-suction system versus an open-suction system: Prospective, randomized study. *Crit Care Med* 1990; 18: 1389–93.
10. Zeitoun SS, de Barros ALcBL, Diccini S. A prospective, randomized study of ventilator-associated pneumonia in patients using a closed vs. open suction system. *J Clin Nurs* 2003; 12: 484–9.
11. Vallés J, Artigas A, Rello J, et al. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. *Ann Int Med* 1995; 122: 179–86.
12. Mahul P, Auboyer C, Jospe R, et al. Prevention of nosocomial pneumonia in intubated patients: Respective role of mechanical subglottic secretions drainage and stress ulcer prophylaxis. *Int Care Med* 1992; 18: 20–5.
13. Kollef MH, Skubas NJ, Sundt TM. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. *Chest* 1999; 116: 1339–46.
14. Smulders K, van der Hoeven H, Weers-Pothoff I, et al. A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. *Chest* 2002; 121: 858–62.
15. Metz CL, Göbel L, Göbel F, et al. Influence of intermittent subglottic lavage on subglottic colonisation and ventilator-associated pneumonia. *Clin Inten Care* 1998; 9: 20–5.
16. Lorente L, Lecuona Ma, Jiménez A, et al. Influence of an endotracheal tube with polyurethane cuff and subglottic secretion drainage on pneumonia. *Am J Resp Crit Care Med* 2007; 176: 1079–83.
17. Poelaert J, Depuydt P, De Wolf A, et al. Polyurethane cuffed endotracheal tubes to prevent early postoperative pneumonia after cardiac surgery: A pilot study. *J Thor Cardiovasc Surg* 2008; 135: 771–6.
18. Rello J, Kollef M, Diaz E, et al. Reduced burden of bacterial airway colonization with a novel silver-coated endotracheal tube in a randomized multiple-center feasibility study. *Crit Care Med* 2006; 34: 2766–72.
19. Boots RJ, George N, Faoagali JL, et al. Double-heater-wire circuits and heat-and-moisture exchangers and the risk of ventilator-associated pneumonia. *Crit Care Med* 2006; 34: 687–93.
20. Dreyfuss D, Djedani K, Gros I, et al. Mechanical ventilation with heated humidifiers or heat and moisture exchangers: effects on patient colonization and incidence of nosocomial pneumonia. *Am J Resp Crit Care Med* 1995; 151: 986–92.
21. Kollef MH, Shapiro SD, Boyd V, et al. A randomized clinical trial comparing an extended-use hygroscopic condenser humidifier with heated-water humidification in mechanically ventilated patients. *Chest* 1998; 113: 759–67.
22. Boots RJ, Howe S, George N, et al. Clinical utility of hygroscopic heat and moisture exchangers in intensive care patients. *Crit Care Med* 1997; 25: 1707–12.
23. Memish ZA, Oni GA, Djazmati W, et al. A randomized clinical trial to compare the effects of a heat and moisture exchanger with a heated humidifying system on the occurrence rate of ventilator-associated pneumonia. *A J Infect Cont* 2001; 29: 301–5.
24. Lacherade J-C, Auburtin M, Cerf C, et al. Impact of humidification systems on ventilator-associated pneumonia: a randomized multicenter trial. *Am J Resp Crit Care Med* 2005; 172: 1276–82.
25. Lorente L, Lecuona MA, Jiménez A, et al. Ventilator-associated pneumonia using a heated humidifier or a heat and moisture exchanger: a randomized controlled trial [ISRCTN88724583]. *Crit Care* 2006; 10: R116.
26. Drakulovic MB, Torres A, Bauer TT, et al. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. *Lancet* 1999; 354: 1851–8.
27. van Nieuwenhoven CA, Vandenbroucke-Grauls C, van Tiel FH, et al. Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: a randomized study. *Crit Care Med* 2006; 34: 396–402.
28. Baker AM, Meredith JW. Bronchoscopically guided management of ventilator-associated pneumonia in trauma patients. *J Bronchol* 2003; 10: 7–16.
29. Alvarez-Lerma F. Modification of empiric antibiotic treatment in patients with pneumonia acquired in the intensive care unit. ICU-Acquired Pneumonia Study Group. *Inten Care Med* 1996; 22: 387–94.
30. Luna CM, Vujacich P, Niederman MS, et al. Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. *Chest* 1997; 111: 676–85.
31. Iregui M, Ward S, Sherman G, et al. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. *Chest* 2002; 122: 262–8.
32. Kollef MH, Ward S. The influence of mini-BAL cultures on patient outcomes: implications for the antibiotic management of ventilator-associated pneumonia. *Chest* 1998; 113: 412–20.
33. Mueller EW, Hanes SD, Croce MA, et al. Effect from multiple episodes of inadequate empiric antibiotic therapy for ventilator-associated pneumonia on morbidity and mortality among critically ill trauma patients. *J Trauma* 2005; 58: 94–101.
34. Heyland DK, Dodek P, Muscedere J, et al. Randomized trial of combination versus monotherapy for the empiric treatment of suspected ventilator-associated pneumonia. *Crit Care Med* 2008; 36: 737–44.
35. Damas P, Garweg C, Monchi M, et al. Combination therapy versus monotherapy: a randomised pilot study on the evolution of inflammatory parameters after ventilator associated pneumonia [ISRCTN31976779]. *Crit Care* 2006; 10: R52.
36. Rubinstein E, Lode H, Grassi C. Ceftazidime monotherapy vs. ceftriaxone/tobramycin for serious hospital-acquired Gram-negative infections. Antibiotic Study Group. *Clin Infect Dis* 1995; 20: 1217–28.
37. Rubinstein E, Cammarata S, Oliphant T, et al. Linezolid (PNU-100766) versus vancomycin in the treatment of hospitalized patients with nosocomial pneumonia: A randomized, double-blind, multicenter study. *Clin Infect Dis* 2001; 32: 402–12.
38. Wunderink RG, Cammarata SK, Oliphant TH, et al. Continuation of a randomized, double-blind, multicenter study of linezolid versus vancomycin in the treatment of patients with nosocomial pneumonia. *Clin Thera* 2003; 25: 980–92.
39. Kohno S, Yamaguchi K, Aikawa N, et al. Linezolid versus vancomycin for the treatment of infections caused by methicillin-resistant *Staphylococcus aureus* in Japan. *J Antimicrob Chemother* 2007; 60: 1361–9.
40. Chastre J, Wolff M, Fagon J-Y, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. *JAMA* 2003; 290: 2588–98.
41. Rumbak MJ, Newton M, Truncala T, et al. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. *Crit Care Med* 2004; 32: 1689–94.

42. Boudierka MA, Fakhir B, Bouaggad A, et al. Early tracheostomy versus prolonged endotracheal intubation in severe head injury. *J Trauma* 2004; 57: 251–4.
43. Rodriguez JL, Steinberg SM, Luchetti FA, et al. Early tracheostomy for primary airway management in the surgical critical care setting. *Surgery* 1990; 108: 655–9.
44. Sugerman HJ, Wolfe L, Pasquale MD, et al. Multicenter, randomized, prospective trial of early tracheostomy. *J Trauma* 1997; 43: 741–7.
45. Saffle JR, Morris SE, Edelman L. Early tracheostomy does not improve outcome in burn patients. *J Burn Care Rehab* 2002; 23: 431–8.
46. Hedrick TL, Smith RL, McElearney ST, et al. Differences in early- and late-onset ventilator-associated pneumonia between surgical and trauma patients in a combined surgical or trauma intensive care unit. *J Trauma* 2008; 64: 714–20.
47. da Silva JM, Rezende E, Guimarães TS, et al. Epidemiological and microbiological analysis of ventilator-associated pneumonia patients in a public teaching hospital. *Braz J Infect Dis* 2007; 11: 482–8.
48. Micek ST, Ward S, Fraser VJ, et al. A randomized controlled trial of an antibiotic discontinuation policy for clinically suspected ventilator-associated pneumonia. *Chest* 2004; 125: 1791–9.

Management of Acute Myocardial Infarction and Cardiogenic Shock

Antonio Hernandez

Question Summary		
Question	Answer	Grade
What is the optimal time from door to PCI that reduces mortality?	90 minutes is the optimal time from door to PCI. Patients who received an intervention within this timeframe experienced a reduction in mortality.	A
What beta-blocker is recommended for management of an acute MI, and is an IV dose superior?	Early initiation of low-dose beta-blocker therapy and careful titration should be the goal until rate control has been achieved.	A
Is a baby aspirin (81 mg) adequate for management of an acute MI?	A minimum of 162 mg aspirin should be administered within 10 minutes of recognizing that the patient is experiencing an acute MI.	A
Is clopidogrel indicated in the management of an acute MI?	Adding clopidogrel to aspirin does improve outcome in non-ST-elevation MI and should be considered. However, caution should be taken in postoperative patients.	A
What ACE-I is indicated for the management of an acute MI, and is an IV dose superior?	The current ACC/AHA recommendations suggest that an oral dose of ACE-I therapy is the optimal treatment. On review of IV ACE-I therapy, mortality is not affected when compared to oral ACE-I therapy, which improved mortality. For LVEF < 40%, it is a class I level A recommendation. For low-risk patients > 40% LVEF, it is IIa level B recommendation.	A
Does the addition of an ARB improve the benefit of an ACE-I?	Addition of an ARB does not improve the outcome of the patient and was noted to introduce more adverse effects. ARBs are as effective as ACE-Is and can be used when ACE-Is are not tolerated by the patient due to adverse reactions.	A
Abbreviations: ACC, American College of Cardiology; ACE-I, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous intervention.		

Cardiovascular disease remains the leading cause of death in the United States. According to the Centers for Disease Control and Prevention, an estimated 12 million persons in the United States had chronic heart disease, of which 1.1 million had an event in 2001 (1). Approximately 650,000 had a primary event, and an estimated 450,000 with have a recurrence. Approximately 220,000 fatal events related to cardiovascular disease occurred in unhospitalized persons. According to the American Heart Association, we are making progress by prevention, and the projections for 2008 are better. However, as of 2005, death related to cardiovascular disease was 652,091, which is 26.6% of all deaths in the United States (2). Our focus in this chapter is related to the incidence of myocardial infarction (MI) and consequent cardiogenic shock in perioperative patients. Although there is good evidence for the use of thrombolytic therapy in ST-elevation MI, based on the 2007 focused update of the American College of Cardiology/American Heart Association (ACC/AHA) (3), thrombolytic therapy is often contraindicated in the postoperative population. Hence, this chapter reviews therapies suggested by the ACC/AHA for ST-elevation and non-ST-elevation MI (4) and how they apply to the postoperative population.

Unlike the rest of the organ systems in the body, the heart's oxygen extraction ratio is significantly higher. The brain, which is metabolically expensive, only extracts 25% of the oxygen at a resting state. In conditions of impaired perfusion, the brain has the luxury of maintaining cerebral metabolism by increasing the oxygen extraction ratio to meet metabolic demands. Unfortunately, at a resting state the heart extracts approximately 50–75% of oxygen, and thus the only way to increase the delivery of oxygen to the myocardial tissue is by increasing blood flow. The basis of this physiology makes it likely to develop "demand/supply" mismatch and consequent ischemia. If the area of ischemia is not reperfused quickly, the ischemic tissue progresses to myocardial necrosis.

DIAGNOSIS

The typical presentation of an electrocardiogram (ECG) for an acute MI include ST segment elevation in two "consecutive" or "contiguous" leads, which represents the same coronary artery territory, and not how they appear in sequence on the ECG. ST elevation should be ≥ 1 mm or

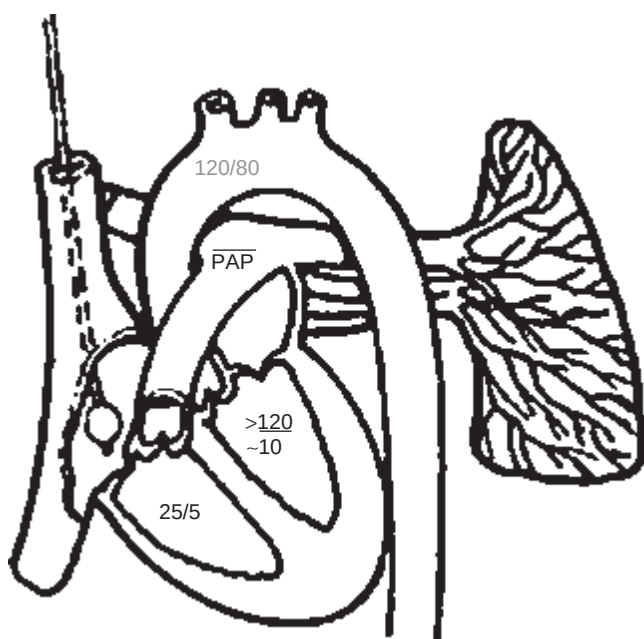


Figure 77.1 Chambers of the heart, greater vessels, and respective pressures. Source: Adapted from *Quick Guide to Cardiopulmonary Care*. Courtesy of P.R. Lichtenthal and Edwards Lifesciences.

0.1 mV. Other ECG findings include inversion of T waves and finally the development of a Q wave. The area that may be elusive on an ECG includes the inferior lateral wall. The presentation here would include increased voltage over the R waves, peaked T waves, and ST depression on leads V_1 – V_2 . Also, the development of a new left bundle branch block should be approached as an acute MI and managed as such until biomarker data exclude the likelihood of an acute event.

The biomarkers follow a pattern of progression that often makes it challenging to assess for reinfarction. At the onset of a MI, creatine phosphokinase and creatine kinase-MB serum levels begin to rise at 4–8 hours, peak at approximately 18 hours, and return to baseline after 2–4 days. Troponin levels are more specific and are the better biomarkers to follow. Troponin serum levels rise at six hours, and may remain elevated for a few days, particularly if the patient has coexisting renal insufficiency. Specific levels of biomarkers should be referenced with the specific institutional standards, as they may vary.

Finally, the role of echocardiography is an excellent complement to the methods described. Echocardiography provides information about specific segments of each wall. Previously we used a 16-segment model for interpretation of systolic function (5) but have recently adopted a 17-segment model for the left ventricle (LV), septum, and true apex. The transthoracic approach is noninvasive and essentially harmless to the patient. In the hands of a skilled echocardiographer, hemodynamic parameters can be estimated, including cardiac output, pulmonary artery systolic pressure and mean arterial pressure, and valvular structural abnormalities including endocarditis; it also provides information about cardiomyopathy patterns, pericardial integrity, and estimation of pericardial volume. Use of a pulmonary artery catheter may

occasionally complement the techniques just described. Information that can be obtained from a pulmonary artery catheter that is not offered from an echocardiogram includes oxygen saturation and oxygen tension of mixed venous blood as a measure of appropriate delivery of oxygen.

MANAGEMENT

Right versus Left Ventricular Infarction

One of the first steps in managing acute MI is to identify which chamber is being affected so that one can implement the appropriate strategy for achieving target hemodynamic goals. As described earlier, the primary method of improving delivery of oxygen to the myocardium is by improving blood flow, because the myocardium is already maximally extracting oxygen at a ratio of approximately 75%. The higher the coronary perfusion pressure, the better the blood flow. At this time we should define the determining variables for coronary perfusion pressure (CPP). For the left ventricle, the CPP is diastolic blood pressure (DBP) minus LV end diastolic pressure (LVEDP) ($CPP = DBP - LVEDP$). This is particularly unique to the left ventricle, because it primarily perfuses during diastole. Figure 77.1 assists in clarifying several issues. Coronary arteries supplying the LV travel epicardially and then into the myocardial wall, where the vessels are surrounded by the myocardium. If the systolic blood pressure (SBP) in the aortic root is 120 mmHg, then the pressure generated within the LV must be greater than 120 mmHg for forward flow to exist. Thus, the pressure surrounding the LV coronary arteries will be greater than the pressure within them, and therefore will not have flow during systole. During diastole, the pressure in the aortic root (according to Fig. 77) is 80 mmHg. Because the aortic valve closes, the pressure in the LV a healthy patient would be approximately 10 mmHg. As a result, the LV coronary branches only have 10 mmHg of resistance. Therefore, the LV CPP, according to Figure 77.1, would be 80 mmHg (DBP) – 10 (LVEDP) for an LV CPP of 70 mmHg. Therefore, to improve blood flow to the LV, one must either increase the DBP or decrease the LVEDP.

Now, referring back to Figure 77.1, let us focus on the right side of the heart. Like the left heart, branches of the right coronary artery enter the right ventricle (RV). However, the RV wall is thinner and the pressure generated within the RV is much lower when compared to the LV in the absence of pulmonary hypertension. The SBP in the aortic root is 120 mmHg, and the RV systolic pressure is 25 mmHg. Again, the pressure surrounding the vessels within the RV will have a resistance of just above 25 mmHg. During systole, the RV CPP would be 120 mmHg (SBP) – 25 mmHg (RV SBP) to generate an RV CPP of approximately 95 mmHg during systole. In this example, during diastole, the DBP in the aortic root is 80 mmHg. In the RV, the diastolic pressure is 5 mmHg. Therefore, the RV CPP during diastole would be 80 mmHg (DBP) – 5 mmHg (RV DBP) to generate a RV diastolic CPP of 75 mmHg. This is why the RV perfuses during the entire cardiac cycle. As a result, the parameters that determine RV CPP are mean arterial pressure–mean pulmonary artery pressure, because this pressure is higher than the RV diastolic pressure and is a better variable for hindrance to perfusion.

Generally, the goals for both LV and RV acute MI are to reduce the oxygen consumption and increase the

delivery of oxygen to the myocardium. However, one of the strategies for the LV in reducing the oxygen consumption will affect the RV in a negative fashion. That is, afterload reduction or reducing LV work will aid in reducing the LV oxygen consumption. If the patient is experiencing RV infarction rather than LV infarction, decreasing the mean arterial pressure will have a negative effect on the delivery of oxygen to the RV and exacerbate the oxygen demand/supply ratio. Therefore, it is imperative to identify which coronary artery territories are being affected before proceeding with management. The following sections describe the management for ST-elevation MI and non-ST-elevation MI independently as per the ACC/AHA guidelines. Overall, the goal is to establish revascularization.

Thrombolytic Therapy

There is good evidence for the use of thrombolytic therapy for revascularization during an acute MI (6). However, in postoperative patients the use of thrombolytic therapy is often contraindicated due to recent surgery. Nevertheless, I include a list of contraindications:

- Active internal bleeding.
- Intracranial neoplasm, aneurysm, or A-V malformation.
- Neurosurgery or cerebral vascular accident within six weeks.
- Trauma or major surgery within two weeks.
- Aortic dissection.

What Is the Optimal Time From Door to PCI That Reduces Mortality?

The following strategies for management of an acute MI will be based on current guidelines forwarded by the ACC/AHA for ST-elevation MI (3) and a review by Hollenberg titled "Myocardial Infarction" in *Multiprofessional Critical Care Review* 2007.

The current recommendation is to establish reperfusion as quickly as possible. For patients experiencing a coronary event, the health system goal should be to have the patient receive an intervention within 90 minutes, from arrival to "balloon" time (7). In the study by Berg et al. information was collected from 60 consecutive patients with ST-elevation MI who underwent percutaneous intervention (PCI) from October 1, 2004, through August 31, 2005 (control group), and compared it to 86 consecutive patients with ST-elevation MI who underwent PCI from September 1, 2005, through June 26, 2006, after implementation of their protocol (treatment group). The following results were generated from their work: the median door-to-balloon time decreased overall (113.5 versus 75.5 minutes; $p < 0.0001$); during regular hours (83.5 versus 64.5 minutes; $p < 0.005$), during off-hours (123.5 versus 77.5 minutes; $p < 0.0001$). Regarding transfer from an outside affiliated emergency department (147 versus 85 minutes; $p < 0.0006$). Treatment within 90 minutes increased from 28% to 71% ($p < 0.0001$). Mean infarct size decreased (peak creatinine kinase, $2,623 \pm 3,329$ versus $1,517 \pm 1,556$ IU/L; $p < 0.0089$), as did hospital length of stay (5 ± 7 versus 3 ± 2 days; $p < 0.0097$) and total hospital costs per admission. For this particular patient population, access to a PCI laboratory should be quite easy.

It has been demonstrated by Krumholz et al. that outcomes are better when patients are cared for in centers of high-volume PCI experience (8). In their analysis of the National Registry of Myocardial Infarction, they compared in-hospital mortality and times to treatment in STEMI across different levels of hospital specialization with PCI. They divided 463 hospitals into quartiles of PCI specialization based on the relative proportion of reperfusion-treated patients who underwent a PCI. After adjusting for patient and hospital characteristics, including percutaneous intervention volume, they found that greater PCI specialization was associated with a lower relative risk of in-hospital mortality in patients treated with PCI (adjusted relative risk comparing the highest and lowest quartiles, 0.64; $p < 0.006$) but not in those treated with fibrinolytic therapy. Because this patient population is likely to have a contraindication to fibrinolytic therapy, prompt arrival to the PCI laboratory is very important.

Answer: Ninety minutes is the optimal time from door to PCI. Patients who received an intervention within this timeframe experienced a reduction in mortality (Grade A recommendation).

What Beta-Blocker Is Recommended for Management of an Acute MI, and Is an Intravenous Dose Superior?

According to the updated guidelines by the ACC/AHA, oral beta-blocker therapy should be initiated in the first 24 hours for patients that do not have the following: (1) signs of heart failure, (2) evidence of a low output state, (3) increased risk for cardiogenic shock, or (4) other relative contraindications to beta-blockade (heart block, asthma, or reactive airway disease) (3). In previous studies, IV beta-blocker therapy had not shown to be superior to the oral route of administration, with the exception of IV atenolol (9). The GUSTO-I experience, aside from comparing one of four thrombolytic strategies, also compared IV versus oral atenolol. The atenolol protocol recommended that patients without hypotension, bradycardia, or signs of heart failure be given atenolol 5mg IV over 5 minutes as soon as possible after enrollment, followed 10 minutes later by another 5mg IV over 5 minutes. Oral atenolol (50mg given 10 minutes after the last intravenous dose, followed by 50–100mg daily) was to be given if no contraindications existed. They compared the 30-day mortality of patients given no atenolol ($n = 10,073$), any atenolol ($n = 30,771$), any IV atenolol ($n = 18,200$), only oral atenolol ($n = 12,545$), and both IV and oral drug ($n = 16,406$), after controlling for baseline differences and for early deaths (before oral atenolol could be given). Patients given any atenolol had a lower baseline risk than those not given atenolol. Adjusted 30-day mortality was significantly lower in atenolol-treated patients, but patients treated with IV and oral atenolol treatment versus oral treatment alone were more likely to die (odds ratio, 1.3; 95% confidence interval, 1.0 to 1.5; $p < 0.02$). IV atenolol use was associated with more heart failure, shock, recurrent ischemia, and pacemaker use than oral atenolol use. The rates of stroke, intracranial hemorrhage, and reinfarction were similar among the IV and oral versus oral atenolol groups. This post hoc analysis of atenolol use identified no significant change in mortality (9,10). Current class I level A recommendations include the initiation of oral beta-blocker (metoprolol) therapy unless

contraindicated within 24 hours of the acute event; this is beneficial for secondary prevention and related complications (11). The oral dose can be titrated to achieve rate control, and vigilance must be maintained to monitor for plausible complications from beta-blocker therapy.

Answer: Early initiation of low-dose beta-blocker therapy and careful titration should be the goal until rate control has been achieved (Grade A recommendation).

Is a Baby Aspirin (81 mg) Adequate for Management of an Acute MI?

Aspirin (162–325 mg) should be initiated on all patients suspected of experiencing an acute MI unless contraindicated. The use of aspirin alone reduces the incidence of reinfarction and mortality by 23% without any other adjuncts (12).

Answer: A minimum of 162 mg of aspirin should be administered within 10 minutes of recognizing that the patient is experiencing an acute MI (Grade A recommendation).

Is Clopidogrel Indicated in the Management of an Acute MI?

The efficacy of thienopyridines in the management of ST-elevation MI, clopidogrel primarily, has been tested in two large trials since the 2004 ACC/AHA guidelines publication. The COMMIT-CCS-2 included 45,852 patients who received 75 mg clopidogrel daily in addition to a daily dose of 162 mg aspirin. This trial achieved an endpoint of all-cause mortality reduction from 8.1% in the placebo group to 7.5% in the clopidogrel group ($p = 0.03$), and the rate of cerebral and major noncerebral bleeding was 0.55% in the placebo group and 0.58% in the clopidogrel group ($p = 0.59$) (13). The other trial was the CLARITY-TIMI 28, which included clopidogrel added to thrombolytic therapy. Although this study is not relevant to the postsurgical population, it is important to note that there was an improvement of the endpoint, which was occluded infarct artery on angiography or death or recurrent MI before angiography. This was reduced from 21.7% in the placebo group versus 15.0% in the clopidogrel group (14). Suffice it to say that clopidogrel is considered a class I level A recommendation for adjuvant therapy for ST-elevation MI. Nevertheless, in the postsurgical and trauma patient population, thienopyridines should be used with caution.

Answer: Adding clopidogrel to aspirin does improve outcome in non-ST-elevation MI and should be considered. However, caution should be taken when used in postoperative patients (Grade A recommendation).

Glycoprotein IIb/IIIa receptor antagonists are used in conjunction with PCI and have no role in independent use as an adjuvant, without the involvement of a PCI specialist.

Anticoagulants

Administration of unfractionated heparin is often done on a weight-based protocol to include a bolus of 60 U/kg up to a maximum of 4,000 U and an initial infusion rate of 12 U/kg per hour with a goal to keep the partial thromboplastin time between 50 and 70 seconds. Unfractionated

heparin currently holds a class IIa level B recommendation. There is increasing evidence that low molecular weight heparin (LMWH) is at least as efficacious than unfractionated heparin, but according to the recent update by the ACC/AHA, LMWH is listed as a class IIa level C recommendation. Both of these are beneficial in patients without thrombolytic therapy, which is representative of this patient population.

Nitrates

Although not addressed by current guidelines, the use of nitrates continues to be the standard of practice. In particular, nitroglycerin (NTG) transdermal, sublingual, or via infusion therapy is frequently initiated to aid in improving angina and perfusion to the injured myocardium until direct revascularization is implemented. It should be noted that there is a lack of evidence to demonstrate an improvement in mortality from nitrates. Recently the GISSI-3 trial compared angiotensin-converting enzyme inhibitor (ACE-I) versus transdermal NTG versus ACE-I with transdermal NTG versus placebo. All patients received aspirin, IV and oral beta-blocker therapy, and thrombolytic therapy. The result demonstrated a benefit from the use of lisinopril, regardless of whether transdermal NTG was added (15). When used IV, the dose of NTG is either 0.25–0.5 mcg/kg per min or 10 mcg/min and titrated to effect as long as the patient is hemodynamically appropriate. Remember to use appropriate tubing to avoid chelating of nitroglycerin before entering the patient.

What ACE-I Is Indicated for the Management of an Acute MI, and Is an IV Dose Superior? Does the Addition of an ARB Improve the Benefit of an ACE-I?

Several trials of demonstrated the benefit of initiating ACE-I therapy as soon as the patient tolerates its use. In the CONSENSUS II trial, 103 Scandinavian centers studied patients with an acute MI and blood pressure above 100/60 mmHg. Subjects were randomly assigned to treatment with either enalapril or placebo, in addition to conventional therapy. Therapy was initiated with an IV infusion of enalapril (enalaprilat) within 24 hours after the onset of chest pain, followed by administration of oral enalapril. Of the 6,090 patients enrolled, 3,046 were assigned to placebo and 3,044 to enalapril. The mortality rates in the two groups at one and six months were not significantly different (6.3% and 10.2% in the placebo group versus 7.2% and 11.0% in the enalapril group, $p = 0.26$). The relative risk of death in the enalapril group was 1.10 (95% confidence interval, 0.93–1.29). Death due to progressive heart failure occurred in 104 patients (3.4%) in the placebo group and 132 (4.3%) in the enalapril group ($p = 0.06$).

As for oral ACE-I therapy, data from the SAVE and later HOPE trials both support the use of oral ACE-I in the post-acute MI setting if not contraindicated. In the SAVE trial, 2,231 patients with left ventricular ejection fraction (LVEF) <40% were randomized to receive either placebo ($n = 1,116$) or oral captopril ($n = 1,115$) within 3–16 days post-acute MI. The initial dose of captopril was 12.5 mg, but the dose was reduced to 6.25 mg for subjects with marked decreases in blood pressure. The target for the study was 25 mg three times a day with a maximum of 50 mg three times a day. Subjects were observed for

two years, and the following data were obtained. All-cause mortality was 20% in the captopril group compared to 25% in the placebo group, with a relative risk reduction of 19% (95% confidence interval, 3–32%; $p = 0.019$). In the HOPE trial, a total of 9,297 high-risk patients who had evidence of vascular disease or diabetes plus one other cardiovascular risk factor and who were not known to have a low ejection fraction or heart failure were randomly assigned to receive ramipril (10 mg once per day orally) or matching placebo for a mean of five years. The primary outcome was a composite of MI, stroke, or death from cardiovascular causes as defined by the investigators. A total of 651 patients received ramipril (14.0%) and reached the primary endpoint, as compared with 826 patients who were assigned to receive placebo (17.8%). Treatment with ramipril reduced the rates of death from cardiovascular causes (6.1%, as compared with 8.1% in the placebo group; relative risk, 0.74; $p < 0.001$), MI (9.9% versus 12.3%; relative risk, 0.80; $p < 0.001$), stroke (3.4% versus 4.9%; relative risk, 0.68; $p < 0.001$), death from any cause (10.4% versus 12.2%; relative risk, 0.84; $p = 0.005$), revascularization procedures (16.0% versus 18.3%; relative risk, 0.85; $p = 0.002$), cardiac arrest (0.8% versus 1.3%; relative risk, 0.63; $p = 0.03$), heart failure (9.0% versus 11.5%; relative risk, 0.77; $p < 0.001$), and complications related to diabetes (6.4% versus 7.6%; relative risk, 0.84; $p = 0.03$). In conclusion, for LVEF $<40\%$, it is a class I level A recommendation; for low-risk patients that have $>40\%$ LVEF, it is IIa level B recommendation.

The SAVE trial (16) demonstrated an improvement in mortality of just over 20%; the HOPE trial (17) improved survival related to cardiac events as well as a reduction in stroke. ACE-I should be initiated within 24 hours if tolerated, and, like beta-blockers, the oral route of administration results in improved outcomes.

The recommendation is to initiate a low dose and titrate the dose as tolerated. For those patients that do not tolerate ACE-I due to the adverse reactions, similar benefits have been noted with angiotensin receptor blockers (ARBs). The VALIANT trial assessed the effect of captopril, valsartan, and the combination of both (18). It was noted that both captopril and valsartan were as effective, but when used together the risks of an adverse effect outweighed the benefit to the patient.

Answer: The current data suggest that an oral dose of ACE-I therapy is the optimal treatment. On review of IV ACE-I therapy, mortality is not affected when compared to oral ACE-I therapy, which improved mortality. Addition of an ARB does not improve the outcome of the patient and was noted to introduce more adverse effects. ARBs are as effective as ACE-I and can be used when ACE-I are not tolerated by the patient due to adverse reactions (Grade A recommendation).

NON-ST-ELEVATION MI

The key for non-ST-elevation MI is to establish reperfusion by thrombolytic therapy if PCI is not available.

Beta-blocker Therapy

Like with ST-elevation MI, the use of oral beta-blockers are more advantageous than IV beta-blockers. The recommendation is a class I level B to initiate within 24 hours of the

acute coronary event, as long as the patient does not have any contraindications as listed in the ST-elevation section (19). Initiate a low dose and titrate to achieve rate control.

Antiplatelet Therapy

As before, the use of aspirin is invaluable and should be initiated within 10 minutes of identifying signs and symptoms of an acute MI, unless contraindicated. The patient should continue to receive this therapy because it not only reduces mortality in the group by nearly 50%, it also reduces reinfarction.

The addition of clopidogrel to this group of 12,562 patients in the CURE trial demonstrated a benefit in mortality, MI, and stroke with only a 1% risk of major non-life-threatening bleeds ($p = 0.001$) (20). The current guidelines recommend either/or clopidogrel 300 mg load or a glycoprotein IIb/IIIa load if an early intervention strategy is anticipated, and this is class I level A recommendation (19). Again, clopidogrel should be used with caution in the postoperative population.

Anticoagulants

Unfractionated heparin as well as LMWH remains a class I level A recommendation. In this patient population, based on the ESSENCE trial, which included 22,000 patients, authors noted a statistically significant reduction in the combined endpoint of death or nonfatal MI at 30 days for enoxaparin versus unfractionated heparin in the overall trial populations (10.1% versus 11.0%; odds ratio, 0.91; 95% confidence interval, 0.83–0.99; number needed to treat, 107) (21). In the TIMI 11B trial, LMWH was demonstrated to be superior to unfractionated heparin without increase risk of bleeding (22). The dose for LMWH is 1 mg/kg every 12 hours subcutaneous. The unfractionated heparin dose is the same as that described in the ST-elevation section.

Nitrates

Like with ST-elevation MI, there is no evidence that nitrates will improve outcome, but they are helpful in managing a patient's symptoms of angina. Initiate at the same doses described, and titrate to effect as long as the patient tolerates its use. Avoid use in patients with a systolic blood pressure below 90 mmHg.

CARDIOGENIC SHOCK

Cardiogenic shock is one of the complications from an acute MI. Management strategies vary, and there is no evidence to clearly guide the choice in agents with improved outcome in a large, multicenter trial. Both dobutamine and milrinone have demonstrated improved cardiac index with their use in LV failure but no conclusive evidence of improved outcome in the setting of acute MI. There is increasing evidence for the use of sildenafil for right ventricular failure, but its role in right ventricular failure in the setting of acute MI is limited. There is limited evidence that support the efficacy of sildenafil as a good agent to reduce pulmonary vascular resistance, while decreasing LVEDP and improving cardiac index (23). RV failure as a

result of pulmonary hypertension will respond well to sildenafil and actually improves the quality of life after 12 weeks (24) and 6 months (25). Because nitrates are the standard of therapy in an acute MI, sildenafil should likely be avoided until more evidence is available.

Intra-aortic balloon counterpulsation (IABCP) in acute MI has been used for nearly 30 years. Unfortunately, there are limited data to determine whether its use impacts mortality, even though a study was performed in which data were collected prospectively including 250 medical centers worldwide and 5,495 patients with acute MI and IABCP (26). Nevertheless, it is a plausible strategy to augment cardiac index but primarily alleviate the LV from added work during an ischemic event.

CONCLUSION

Diagnosis of an MI in the postoperative patient requires that the clinician have a high index of suspicion because often this patient population is sedated and intubated or under the influence of analgesic therapy. Thus, reliance on

monitors and biomarkers is key, as is rapid implementation of a plan to establish reperfusion and anti-ischemic therapy. Overall, the oral route of administration for both beta-blocker therapy and ACE-I therapy is more efficacious, even when low-dose therapy is initiated and titrated carefully. Antiplatelet therapy is of utmost importance, regardless of whether the patient will receive thrombolytic therapy. Aspirin of 162–325mg should be initiated and continued indefinitely unless contraindicated. Anticoagulation with unfractionated heparin has been the standard for some time and presently receives the most evidence for its use, but emerging data support the superiority of LMWH over unfractionated heparin. Regardless, anticoagulation is an adjuvant to antiplatelet therapy in establishing reperfusion and reducing the risk of restenosis in the acute phase. Finally, implementation of a plan that is easily reproducible and communicated is key to successful delivery of evidence-based care. Development of protocol- or algorithm-driven therapy is the key to eliminating deviation from evidence-based practice in a setting of a variety of practitioners from different training backgrounds.

Levels of Evidence

Question	Answer	Class, level	Refs.
What is the optimal time from door to PCI that reduces mortality?	90 minutes is the optimal time from door to PCI. Patients who received an intervention within this timeframe experienced a reduction in mortality.	Class I, Level A	3, 7
What beta-blocker is recommended for management of an acute MI, and is an IV dose superior?	Early initiation of low-dose beta-blocker therapy and careful titration should be the goal until rate control has been achieved.	Class I, Level A	3, 10, 11
Is a baby aspirin (81 mg) adequate for management of an acute MI?	A minimum of 162 mg aspirin should be administered within 10 minutes of recognizing that the patient is experiencing an acute MI.	Class I, Level A	3
Is clopidogrel indicated in the management of an acute MI?	Adding clopidogrel to aspirin does improve outcome in non-ST-elevation MI and should be considered. However, caution should be taken in postoperative patients.	Class I, Level A	3, 20
What ACE-I is indicated for the management of an acute MI, and is an IV dose superior?	The current ACC/AHA recommendations suggest that an oral dose of ACE-I therapy is the optimal treatment. On review of IV ACE-I therapy, mortality is not affected when compared to oral ACE-I therapy, which improved mortality. For LVEF < 40%, it is a class I level A recommendation. For low-risk patients > 40% LVEF, it is IIa level B recommendation.	Class I, Level A; and Class IIa Level B	3
Does the addition of an ARB improve the benefit of an ACE-I?	Addition of an ARB does not improve the outcome of the patient and was noted to introduce more adverse effects. ARBs are as effective as ACE-Is and can be used when ACE-Is are not tolerated by the patient due to adverse reactions.	Class I, Level A	3, 18

Abbreviations: ACC, American College of Cardiology; ACE-I, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous intervention.

REFERENCES

- American Heart Association. 2001 Heart and Stroke Statistical Update. Dallas, TX: American Heart Association, 2000. Available at <http://www.americanheart.org/statistics/index.html>; accessed February 2001.
- CDC National Vital Statistics Reports. Deaths: Final data for 2005. Nat Vital Stat Rep 2008; 56: 1–121.
- American College of Cardiologists. 2007 focused update of the ACC/AHA 2004 guidelines for management of patients with ST-elevation myocardial infarction. J Am Coll Cardiol 2008; 51: 210–47.
- American College of Cardiologists. 2007 update to the ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: implications for emergency department practice. Ann Emerg Med 2007; 51: 591–606.
- Shanewise JS, Cheung AT, Aronson S, et al. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. Anesth Analg 1999; 89: 870–84.
- The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Eng J Med 1993; 329: 673–82.
- Khot UN, Johnson ML, Ramsey C, et al. Emergency department physician activation of the catheterization laboratory

- and immediate transfer to an immediately available catheterization laboratory reduce door-to-balloon time in ST-elevation myocardial infarction. *Circulation* 2007; 116: 67–76.
8. Nallamothu BK, Wang Y, Magid DJ, et al. Relation between hospital specialization with primary percutaneous coronary intervention and clinical outcomes in ST-segment elevation myocardial infarction: National Registry of Myocardial Infarction-4 analysis. *Circulation* 2006; 113: 222–9.
 9. Pfisterer M, Cox JL, Granger CB, et al. Atenolol use and clinical outcomes after thrombolysis for acute myocardial infarction: The (ateplase) for occluded coronary arteries. *J Am Coll Cardiol* 1998; 32: 634–40.
 10. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004; 44: e1–e211.
 11. Lopez-Sendon J, Swedberg K, McMurray J, et al. Expert consensus document on beta-adrenergic receptor blockers. *Eur Heart J* 2004; 25: 1341–2.
 12. ISIS-2 Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988; 2: 349–60.
 13. Chen ZM, Jiang LX, Chen YP, et al. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomized placebo-controlled trial. *Lancet* 2005; 366: 1607–21.
 14. Scirica BM, Sabatine MS, Morrow DA, et al. The role of clopidogrel in early and sustained arterial patency after fibrinolysis for ST-segment elevation myocardial infarction: the ECG CLARITY-TIMI 28 study. *J Am Coll Cardiol* 2006; 48: 37–42.
 15. GISSI-3 Investigators. Causes of death in patients with acute myocardial infarction treated with angiotensin-converting enzyme inhibitors: findings from the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto (GISSI)-3 trial. *Am Heart J* 2008; 155: 388–94.
 16. Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *N Engl J Med* 1992; 327: 669–77.
 17. Yusuf S, Sleight P, Pogue J, et al. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000; 342: 145–53.
 18. Pfeffer MA, McMurray JJ, Velazquez EJ, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med* 2003; 349: 1893–906.
 19. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction): Developed in collaboration with the American College of Emergency Physicians, American College of Physicians, Society for Academic Emergency Medicine, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2007; 50: e1–e157.
 20. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; 345: 494–502.
 21. Petersen JL, Califf RM, et al. Efficacy and bleeding complications among patients randomized to enoxaparin or unfractionated heparin for antithrombin therapy in non-ST-segment elevation acute coronary syndromes. A systematic overview. *JAMA* 2004; 292: 89–96.
 22. Antman EM, McCabe CH, Braunwald E; TIMI 11B investigators. Enoxaparin prevents death and cardiac ischemic events in unstable angina/non-Q-wave myocardial infarction results of the Thrombolysis In Myocardial Infarction (TIMI) 11B trial. *Circulation* 1999; 100: 1593–601.
 23. Michelakis E, Tymchak W, Archer S, et al. Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension. Comparison with inhaled nitric oxide. *Circulation* 2002; 105: 2398–403.
 24. SUPER Study Group. Sildenafil citrate therapy for arterial pulmonary hypertension. *N Engl J Med* 2005; 353: 2148–57.
 25. Pepke-Zaba J, Gilbert C, Collings L, et al. Sildenafil improves health-related quality of life in patients with pulmonary arterial hypertension. *Chest* 2008; 133: 183–9.
 26. Stone GW, Ohman EM, Ferguson JJ III, et al. Contemporary utilization and outcomes of intra-aortic balloon counterpulsation in acute myocardial infarction. *J Am Coll Cardiol* 2003; 41: 1940–5.

Perioperative Arrhythmias

Bipin K. Ravindran and Mohan N. Viswanathan

Clinical Questions		
Question	Answer	Grade of recommendation
What are effective and safe pharmacologic strategies for prevention of postoperative atrial fibrillation after coronary artery bypass surgery?	Beta-blockers Amiodarone	A B
Are there intraoperative strategies to consider that may reduce incident atrial fibrillation after cardiothoracic surgery?	Applying mild hypothermia, performing a posterior pericardiotomy, and by using heparin-coated bypass circuits	C
What drugs should be avoided in patients with atrial fibrillation with underlying Wolff-Parkinson-White syndrome?	Adenosine, beta-blockers, and calcium channel blockers	A
Is elective cardioversion, chemically or by direct current, a reasonable option in the postoperative atrial fibrillation patient?	Yes. It may reduce length of hospital stay and prolong duration in normal sinus rhythm.	B
Should warfarin be given in postoperative atrial fibrillation that is recurrent or persists for more than 24 hours?	Warfarin anticoagulation should be initiated for at least 4 weeks to mitigate the risk of stroke.	B

ATRIAL ARRHYTHMIAS

Atrial tachyarrhythmias in the early perioperative period are extremely common and encompass atrial fibrillation (AF), atrial flutter, and atrial tachycardia, and certain other reentrant supraventricular tachyarrhythmias. These rhythm disturbances are all closely related in terms of risk factors and management. AF greatly outweighs the incidence of the others and has been the focus of essentially all the existing retrospective, observational, and prospective randomized controlled trials. Accordingly, AF is the focus of this discussion.

AF is the most frequently encountered arrhythmia in outpatient clinical practice, and therefore it is no surprise that it is also the most commonly encountered perioperative arrhythmia. AF occurs in 4–20% of patients following non-cardiac surgery, depending on the complexity of the operation, with the highest incidence occurring with vascular and major abdominal surgeries (1–3). In fact, in coronary artery bypass grafting (CABG), AF occurs in 25–33% of patients (4–7). Adding valvular surgery to CABG increases the incidence of AF up to 60% with aortic valve replacement and up to 63% with mitral valve replacement (6).

The exact pathophysiology of AF is poorly defined. The rhythm is characterized by multiple, simultaneously occurring atrial depolarizations that propagate chaotically throughout the atria (8–10). Even less is known about the development of AF in the perioperative setting, but it is thought to be related to (a) catecholamine excess (11), (b)

autonomic imbalance (12), (c) inflammation (12,13), and (d) shifts in volume and pressure in the atria that can all affect electrical stability (14,15).

AF is commonly thought of as a disease of the elderly. Increasing age is the greatest risk factor for incident AF in both the outpatient and perioperative setting. In a study of 570 consecutive patients undergoing CABG, the risk of developing AF in those less than 60 was 18% and in those over 80 was as high as 52% (5). Additional independent risk factors for AF include prior AF, male gender, reduced left ventricular systolic function, valvular surgery, chronic obstructive pulmonary disease, chronic renal insufficiency, and diabetes mellitus (16).

PREVENTION

What Are Effective and Safe Pharmacologic Strategies for Prevention of Postoperative AF After Coronary Artery Bypass Surgery?

Answer: Beta-blockers consistently demonstrate a reduction in AF with an acceptable safety profile. In high-risk patients, amiodarone is also a reasonable strategy; however, there remains some uncertainty regarding its safety profile. Grade of recommendation: A.

Beta-adrenergic Receptor Antagonists

Beta-blockers are the most studied drug in preventing AF after cardiothoracic surgery and have established benefit.

Although numerous studies have been performed, there exists significant heterogeneity in study designs, specifically in regard to the number of patients enrolled, primary endpoints, specific beta-blocker studied, and even timing of initial therapy. Two meta-analyses looking collectively at these studies demonstrated that beta-blockers reduced the incidence of AF postcardiothoracic surgery by 61–64% compared with control subjects (17,18).

The largest and probably best designed beta-blocker study enrolled more than 500 patients in a randomized, double-blinded, placebo-controlled trial, named the Beta-blocker Length of Stay study (19). The investigators set out to determine if the expected reduction in postoperative AF with oral metoprolol was associated with a shortened hospital length of stay. The treatment group received either 100 or 150mg oral metoprolol daily after arrival to the intensive care unit (ICU). Despite a 20% reduction in postoperative AF in the treatment group, the authors were surprised to find that the length of stay was not statistically different between the groups. This may have been for several reasons. First, all nonstudy beta-blockers were allowed to be continued in both study groups, which accounted for 40% of the control group. This might have decreased the observed effect of beta-blocker therapy. Second, it is also possible that the beta-blockers might have caused adverse complications due to bradycardia or hypotension, which could attenuate any of benefits of having reduced the total AF burden. Last, the observed reduction in AF from beta-blockers was much lower than expected, and this could render this study underpowered to detect a difference in length of stay.

In summary, there is overwhelming evidence that patients on preoperative beta-blockers should be continued on their current therapy and patients who are naive to beta-blockers should be initiated on beta-blocker therapy and be continued throughout the perioperative period.

Amiodarone: Class III Antiarrhythmic

Amiodarone is a unique antiarrhythmic drug that has been shown to reduce AF after cardiothoracic surgery. The drug works via its complex actions on potassium channels, sodium channels, and calcium channels as well as possessing antiadrenergic properties that might aid in attenuating the heightened sympathetic tone seen after surgery. In the AFIST II study, an IV amiodarone study of 160 patients undergoing CABG ± valve surgery, patients received either the treatment drug beginning within the first six hours postoperatively or received placebo. The treatment group had an encouraging reduction in AF incidence at 22.1% compared to the 38.6% seen in the placebo arm (20). Instead of IV amiodarone, the PAPABEAR study used oral amiodarone, which was initiated six days preoperatively and demonstrated a significant reduction in AF incidence at only 16.1% seen in the treatment group and 29.5% seen in the placebo arm (21).

Though these results are encouraging, amiodarone is not a completely benign therapy, especially given the numerous reported complications seen in the outpatient setting. Several case reports draw particular attention to the possibility of developing pulmonary toxicity and even fulminant acute respiratory distress syndrome (ARDS). However, two studies looking specifically to identify ARDS as a possible risk failed to demonstrate that amiodarone increases the risk of ARDS in postcardiothoracic surgical patients (22,23).

A recent meta-analysis looked at the safety profile of amiodarone in over 18 different postcardiothoracic surgery trials (24). This study showed that amiodarone had the benefits of fewer episodes of ventricular arrhythmias and fewer neurologic events (transient ischemic attacks or stroke). However, there were increased episodes of bradycardia and hypotension, but the authors note that more of these episodes were seen using IV amiodarone compared to oral amiodarone.

Sotalol: Class III Antiarrhythmic

Numerous studies have evaluated the potential of sotalol to reduce AF after cardiothoracic surgery due to the effects imparted by both its antiarrhythmic properties coupled with its beta-blocking properties. All of these studies have consistently demonstrated a significant reduction in AF with a recent meta-analysis reporting there to be a 63% risk reduction in AF (odds ratio 0.37 with 95% confidence interval 0.29–0.48) (18). It was found to be more effective than beta-blockers alone by 10%. Although these results are certainly promising, there is significant potential for side effects, including bradycardia, hypotension, and even proarrhythmia with the development of torsades de pointes (TdP) due to sotalol's QT-prolonging effects. The same meta-analysis noted that sotalol was not tolerated well and that patients discontinued treatment compared to placebo due to side effects of bradycardia, hypotension, and prolongation of the QTc interval (6.0 versus 1.9%, $p = 0.004$) (18). Even though no significant difference was seen with rates of withdrawal from treatment between sotalol compared to beta-blockers, this may have been because the individual studies had small numbers of enrollees and therefore may not have adequately represented all the potential for sotalol side effects.

Sotalol does hold promise as an effective prophylactic agent; however, large randomized, placebo-controlled trials need to be performed before it can be recommended as a primary agent.

Are There Intraoperative Strategies to Consider That May Reduce Incident AF After Cardiothoracic Surgery?

Answer: Applying mild hypothermia, performing a posterior pericardiotomy, and using heparin-coated bypass circuits have all suggested a benefit in reducing the risk of supraventricular tachycardias. Grade of recommendation: C.

Intraoperative Techniques

Varying degrees of hypothermia have demonstrated a significant reduction in postoperative AF, and greater reduction is seen in patients cooled to mild hypothermia (34°C) compared to moderate hypothermia (28°C). Induction of systemic hypothermia is common during CABG surgery for both myocardial and cerebral protection. Although the exact nature of the mechanism of benefit is unclear, it has been proposed that rewarming from only mild hypothermia may reduce autonomic fluctuations that increase risk of AF (25).

Incision of the posterior pericardium in addition to the typical anterior incision has also been shown to reduce postoperative AF. The typical surgical approach is for the surgeon to make an anterior incision to expose the great vessels and underlying heart. The addition of the posterior

incision is thought to facilitate drainage of blood and fluid that collects as a product of perimyocardial inflammation. This would then theoretically minimize inflammation and irritation to the myocardium (26).

Cardiac perfusion bypass circuits have long been associated with systemic inflammation and may contribute to AF. Heparin-coated circuits were created in an attempt to minimize the inflammation that leads to AF. Results from two randomized, controlled trials looking at the benefits of heparin-coated circuits did demonstrate a reduction in AF. The specific brand of heparin-coated circuits used did yield variable results and thus should be taken into account (27,28).

Cardiac Pacing

The usefulness of atrial pacing to prevent postoperative AF remains inconclusive. The theoretical goals of atrial pacing are to reduce the premature atrial complexes that are frequently seen in the minutes to hours prior to the onset of AF (29) by overdrive pacing and to minimize dispersion of atrial repolarization (30). Studies to date have collectively yielded conflicting results. Several studies looking separately at right atrial pacing, left atrial pacing, and biatrial pacing have yielded a reduction in AF in some with no benefit in others. Of these different modalities, biatrial pacing appears to confer the most benefit with the largest randomized controlled trial of 130 patients demonstrating a reduction in AF of 13.8% versus 38.5% ($p = 0.001$) (31). However, these studies all suffer from small sample sizes and variable results, making a clear benefit questionable. At this time, despite the small amount of risk involved in placing epicardial leads at the time of surgery, atrial pacing cannot be strongly recommended for prevention of postoperative AF.

TREATMENT

All hemodynamically unstable tachyarrhythmias should receive emergent direct current (DC) cardioversion. Otherwise, if hemodynamically stable, supraventricular arrhythmias, except for AF, atrial flutter, and most atrial tachycardias, can be terminated using IV adenosine by disrupting conduction at the level of the atrioventricular (AV) node. Typically this is done using sequential attempts first with 6mg, then 12mg, and then a repeat attempt with an additional 12mg of adenosine.

In hemodynamically stable patients, the management encompasses the control of ventricular rate, mitigating the risk of thromboembolic events, and the option of restoring and maintaining normal sinus rhythm via direct current cardioversion.

What Drugs Should Be Avoided in Patients with AF with Underlying Wolff-Parkinson-White Syndrome?

Answer: Adenosine, beta-blockers, and calcium channel blockers. It is important to avoid AV-nodal blocking agent, such as adenosine, beta-blockers, and calcium channel blockers (CCBs) if AF or atrial flutter occurs in a patient known to have ventricular pre-excitation, namely, the Wolff-Parkinson-White Syndrome (32,33). If given, AV-nodal blocking agents will cause conduction block in the AV

node, thereby favoring anterograde conduction over the accessory pathway at dangerously high conduction rates, and the rhythm could then degenerate into ventricular fibrillation. Grade of recommendation: A.

Is Elective Cardioversion, Chemically or by DC Cardioversion, a Reasonable Option in the Postoperative AF Patient?

Answer: Yes. It may reduce length of hospital stay and prolong duration in normal sinus rhythm. Grade of recommendation: B.

Rate Control and Rhythm Control Strategies

The first step in managing hemodynamically stable AF is to control the ventricular response, which is often rapid due to the heightened sympathetic tone seen in the immediate postoperative period. Beta-blockers are the first choice with either IV short-acting esmolol or IV metoprolol. Non-dihydropyridine CCBs can also be used, but beta-blockers remain first-line agents due to their antiadrenergic properties. Digoxin is considered less useful in the immediate postoperative setting because of its slow onset of action. At times, it is useful in patients with congestive heart failure or if added to beta-blockers or CCBs for its synergistic rate-controlling effect.

It is important to emphasize that most episodes of AF are self-limited and will frequently spontaneously convert to normal sinus rhythm (NSR) without antiarrhythmic therapy. In one study, up to 80% of patients spontaneously converted to NSR within 24 hours with only an AV-nodal blocking agent given for rate control (34). However, if the patient remains in AF, there are advantages to pursuing elective cardioversion (either chemically or by DC application) including decreased hospital length of stay and prolonged maintenance of sinus rhythm (35).

Either chemical cardioversion using agents such as amiodarone, ibutilide, sotalol, or propafenone or direct current cardioversion are reasonable options. The advantage of chemical cardioversion is mainly the convenience of its administration; however, all antiarrhythmic medications confer some risk for complications, albeit usually small.

Amiodarone is the agent of choice when looking to chemically convert postoperative AF. When given IV, it will convert AF to NSR ~40–90% of the time after cardiac surgery in 12–24 hours (36–38). It possesses significant advantages over other class IC and III agents. Essentially, all antiarrhythmic drugs are associated with an increased risk of proarrhythmia either due to prolongation of the QTc interval, resulting in TdP, or through their modulation of refractory periods. However, this appears to be a very rare complication of amiodarone. In addition to having less proarrhythmia, its beta-blocking properties help with rate control while the patient is in AF. Finally, it also has the advantage of being easily converted to an oral form if it needs to be taken after discharge in the outpatient setting.

Ibutilide is a class III antiarrhythmic that has proven effective in converting AF to NSR after cardiac surgery. In one study, at the 1 mg IV dose, it successfully converted 57% of patients to NSR, which was significantly higher than placebo. There is an increased risk of TdP due to its QT-prolonging effects, which was seen in 1.8% of patients

receiving ibutilide. Given this proarrhythmia risk, certain precautions must be taken before administering ibutilide. One must make sure the QTc interval is not prolonged on a 12-lead electrocardiogram (ECG) and that all electrolyte abnormalities have been corrected (39).

Should Warfarin Be Given in Postoperative AF That Is Recurrent or Persists for More than 24 Hours?

Answer: Warfarin anticoagulation should be initiated for at least four weeks to mitigate the risk of stroke. Grade of recommendation: B.

Anticoagulation

Anticoagulation for persistent AF (lasting greater than 48 hours) must be strongly considered after cardiac surgery to reduce the devastating risk of stroke. The benefits of anticoagulation with heparin or warfarin need to be weighed against the risk of bleeding from the performed surgical procedure. The exact duration of anticoagulation, whether for the short term or the long term, needs to be individualized. The major factors that increase the risk of stroke in patients with AF are congestive heart failure, diabetes, hypertension, age >75 years, and prior history of transient ischemic attacks or stroke (40).

BRADYARRHYTHMIAS

Conduction system disturbances following noncardiac surgery resulting in permanent pacemaker (PPM) placement are rare. On the other hand, it is relatively common following cardiac surgery, occurring in up to 2–3% of patients (41,42). The risk of requiring PPM placement increases with the complexity of the cardiac surgery. Repeat valve surgery results in up to 10% of patients requiring a PPM (43), whereas multivalve surgery results in PPM placement in 10% for aortic + mitral valves, 16% for mitral + tricuspid valves, and 25% for aortic + mitral + tricuspid valves (43).

The conduction disturbances resulting in sinus node dysfunction or varying degrees of heart block are either due to surgical trauma to the areas of the sinoatrial node, AV node, or His-Purkinje specialized conduction system or possibly to ischemic injury associated with cardioplegia.

In sinus node dysfunction or if significant heart block develops, management in the perioperative period is similar to other bradycardic presentations. Electrolyte imbalances need to be corrected, and nonessential drugs contributing to bradycardia should be discontinued. Generally, no acute therapy is needed if there is no hemodynamic compromise and particularly if the arrhythmia is transient. Most of the bradyarrhythmias that occur immediately postoperatively are self-limited and resolve by postoperative day 7. In fact, it is noteworthy that up to 40% of patients who receive a PPM eventually will not require use of their implanted device (44).

In the acute setting, if sinus node dysfunction is persistent and results in end organ hypoperfusion, then immediate management is needed. The sinus rate can be augmented by giving an anticholinergic agent (such as IV atropine) or by infusing a beta-agonist (such as dopamine).

If second degree, Mobitz II AV block, high grade AV block, or complete heart block occurs, then temporary

pacing should be sought by either previously placed epicardial pacing wires, percutaneous transvenous pacing, or transcutaneous pacing. Temporary epicardial wires are often routinely implanted at the time of cardiac surgery, especially in patients who are at high risk for developing conduction disturbances.

The long-term management of persistent bradyarrhythmias is essentially the same postoperatively as in the outpatient setting and may require placement of a PPM as detailed by the ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities (45).

VENTRICULAR ARRHYTHMIAS

Ventricular tachyarrhythmias after noncardiac surgery are uncommon. In two series, the incidence is reported to be up to 3%; however, the vast majority of these included hemodynamically insignificant ectopic ventricular beats (46,47). However, after cardiothoracic surgery, sustained monomorphic ventricular tachycardia (VT), polymorphic VT, and ventricular fibrillation (VF) are seen in up to 1–3% of patients (48,49). In the same studies, not surprisingly, the presence of ventricular conduction disturbances was associated with a significantly worse outcome compared to similar patients who did not develop these arrhythmias.

The entire spectrum of ventricular arrhythmias that can occur in the perioperative period includes isolated premature ventricular complexes (PVCs), nonsustained VT, sustained monomorphic VT (either with or without hemodynamic compromise), and VF.

PVCs in patients with structurally normal hearts have a benign prognosis and require no further therapy. However, beta-blockers can be used to suppress PVCs in symptomatic patients. In patients with structurally abnormal hearts (including those with either a nonischemic cardiomyopathy or an ischemic cardiomyopathy), like many of those who undergo cardiothoracic surgery, PVCs and nonsustained VT are associated with an increased risk of sudden death. Despite this increased risk, the CAST trials have shown that in patients who have suffered a prior myocardial infarction, suppression of PVCs and episodes of nonsustained VT with class I antiarrhythmic drugs (encainide, flecainide, and moricizine) increases mortality (50). Therefore, the use of these drugs for suppression of PVCs and episodes of nonsustained VT should be avoided due to their proarrhythmic nature.

All patients who develop sustained VT and polymorphic VT associated with hemodynamic instability should receive emergent DC cardioversion. Additionally, an immediate evaluation is required to identify reversible causes, such as ischemia, electrolyte imbalances, or the presence of QT-prolonging drugs that may result in a specific type of polymorphic VT, namely TdP.

Beta-blockers are considered the cornerstone of antiarrhythmic drug therapy and have been shown to safely and effectively reduce the recurrence of the entire spectrum of ventricular arrhythmias in those with and without structural heart disease (51,52). Patients with structural heart disease should be given beta-blockers as long as they can hemodynamically tolerate a drug.

Patients with episodes of sustained monomorphic VT at risk of circulatory collapse but currently hemodynamically

stable can be given antiarrhythmic drugs for acute termination and to suppress recurrence. Amiodarone is considered the first-line agent for the acute termination of hemodynamically stable monomorphic VT and to suppress recurrent VT as outlined in the most recent ACLS guidelines (53,54). Lidocaine was historically used as a first-line agent (55); however, it has since fallen out of favor given that its effectiveness appears to be limited to myocardial tissue subjected to ongoing ischemia (56,57). Other pharmacologic options include procainamide and sotalol.

Polymorphic VT is characterized by a wide complex tachycardia with a continuously shifting QRS morphology, amplitude, and axis. The acute management is similar to monomorphic VT and VF with attention given to immediate DC cardioversion, antiarrhythmic therapy, and identification of reversible causes. Particular attention needs to be given to the patient's 12-lead ECG to accurately measure the QTc interval. If this interval is not prolonged or only mildly prolonged (<440 milliseconds), this would be highly suggestive of ischemia as a precipitating factor. If this interval is prolonged, a thorough medication review is warranted to identify and remove any nonessential QT-prolonging drugs.

There are other rare causes for polymorphic VT, such as the congenital long QT syndromes resulting from defects found in ion channels. However, the drug-induced causes occur with much more frequency.

REFERENCES

- Goldman L, Caldera DL, Southwick FS, et al. Cardiac risk factors and complications in non-cardiac surgery. *Medicine (Baltimore)* 1978; 57: 357–70.
- Walsh SR, Thomas C, Manohar S, et al. Early management of atrial fibrillation in general surgical in-patients. *Int J Surg* 2006; 4: 115–17.
- Polanczyk CA, Goldman L, Marcantonio ER, et al. Supraventricular arrhythmia in patients having noncardiac surgery: clinical correlates and effect on length of stay. *Ann Intern Med* 1998; 129: 279–85.
- Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? *Ann Surg* 1997; 226: 501–11; discussion 511–13.
- Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation* 1996; 94: 390–7.
- Creswell LL, Schuessler RB, Rosenbloom M, et al. Hazards of postoperative atrial arrhythmias. *Ann Thorac Surg* 1993; 56: 539–49.
- Fuller JA, Adams GG, Buxton B. Atrial fibrillation after coronary artery bypass grafting. Is it a disorder of the elderly? *J Thorac Cardiovasc Surg* 1989; 97: 821–5.
- Moe GK, Abildskov JA. Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge. *Am Heart J* 1959; 58: 59–70.
- Moe GK, Rheinboldt WC, Abildskov JA. A computer model of atrial fibrillation. *Am Heart J* 1964; 67: 200–20.
- Waldo AL. Experimental models of atrial fibrillation—what have we learned? *Semin Interv Cardiol* 1997; 2: 195–201.
- Kalman JM, Munawar M, Howes LG, et al. Atrial fibrillation after coronary artery bypass grafting is associated with sympathetic activation. *Ann Thorac Surg* 1995; 60: 1709–15.
- Levy MN. Sympathetic-parasympathetic interactions in the heart. *Circ Res* 1971; 29: 437–45.
- Tselentakis EV, Woodford E, Chandy J, et al. Inflammation effects on the electrical properties of atrial tissue and inducibility of postoperative atrial fibrillation. *J Surg Res* 2006; 135: 68–75.
- Ravelli F, Allesie M. Effects of atrial dilatation on refractory period and vulnerability to atrial fibrillation in the isolated Langendorff-perfused rabbit heart. *Circulation* 1997; 96: 1686–95.
- Deroubaix E, Folliguet T, Rucker-Martin C, et al. Moderate and chronic hemodynamic overload of sheep atria induces reversible cellular electrophysiologic abnormalities and atrial vulnerability. *J Am Coll Cardiol* 2004; 44: 1918–26.
- Baker WL, White CM. Post-cardiothoracic surgery atrial fibrillation: a review of preventive strategies. *Ann Pharmacother* 2007; 41: 587–98.
- Crystal E, Connolly SJ, Sleik K, et al. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: a meta-analysis. *Circulation* 2002; 106: 75–80.
- Burgess DC, Kilborn MJ, Keech AC. Interventions for prevention of post-operative atrial fibrillation and its complications after cardiac surgery: a meta-analysis. *Eur Heart J* 2006; 27: 2846–57.
- Connolly SJ, Cybulsky I, Lamy A, et al. Double-blind, placebo-controlled, randomized trial of prophylactic metoprolol for reduction of hospital length of stay after heart surgery: the beta-blocker length of stay (BLOS) study. *Am Heart J* 2003; 145: 226–32.
- White CM, Caron MF, Kalus JS, et al. Intravenous plus oral amiodarone, atrial septal pacing, or both strategies to prevent post-cardiothoracic surgery atrial fibrillation: the Atrial Fibrillation Suppression Trial II (AFIST II). *Circulation* 2003; 108(Suppl 1): II200–II206.
- Mitchell LB, Exner DV, Wyse DG, et al. Prophylactic oral amiodarone for the prevention of arrhythmias that begin early after revascularization, valve replacement, or repair: PAPABEAR: a randomized controlled trial. *JAMA* 2005; 294: 3093–100.
- Crystal E, Kahn S, Roberts R, et al. Long-term amiodarone therapy and the risk of complications after cardiac surgery: results from the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT). *J Thorac Cardiovasc Surg* 2003; 125: 633–7.
- Kaushik S, Hussain A, Clarke P, et al. Acute pulmonary toxicity after low-dose amiodarone therapy. *Ann Thorac Surg* 2001; 72: 1760–1.
- Patel AA, White CM, Gillespie EL, et al. Safety of amiodarone in the prevention of postoperative atrial fibrillation: a meta-analysis. *Am J Health Syst Pharm* 2006; 63: 829–37.
- Adams DC, Heyer EJ, Simon AE, et al. Incidence of atrial fibrillation after mild or moderate hypothermic cardiopulmonary bypass. *Crit Care Med* 2000; 28: 309–11.
- Kuralay E, Ozal E, Demirkili U, Tatar H. Effect of posterior pericardiotomy on postoperative supraventricular arrhythmias and late pericardial effusion (posterior pericardiotomy). *J Thorac Cardiovasc Surg* 1999; 118: 492–5.
- Ovrum E, Am Hølen E, Tangen G, et al. Heparinized cardiopulmonary bypass and full heparin dose marginally improve clinical performance. *Ann Thorac Surg* 1996; 62: 1128–33.
- Svenmarker S, Sandstrom E, Karlsson T, et al. Neurological and general outcome in low-risk coronary artery bypass patients using heparin coated circuits. *Eur J Cardiothorac Surg* 2001; 19: 47–53.
- Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. *Ann Intern Med* 2001; 135: 1061–73.
- Satoh T, Zipes DP. Unequal atrial stretch in dogs increases dispersion of refractoriness conducive to developing atrial fibrillation. *J Cardiovasc Electrophysiol* 1996; 7: 833–42.
- Levy T, Fotopoulos G, Walker S, et al. Randomized controlled study investigating the effect of atrial pacing in prevention of atrial fibrillation after coronary artery bypass grafting. *Circulation* 2000; 102: 1382–7.

32. Garratt C, Antoniou A, Ward D, et al. Misuse of verapamil in pre-excited atrial fibrillation. *Lancet* 1989; 1: 367–9.
33. McGovern B, Garan H, Ruskin JN. Precipitation of cardiac arrest by verapamil in patients with Wolff-Parkinson-White syndrome. *Ann Intern Med* 1986; 104: 791–4.
34. Soucier RJ, Mirza S, Abordo MG, et al. Predictors of conversion of atrial fibrillation after cardiac operation in the absence of class I or III antiarrhythmic medications. *Ann Thorac Surg* 2001; 72: 694–7; discussion 697–8.
35. Lee JK, Klein GJ, Krahn AD, et al. Rate-control versus conversion strategy in postoperative atrial fibrillation: trial design and pilot study results. *Card Electrophysiol Rev* 2003; 7: 178–84.
36. Cochrane AD, Siddins M, Rosenfeldt FL, et al. A comparison of amiodarone and digoxin for treatment of supraventricular arrhythmias after cardiac surgery. *Eur J Cardiothorac Surg* 1994; 8: 194–8.
37. McAlister HF, Luke RA, Whitlock RM, et al. Intravenous amiodarone bolus versus oral quinidine for atrial flutter and fibrillation after cardiac operations. *J Thorac Cardiovasc Surg* 1990; 99: 911–18.
38. Installe E, Schoevaerdt JC, Gadisseux P, et al. Intravenous amiodarone in the treatment of various arrhythmias following cardiac operations. *J Thorac Cardiovasc Surg* 1981; 81: 302–8.
39. VanderLugt JT, Mattioni T, Denker S, et al. Efficacy and safety of ibutilide fumarate for the conversion of atrial arrhythmias after cardiac surgery. *Circulation* 1999; 100: 369–75.
40. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *J Am Coll Cardiol* 2006; 48: 854–906.
41. Goldman BS, Hill TJ, Weisel RD, et al. Permanent cardiac pacing after open-heart surgery: acquired heart disease. *Pacing Clin Electrophysiol* 1984; 7: 367–71.
42. Del Rizzo DF, Nishimura S, Lau C, et al. Cardiac pacing following surgery for acquired heart disease. *J Card Surg* 1996; 11: 332–40.
43. Lewis JW Jr., Webb CR, Pickard SD, et al. The increased need for a permanent pacemaker after reoperative cardiac surgery. *J Thorac Cardiovasc Surg* 1998; 116: 74–81.
44. Glikson M, Dearani JA, Hyberger LK, et al. Indications, effectiveness, and long-term dependency in permanent pacing after cardiac surgery. *Am J Cardiol* 1997; 80: 1309–13.
45. Epstein AE, Dimarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices): Developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *Circulation* 2008; 117: 2820–40.
46. Walsh SR, Tang T, Wijewardena C, et al. Postoperative arrhythmias in general surgical patients. *Ann R Coll Surg Engl* 2007; 89: 91–5.
47. Batra GS, Molyneux J, Scott NA. Colorectal patients and cardiac arrhythmias detected on the surgical high dependency unit. *Ann R Coll Surg Engl* 2001; 83: 174–6.
48. Ascione R, Reeves BC, Santo K, et al. Predictors of new malignant ventricular arrhythmias after coronary surgery: a case-control study. *J Am Coll Cardiol* 2004; 43: 1630–8.
49. Yeung-Lai-Wah JA, Qi A, McNeill E, et al. New-onset sustained ventricular tachycardia and fibrillation early after cardiac operations. *Ann Thorac Surg* 2004; 77: 2083–8.
50. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991; 324: 781–8.
51. Reiter MJ, Reiffel JA. Importance of beta blockade in the therapy of serious ventricular arrhythmias. *Am J Cardiol* 1998; 82: 91–191.
52. Ellison KE, Hafley GE, Hickey K, et al. Effect of beta-blocking therapy on outcome in the Multicenter UnSustained Tachycardia Trial (MUSTT). *Circulation* 2002; 106: 2694–9.
53. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). *J Am Coll Cardiol* 2006; 48: e247–e346.
54. Dorian P, Cass D, Schwartz B, et al. Amiodarone as compared with lidocaine for shock-resistant ventricular fibrillation. *N Engl J Med* 2002; 346: 884–90.
55. Griffith MJ, Linker NJ, Garratt CJ, et al. Relative efficacy and safety of intravenous drugs for termination of sustained ventricular tachycardia. *Lancet* 1990; 336: 670–3.
56. Kowey PR, Marinchak RA, Rials SJ, et al. Intravenous antiarrhythmic therapy in the acute control of in-hospital destabilizing ventricular tachycardia and fibrillation. *Am J Cardiol* 1999; 84: 46R–51R.
57. Gorgels AP, van den Dool A, Hofs A, et al. Comparison of procainamide and lidocaine in terminating sustained monomorphic ventricular tachycardia. *Am J Cardiol* 1996; 78: 43–6. Perioperative Arrhythmias

Feeds and Feeding Surgical Patients

Jayson D. Aydelotte

Clinical Questions		
Question	Answer	Grade of recommendation
Is TPN or tube feedings better for the patient?	Enteral feeds have fewer and less severe infective complications and faster return of bowel function.	A
What is the safest and most effective, feeding the stomach or the small bowel?	Complication rates are the same for both methods. Gastric feeds have faster onset of goal feeds.	A
Does immunonutrition improve outcome?	Yes, immunonutrition is linked to shorter hospital stay and vent days as well as overall infection. Mortality unchanged.	A
What's the best way to start and advance postoperative patients on a diet?	Give them a diet of choice as soon as possible. Waiting for flatus and physician-dictated diets drag things out longer with no decrease in complications.	A
Is glutamine a beneficial additive to feedings?	Yes, glutamine is readily available and relatively cheap. Multiple studies link glutamine to lower infections and decreased morbidity.	A
How early can tube feeds be safely started?	Enteral feeds can be safely started within 12–24 hours. Early tube feeds are linked to lower septic morbidity.	A
Abbreviations: TPN, total parenteral nutrition.		

Nutrition is one of the key components of good wound healing. From the moment a patient is injured or undergoes a significant surgical procedure, he or she is dependent on the building blocks of nutrients. Surgeons have traditionally been faced with answering questions such as when to start someone on enteral feeds? Should patients just get total parenteral nutrition (TPN) instead of tube feeds? Should we feed the stomach or feed past the pylorus? Is immunonutrition beneficial? Is glutamine beneficial as an additive to feedings? What is the best way to start someone on an oral diet after abdominal surgery? Nutrition lends itself to quality research. Most of the research is done in controlled hospital settings with a relatively standard patient population. Because of this there have been many randomized controlled trials looking at many of these questions.

DO I HAVE TO USE THE GUT AFTER A MAJOR ABDOMINAL OPERATION, OR CAN I JUST GIVE THE PATIENT TPN?

Apprehension in using the bowel after major abdominal surgery or trauma leads many surgeons to deliver nutrition to patients without using the gut. This makes a certain amount of common sense, and several studies have been done to address this very question.

One randomized prospective trial divided two groups of trauma patients at the time of laparotomy into needle jejunostomy enteral feeds versus isocaloric/isonitrogenous TPN starting 12 hours after surgery. Eighty-six percent of the patients receiving enteral feeds tolerated a full feeding rate. There were no differences in nitrogen balance in the two groups, but the enteral feeding group had significantly less hyperglycemia and septic complications (12) (Level Ib evidence). Another study was done randomizing patients with both blunt and penetrating abdominal trauma to TPN and protein/calorie matched enteral feeds. The results were very similar. Overall, there were fewer infections in fewer patients in the enterally fed group. There was no difference in mortality (13) (Level Ib evidence). Another prospective randomized trial looked at standard enteral feeds versus TPN versus immune-enhanced enteral feeds and found that only 94% of the patients receiving enteral feeds tolerated the feeds well (1) (Level IIb evidence). A meta-analysis of 13 prospective random assignment trials concluded enteral nutrition had fewer infective complications without any decrease in mortality or hospital stay than TPN (14) (Level Ia evidence).

Answer: Enteral tube feedings started within the first 24 hours after abdominal trauma or abdominal surgery is safe and the preferred method of nutrition delivery over parenteral nutrition (Grade A recommendation).

WHEN SHOULD ENTERAL FEEDS BE STARTED?

This question was indirectly asked during some of the trials listed in the question regarding TPN versus enteral feeds. Traditionally, surgeons are apprehensive in starting enteral feeds in patients before they demonstrate return of bowel function as manifested by many different clinical signs, such as passing flatus or return of bowel sounds. In an effort to objectify things, some authors set out to start tube feeds at a certain time postoperatively or after injury and see how the patients tolerated this and, more important, to see if this made any difference in outcome. In Moore's study, enteral feeding was started 12 hours postoperatively in patients who had undergone abdominal surgery. These feeds were tolerated well, and the patients fed enterally had fewer septic complications (12) (Level Ib evidence). Another study looking at nontrauma septic patients with peritonitis from perforation started enteral feeds within 12 hours of surgery. Only 18% of the studied subjects needed the feeds temporarily held for abdominal distention. The studied group had a positive nitrogen balance by the third postoperative day and suffered fewer septic complications than the controls (11) (Level Ib evidence).

Answer: Enteral feeds can safely be started in trauma patients and patients who undergo major abdominal surgery within the first 24 hours in most cases (Grade A recommendation).

CAN WE JUST FEED THE STOMACH, OR DO WE NEED TO FEED PAST THE PYLORUS INTO THE SMALL BOWEL?

Much like the notion that not using the gut after major surgery or trauma makes common sense to some surgeons, the idea that feeding beyond the ligament of Treitz or beyond the pylorus makes some sense as well. The idea is that the tube feeds would not be in the stomach and easily aspirated into the lungs. Or, more commonly, the tube feeds would not be in a stomach that may or may not be emptying well because of the overall poor physical condition of the patient. For this reason, many surgeons and nonsurgeons advocate the placement of a small bowel feeding catheter instead of feeding a gastric tube. The problem is that placing these tubes is not always as easy as it seems, and they often become displaced from the small bowel. Several studies were done to see if feeding the stomach is as safe and effective as feeding the small bowel. Neuman and colleagues randomized 60 patients to receive gastric feeds or have a postpyloric tube placed. Patients receiving gastric feeds had their feeds started sooner and had an earlier time to goal feeding while having no increased aspiration as compared to the patients randomized to the postpyloric group (7) (Level Ib evidence). Another study with similar numbers in children came to the opposite conclusion. The postpyloric group had a higher percentage of daily caloric goal achieved but had the same complication rate as stomach feeding. However, in this study the investigators suffered from the same problem that lead to the original question in that nearly 30% of the patients randomized to the postpyloric group could not have their tube placed properly and were then switched to the gastric feeding group (6). (Level IIb evidence).

This study, however, is helpful to partly answer the question. That is, there were no significant differences in complications between gastric and postpyloric tube feeding complications.

Answer: It is safe to feed a working stomach. Placing a small bowel feeding tube delays time to goal feeds and does not lower complication rates (Grade A recommendation).

IS IMMUNONUTRITION BENEFICIAL?

Enteral tube feedings have been adjusted and manipulated for many different reasons to give different desired results. One particular way tube feeds can be adjusted is by adding certain "immune-enhancing" agents to the feeding. There are a variety of specific immune enhancing agents that have been studied, such as arginine, glutamine, nucleic acids, eicosapentanoic acid, and omega-3-fatty acids. Different manufacturers produce different combinations of these agents to make proprietary products. There have been randomized trials looking at specific products and outcomes. One study evaluated preoperative and postoperative immunonutrition with arginine, omega-3-fats, and RNA nucleotides in patients undergoing upper gastrointestinal surgery for cancer. Treated subjects had a lower incidence of postoperative infective complications with no difference in mortality (9) (Level Ib evidence). Another study evaluated immunonutrition using the same additives in critically ill patients. Subjects receiving immunonutrition had a decrease in ventilator days and hospital stay with no change in mortality (10) (Level Ib evidence). A meta-analysis was done on a total of 15 prospective randomized studies using immunonutrition and comprising many different products. Overall conclusions of this study were that immunonutrition as a whole showed a significant decrease in ventilator days, hospital days, and infection complications (8). (Level Ia evidence).

Answer: Immunonutrition is associated with a decrease in hospital days, ventilator days, and postoperative infection in seriously ill patients and may decrease postoperative infections in patients undergoing major abdominal operations for cancer (Grade A recommendation).

IS GLUTAMINE HELPFUL AS A FEED ADDITIVE?

Glutamine is a nonessential amino acid and a preferential nutrient of the enterocyte. Glutamine is relatively cheap and can be easily added to standard tube feed products. Several randomized prospective trials evaluating the addition of glutamine to both tube feeds and parenteral formulas have been done. One randomized study in burn patients found an association of lower mortality and decreased infection (2) (Level Ib evidence). Another study in patients with multitrauma found a lower incidence of pneumonia, bacteremia, and sepsis in the glutamine-treated group (3) (Level Ib evidence). A large, French, multicenter randomized trial found glutamine addition to TPN decreased pneumonia and incidence of hyperglycemia (5) (Level Ib evidence).

Answer: Glutamine is effective as an additive in both enteral and parenteral feeds to decrease the incidence of infectious complications (Grade A recommendation).

WHAT IS THE BEST WAY TO START AND PROGRESS A DIET IN A PATIENT AFTER ABDOMINAL SURGERY?

The traditional surgical thinking regarding the starting of oral intake after abdominal surgery is to wait for hard signs of return of bowel function and then slowly progress to a regular diet in a stepwise fashion from clear liquids through a range of food qualities to regular diet over the course of several days. Recently, this thought process has been challenged. One trial randomly assigned gynecologic oncology patients into two groups: those who were to be given clear liquids on the first postoperative day and advance as tolerated and those who were to be nothing per oral until passage of flatus. There was no difference in vomiting or other complications, although the treatment group trended toward more nausea. There was a one day shorter hospital stay and 2.5 fewer days to tolerating a

regular diet (15) (Level Ib evidence). A similar prospective randomized study by the same authors looked at the same patient population and divided groups into regular diet as first diet of choice versus clear liquids and progression as tolerated. There was no difference in complication or hospital stay but a decrease in time to tolerating regular diet (17) (Level Ib evidence). Another study assigned patients undergoing elective aortic and colorectal surgery randomly to two groups: the treatment group, which was provided a patient-controlled diet of choice, and the control was nothing by mouth for five days. There was no difference in hospital days, complications, or nasogastric tube reinsertion rate. The patients in the treatment group had a shorter time until they were tolerating a diet (16) (Level Ib evidence).

Answer: Provide a patient-controlled diet as soon as possible postoperatively (Grade A recommendation).

Levels of Evidence

Author	Ref.	Year	Level of evidence	Groups	Design	Endpoint
Braga	1	1998	Ib	TPN versus immune enhanced feeds versus standard enteral feeds	RCS	Infection, toleration of feedings
Garrel	2	2003	Ib	Enteral glutamine versus no glutamine	RCS	Infection, pneumonia, death
Houdijk	3	1998	Ib	glutamine versus no glutamine enteral diet	RCS	Infection, pneumonia, mortality
Dechelotte	4	2006	Ib	Glutamine versus no glutamine TPN	RCS	Infection and glucose intolerance
Saalwachter	5	2006	Ib	Glutamine versus no glutamine enteral feeds	RCS	Infection, pneumonia
Meert	6	2004	Ib	Gastric versus small bowel feeding in children	RCS	Time to goal feeds, total calories, aspiration
Neumann	7	2002	Ib	Gastric versus small bowel feeding	RCS	Time to feeds, total calories, aspiration
Beale	8	1999	Ia	Immunonutrition in the critically ill	SR	Mortality, infection
Senkal	9	1999	Ib	Perioperative immunonutrition versus standard enteral nutrition	RCS	Infection, mortality
Atkinson	10	1998	Ib	Enteral immunonutrition versus standard enteral nutrition	RCS	Vent days, hospital days, mortality
Singh	11	1998	Ib	Early enteral feeds after peritonitis	RCS	Infection, nitrogen balance
Moore	12	1989	Ib	Early enteral feeding after abdominal trauma versus TPN	RCS	Infection, mortality, tolerate feeds
Kudsk	13	1992	Ib	TPN versus enteral feeding after abdominal trauma	RCS	Mortality, infection
Gramlich	14	2004	Ia	TPN versus enteral nutrition in critically ill	SR	Infection, mortality, hospital days
Pearl	15	1998	Ib	Early postoperative feeding versus waiting for return of bowel function to feed	RCS	Hospital days, days to regular diet, aspiration, need for NGT insertion
Han-Guerts	16	2001	Ib	Patient controlled versus fixed regimen feeding after elective abdominal surgery	RCS	Hospital days, aspiration, days to regular diet
Pearl	17	2002	Ib	Regular diet as first meal versus clear liquids and progression determined by physicians	RCS	Hospital stay, NGT insertion, aspiration

Abbreviations: NGT, nasogastric tube; RCS, randomized controlled study; SR, systematic review; TPN, total parenteral nutrition.

REFERENCES

- Braga M, Gianotti L, Vignali A, et al. Artificial nutrition after major abdominal surgery: Impact of route of administration and composition of the diet. *Crit Care Med* 1998; 26: 24–30.
- Garrel D. Decreased mortality and infectious morbidity in adult burn patients given enteral glutamine supplements: a prospective, controlled, randomized clinical trial. *Crit Care Med* 2003; 31: 2444–9.
- Houdijk A, Alexander PJ, Rijnsburger E, et al. Randomised trial of glutamine-enriched enteral nutrition on infectious morbidity in patients with multiple trauma. *Lancet* 1998; 352: 772–6.
- Dechelotte P, Hasselmann M, Cynober L. L-alanyl-glutamine dipeptide-supplemented total parenteral nutrition reduces infectious complications and glucose intolerance in critically ill patients: the French controlled, randomized, double-blind, multicenter study. *Crit Care Med* 2006; 34: 598–604.
- Saalwachter A, Schulman K, Willcutts J. Does enteral glutamine supplementation decrease infectious morbidity? *Surg Infect* 2006; 7: 29–35.

6. Meert K, Daphtary K, Metheny N. Gastric vs small-bowel feeding in critically ill children receiving mechanical ventilation: a randomized controlled trial. *Chest* 2004; 126: 872–8.
7. Neumann D, Delegge M. Gastric versus small-bowel tube feeding in the intensive care unit: a prospective comparison of efficacy. *Crit Care Med* 2002; 30: 1436–8.
8. Beale R, Bryg D, Bihari D. Immunonutrition in the critically ill: a systematic review of clinical outcome. *Crit Care Med* 1999; 27: 2799–805.
9. Senkal M, Zumbobel V, Bauer K. Outcome and cost-effectiveness of perioperative enteral immunonutrition in patients undergoing elective upper gastrointestinal tract surgery: a prospective randomized study. *Arch Surg* 1999; 134: 964–70.
10. Atkinson S, Sieffert E, Bihari D. A prospective, randomized, double-blind, controlled clinical trial of enteral immunonutrition in the critically ill. *Guy's Hospital Intensive Care Group. Crit Care Med* 1998; 26: 1164–72.
11. Singh G, Ram RP, Khanna SK. Early postoperative enteral feeding in patients with nontraumatic intestinal perforation and peritonitis. *J Am Coll Surg* 1998; 187: 142–6.
12. Moore F, Moore E, Jones T, et al. TEN versus TPN following major abdominal trauma—reduced septic morbidity. *J Trauma* 1989; 29: 916–22.
13. Kudsk K, Croce M, Fabian T, et al. Enteral versus parenteral feeding. Effects on septic morbidity after blunt and penetrating abdominal trauma. *Ann Surg* 1992; 215: 503–11.
14. Gramlich L, Krikor K, Pinilla J. Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature. *Nutrition* 2004; 20: 843–8.
15. Pearl M, Valea F, Fischer M. A randomized controlled trial of early postoperative feeding in gynecologic oncology patients undergoing intra-abdominal surgery. *Obstet Gynecol* 1998; 92: 94–7.
16. Han-Guerts I, Jeekel J, Tilanus H, et al. Randomized clinical trial of patient-controlled versus fixed regimen feeding after elective abdominal surgery. *Br J Surg* 2001; 88: 1578–82.
17. Pearl M, Frandina M, Mahler L, et al. A randomized controlled trial of a regular diet as the first meal in gynecologic oncology patients undergoing intra-abdominal surgery. *Obstet Gynecol* 2002; 100: 230–4.

Evidence-Based Surgery: Acute Lung Injury/Acute Respiratory Distress Syndrome

Juan J. Blondet and Greg J. Beilman

Clinical Questions		
Question	Answer	Grade of recommendation
What are risk factors for development of ALI/ARDS?	Risk factors for ARDS/ALI include severe sepsis, multiple system trauma, massive blood transfusion, aspiration, and others	B
What is appropriate ventilator management in ALI/ARDS?	Low tidal volume ventilation (V_T <8 ml/kg predicted body weight) PEEP/ FiO_2 titrated to adequate oxygenation (SpO_2 88–95%)	A
What are common causes of poor outcome in ALI/ARDS?	Age, immunocompromise, severity of illness, organ failure	B
Is there a risk of PEEP >10, FiO_2 >0.5?	Major risk of PEEP is barotrauma (hazard ratio of 1.67 for every 5 cm H_2O PEEP) Risk of higher percentage of FiO_2 not well characterized Titration of PEEP/ FiO_2 should be carried out in graded fashion	A D
Salvage therapies for severe hypoxemia?	No significant outcome benefit for salvage therapies in patients with severe ARDS	A
How should I wean my patient from the ventilator?	Daily SBT in appropriate patients Method of SBT: Pressure support, continuous positive airway pressure, T-piece all equivalent Daily interruption of sedation decreased time on ventilator, ICU, hospital	A
Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; PEEP, positive end-expiratory pressure; SBT, spontaneous breathing trial.		

INTRODUCTION

The first description of acute respiratory distress syndrome (ARDS) appeared in a landmark case series reported in 1967 (1). In 1994, a consensus conference of American and European investigators published their definition of ARDS, which has since been widely adopted (2) (Table 80.1). ARDS was defined as a syndrome of acute onset with bilateral infiltrates on chest radiography consistent with pulmonary edema, pulmonary artery occlusion pressure less than or equal to 18 mmHg (or absence of clinical evidence of left atrial hypertension), and hypoxemia as measured by the ratio of the arterial partial pressure of oxygen (PaO_2) to the fraction of oxygen inspired (FiO_2). Recognizing the spectrum of severity of the disease, the consensus panel recommended that a PaO_2/FiO_2 ratio of less than or equal to 300 define an entity called *acute lung injury* (ALI). ARDS is a more severe form of ALI and is defined as occurring if the PaO_2/FiO_2 ratio is less than or equal to 200.

A useful categorization of patients with ALI and ARDS considers that “direct,” “primary,” or “pulmonary” ARDS, in which lung injury is initiated from the epithelial or pulmonary side, behaves somewhat differently from ARDS caused by injury to the vascular endothelium (“indirect,” “secondary,”

or “extrapulmonary”) through the activation of systemic inflammation, presumably related to elevated blood cytokines and other biochemical and cellular mediators.

The reported incidence and mortality of patients with ALI/ARDS are high. In a recent analysis of the ARDS Network database, Goss and colleagues estimated the incidence of ARDS in the United States at 64 per 100,000 (3). A report from 78 intensive care units (ICUs) from 10 European countries found that ALI occurred in 7.1% of all ICU admissions and 16.1% of all mechanically ventilated patients (4). In the recent international survey of mechanically ventilated patients (5), the ICU mortality rate of the 231 patients with ARDS on ICU admission was reported as high as 52%. The regional differences in genetic or environmental factors and in disease-specific associations, such as trauma or lung reperfusion injury after cardiopulmonary bypass or lung transplantation, may account for some of the regional variability in the reported incidences of ARDS and ALI in the literature (6).

In this chapter, we review the latest literature concerning the most relevant questions on risk factors, management, and prevention of ALI and ARDS and provide recommendations as supported by the current level of evidence.

Table 80.1 American-European Consensus Conference Criteria for ARDS

	Timing	Oxygenation	Frontal Chest Radiograph	Pulmonary Artery Wedge Pressure
ALI	Acute	$\text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mm Hg}^*$	Bilateral infiltrates	$\leq 18 \text{ mmHg}$ if measured, or no clinical evidence of left atrial hypertension
ARDS	Acute	$\text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mm Hg}^*$	Bilateral infiltrates	$\leq 18 \text{ mmHg}$ if measured, or no clinical evidence of left atrial hypertension

*Regardless of positive end-expiratory pressure.

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome.

Source: Adapted from (2).

WHAT ARE RISK FACTORS FOR THE DEVELOPMENT OF ALI/ARDS?

Overall, sepsis syndrome has historically carried the highest risk for the development of ALI/ARDS (4,7,8), and the specific infections related to severe sepsis vary considerably by geographic area. In a prospective study of 695 critically ill patients published in 1995, almost 40% of patients with sepsis went on to develop ARDS. The investigators also found that the presence of more than one presumed clinical risk factor increased significantly the incidence of ARDS (7). In this last series, over a third of the patients receiving massive blood transfusion and a quarter of patients with multiple trauma (one or more of pulmonary contusion, multiple fractures, and multiple transfusions) developed ARDS (7). Other factors shown to increase ARDS risk following predisposing clinical conditions include age, female gender (in trauma only), severity of illness (by Injury Severity Score or Acute Physiology And Chronic Health Evaluation [APACHE] II scores), cigarette smoking, and chronic alcohol abuse (8).

A recent meta-analysis of studies published from January 1987 to June 2007, including 4,311 patients with ARDS, found no difference in mortality when comparing patients with direct or pulmonary ARDS (2,330 patients) and patients with indirect or extrapulmonary ARDS (1,981 patients) [odds ratio (OR) 1.11, 95% confidence interval (CI), 0.88–1.39, as determined by a random-effects model; 1.04, 95% CI, 0.92–1.18, as determined by a fixed-effects model; and 1.04, 95% CI, 0.92–1.18, as determined by an exact method] despite stratifying by either the prospective or retrospective nature of the studies or whether they had small or large sample sizes (9). Future studies should focus on specific etiologies within these subgroups.

There is increasing evidence that mechanical ventilation by itself can trigger inflammatory pulmonary edema in both animal models (10) and human patients (11). Some studies have shown that higher tidal volumes (V_T) are associated with more cases of ARDS and ALI in patients without these conditions at the onset of mechanical ventilation (12,13). In a retrospective cohort study published recently (14) that included 1,366 ICU patients requiring mechanical ventilation for more than 48 hours who did not have ARDS at admission, 152 (19%) of them developed bilateral infiltrates and met ARDS criteria on an average of 3.3 days after initiation of mechanical ventilation. In their univariate and multivariate logistic regression analyses, the authors found that high airway pressures [high peak inspiratory pressures, plateau pressures, positive end-expiratory pressure (PEEP)], and V_T were the most important ventilator-associated risk factors for the development of new ARDS. Transfusion of blood products, especially

fresh frozen plasma, and high net fluid balance were also strongly associated with new ARDS. Massive transfusion in a trauma patient population, defined as >15 units of packed red blood cells in 24 hours, was associated with a 40% risk of development of ARDS (7).

Recommendation: It may be possible to reduce the occurrence of ARDS in mechanically ventilated patients with careful ventilator management and transfusion reduction or avoidance. Clinicians should consider minimizing these potentially deleterious interventions in patients without ALI at the onset of mechanical ventilation (Level of evidence IIc, Grade B recommendation).

WHAT IS THE EVIDENCE THAT JUSTIFIES CURRENT VENTILATOR MANAGEMENT IN ALI/ARDS?

Low V_T Ventilation

Early interest in low V_T ventilation was prompted by animal studies showing that ventilation with large V_T and high inspiratory pressures not only resulted in increased levels of inflammatory mediators [tumor necrosis factor- α , interleukin (IL)-6, and IL-10] but also in the development of ALI (15–18). These studies prompted Hickling and colleagues (19) to use a low VT/low inspiratory pressure strategy of ventilation in patients with severe ARDS, and a retrospective analysis of a series of 50 such patients indicated that mortality was significantly lower than that predicted by APACHE II scores (16% versus 39.6%, respectively; $p < 0.001$).

In the late 1990s, four randomized controlled trials (RCTs) (20–23) were conducted to evaluate the benefit of low V_T ventilation in ARDS patients compared with traditional V_T ventilation. Only one of these trials (20) showed a significant reduction in mortality in the experimental treatment group. Because all four studies had limited statistical power due to small sample sizes, a large, multicenter RCT was conducted between 1996 and 1999 by the National Heart, Lung, and Blood Institute ARDS Network that included 861 patients at 10 institutions, known as the Respiratory Management in Acute Lung Injury/ARDS (ARMA) trial (24). ARMA compared a ventilatory protocol using V_T of $\leq 6 \text{ ml/kg}$ of predicted body weight (calculated from sex and height) and maintaining plateau pressures of $\leq 30 \text{ cmH}_2\text{O}$ with conventional mechanical ventilation using higher V_T . The hospital mortality rate was significantly reduced in the low V_T group compared with the control group (31% versus 39.8%, respectively; $p = 0.007$). Additionally, patients treated with low V_T ventilation had a greater mean $\pm$ SD number of days free of mechanical ventilation (12 ± 11 versus 10 ± 11 days, respectively; $p = 0.007$) and a greater number of days free of nonpulmonary

organ failure (15 ± 11 versus 12 ± 11 days, respectively; $p = 0.006$).

Since the publication of ARMA, low V_T ventilation has remained underutilized in the treatment of patients with ARDS (25–28) and recent publications addressed concerns regarding physicians' underrecognition of less severe cases of ALI, hypercapnia, patient discomfort, and acidosis (27,29–33). Some investigators have suggested that V_T reduction should not be used for all ARDS patients but adjusted individually according to surrogate markers of ventilator-induced lung injury, such as inspiratory airway pressures (30).

A very controversial meta-analysis of the existing five RCTs testing mechanical ventilation with low V_T in patients with ALI and ARDS, including ARMA (34), concluded that significant differences in the control arms of these studies provide the basis for their contradictory results and that further clinical trials are necessary to determine the survival benefit of low V_T (5–7 ml/kg measured body weight) when compared to intermediate V_T (8–9 ml/kg). Another meta-analysis published in 2005 (32) of the same five RCTs using a different statistical method of meta-regression of covariates on treatment effect with respect to 28-day mortality found that the pooled estimate of treatment effect with V_T less than 7.7 ml/kg predicted favors protective ventilation strategies, but it failed to achieve statistical significance on random effects estimation. The authors concluded that in ALI/ARDS, mechanical ventilation with low V_T is not detrimental and may have advantage below threshold levels of 7.7 ml/kg predicted.

Recommendation: Low V_T ventilation (≤ 6 –8 ml/kg predicted body weight) should be the *initial* target in all patients with ALI/ARDS because it is the only method of mechanical ventilation demonstrating improved survival. After reaching this initial goal, titration of V_T according to indices of pulmonary compliance (such as peak or plateau inspiratory pressures) should be based on clinical judgment (Level of evidence Ib, Grade A recommendation).

PEEP and Alveolar Recruitment

PEEP is an essential component of mechanical ventilation for patients with ALI/ARDS that should be used to increase the proportion of nonaerated lung, resulting in improved oxygenation. Traditionally, PEEP levels of 5–12 cm H_2O have been used for patients with ARDS (5). However, it currently remains unclear whether these values are ideal because RCTs have not shown that higher levels of PEEP lead to a reduction in mortality rate (24,35,36). Neither high PEEP nor a combination approach (low V_T ventilation, high PEEP, plus recruitment maneuvers) have been shown to improve mortality in patients with ARDS, although both improve other outcome measures.

In late 2007, a meta-analysis was published of the relevant RCTs that evaluate the effects of high PEEP versus conventional PEEP on mortality and on the risk of barotrauma in patients with ARDS (37). Four studies were selected for the meta-analysis on mortality (20,36,38,39), and three for the meta-analysis on barotrauma (20,36,38). No effects of PEEP level on mortality were found [relative risk (RR) 0.73, 95% CI 0.49–1.10] or in the incidence of barotrauma (RR 0.50, 95% CI 0.43–0.82). Interestingly, when

analyzing only the three studies in which PEEP was individualized in function of pulmonary mechanics (lower inflection point of the pressure-volume curve of the respiratory system) (20,36,39), the use of high PEEP was associated with a significant decrease in the risk of death (RR 0.59, 95% CI 0.43–0.82, $p = 0.001$).

In 2008, a multicenter RCT enrolled 767 patients receiving low V_T ventilation for ARDS (40). Patients were randomly assigned to receive a high PEEP strategy or a low PEEP strategy. There were no statistically significant differences in mortality. However, the high PEEP group had a higher median ventilator free days and nonpulmonary organ failure-free days, as well as a decreased need for rescue therapies. The same year, another multicenter RCT randomly assigned 983 patients with ARDS to receive the combination approach (low V_T ventilation, high PEEP, plus recruitment maneuvers) or low V_T ventilation alone (41). There was no significant difference in all-cause hospital mortality, although the composite intervention group had less refractory hypoxemia and needed fewer rescue interventions.

Recommendation: PEEP is an essential component of mechanical ventilation for patients with ALI/ARDS. Higher levels of PEEP have not been shown to improve survival but may result in improvement in other respiratory variables (e.g., hypoxemia, ventilator-free days) (Level of evidence Ia, Grade A recommendation).

WHAT ARE THE MOST COMMON CAUSES OF POOR OUTCOME IN ALI/ARDS?

In 2004, the ALIVE study (Acute Lung Injury Verification of Epidemiology) published the results of their prospective, multinational, cohort study, conducted in 78 ICUs across 10 European countries (4). Their purpose was to study the occurrence, etiologies, outcomes, and factors associated with survival in patients with ALI/ARDS. They found that in these patients, mortality varied according to the cause of lung injury and whether the lung injury was from a direct cause (e.g., pneumonia), an indirect cause (e.g., extrapulmonary sepsis), or a combined insult (pneumonia and septic shock), where the latter had the worst outcome. When focusing on a single factor associated with poor outcome, they found that mortality at hospital discharge was the highest in patients with sepsis (43%), lower in patients with pneumonia (36%) or aspiration (37%), and the lowest in patients with trauma (11%). After multivariable logistic regression analysis of risk factors for death in the whole cohort of ALI/ARDS patients, the authors found that the following variables remained significantly associated with mortality: age [OR = 1.2 per 10 years (1.05–1.36, 95% CI), $p = 0.006$], immunocompetence [OR = 2.88 (1.57–5.28, 95% CI), $p = 0.0006$], air leak in the first two days [OR 3.16 (1.59–6.28, 95% CI), $p = 0.001$], the Simplified Acute Physiology Score II on admission [OR = 1.16 per 10% expected mortality (1.02–1.31, 95% CI), $p = 0.024$], Logistic Organ Dysfunction score [OR = 1.25 per point (1.13–3.18, 95% CI), $p < 0.0001$], and a pH of 7.30 or less [OR = 1.88 (1.11–3.18, 95% CI), $p = 0.019$].

Recommendation: Common causes of poor outcome in patients with ALI/ARDS include sepsis, etiology, age, immunosuppression, and nonpulmonary organ failure (Level of evidence IIb, Grade B recommendation).

IS THERE A RISK OF PEEP ABOVE 10 OR FiO_2 ABOVE 0.5?

The goal in mechanical ventilation and oxygen therapy in ALI/ARDS is to increase oxygen delivery and relieve excessive breathing workload while preventing further damage from oxygen toxicity, barotrauma, ventilator-induced lung injury, infection, and other iatrogenic complications. Clinicians must decide how to balance risks of PEEP, including circulatory depression and barotrauma, versus risks of oxygen toxicity from high FiO_2 .

The optimal ventilatory strategy is still unknown (42), and high PEEP has been used in various studies, but this approach may prove deleterious in certain conditions. In a retrospective analysis of the ARDS Network trials (43), Eisner and colleagues investigated the association between airway pressures and the risk of early barotrauma (in the first four study days) in a cohort of 718 patients with ALI/ARDS and no baseline barotrauma. The incidence of barotrauma in the first four study days was 13% (93 patients). In forward stepwise Cox proportional hazards analysis using time-dependent variables, and also using a multivariate analysis, the authors found that higher concurrent PEEP was associated with an increased risk of early barotrauma and that no other airway pressure was related to barotrauma (including plateau pressures), even after controlling for markers of acute and chronic disease severity. The authors found that for every 5 cm H_2O concurrent PEEP increment, the relative hazard of developing barotrauma increased by 1.67 (95% CI, 1.35–2.07).

Based on experimental studies, the particular level of PEEP that was injurious appeared to depend on a number of factors, including the specific experimental model, the animal species, and end-inspiratory lung volume (44).

Very high FiO_2 can safely be used for brief periods of time, as efforts are made to correct the underlying process, but sustained elevations of FiO_2 greater than 0.6 have been proven to result in inflammatory changes and eventual fibrosis in experimental models. The toxic FiO_2 threshold in humans with ALI/ARDS remains unknown and has not been the topic of carefully performed prospective trials.

Methods of titrating PEEP and FiO_2 in patients with ALI/ARDS have been reported in trials of ALI/ARDS treatment (24,36). Until further information is available, it seems reasonable to use parameters as described in these trials as guidelines to titrate PEEP/ FiO_2 in patients with ARDS/ALI.

Recommendations: Higher levels of PEEP are associated with increased risk of barotrauma but not increased risk of death. The clinician must balance the need for adequate oxygenation with the risk of barotrauma (Level of evidence Ib, Grade A recommendation). The clinician should use FiO_2 percentage adequate to allow appropriate oxygenation with the goal to reduce $\text{FiO}_2 < 0.4$ when possible (Level of evidence V, Grade D recommendation). Titration of PEEP/ FiO_2 should be carried out in a graded fashion, with increased PEEP and FiO_2 levels used for increasing hypoxemia (Level of evidence Ib, Grade B recommendation).

WHAT IS THE EVIDENCE TO SUPPORT SALVAGE THERAPIES FOR SEVERE HYPOXEMIA?

Some investigators have proposed that high-frequency oscillatory ventilation is an ideal mode of ventilation for ARDS patients because it is the natural culmination of low

VT ventilation. This mode of ventilation rapidly delivers small tidal volumes that are typically 1–5 ml/kg (45), possibly improving gas exchange and reducing ventilator-induced lung injury. However, both randomized controlled trials that have been conducted to date to evaluate the efficacy of high-frequency oscillatory ventilation in the treatment of ARDS have failed to demonstrate an improvement in mortality (46,47). Similarly, so far most of the other promising interventions found to reduce lung injury and improve outcome in animal studies (e.g., prone position, surfactant supplementation, nitric oxide, lung recruitment maneuvers) have not been found significantly to improve patient survival or outcome on adult ICU patients with ALI/ARDS (48–55). In the case of prone positioning to improve ventilation in patients with ARDS, in a well-done RCT Guerin et al. (50) found no reduction in mortality, but the method improved oxygenation and reduced the incidence of ventilator-associated pneumonia (VAP). As some investigators have asked, should we abandon this approach (or any other) simply because no RCT has shown a reduction in mortality (42,49)? Perhaps this may benefit the most severe patients, as suggested by Gattinoni et al. (49). However, the beneficial impact on VAP should drive the development of more RCTs (50,56).

A recent meta-analysis on the use of steroids in ALI/ARDS (57) (nine randomized trials were selected using variable dose and duration of steroids: four studies on preventive use of steroids and five studies with steroid administration after onset of ARDS) found some evidence that suggested that giving corticosteroids *to prevent* the development of ARDS was actually associated with the subsequent development of ARDS and was also associated with a weakly increased risk of death in patients who subsequently developed ARDS. The authors also found that giving corticosteroids *after* the onset of ARDS was associated with a trend toward reduced mortality. Steroid therapy was also associated with substantially more ventilator-free days compared with controls (mean difference 4.05 days, 95% credible interval 0.22–8.71), no evidence was found of an association between odds of mortality and time to treatment in hours, and corticosteroids were not associated with increase in risk of infection, but a trend was found toward increased risk of infection with increasing steroid dose. The reader should be aware that meta-analyses on the basis of small number of trials with sparse data like this one must have limitations in estimation of treatment effects, and more studies are necessary to make a definitive recommendation.

Tracheal gas insufflation (TGI) is an adjunct to mechanical ventilation that lowers alveolar and arterial P_{CO_2} without rising VT or respiratory rate by washing CO_2 out of large airways during exhalation. Therefore, TGI increases efficiency of CO_2 clearance by reduction of dead space. Two small prospective randomized clinical trials (one of them in 14 adults with early onset, primary, severe ARDS and the other one in 34 preterm neonates with hyaline membrane disease) suggest that the use of TGI could improve some of the respiratory parameters (58,59).

The role of extracorporeal membrane oxygenation (ECMO), also known as extracorporeal life support has not yet been validated for patients with ARDS. Only two RCTs have been reported in the literature, and both trials failed to demonstrate benefit on outcome or survival (60–62).

The Conventional Ventilatory Support versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure trial (63) is a recently completed RCT from the United Kingdom that will assess whether in patients with severe but potentially reversible respiratory failure, ECMO will increase the rate of survival without severe disability by six months postrandomization and be cost-effective, compared to conventional ventilatory support. Its results will elucidate the role of ECMO as rescue therapy for ARDS, but until then, ECMO appears to be an unvalidated rescue treatment option.

Recommendation: Current evidence does not demonstrate benefit for salvage therapies with respect to improved outcomes in the management of patients with severe ARDS. The use of these therapies is at the discretion of the treating physician (Level of evidence Ib, Grade A recommendation).

WHAT IS CURRENT EVIDENCE TO SUPPORT USE OF WEANING PROTOCOLS FOR MECHANICAL VENTILATION?

In 1999, the Agency for Healthcare Policy and Research (AHCPR) and the McMaster University Evidence Based Practice Center published the first evidence-based report on the criteria for discontinuation of mechanical ventilation (64). At the same time, the American College of Chest Physicians, the Society for Critical Care Medicine, and the American Association for Respiratory Care formed a task force to incorporate the recommendations from the AHCPR-McMaster University report and produce evidence-based clinical practice guidelines for managing the weaning process of mechanically ventilated patients (65). These guidelines were developed from data derived from multiple meta-analyses and individual RCTs. The most important recommendation includes the use of spontaneous breathing to assess the potential for formal discontinuation of ventilatory support. The technique as described includes the use of a 30–120-minute spontaneous breathing trial (SBT) to identify candidates for permanent ventilator discontinuation, evaluation and treatment of causes of

failed SBT, and daily reevaluation with SBT. Candidates for SBT include those patients with evidence for improvement in their underlying process, adequate oxygenation ($PEEP \leq 5-8$ cm H_2O , and $FiO_2 \leq 0.4-0.5$), hemodynamic stability, and the capability to initiate an inspiratory effort. SBT can be accomplished by using low levels of continuous positive airway pressure (5 cm H_2O), low levels of pressure support (5–7 cm H_2O), or “T-piece” breathing.

Recently, a multicenter RCT compared 168 mechanically ventilated patients randomized to daily use of spontaneous awakening trial (daily interruption of sedatives) followed by a SBT (intervention group) to another 168 mechanically ventilated patients randomized to usual care (with sedation) with daily SBT (control group) (66). Their results showed that patients with daily interruption of sedatives had more ventilator-free days (14.7 days versus 11.6 days; mean difference 3.1 days, 95% CI, 0.7–5.6; $p = 0.02$) and were discharged earlier from the ICU (median time in the ICU 9.1 days versus 12.9 days, $p = 0.01$) and from the hospital (median time in the hospital 14.9 days versus 19.2 days; $p = 0.04$). Not surprisingly, more patients in the intervention group self-extubated than in the control group, but the number of patients that required reintubation were similar. Interestingly, at any time point during the one-year follow-up, patients in the intervention group were 32% less likely to die than were patients in the control group (hazard ratio 0.68, 95% CI 0.5–0.92; $p = 0.01$). This survival benefit remains to be validated in a larger study.

Recommendation: The use of a SBT is the most direct way to assess how a patient will perform without ventilatory support. Use of SBT to evaluate candidates for liberation from the ventilator has been shown to reduce ventilator, ICU, and hospital days (Level of evidence Ia, Grade A recommendation). Daily removal of sedation (spontaneous awakening trial) coupled with SBT has been shown to decrease ICU, hospital, and ventilator days and should be used in appropriate ventilated patients. Additional multicenter trials should be conducted to confirm the benefits of this approach (Level of evidence Ib, Grade B recommendation).

Levels of Evidence

Question	Answer	Level of evidence	Grade of recommendation	Refs.
What are risk factors for development of ALI/ARDS?	Risk factors for ARDS/ALI include severe sepsis, multiple system trauma, massive blood transfusion, aspiration, and others	Ilc	B	4, 7–14
What is appropriate ventilator management in ALI/ARDS?	Low tidal volume ventilation ($V_T < 8$ ml/kg predicted body weight)	Ib	A	15–41
What are common causes of poor outcome in ALI/ARDS?	PEEP/ FiO_2 titrated to adequate oxygenation (SpO_2 88–95%)	Ia		
Is there a risk of PEEP >10, $FiO_2 > 0.5$?	Age, immunocompromise, severity of illness, organ failure	Ilb	B	4
Salvage therapies for severe hypoxemia?	Major risk of PEEP is barotrauma (hazard ratio of 1.67 for every 5 cm H_2O PEEP)	Ib	A	42–44
How should I wean my patient from the ventilator?	Risk of higher percentage of FiO_2 not well characterized	V	D	
	Titration of PEEP/ FiO_2 should be carried out in graded fashion	Ib		
	No significant outcome benefit for salvage therapies in patients with severe ARDS	Ib	A	42, 45–63
	Daily SBT in appropriate patients	Ia	A	64–66
	Method of SBT: Pressure support, continuous positive airway pressure, T-piece all equivalent	Ia		
	Daily interruption of sedation decreased time on ventilator, ICU, hospital	Ib		

Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; PEEP, positive end-expiratory pressure; SBT, spontaneous breathing trial.

REFERENCES

- Ashbaugh DG, Bigelow DB, Petty TL, et al. Acute respiratory distress in adults. *Lancet* 1967; 2: 319–23.
- Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med* 1994; 149: 818–24.
- Goss CH, Brower RG, Hudson LD, et al. Incidence of acute lung injury in the United States. *Crit Care Med* 2003; 31: 1607–11.
- Brun-Buisson C, Minelli C, Bertolini G, et al. for the ALIVE study group. Epidemiology and outcome of acute lung injury in European intensive care units. Results from the ALIVE study. *Inten Care Med* 2004; 30: 51–61.
- Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002; 287: 345–55.
- Rubenfeld GD. Epidemiology of acute lung injury. *Crit Care Med* 2003; 31: S276–S284.
- Hudson LD, Milberg JA, Anardi D, et al. Clinical risks for development of the acute respiratory distress syndrome. *Am J Respir Crit Care Med* 1995; 151: 293–301.
- Steinberg KP, Hudson LD. Acute lung injury and acute respiratory distress syndrome. The clinical syndrome. *Clin Chest Med* 2000; 21: 401–17.
- Agarwal R, Srinivas R, Nath A, et al. Is the mortality higher in the pulmonary vs the extrapulmonary ARDS? A meta analysis. *Chest* 2008; 133: 1463–73.
- Gurkan OU, O'Donnell C, Brower R, et al. Differential effects of mechanical ventilatory strategy on lung injury and systemic organ inflammation in mice. *Am J Physiol Lung Cell Mol Physiol* 2003; 285: L710–L718.
- Slutsky AS. Lung injury caused by mechanical ventilation. *Chest* 1999; 116(1Suppl): 9S–15S.
- Gajic O, Dara SI, Mendez JL, et al. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. *Crit Care Med* 2004; 32: 1817–24.
- Gajic O, Frutos-Vivar F, Esteban A, et al. Ventilator settings as a risk factor for acute respiratory distress syndrome in mechanically ventilated patients. *Intens Care Med* 2005; 31: 922–6.
- Jia X, Malhotra A, Saeed M, et al. Risk factors for ARDS in patients receiving mechanical ventilation for >48h. *Chest* 2008; 133: 853–61.
- Kolobow T, Moretti MP, Fumagalli R, et al. Severe impairment in lung function induced by high peak airway pressure during mechanical ventilation: an experimental study. *Am Rev Respir Dis* 1987; 135: 312–15.
- Dreyfuss D, Basset G, Soler P, et al. Intermittent positive-pressure hyperventilation with high inflation pressures produces pulmonary microvascular injury in rats. *Am Rev Respir Dis* 1985; 132: 880–4.
- Tremblay L, Valenza F, Ribeiro SP, et al. Injurious ventilatory strategies increase cytokines and c-fos m-RNA expression in an isolated rat lung model. *J Clin Invest* 1997; 99: 944–52.
- von Bethmann AN, Brasch F, Nusing R, et al. Hyperventilation induces release of cytokines from perfused mouse lung. *Am J Respir Crit Care Med* 1998; 157: 263–72.
- Hickling KG, Henderson SJ, Jackson R. Low mortality associated with low volume pressure limited ventilation with permissive hypercapnia in severe adult respiratory distress syndrome. *Intensive Care Med* 1990; 16: 372–7.
- Amato MB, Barbas CS, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med* 1998; 338: 347–54.
- Stewart TE, Meade MO, Cook DJ, et al. Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome: pressure- and Volume-Limited Ventilation Strategy Group. *N Engl J Med* 1998; 338: 355–61.
- Brochard L, Roudot-Thoraval F, Roupie E, et al. Tidal volume reduction for prevention of ventilator-induced lung injury in acute respiratory distress syndrome. Multicenter Trial Group on Tidal Volume Reduction in ARDS. *Am J Respir Crit Care Med* 1998; 158: 1831–8.
- Brower RG, Shanholtz CB, Fessler HE, et al. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal volume ventilation in acute respiratory distress syndrome patients. *Crit Care Med* 1999; 27: 1492–8.
- The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342: 1301–8.
- Weinert CR, Gross CR, Marinelli WA. Impact of randomized trial results on acute lung injury ventilator therapy in teaching hospitals. *Am J Respir Crit Care Med* 2003; 167: 1304–9.
- Young MP, Manning HL, Wilson DL, et al. Ventilation of patients with acute lung injury and acute respiratory distress syndrome: has new evidence changed clinical practice? *Crit Care Med* 2004; 32: 1260–5.
- Kalhan R, Mikkelsen M, Dedhiya P, et al. Underuse of lung protective ventilation: analysis of potential factors to explain physician behavior. *Crit Care Med* 2006; 34: 300–6.
- Young MP. Tidal volumes used in acute lung injury: Why the persistent gap between intended and actual clinical behavior? *Crit Care Med* 2006; 34: 543–4.
- Rubenfeld GD, Cooper C, Carter G, et al. Barriers to providing lung-protective ventilation to patients with acute lung injury. *Crit Care Med* 2004; 32: 1289–93.
- Deans KJ, Minneci PC. Mechanical ventilation in ARDS: one size does not fit all. *Crit Care Med* 2005; 33: 1141–3.
- Gattinoni L, Caironi P, Carlesso E. How to ventilate patients with acute lung injury and acute respiratory distress syndrome. *Curr Opin Crit Care* 2005; 1: 69–76.
- Moran JL, Bersten AD, Solomon PJ. Meta-analysis of controlled trials of ventilator therapy in acute lung injury and acute respiratory distress syndrome: an alternative perspective. *Intens Care Med* 2005; 31: 227–35.
- Petrucchi N, Iacovelli W. Ventilation with smaller tidal volumes: a quantitative systematic review of randomized controlled trials. *Anesth Analg* 2004; 1: 193–200.
- Eichacker PQ, Gerstenberger EP, Banks SM, et al. Meta-analysis of acute lung injury and acute respiratory distress syndrome trials testing low tidal volumes. *Am J Respir Crit Care Med* 2002; 166: 1510–14.
- The National Heart Lung and Blood Institute ARDS Clinical Trials Network. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med* 2004; 351: 327–36.
- Villar J, Kacmarek RM, Pérez-Méndez L, et al. for the ARIES Network. A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. *Crit Care Med* 2006; 34: 1311–18.
- Gordo-Vidal F, Gómez-Tello V, Palencia-Herrejón E, et al. High PEEP vs. conventional PEEP in the acute respiratory distress syndrome: a systematic review and meta-analysis. *Med Intensiva* 2007; 31: 491–501.
- Brower RG, Lanken PN, MacIntyre N, et al. National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med* 2004; 351: 327–36.
- Ranieri VM, Suter PM, Tortorella C, et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 1999; 282: 54–61.

40. Mercat A, Richard JC, Vielle B, et al. Expiratory Pressure (Express) Study Group. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 2008; 299: 646–55.
41. Meade MO, Cook DJ, Guyatt GH, et al. Lung Open Ventilation Study Investigators. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 2008; 299: 637–45.
42. Dreyfuss D, Saumon G. Evidence-based medicine or fuzzy logic: what is best for ARDS management? *Intensive Care Med* 2002; 28: 230–4.
43. Eisner MD, Thompson BT, Schoenfeld D, et al. and the Acute Respiratory Distress Syndrome Network. Airway pressures and early barotrauma in patients with acute lung injury and acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2002; 165: 978–82.
44. Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med* 1998; 157: 294–323.
45. Ferguson ND, Stewart TE. New therapies for adults with acute lung injury: high-frequency oscillatory ventilation. *Crit Care Clin* 2002; 18: 91–106.
46. Derdak S, Mehta S, Stewart TE, et al. High-frequency oscillatory ventilation for acute respiratory distress syndrome in adults: a randomized, controlled trial. *Am J Respir Crit Care Med* 2002; 166: 801–8.
47. Bollen CW, van Well GT, Sherry T, et al. High frequency oscillatory ventilation compared with conventional mechanical ventilation in adult respiratory distress syndrome: a randomized controlled trial. *Crit Care* 2005; 9: R430–R439.
48. Spragg RG, Lewis JF, Walrath H, et al. Effect of recombinant surfactant protein c-based surfactant on the acute respiratory distress syndrome. *N Engl J Med* 2004; 351: 884–92.
49. Gattinoni L, Tognoni G, Presenti A, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 2001; 345: 568–73.
50. Guerin C, Gaillard S, Lemasson S, et al. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. *JAMA* 2004; 292: 2379–87.
51. Kallet RH. Evidence-based management of acute lung injury and acute respiratory distress syndrome. *Respir Care* 2004; 49: 793–809.
52. Adhikari NK, Burns KE, Friedrich JO, et al. Effect of nitric oxide on oxygenation and mortality in acute lung injury: systematic review and meta-analysis. *Br Med J* 2007; 334: 757–8.
53. Sokol J, Jacobs SE, Bohn D. Inhaled nitric oxide for acute hypoxic respiratory failure in children and adults: a meta-analysis. *Anesth Analg* 2003; 97: 989–98.
54. Mancebo J, Fernández R, Blanch L, et al. A multicenter trial of prolonged prone ventilation in severe acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2006; 173: 1233–9.
55. Adhikari N, Burns KE, Meade MO. Pharmacologic therapies for adults with acute lung injury and acute respiratory distress syndrome. *Cochrane Database Syst Rev* 2004; 4: CD004477.
56. Drakulovic MB, Torres A, Bauer TT, et al. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomized trial. *Lancet* 1999; 345: 1851–8.
57. Peter JV, John V, Graham PL, et al. Corticosteroids in the prevention and treatment of acute respiratory distress syndrome (ARDS) in adults: meta-analysis. *Br Med J* 2008; 336: 1006–9.
58. Mentzelopoulos SD, Roussos C, Koutsoukou A, et al. Acute effects of combined high frequency oscillation and tracheal gas insufflation in severe acute respiratory distress syndrome. *Crit Care Med* 2007; 35: 1500–8.
59. Dassieu G, Brochard L, Benani M, et al. Continuous tracheal gas insufflation in preterm infants with hyaline membrane disease. *Am J Respir Crit Care Med* 2000; 162: 826–31.
60. Zapol WM, Snider MT, Hill JD, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure: a randomized prospective study. *JAMA* 1979; 242: 2193–6.
61. Morris AH, Wallace CJ, Menlove RL, et al. Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO₂ removal for adult respiratory distress syndrome. *Am J Respir Crit Care Med* 1994; 149: 295–305.
62. Chalwin RP, Moran JL, Graham PL. The role of extracorporeal membrane oxygenation for treatment of the adult respiratory distress syndrome: review and quantitative analysis. *Anaesth Intensive Care* 2008; 36: 152–61.
63. Peek GJ, Clemens F, Elbourne D. CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. *BMC Health Serv Res* 2006; 6: 163.
64. Cook D, Meade M, Guyatt G, et al. Evidence Report on Criteria for Weaning from Mechanical Ventilation. Rockville, MD: Agency for Health Care Policy and Research, 1999.
65. MacIntyre NR, Cook DJ, Ely EW Jr., et al. Evidence-based guidelines for weaning and discontinuing ventilatory support: A collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest* 2001; 120: 375S–95S.
66. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet* 2008; 371: 126–34.

Acute Renal Failure

Teofilo Lama

Question Summary		
Question	Answer	Grade of recommendation
Which surgical patients are at higher risk of developing ARF?	Cardiac, vascular, transplant, and multiple-trauma patients are the higher risk surgical patients. Patients with preexistent morbidities, diabetes, or renal dysfunction consider as higher risk.	C
Which are the signs for early recognition of AKI or ARF?	The first signs of ARF are decrease urine output and elevation of BUN and creatinine.	C
Diuretics, dopamine, fenoldopam, and others: Do they play any role in preventing ARF?	Dopamine should not be used. Diuretics and fenoldopam can be use in the early stages, the data are clear for the need of more multicenter randomized controlled trials.	C
ARF in surgical patients: What are the treatment modalities?	Current modalities include IHD and CRRT. The new techniques SLED and CRRT with high volumes, but there is the need of more prospective randomized trials.	C
Is CRRT better than IHD in patients with ARF after surgery?	No significant difference in the mortality rate or the progression to ESRD in patients with ARF treated with IHD or CRRT. CRRT has shown advantages in patients with low blood pressure.	B
Does CRRT has a role in the critical ill trauma patient without ARF?	Has shown some benefits in the critically ill patient without evidence of ARF, specially in sepsis and ARDS, but there isn't enough data to support its use.	C
How does ARF impact the morbidity and mortality of surgical patients?	ARF has a tremendous impact in the morbidity and mortality not only in surgical patients.	C
Abbreviations: AKI, acute kidney injury; ARF, acute renal failure; BUN, blood urea nitrogen; CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; IHD, intermittent hemodialysis; SLED, slow extended daily dialysis.		

HISTORY

The first evidence of medical description and speculation of the etiology, signs, treatment, and prognosis of acute renal failure (ARF) comes from the ancient Greek and Byzantine periods (1). Hippocrates is considered the founder of clinical nephrology. He is known for the aphorism "Bubbles appearing on the surface of the urine indicate diseases of the kidneys and a prolonged illness" (2). The Greeks described several pathological conditions, including renal inflammation, destruction of renal parenchyma, crush syndrome, poisoning, breakage of capillaries into the kidney with thrombosis, and so on. They also describe several causes for ARF, such as wounds, crushes, and poisoning (1).

The Byzantines (14th century) described the relationship between severe systemic diseases and ARF, as well as defining the oliguric, anuric, and polyuric phases of the disease. They also published *Uroscopy*, a work in 12 editions spanning the 14th through the 17th centuries.

Thomas Graham (Scotland) introduced the term dialysis in 1854. George Haas in 1924 in the town of Giessen, Germany (3), performed the first human hemodialysis. In 1942, Willem Kolff (Holland) developed the first clinically useful artificial kidney for the treatment of ARF.

During the bombing of London in World War II, Bywaters and Beall described an acute loss of kidney function that occurred in victims with crush injury. The term used was acute tubular necrosis. During that period, the mortality rate of ARF approached 100%. Acute hemodialysis was used clinically during the Korean War (1950), where the mortality rate for ARF decreased to 50%. Improvement in transportation and fluid resuscitation decreased the incidence of ARF in severely wounded patients from 1 in 200 during the Korean War to 1 in 600 in the Vietnam War.

Hemodialysis has changed in the last decade from standard intermittent hemodialysis (IHD) to continuous venovenous hemofiltration (CVVH) and the newer modalities

that include high-volume hemofiltration and extended daily hemodialysis.

EPIDEMIOLOGY

ARF is a common complication in surgical critical care. Cardiac, vascular, transplant, and multiple-trauma patients, as well as any surgical patient with a previous history of renal impairment, have the highest risk of developing this complication. The incidence varies from 1% to 25%; regardless of the advancements in the treatment modalities of ARF, the mortality rate in this group remains as high as 30–65% and is usually associated with multiple organ failure.

PHYSIOLOGY

The accumulation of nitrogenous waste in blood has three clear etiologies: prerenal, renal, and postrenal. The prerenal azotemia develops in prolonged states of shock regardless of its etiology. Postrenal azotemia etiology is related to an obstruction at any level of the urinary tract.

When ARF is of renal etiology, there is usually an ischemic insult that affects the kidney, creating a cascade of events. This includes loss of the vascular autoregulation, tubular dysfunction with decrease reabsorption of sodium, structural changes associated with shedding, and excretion of proximal tubule brush membranes and epithelium that eventually create the substrate for intraluminal obstruction at the distal nephrons. That, in conjunction with cast deposits from the ascending limb, explains the findings from microdissection of individual nephrons that demonstrated dilated proximal tubules with obstructing casts in the distal tubules and collecting ducts.

INITIAL EVALUATION AND DIAGNOSIS

The sudden loss of the ability of the kidneys to excrete wastes, concentrate urine, conserve electrolytes, and maintain fluid balance is a frequent clinical problem, particularly in the intensive care unit (ICU). The progression from an azotemic state associated with renal vasoconstriction and intact tubular function to established ARF with tubular dysfunction occurs if the renal ischemia is prolonged.

It is important to ensure that an early diagnosis of acute renal vasoconstriction can be made before the occurrence of tubular dysfunction. Early intervention with fluid resuscitation has shown to prevent the progression from prerenal azotemia to established ARF.

At the earliest signs of oliguria and increased levels of creatinine and blood urea nitrogen (BUN), it is a common clinical practice to challenge the patient with fluids. Responses with decreasing levels of BUN indicate the presence of reversible vasoconstriction, whereas accumulation of them is an indication of established ARF.

Many complications, including massive fluid overload, pulmonary congestion, and respiratory failure with intubations and ventilatory support have resulted from this approach. The evaluation of urine sediments and chemistry helps differentiate between renal vasoconstriction with intact tubular function and established ARF.

If the tubular function is intact, the reabsorption of sodium is enhanced to more than 99%. Thus a fractional excretion of Na (FENa) ($\text{urine Na} \times \text{plasma creatinine} / (\text{plasma Na} \times \text{urine creatinine})$) of less than 1% indicates an intact tubular function. With the use of diuretics including mannitol, patients with glucosuria and patients with chronic renal failure will have FENa >1. Once ARF is established, the urine-concentrating capacity is abolished, and the measurement of urine osmolality may complement the use of FENa. The increased amount of tubular epithelial cells present in the urine sediment is also indicative of ARF with tubular dysfunction.

The traditional definition of ARF has been used for the patient in the ICU with decreased renal function and need for renal replacement therapy (RRT). Because even modest changes in renal function have shown to increase the morbidity and mortality of the patients, another term has been used to define patients that have any clinical evidence of renal dysfunction: acute kidney injury (AKI).

The lack of universal definition of AKI and ARF has created a large discrepancy in the reported data regarding incidence and prognosis for these patients. An expert panel under the auspices of the Acute Dialysis Quality Initiative has developed the RIFLE classification of AKI. The acronym RIFLE defines three grades of increasing severity of ARF (risk, injury, and failure) and two outcome variables (loss and end-stage kidney disease). The severity of renal dysfunction is based on a change in serum creatinine, reflecting changes in glomerular filtration rate (GFR) or duration and severity of decline in urine output from the baseline. Multiple studies have validated the use of the RIFLE criteria, and it is becoming the universal choice to describe patients with AKI.

MANAGEMENT

The best treatment of ARF is prevention. Nonpharmacologic approaches include:

- Hydration and volume repletion;
- Adequate renal perfusion pressure: avoidance of systemic arterial hypotension and or increased intra-abdominal pressure;
- Limiting nephrotoxin exposure: most common agents used in the ICU are antibiotics like aminoglycosides and amphotericin B and radio-contrast agents.

The pharmacologic strategies include the following:

- Diuretics and mannitol: there is no clear evidence in the literature to support the use of these agents in prevention of ARF.
- Dopamine and fenoldopam: dopamine increases the GFR by vasodilation through dopamine receptors, increasing the cardiac output by β -adrenergic stimulation, or increasing perfusion pressure via α -stimulation. Review of the data has not shown any benefits of dopamine in preventing ARF. Fenoldopam is a selective dopamine-1 receptor agonist that has shown to improve renal perfusion and decrease the creatinine level but has not been clearly shown to decrease the occurrence of ARF in the critical care population.

- c. N-acetylcysteine and theophylline do not have any role in the prevention of radio-contrast nephropathy and should not be used.

Once the patients develop acute renal failure, the treatment of choice is dialysis. The indications for acute hemodialysis are clear: fluid management, severe acidosis, electrolyte (potassium) abnormalities, and increased ammonia levels with clinical manifestations. The multiple types of dialysis are discussed in detail in one of the questions in this chapter.

Which Surgical Patients Are at Higher Risk of Developing ARF?

AKI is a well-known complication in the surgical patient. It can occur in any surgical patient who develops sepsis or multiple organ failure but is most frequent in patients after cardiac, vascular (4), and transplant surgeries and in patients with multiple trauma. The incidence ranges from 1% to 8% in the cardiac group (5–7), to as high as 40–90% in the liver transplant group (8). Cardiac, vascular, and transplant patients share an association of multiple comorbidities in their medical histories that include some degree of renal dysfunction. In multiple-trauma patients, the severity of the injury is directly related to the incidence of multiple organ failure, including ARF.

Answer: Cardiac, vascular, transplant, and multiple-trauma patients are higher risk surgical patients. Any surgical patients with preexistent morbidities, such as diabetes or renal dysfunction, should be considered at higher risk. Grade of recommendation: C.

What Are the Signs for Early Recognition of AKI or ARF?

The first clinical signs of AKI are a decrease of the urine output with an increase in blood levels of BUN and creatinine. An investigational alternative for early detection of a decrease in GFR is the monitoring of serum levels of cystatin C, a 13-kDa endogenous cysteine proteinase housekeeping protein. It has been shown to indicate AKI risk one to two hours earlier. This procedure is currently still being researched, and its use is limited. Creatinine levels, urine output, and cystatin C represent only the excretory function of the kidney, and they are only indirect markers of kidney injury.

There is not a consistent marker for the early detection of kidney damage. Several markers are in the investigational phase. The most promising are Kidney Injury Molecule 1, neutrophil gelatinase-associated lipocalin, IL-18, sodium/hydrogen exchanger isoform 3, n-acetyl- β -D-glucosaminidase, and matrix metalloproteinase 9 (9). These markers are not available for the clinical use, and further data are needed to consider their clinical value. Most important, the data suggest that there is a significant discrepancy in the incidence (1–31%), mortality (19–83%), optimal treatment, and prevention in patients with AKI. The main reason is a lack of a clear and universal definition.

The use of the RIFLE classification (10) and criteria for the definition of AKI have been tested in clinical practice and seem to be at least coherent with regards to outcome of the patients with AKI (11–15). The RIFLE classification

is becoming the universal guideline for the definition and stratification of patients with AKI. This helps recognize the patients at risk, which allows an earlier intervention to prevent progression to renal failure.

Answer: The first signs of ARF are decreased urine output and elevation of BUN and creatinine. The universal definition and stratification or AKI helps in the design of more trials to create new markers for earlier recognition of ARF. Grade of recommendation: C.

Diuretics, Dopamine, Fenoldopam, and Others: Do They Play Any Role in Preventing ARF?

Diuretics are a common intervention in the critically ill patient with AKI. There have been several reviews and data concluding that the use of loop diuretics is associated with shorter duration of RRT and increased urine output in critically ill patients, but no improvement in mortality or decrease in the need for RRT in patients with ARF (16,17). Bagshaw and Bellomo conducted a multinational multicenter survey (16) about the use of diuretics in AKI. It generated 331 responses from 16 countries. The conclusion of the survey was that diuretics are frequently used in AKI. Clinicians are most familiar with furosemide given intravenously and titrated to a physiologic endpoint of urine output. Most clinicians agree that a randomized controlled trial on diuretic use in AKI is justified and ethical.

The systematic review of the use of dopamine for the prevention and treatment of ARF showed that it did not prevent the onset of ARF, decrease the need for dialysis, or decrease the mortality rate. The use of fenoldopam in the early stages of AKI has shown that it may decrease the incidence of death and RRT (18,19).

Answer: Dopamine should not be used for the treatment of AKI. Diuretics and fenoldopam can be used in the early stages of AKI. Even though these drugs have been used for a long time, the data are clear for the need of more multicenter randomized controlled trials to validate them. Grade of recommendation: C.

ARF in Surgical Patients: What Are the Treatment Modalities?

Current treatment modalities include peritoneal dialysis and hemodialysis. Currently peritoneal dialysis has been left for the treatment of end-stage renal disease in the chronic phase. The most common modality used in the acute renal failure is hemodialysis. There are multiple modes of hemodialysis, including IHD and continuous RRT (CRRT). Neither of them has shown a significant difference in the mortality rate of critically ill patients (20,21). A new approach in renal replacement therapy is a slow extended daily dialysis that combines the advantages of CRRT and IHD. The initial reports of this new technique are promising, but further investigation is needed.

Two interesting aspects of the evolution of renal replacement therapy in the ICU over the past decade are the adequate intensity of dialysis and the potential of high-intensity therapy for the treatment of sepsis. The adequate dose, 35 ml/kg/hour, has shown to improve survival (22). The second concept introduces the rationale for high-volume hemofiltration (HVHF) in patients with sepsis with or without renal failure. HVHF is a

variant of continuous veno-venous hemodialysis (CVVHD) that requires higher surface area hemofilters and employs volumes of 35–80 ml/kg/hour.

Data suggest that the high-volume approach provides higher clearances of middle/high molecular weight solutes, that seem to be involved in the systemic inflammatory response syndrome, but at the same time this approach clears other molecules that are beneficial. More data are needed to prove the efficacy of HVHF as an immunomodulatory technique in the treatment of sepsis.

Answer: Current modalities that have proved their efficacy include IHD and CRRT. The new techniques include slow extended daily dialysis and CRRT with high volumes, but more prospective randomized trials are needed. Grade of recommendation: C.

Is CRRT Better than IHD in Patients with ARF After Surgery?

The advantages of CVVHD versus IHD were not documented in the early stages of the new modality. In 1999, a study from Bellomo and Ronco (23) compared two groups (about 47 patients each). That study showed that continuous hemofiltration is associated with improved daily control of azotemia. The superior adequacy of small solute clearance achieved during CVVHD provides additional support for its preferential use in the management of ARF in the ICU.

Waldrop and Barker published a retrospective review of trauma/surgical critical care patients requiring renal support (24). They found that CRRT provides a better control of azotemia and patients maintain a higher mean arterial pressure. Uehlinger and Frey conducted a study of 125 patients who were randomized into two groups: CVVHDF 70 and IHD 55 (25). The two groups were very similar. Their conclusion was that there is no survival benefit of continuous versus intermittent RRT in ICU patients with ARF.

The Cochrane Database Systematic Review (26) presented a meta-analysis of about 15 studies (1,550 patients) comparing CCRT with IHD. It did not find any statistical differences between in-hospital or ICU mortality rate, number of surviving patients not requiring RRT, hemodynamic stability or hypotension, and the need for escalation of vasopressor therapy. The only significant difference was in terms of higher mean arterial pressure and higher risk of clotting the dialysis filters in the CRRT group.

Recently, a pilot study that randomized controlled comparisons of CVVHD and extended daily dialysis with filtration (27) showed no significant difference in controlling the urea, creatinine, and electrolyte levels. Acidosis was better controlled with CVVHD.

Answer: There is no significant difference in the mortality rate or the progression to end-stage renal disease in patients with ARF treated with IHD or CRRT. CRRT has

shown advantages in patients with hemodynamic instability. Grade of recommendation: B.

Does CRRT Have a Role in the Critically Ill Trauma Patient Without ARF?

There has been a lot of interest in the role of CRRT as a therapeutic strategy for systemic inflammatory response syndrome (SIRS). There are some animal data showing that CVVHDF has a positive effect on hemodynamics in piglets with SIRS induced by cecum-perforated peritonitis (28). A pilot study comparing high-adsorption CVVH with standard CVVH in septic shock patients (29) showed that the group with high-adsorption filtration registered a decreased norepinephrine requirement to maintain the mean arterial blood pressure and also decreased plasma concentrations of cytokines.

There are some data that suggests that CVVH can remove some cytokines in plasma, reduce the APACHE II score and improve hemodynamics and oxygenation in patients with multiple organ dysfunction syndrome (30,31). HVHF when compared with standard volume CVVH has shown a decreased need for vasopressors and decreased cytokine levels in human septic shock (32,33).

Answer: The use of CVVHD (standard and high volumes) has shown benefits in critically ill patients without evidence of ARF, especially in sepsis and acute respiratory distress syndrome, but there aren't enough data to support its use. Grade of recommendation: C.

How Does ARF Impact the Morbidity and Mortality of Surgical Patients?

The negative impact of mild to moderate renal dysfunction on patient morbidity and mortality has been underestimated. Brandt and Horst (34) presented a retrospective study of all surgical patients admitted to an ICU. They found that patients that developed any kind of renal dysfunction would record an increase in the length of stay, ventilator days, mortality, and cost in the ICU.

A national survey using the 2001 National Hospital Discharge Survey (35), reviewed the discharge disposition of about 29 million patients and identified 558,032 cases of ARF with a frequency of 19.2 per 1,000 hospitalizations. It was associated with increased length of stay, increased hospital mortality, and a greater requirement for posthospitalization care. In a review of data from critically ill post-trauma patients (1,033) Brandt and Horst (36) found that patients with any level of AKI had an increase in ventilator days, length of stay, morbidity, and mortality rate compared with patients with normal renal function.

Answer: ARF has a tremendous impact in the morbidity, mortality, and cost in surgical patients. Grade of recommendation: C.

Levels of Evidence

Ref.	Year	Level	Findings
3	2007	IIc	AKI is frequent in infrarenal aortic aneurysm repair.
6	1998	Ic	Bypass surgery is associated with AKI, increase LOS, and mortality.
7	2007	IIc	AKI associated with bypass surgery has increased.
16	2007	IIb	Loop diuretics did not improve mortality, but decrease length of RRT and increased urine output.
17	2007	IIc	Loop diuretics did not improve mortality, but decrease length of RRT and increased urine output.
18	2006	IIa	Fenoldopam decreases the need for RRT and mortality in AKI.
19	2005	Ic	Fenoldopam does not reduce mortality or dialysis in ICU patients with early acute tubular necrosis
24	2005	IIc	CRRT is better than IHD to control azotemia and for patients with hemodynamic instability.
25	2005	IIb	No survival benefits of CRRT versus IHD in ARF patients.
26	2007	IIa	In hemodynamically stable patients, CRRT is not better than IHD in ARF patients.
27	2007	IIc	CVVH and SLED achieved similar control of urea, creatinine, and electrolytes.
29	2007	IIc	High-adsorption CVVH appears more effective than standard CVVH to decrease pressors requirements and cytokines in septic shock patients.
30	1998	III	CVVH decreases levels of cytokine in trauma patients as well as their clinical status.
31	2006	III	CVVH can remove cytokines in plasma, reduce APACHE II score, and improve hemodynamics and oxygenation in multiple-organ dysfunction syndrome.
32	2001	IIc	HVHF decreases vasopressor use in septic shock and affects anaphylatoxin levels differently than standard CVVH.
33	2006	IIc	HVHF at 6 L/h may seem to successfully remove some inflammatory cytokines in septic patients compared to CVVH.
34	2007	IIc	Mild to moderate renal failure increase mortality, LOS, ventilator days, and cost in ICU.
35	2006	IIb	AKI as a complication, increase mortality, LOS, ventilatory days, and cost.
36	2007	IIc	Early detection and treatment of AKI will decrease cost and improve patient outcomes.

Abbreviations: AKI, acute kidney injury; ARF, acute renal failure; BUN, blood urea nitrogen; CRRT, continuous renal replacement therapy; CVVH, continuous veno-venous hemofiltration; ESRD, end-stage renal disease; HVHF, high-volume hemofiltration; ICU, intensive care unit; IHD, intermittent hemodialysis; LOS, length of stay; RRT, renal replacement therapy; SLED, slow extended daily dialysis.

REFERENCES

- Marketos SG, et al. Acute renal failure according to ancient Greek and Byzantine medical writers. *J Roy Soc Med* 1993; 86: 290–1.
- Black D. The story of nephrology. *J Roy Soc Med* 1980; 73: 514.
- Paskalev D. Georg Haas the forgotten hemodialysis pioneer. *Dial Transp* 2001; 30: 828–32.
- Tallgren M, Hynninen M. Acute renal injury and dysfunction following elective abdominal aortic surgery. *Eur J Vasc Endovasc Surg* 2007; 33: 550–5.
- Lassnigg A, et al. Impact of minimal increases in serum creatinine on outcome in patients after cardiothoracic surgery: do we have to revise current definitions of acute renal failure? *Crit Med* 2008; 36: 1370–2.
- Mangano CM, et al. Renal dysfunction after myocardial revascularization: Risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. *Ann Int Med* 1998; 128: 194–203.
- Swaminathan M, et al. Trends in acute renal failure associated with coronary artery bypass graft surgery in the United States. *Crit Care Med* 2007;35.
- Yalavarthy G, et al. Acute renal failure and chronic kidney disease following liver transplantation. *Hemodialysis Int* 2007; 11(Suppl 3): 7–12.
- Zhou H, Star RA. Acute kidney injury biomarkers: needs, present status and future promise. *NephSAP* 2006; 5: 63–71.
- Van Biesen V, Lameire N. Defining acute renal failure: RIFLE and beyond. *Clin J Am Soc Nephrol* 2006; 1: 1314–19.
- Abosaif NY, El Nahas AM. The outcome of acute renal failure in the intensive care unit according to RIFLE: model application, sensitivity and predictability. *Am J Kidney Dis* 2005; 46: 1038–48.
- Bell M, Martling CR. Optimal follow-up time after continuous renal replacement therapy in actual renal failure patients stratified with the RIFLE criteria. *Nephrol Dial Transplant* 2005; 20: 354–60.
- Hoste EA, Kellum JA. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. *Crit Care* 2006; 10: R73–R83.
- Kuitunen A, Pettila V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg* 2006; 81: 542–6.
- Uchino S, Bellomo R, Ronco C. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. *Crit Care Med* 2006; 34: 1913–17.
- Bagshaw SM, Bellomo R. Loop diuretics in the management of acute renal failure: a systematic review and meta-analysis. *Crit Care Resusc* 2007; 9: 60–8.
- SamPATH S, Abrams KR. The efficacy of loop diuretics in acute renal failure: assessment using Bayesian evidence synthesis techniques. *Crit Care Med* 2007; 35: 2516–24.
- Landoni G, Zangrillo A. Beneficial impact of fenoldopam in critically ill patients with or at risk for acute renal failure: a meta-analysis of randomized clinical trials. *Am J Kidney Dis* 2007; 49: 56–68.
- Tumlin J, Shaw AD. Fenoldopam mesylate in early acute tubular necrosis: a randomized, double-blind, placebo-controlled clinical trial. *Am J Kidney Dis* 2005; 46: 26–34.
- Eachempati SR, Barie PS. Acute renal failure in critically ill surgical patients: persistent lethality despite new modes for renal replacement therapy. *J Trauma* 2007; 63: 987–93.
- Fuiano G, Mazza G. Guidelines for dialysis. Replacement therapy for acute renal failure in critically ill patients. *G Ital Nephrology* 2004; 21(Suppl 28): S1–S10.
- Ronco C, Bellomo R. Effects of different doses of continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomized trial. *Lancet* 2000; 356: 26–30.

23. Bellomo R, Ronco C. Changing acute renal failure treatment from intermittent hemodialysis to continuous hemofiltration: impact on azotemic control. *Int J Artif Organs* 1999; 22: 145–50.
24. Waldrop J, Barker DE. A comparison of continuous renal replacement therapy to intermittent dialysis in the management of renal insufficiency in the acutely ill surgical patient. *Am Surg* 2005; 71: 36–9.
25. Uehlinger DE, Frey FJ. Comparison of continuous and intermittent renal replacement therapy for acute renal failure. *Nephrol Dial Transplant* 2005; 20: 1630–7.
26. Rabindranath K. Intermittent versus continuous renal replacement therapy for acute renal failure in adults. *Cochrane Database Syst Rev* 2007;3.
27. Baldwin I, Bellomo R. A pilot randomized controlled comparison of continuous veno-venous haemofiltration and extended daily dialysis with filtration: Effect on small solutes and acid-base balance. *Intensive Care Med* 2007; 33: 830–5.
28. Gong JY, Zhang LE. Therapeutic effect of continuous veno-venous hemodiafiltration on systemic inflammatory response syndrome induced by cecum perforated peritonitis in piglets. *Zhongguodang Dai Er Ke Za Zhi* 2007; 9: 237–40.
29. Haase M, Bellomo R. A pilot study of high-adsorption hemofiltration in human septic shock. *Int J Artif Organs* 2007; 30: 108–17.
30. Koperna T, Germann P. Cytokine patterns in patients who undergo hemofiltration for treatment of multiple organ failure. *World J Surg* 1998; 22: 443–7.
31. Kou QY, Guan XD. Effect of continuous veno-venous hemofiltration on the plasma level of cytokines in patients with multiple organ dysfunction syndrome. *Zhong Hua Waike Za-Zhi* 2006; 44: 1197–9.
32. Cole L, Tipping P. High-volume hemofiltration in human septic shock. *Intensive Care Med* 2001; 27: 978–86.
33. Ghani RA, Ismail R. Serum IL-6 and IL-1-ra with sequential organ failure assessment scores in septic patients receiving high-volume hemofiltration and continuous veno-venous hemofiltration. *Nephrology* 2006; 11: 386–93.
34. Brandt MM, Horst HM. The impact of mild renal dysfunction on postoperative mortality in the surgical intensive care unit. *Am Surg* 2007; 73: 743–6.
35. Liangos O, Jaber BL. Epidemiology and outcomes of acute renal failure in hospitalized patients: A national survey. *Clin J Am Soc Nephrol* 2006; 1: 43–51.
36. Brandt MM, Horst HM. Renal dysfunction in trauma: even a little costs a lot. *J Trauma* 2007; 62: 1362–4.

Hyperglycemia

Balachundhar Subramaniam and Alan Lisbon

Evidence-Based Practice of Tight Glucose Control in the Perioperative Setting		
Issues	Answers	Recommendation grade
TGC in the cardiac and neurosurgical ICU	It is beneficial.	A
TGC in the general surgical ICU	It is beneficial.	B
TGC in medical surgical ICU	It is beneficial after 3 days of ICU stay.	B
TGC in the cardiac surgical OR	It is beneficial with a target blood sugar around 150 mg/dl.	B
TGC in the noncardiac surgical OR	It may be beneficial in critically ill.	C
Target glucose level in diabetics and nondiabetics	No difference in their target glucose values.	C
Prevention of glucose toxicity or insulin	Both play a role in providing TGC benefits.	B
Optimum target blood glucose value with least adverse effects	TGC 80–110 mg/dl may not be the same in all surgical settings to provide maximum benefits with least adverse effects.	B
Blood glucose variability and outcome	Decreasing variability by continuous insulin infusion increases good outcome.	B
Cost savings	TGC decreases cost and health care utilization.	B

Abbreviations: ICU, intensive care unit; OR, operating room; TGC, tight glucose control.

INTRODUCTION

Diabetes affects 6.3% of the population or about 18.2 million people in the United States. One-third of them may be undiagnosed. The risk of heart disease and stroke is about two to four times higher than adults without diabetes. Poorly controlled inpatient glucose levels are associated with increased morbidity and mortality and higher hospital costs (1). Acute and chronic hyperglycemia is associated with poor outcomes (1). Recent interventional studies have shown an improved outcome with glucose control in patients undergoing cardiac surgery (2,3), those with acute myocardial infarction (4–6), and the critically ill (7–9).

The aim of this chapter is to analyze the current evidence in the intensive care unit (ICU) and in the perioperative setting of the benefits, efficacy, and adverse effects of intensive glycemic control.

DOES INTENSIVE GLUCOSE MANAGEMENT IMPROVE OUTCOME IN THE SURGICAL CRITICAL CARE UNIT? IF SO, WHAT ARE THE BENEFITS AND WHO ARE THE PATIENTS THAT BENEFIT?

The Leuven trials (7,8), Stamford trial (9), and the Portland diabetic project (2) show a mortality benefit in critically ill patients. In the Leuven trials, intensive insulin therapy

titrated to a target of 80–110 mg/dl reduced mortality by 34%, sepsis by 46%, blood transfusion by 50%, critical illness polyneuropathy by 44%, and renal failure requiring dialysis by 41%. Krinsley (9) largely confirmed this result in a medical-surgical population. In the Leuven II trial (8), the mortality benefit was seen only for patients who stayed three or more days in the medical ICU. Pittas et al. (10) in their meta-analysis of clinical trials evaluating the effect of insulin therapy on mortality in hospitalized patients with critical illness found that short-term mortality was decreased by 15% in variety of clinical settings. In the ICU, true randomized trials are few. Two trials, VISEP (11) and Glucontrol (12), have not shown benefits. They should be interpreted as failed trials and not lack of positive benefit. See Figure 82.1.

The Leuven I trial had 65% of the study population as post-cardiac surgery patients. This study along with the Portland diabetic project confirm that tight blood glucose control decreases the incidence of deep sternal wound infection and may confer mortality benefit. However, mortality benefits have not been reproducible in other trials, such as Glucontrol (12) and VISEP (11). It is important to note that the Stamford trial had retrospective controls and may be susceptible to bias. The argument against a 30% reduction in mortality seen in Leuven I is that there may be a too high a benefit to be explained by glucose control alone. It is possible that reduced mortality is secondary to a Hawthorne

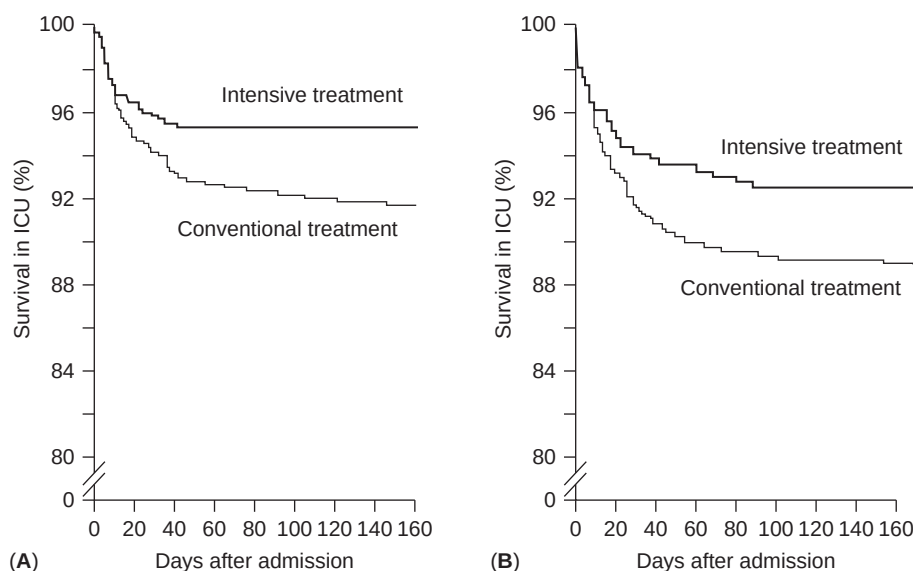


Figure 82.1 Survival beneficial effects of tight glucose control in critically ill patients

effect (tight glucose control = investigator commitment and bedside presence, more tests, more attention, more patient visits, more interventions, and overall better care). Tight glucose control of 80–110mg/dl causes a sixfold risk of hypoglycemia. The target blood glucose level for the non-cardiac ICU population cannot be kept at 80–110mg/dl due to the lack of evidence and possible higher incidence of hypoglycemia.

Both Glucontrol and VISEP were stopped due to the increased incidence of severe hypoglycemic episodes. The numbers in both studies were not enough to confirm or reject mortality benefit. It is a good practice to control the blood sugars without exposing the patients to severe hypoglycemic episodes. One has to await the NICE-SUGAR (13) study to reproduce the Leuven and Stamford trials before tight glucose control (80–110mg/dl) should be adapted as a standard of care in the noncardiac ICU population (14).

Recommendations: It is important to keep the blood sugar less than 150mg/dl. Tight glucose control (80–110mg/dl) is beneficial in cardiac and neurosurgical ICU; Level of evidence: Ib; strength of recommendation: Grade A. Tight glucose control (100–150mg/dl) is beneficial in general surgical ICU; Level of evidence: Ib; strength of recommendation: Grade B. Tight glucose control (100–150mg/dl) is beneficial in medical surgical ICU; Level of evidence: IIb; strength of recommendation: Grade B.

DOES TIGHT PERIOPERATIVE GLUCOSE CONTROL IN THE OPERATING ROOM IMPROVE SURGICAL OUTCOME? WHAT ARE THE BENEFITS?

Hyperglycemia predicts infection in diabetics undergoing cardiac surgery (15). Hyperglycemia in the first 48 postoperative hours has a 200% increase in surgical site

infections among cardiothoracic surgical patients (16). Gandhi and colleagues (17) evaluated a tight 80–110mg/dl control versus <200mg/dl in cardiac surgical patients. All the patients had a similar postoperative intensive care regimen. They found that patients with tight control in the operating room had no benefit. Their secondary outcome, stroke, was indeed higher in the intraoperative tight glucose control group.

The Leuven I trial (7) and Portland diabetic project (2) show that intensive perioperative glycemic control is beneficial in patients undergoing cardiac surgery. The Leuven I trial has also shown these benefits in patients undergoing thoracic surgery and vascular surgery subgroups, even though it was a subgroup analysis benefit. Other than these trials, there is no study in the literature evaluating the benefit of intensive glycemic control in different operative settings. We recommend caution against a very tight control such as 80–110mg/dl in the intraoperative period for fear of severe hypoglycemic episodes without proven benefit in this setting. We recommend keeping the intraoperative blood sugars to 100–150mg/dl in all major surgery or patients who are expected to go to the ICU after the surgery.

Recommendations: Beneficial effects of intraoperative glycemic control (100–150mg/dl), cardiac surgery: Level of evidence: Ib; strength of recommendation: Grade B. Non-cardiac surgery: Level of evidence: not available; strength of recommendation Grade C.

ARE THE BENEFITS AND SIDE EFFECTS OF TIGHT GLUCOSE CONTROL SIMILAR IN DIABETIC AND NONDIABETIC SURGICAL PATIENTS?

Rady et al. (18) with a database of 7,285 patients (1,083 had a previous diagnosis of diabetes mellitus) evaluated whether

glycemic control predicted similar outcomes in diabetic and nondiabetic patients. In their study, the presence of diabetes modified the relationship between glycemic control and mortality. For the same lower median values of blood glucose, nondiabetics had a twice as high mortality compared to the diabetics. Within the control group, diabetics and nondiabetics had a similar mortality rates even if the latter had higher blood glucose levels. These findings suggest that the target blood glucose levels in the two groups may not be the same to obtain beneficial effects with the tight glucose control regimen. As of now there is no more evidence to confirm or reject these findings.

Recommendations: Target glucose level and differential beneficial effects of intraoperative glycemic control in diabetics and nondiabetics: there is no difference between the recommended target glucose levels between diabetics and nondiabetics in the perioperative period. Level of evidence: II; strength of recommendation: Grade C.

IS IT GLYCEMIC CONTROL OR OTHER METABOLIC OR NONMETABOLIC EFFECTS OF INSULIN THAT PROVIDE THE BENEFICIAL EFFECTS?

Hyperglycemia accompanies critical illness in different settings, such as acute coronary syndrome (19,20), stroke, trauma (21,22), and in medical and surgical ICUs (9) and is a marker for adverse outcome. Insulin resistance and hyperglycemia coexist in critically ill patients and is called diabetes of stress (23). Control of this hyperglycemia has been shown to decrease ICU mortality (7–9). The mechanism of this benefit could be due to control of glucose levels or a direct effect of insulin. Insulin partially corrects abnormal serum lipid profiles and counteracts the catabolic state evoked by critical illness. The direct effect of insulin and the lowering of blood glucose both lead to myocardial protection and decrease in inflammation. Both the liver and skeletal muscles suffer from insulin resistance in the critically ill. Insulin lowers blood glucose predominantly through increased skeletal muscle glucose uptake (24). In the critically ill, adipose tissue and skeletal muscle are relatively insulin-responsive compared to the liver. All organs that passively take up glucose into the cell are at a higher risk of direct glucose overload due to loss of cellular protection against this increased uptake. Increased intracellular glucose metabolism leads to increased production of superoxide and peroxynitrite and thereby mitochondrial dysfunction. This may lead to shuttling of glucose into toxic pathways and increased apoptosis.

Recommendation: Both insulin and glucose control provide beneficial effects in the perioperative period. Level of evidence II. Strength of recommendation Grade B.

WHAT IS THE OPTIMUM TARGET BLOOD GLUCOSE LEVEL IN THE OPERATING ROOM AND THE ICU TO DERIVE MAXIMUM BENEFIT WITH THE LEAST ADVERSE EFFECTS?

There was a linear correlation between the degree of hyperglycemia and the risk of death in patients enrolled in Leuven

I trial (25). This persisted even after correction for insulin dose and illness severity scores. Maximum benefit was seen in the group who had their blood glucose levels below 110mg/dl, including organ protection effects such as reduced incidence of renal failure, anemia, and blood transfusions. The group of patients with blood glucose level between 110 and 150mg/dl had moderate benefits compared to the group with blood glucose between more than 150mg/dl.

The trade-off of such tight control of blood glucose in critically ill patients is the incidence of hypoglycemia. Severe hypoglycemia is defined as blood glucose <40mg/dl. The rate of severe hypoglycemia in Leuven I trial was 5.1% in intervention group compared to 0.8% in the control group. This incidence increased to 18.7% in the subsequent Leuven II trial compared to 3.1% in the control group. In the Leuven II trial, medical ICU patients may have had severe illness scores and a higher sepsis incidence on admission. Logistic regression analysis identified hypoglycemia induced by intensive insulin therapy as an independent risk factor for death by itself, and this may offset the beneficial effects of tight glucose control (8). The method of glycemic monitoring could influence the blood glucose values and thereby their incidence.

The VISEP and Glucontrol trials were stopped due to a higher incidence of severe hypoglycemic episodes in the tight glucose control arms. This should be considered as failure of study protocols and does not give any insight into any beneficial effect (or lack thereof) (26). Even a single episode of severe hypoglycemia was associated with increased risk of mortality. The Stamford trial had a rate of 0.35% hypoglycemia before and after the induction of tight glucose control regimen. Krinsley and Grover (27) showed that in their population of mixed critically ill patients that diabetes, septic shock, renal insufficiency, mechanical ventilation, severity of illness reflected by APACHE II score with the age component deleted, and treatment in the tight glycemic control period were independent risk factors for the development of hypoglycemia. Mortality was 55.9% among the patients with severe hypoglycemia and 39.5% among the controls. The increase in the risk of severe hypoglycemia would negate the benefits of tight glucose control.

Avoidance of hypoglycemia is a key element when attempting intensive insulin therapy. Choosing the right glycemic target for a given population (26), training nurses and physicians in the glucose protocols, understanding the strength and weakness of various monitoring tools, frequent monitoring of patients, paying attention to the rapidity of change in glucose values, and concomitant adjustment of insulin infusion can decrease the hypoglycemic events and increase the beneficial effects.

Recommendation: Control of blood glucose level to 80–110mg/dl may not be beneficial in all surgical populations because it may be associated with increased risk of hypoglycemia and adverse outcomes. Strength of evidence: Ib; level of recommendation: Grade B.

CAN THE VARIABILITY IN BLOOD GLUCOSE LEVELS AFFECT THE OUTCOME INDEPENDENT OF SET TARGET BLOOD GLUCOSE LEVELS?

Less variability in blood glucose values provided survival benefit in a retrospective study of 7,049 critically ill patients

(28). The standard deviation of the values of blood glucose recorded in each patient was closely related to survival in this multivariate logistic regression analysis. In this study, the authors showed that the variability of glucose levels was a stronger predictor of ICU mortality than the absolute blood glucose value. They also found that unlike nondiabetic subjects, patients with diabetes did not display an association between increasing levels of blood glucose or glucose variability and ICU or hospital mortality. This suggests that diabetic patients may have unique response to the biologic effects of hyperglycemia. Hirsh and Brownlee recently (29) stressed the importance of glucose variability. Glucose fluctuations may increase the oxidative stress (30). Cell damage was most prominent when the glucose level increased rapidly from a normal level (31). Decreasing variability of blood glucose concentration might be an important factor by which intensive insulin therapy exerts its beneficial effects. Continuous IV administration is better than continuous and bolus subcutaneous administration, which is better than bolus IV administration (32). This is a consideration along with target blood glucose level when evaluating a blood glucose protocol for tight blood glucose in intensive care.

Recommendation: Decreasing variability in perioperative blood glucose levels by continuous insulin infusion provides beneficial outcome. Strength of evidence: II; level of recommendation: Grade C.

DOES INTENSIVE INSULIN THERAPY REDUCE HEALTH CARE RESOURCE UTILIZATION AND PROVIDE COST SAVINGS?

The Leuven trials (7,8) provided positive beneficial effects on organ injury as well as mortality when tight glucose control was used as an intervention in their critical care units. This led to a position statement from American College of Endocrinology for inpatient management of hyperglycemia. It is possible that intensive insulin glucose control could lead to increased costs because of increased patient blood checks and personnel involvement. The same group evaluated the cost of intensive insulin therapy (33). The post hoc health care resource utilization analysis has shown intensive insulin therapy to be associated with a substantial reduction in hospital costs (cost savings of \$4,200). These savings were attributed to the reduction in renal failure, sepsis, blood transfusions, dependency on mechanical ventilation, and length of ICU stay. Though the cost of additional monitoring was \$115, the overall benefit was substantial in this treatment group. The length of hospital stay was 8.6 days in the conventionally treated group, compared to 6.6 days in the treatment group. The net annualized decrease in cost was \$1,580 per patient in a mixed critically ill patient population (34).

Recommendation: Tight perioperative blood glucose control decreases health care costs and resource utilization. Strength of evidence: II; level of recommendation: Grade B.

Tight Glucose Control in the Operating Rooms and Outcome

Trial	Year (Ref no)	Level of evidence	Randomized groups (n)	Intervention/Design	Minor endpoint	Major endpoint	Interpretation/Comments
1	2007 Mayo (17)	I	2 (n = 400), 157 to 114	IV insulin infusion/ randomized	Length of ICU and hospital stay	No decrease in composite of death, sternal infection, ventilation, stroke, renal failure within 30 days	Single center, similar postoperative regimen and targets between the groups
2	2005 Outtara (36)	II	200 consecutive; intervention during surgery, >200 was defined as poor control	IV insulin infusion in all/case control	Hospital stay	↓ Combined cardiovascular, respiratory, neurological, renal, infectious	Poor intraoperative BS had 7.2 odds of severe adverse in-hospital outcome
3	2004 Lazaar (37)	I	2 (n = 141), 260 to 138	IV insulin infusion/ randomized (GIK)		↓ Atrial fibrillation, ↓ length of stay, ↓ 2-year mortality, ↓ wound infection, ↓ recurrent ischemia	Better combined outcome; control group BS very high at 260
4	2003 Portland (2)	II	Case control, 213 to 177	IV infusion/intermittent SC insulin	—	↓ Mortality	Reduction in mortality by 66%
5	1999 Portland (3)	II	Case control, 200 to <150	IV infusion/intermittent SC insulin	—	↓ Sternal infection	Deep sternal wound infection reduced by 57%

Abbreviations: BS, blood sugar; ICU, intensive care unit.

Tight Glucose Control Studies in ICUs and Outcome

Trial	Year (Ref.)	Level of evidence	Randomized groups (n)	Intervention/Design	Minor endpoint	Major endpoint	Interpretation/Comments
1	2001 Leuven I (7)	Ib	2 (n = 1,548); 153 to 103; 73% <110	IV insulin infusion/prospective randomized	↓ Renal failure, ↓ ventilatory support, ↓ bilirubin, ↓ sepsis, ↓ polyneuropathy, ↓ transfusion	↓ ICU and ↓ hospital mortality (pronounced in ICU >5 days)	Single-center study; surgical patients only
2	2006 Leuven II (8)	Ib	2 (n = 1,200); 160 to 105; 64% <110	IV insulin infusion/prospective randomized	↓ Renal failure, ↓ ventilatory support, ↓ hospital stay ↓ bilirubin	↓ Mortality (if ICU >3 days); ↓ hospital mortality	Single-center study; medical patients only
3	2006 Leuven I and II (35)	Ib	2 (n = 2,748); 152 to 105; 70% < 110	IV insulin infusion/prospective randomized	↓ Renal failure, ↓ ventilatory support, ↓ polyneuropathy	↓ Mortality	Meta-analysis of study 1 and study 2
4	2004 Stamford (9)	IIIb	2 (n = 1,600); 152 to 131	IV insulin Infusion/case control study	↓ Renal failure, ↓ ventilatory support, ↓ ICU stay, ↓ anemia	↓ Mortality	Retrospective controls
5	Glucontrol 2006	Unpublished	2 (n = 855) medical/surgical	Two arms	Unreported	No mortality benefits	Stopped; severe Hypoglycemia; less power
6	WISEP 2008 (11)	Ib	4 (n = 488) sepsis/septic shock patients	Four-arm study with fluid and glucose	Unreported	No mortality benefits	Stopped; severe Hypoglycemia; less power
7	NICE (13)	Ongoing	2 (n = 6,100) ICU patients 180 to 108	IV insulin infusion/randomized	Ongoing	Mortality	Multicenter, ongoing
8	Portland 2003 (2)	IIIb		IV insulin infusion/randomized		↓ Mortality	Single center

Abbreviation: ICU, intensive care unit.

REFERENCES

- Control CfD. National Diabetes Fact Sheet. 2002. Available at www.cdc.gov/diabetes
- Furnary AP, Gao G, Grunkemeier GL, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003; 125: 1007–21.
- Furnary AP, Zerr KJ, Grunkemeier GL, et al. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg* 1999; 67: 352–60; discussion 360–2.
- Malmberg K, Norhammar A, Wedel H, et al. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. *Circulation* 1999; 99: 2626–32.
- Malmberg K. Prospective randomized study of intensive insulin treatment on long-term survival after acute myocardial infarction in patients with diabetes mellitus. DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) Study Group. *Br Med J* 1997; 314: 1512–15.
- Ishihara M, Kojima S, Sakamoto T, et al. Acute hyperglycemia is associated with adverse outcome after acute myocardial infarction in the coronary intervention era. *Am Heart J* 2005; 150: 814–20.
- Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med* 2001; 345: 1359–67.
- Van den Berghe G, Wilmer A, Hermans G, et al. Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006; 354: 449–61.
- Krinsley JS. Effect of an intensive glucose management protocol on the mortality of critically ill adult patients. *Mayo Clin Proc* 2004; 79: 992–1000.
- Pittas AG, Siegel RD, Lau J. Insulin therapy for critically ill hospitalized patients: a meta-analysis of randomized controlled trials. *Arch Intern Med* 2004; 164: 2005–11.
- Brunkhorst FM, Engel C, Bloos F, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med* 2008; 358: 125–39.
- Vanhorebeek I, Langouche L, Van den Berghe G. Tight blood glucose control with insulin in the ICU: facts and controversies. *Chest* 2007; 132: 268–78.
- George Institute for International Health. Normoglycaemia in intensive care evaluation and survival using glucose algorithm regulation—NICE-SUGAR. 2007. Available at <http://www.thegeorgeinstitute.org/research/critical-care-&-trauma/research/normoglycaemia-in-intensive-care-evaluation—nice.cfm>
- Bellomo R, Egi M. Glycemic control in the intensive care unit: why we should wait for NICE-SUGAR. *Mayo Clin Proc* 2005; 80: 1546–8.
- Golden SH, Peart-Vigilance C, Kao WH, et al. Perioperative glycemic control and the risk of infectious complications

- in a cohort of adults with diabetes. *Diabetes Care* 1999; 22: 1408–14.
16. Latham R, Lancaster AD, Covington JF, et al. The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Control Hosp Epidemiol* 2001; 22: 607–12.
 17. Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med* 2007; 146: 233–43.
 18. Rady MY, Johnson DJ, Patel BM, et al. Influence of individual characteristics on outcome of glycemic control in intensive care unit patients with or without diabetes mellitus. *Mayo Clin Proc* 2005; 80: 1558–67.
 19. Kosuge M, Kimura K, Ishikawa T, et al. Persistent hyperglycemia is associated with left ventricular dysfunction in patients with acute myocardial infarction. *Circ J* 2005; 69: 23–8.
 20. Timmer JR, van der Horst IC, Ottervanger JP, et al. Prognostic value of admission glucose in non-diabetic patients with myocardial infarction. *Am Heart J* 2004; 148: 399–404.
 21. Juvela S, Siironen J, Kuhmonen J. Hyperglycemia, excess weight, and history of hypertension as risk factors for poor outcome and cerebral infarction after aneurysmal subarachnoid hemorrhage. *J Neurosurg* 2005; 102: 998–1003.
 22. Sung J, Bochicchio GV, Joshi M, et al. Admission hyperglycemia is predictive of outcome in critically ill trauma patients. *J Trauma* 2005; 59: 80–3.
 23. McCowen KC, Malhotra A, Bistrian BR. Stress-induced hyperglycemia. *Crit Care Clin* 2001; 17: 107–24.
 24. Mesotten D, Swinnen JV, Vanderhoydonc F, et al. Contribution of circulating lipids to the improved outcome of critical illness by glycemic control with intensive insulin therapy. *J Clin Endocrinol Metab* 2004; 89: 219–26.
 25. Van den Berghe G, Wouters PJ, Bouillon R, et al. Outcome benefit of intensive insulin therapy in the critically ill: insulin dose versus glycemic control. *Crit Care Med* 2003; 31: 359–66.
 26. Krinsley J. Glycemic control in critically ill patients: leuven and beyond. *Chest* 2007; 132: 1–2.
 27. Krinsley JS, Grover A. Severe hypoglycemia in critically ill patients: risk factors and outcomes. *Crit Care Med* 2007; 35: 2262–7.
 28. Egi M, Bellomo R, Stachowski E, et al. Variability of blood glucose concentration and short-term mortality in critically ill patients. *Anesthesiology* 2006; 105: 244–52.
 29. Hirsch IB, Brownlee M. Should minimal blood glucose variability become the gold standard of glycemic control? *J Diabetes Comp* 2005; 19: 178–81.
 30. Monnier L, Mas E, Ginet C, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. *JAMA* 2006; 295: 1681–7.
 31. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. *Nature* 2001; 414: 813–20.
 32. Van den Berghe G, Wouters PJ, Kesteloot K, et al. Analysis of healthcare resource utilization with intensive insulin therapy in critically ill patients. *Crit Care Med* 2006; 34: 612–16.
 33. Ouattara A, Grimaldi A, Riou B. Blood glucose variability. A new paradigm in critical care? *Anesthesiology* 2006; 105: 233–4.
 34. Krinsley JS, Jones RL. Cost analysis of intensive glycemic control in critically ill adult patients. *Chest* 2006; 129: 644–50.
 35. Van den Berghe G, Wilmer A, Milants I, et al. Intensive insulin therapy in mixed medical/surgical intensive care units: benefit versus harm. *Diabetes* 2006; 55: 3151–9.
 36. Ouattara A, Lecomte P, Le Manach Y, et al. Poor intraoperative blood glucose control is associated with a worsened hospital outcome after cardiac surgery in diabetic patients. *Anesthesiology* 2005; 103: 687–94.
 37. Lazar HL, Chipkin SR, Fitzgerald CA, et al. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. *Circulation* 2004; 109: 1497–502.

Abdominal Compartment Syndrome

James C. Doherty

Clinical Questions		
Question	Answer	Grade of recommendation
Are there risk factors that can be used to identify patients at-risk for ACS/IAH ?	Abdominal surgery; ileus; pulmonary, hepatic, or renal dysfunction; >3.5 L/24 hour resuscitation, hypothermia, oliguria, anemia, base deficit, high GAP CO ₂	B
How should patients be screened for ACS/IAH?	Intermittent IAP measurement via urinary bladder (B) with repeat measurements if IAH is present (C)	B, C
Is there a threshold level of IAP that mandates intervention?	There appears to be benefit in keeping APP ≥50–60 mmHg	C
Are there any effective nonsurgical strategies for treating ACS/IAH?	Decompressive laparotomy (B), neuromuscular blockade (C), supine positioning (C), avoid overly zealous fluids (B), colloid or hypertonic crystalloid (C), percutaneous catheter drainage (C)	B, C
Is there a preferred technique for temporary abdominal closure?	No	N/A
Is there a predictable time frame or preferred technique for definitive abdominal closure?	No	N/A
Is there a role for abdominal decompression in the management of intracranial hypertension	Decompressive laparotomy should be considered in cases of refractory intracranial hypertension	B
Abbreviations: ACS, abdominal compartment syndrome; APP, abdominal perfusion pressure; GAP CO ₂ , gastric-to-arterial PCO ₂ difference IAH, intra-abdominal hypertension; IAP, intra-abdominal pressure; N/A, not available.		

INTRODUCTION

The concept of abdominal compartment syndrome (ACS) is less than 25 years old, but it represents one of the most influential recent developments in trauma and critical care. First described by Kron et al. in 1984, ACS has evolved conceptually from a postoperative concern of trauma surgeons to a potential preventable cause of multiple organ dysfunction for all critically ill patients (1). Accompanying the proliferation of literature regarding ACS over the past two decades has been the confusing emergence of a number of varying definitions and classification systems. To resolve this confusion, an International ACS Consensus Definitions Conference of the World Society of the Abdominal Compartment Syndrome (WSACS) met in 2004 and established a series of definitions to guide clinicians in the diagnosis of ACS (2). The conference also published evidence-based recommendations for the diagnosis, management, and prevention of ACS (3).

The WSACS conference defined intra-abdominal hypertension (IAH) as “sustained or repeated pathological elevation

in intra-abdominal pressure (IAP) ≥12 mmHg.” Furthermore, it defined ACS as “sustained IAP >20 mmHg . . . that is associated with new organ dysfunction/failure.” It also subclassified ACS into primary ACS (due to primary abdominal or pelvic pathology), secondary ACS (due to nonabdominal/nonpelvic pathology), and recurrent ACS (redevelopment of ACS after treatment). The conference also established intermittent IAP measurement via the urinary bladder as the reference standard for intermittent IAP measurement and detailed specific requirements for standardization and accuracy of measurements. These included maximal bladder instillation volume of 25 ml sterile saline, measurement in supine position at end-expiration, and a zero point for pressure transduction at the midaxillary line.

The remainder of this chapter use a systematic review of the medical literature to provide timely, evidence-based recommendations for the diagnosis and treatment of ACS. Specific questions are used to frame the discussions and develop appropriate recommendations supported by the existing literature.

ARE THERE RISK FACTORS THAT CAN BE USED TO IDENTIFY PATIENTS TO BE SCREENED FOR THE DEVELOPMENT OF IAH/ACS?

Because of the various inconsistent criteria used to define IAH and ACS, no consistent data exist regarding the incidence of these entities in clinical practice. Nevertheless, IAH and ACS do occur with some frequency in the intensive care unit (ICU) and are associated with organ dysfunction and mortality (4–7). Several prospective studies have identified risk factors for the development of IAH and ACS. Malbrain et al. associated the development of IAH with the presence of abdominal surgery, ileus, pulmonary dysfunction, liver dysfunction, renal dysfunction, and large volume fluid administration (>3.5 L/24 hours) (7). In a prospective study of blunt torso trauma, hypothermia, anemia, oliguria, base deficit, large volume of crystalloid resuscitation, and high gastric-to-arterial PCO_2 difference (GAP CO_2) by gastric tonometry all were found to be predictors of ACS development (8).

Recommendation: Given the presence of identifiable risk factors for IAH and ACS and the high morbidity and mortality associated with untreated ACS, identification of at-risk individuals using criteria such as those listed may provide an opportunity for screening and early intervention in IAH and ACS. This Grade B recommendation in favor of risk assessment and screening is offered with the recognition that future studies may identify additional risk factors to be considered.

HOW SHOULD PATIENTS BE SCREENED AND/OR MONITORED FOR THE DEVELOPMENT OF IAH/ACS?

Physical examination has been shown to lack sufficient sensitivity to diagnose IAH (9,10). Thus, direct measurement of IAP is the preferred diagnostic test for IAH. As mentioned previously, the WSACS conference established intermittent IAP measurement via the urinary bladder as the reference standard for measurement of IAP. This determination was based on the reliability, simplicity, and low cost associated with such measurement, especially when performed in a standardized fashion (11–13).

No data exist regarding the ideal frequency of IAP measurements in at-risk individuals. Well-designed studies are needed to resolve this issue. A recently published study demonstrated that a continuous IAP measurement technique using a standard three-way bladder catheter yields IAP measurements that closely correlate with those obtained using the intermittent technique (14). Moreover, specialized urinary catheters designed for continuous measurement of IAP are now commercially available. If such techniques prove to be cost-effective and can be further validated clinically, continuous monitoring may replace traditional intermittent monitoring, and the frequency issue may become irrelevant.

Recommendation: Intermittent IAP measurement via the urinary bladder should be performed in patients identified to be at risk for IAH/ACS based on assessment of the risk factors mentioned earlier (Grade B recommendation). At-risk individuals demonstrating IAH (IAP ≥ 12 mmHg) should have repeat measurements performed during their ICU course to monitor for the development

of worsening IAH or ACS requiring intervention (Grade C recommendation).

IS THERE AN IAP THRESHOLD LEVEL THAT MANDATES INTERVENTION IN IAH/ACS?

As mentioned previously, IAP >20 mmHg in the presence of organ dysfunction defines ACS, a condition requiring acute intervention. Nevertheless, no threshold value for IAP exists that can be universally applied to all patients. An alternative parameter, abdominal perfusion pressure (APP), defined as the difference of mean arterial pressure and IAP, has been studied as a resuscitation endpoint. One retrospective trial identified an APP value of ≥ 50 mmHg as correlated with lower mortality in surgical and trauma patients (15). Several other studies in mixed populations of medical and surgical patients identified a critical APP value of ≥ 60 mmHg as imparting improved survival (16,17).

Recommendation: In patients being monitored for IAP, there appears to be benefit in keeping APP ≥ 50 –60 mmHg (Grade C recommendation). This can be accomplished by using some of the therapies listed in the next two sections.

ARE THERE ANY EFFECTIVE NONSURGICAL STRATEGIES FOR TREATING IAH/ACS?

The standard treatment for ACS remains decompressive laparotomy. Nevertheless, the use of screening IAP measurement inevitably leads to the identification of a population of patients with isolated IAH or with evolving ACS. Such patients may be candidates for nonsurgical interventions aimed at reducing IAP. Such interventions may theoretically prevent the development of ACS and its associated organ dysfunction while simultaneously sparing the patient the morbidity associated with an open abdomen. These interventions include sedation and/or analgesia, diuretics and/or hemofiltration/ultrafiltration, gastrointestinal decompression and/or prokinetic agents, neuromuscular blockade, supine positioning, limitation of fluid resuscitation, and catheter decompression.

Although sedation and analgesia might be expected to have favorable effects on IAH by decreasing abdominal muscle tone, no clinical data exist to support such intervention. Similarly, no clinical studies of active fluid withdrawal by either diuretic therapy or renal replacement therapies have been conducted. Thus, no medical evidence exists to support such potentially dangerous therapies in the treatment of IAH. Similarly, neither gastrointestinal decompression nor prokinetic drug therapy have been studied as treatments for IAH.

A small prospective trial using single-dose cisatracurium demonstrated the effectiveness of neuromuscular blockade in reducing IAP, but the effectiveness of therapy appeared to be diminished at higher levels of IAP (18). The adverse effects of paralytics (myopathy, neuropathy, prolonged mechanical ventilation) must be carefully weighed in to the decision to use these agents. Both prone positioning and elevation of the head of the bed have been shown to increase IAP. Both positioning maneuvers are becoming more common in the ICU. Head elevation is used to reduce aspiration risk, and prone positioning is used as an adjunct

to mechanical ventilation in the management of patients with adult respiratory distress syndrome (ARDS). Although supine positioning may minimize IAP, no evidence exists as to whether the IAP benefit is of sufficient magnitude to offset the greater risk of aspiration or to contraindicate prone positioning in the ARDS patient.

Fluid administration is a critical consideration in the management of IAH/ACS. Volume resuscitation is necessary to maintain adequate intravascular volume and support organ perfusion in the critically ill patient. However, excessive or "supranormal" fluid resuscitation is an independent risk factor for IAH and ACS and represents a frequent cause of secondary ACS (8,19,20). In one retrospective study, volume resuscitation to a supranormal level of oxygen delivery was found to be associated with a significantly increased incidence of IAH and ACS, as well as decreased survival (20). A single prospective, randomized controlled trial of fluid administration in IAH/ACS has also been performed. This study demonstrated higher IAP in burn patients receiving large volume crystalloid resuscitation as opposed to those receiving a lower volume, colloid-based resuscitation strategy (21). In another study, limitation of fluid administration accomplished by the use of a hypertonic resuscitation strategy has been associated with higher APP, lower IAP, and lower peak inspiratory pressures (22).

The use of catheter decompression to reduce IAP may be an effective alternative to decompressive laparotomy, especially when the elevation in IAP results from intraperitoneal fluid accumulations, such as hemoperitoneum, ascites, or abscess. Percutaneous decompression has been reported as a successful treatment for ACS in a number of retrospective case series (23–27). Furthermore, a small prospective study demonstrated its effectiveness in decreasing IAP in 33 of 35 patients with IAH secondary to malignant ovarian ascites (28). A second small prospective study demonstrated that percutaneous catheter drainage performed in conjunction with aggressive IAP/APP monitoring resulted in successful reduction of IAP and augmentation of APP in 8 of 12 trauma patients (29).

Recommendation: Decompressive laparotomy remains the standard treatment of ACS (Grade B recommendation). Neuromuscular blockade and supine positioning may be used as adjunctive measures in the treatment of IAH after careful consideration of the potential adverse consequences of such therapies (Grade C recommendation). In patients at risk for IAH or ACS, care must be taken to provide sufficient resuscitation to support adequate organ perfusion while avoiding overly zealous volume administration (Grade B recommendation). Colloids and hypertonic crystalloid administration may serve as alternatives to conventional isotonic crystalloid resuscitation to prevent IAH/ACS (Grade C recommendation). Percutaneous catheter decompression may be an option in cases of IAH/ACS due to intraperitoneal fluid collections (abscess, blood, ascites) (Grade C recommendation).

IS THERE A PREFERRED TECHNIQUE FOR TEMPORARY ABDOMINAL CLOSURE AFTER DECOMPRESSIVE LAPAROTOMY?

Once abdominal decompression is completed, the patient's abdomen must be left open to prevent recurrence of

IAH/ACS. Maintenance of the open abdomen requires some type of protective dressing to isolate the exposed abdominal contents from the external environment while accommodating further postoperative visceral expansion. Failure to provide for such expansion may lead to recurrence of IAH/ACS. A number of temporary abdominal closure techniques have been described. These include the towel clip skin closure, the vacuum-pack closure, the "Bogota bag," the Wittmann patch (Star Surgical, Burlington, WI), and the abdominal vacuum-assisted closure (30–34). All of these techniques have been validated clinically, but no data exist that would render any one technique superior to the others.

Recommendation: No technique for temporary abdominal closure is favored by the existing medical literature, and therefore no recommendation can be made.

IS THERE A PREDICTABLE TIMEFRAME OR PREFERRED TECHNIQUE FOR DEFINITIVE ABDOMINAL CLOSURE AFTER DECOMPRESSIVE LAPAROTOMY?

In general, primary fascial closure is possible within five to seven days if critical illness resolves and progressive organ failure does not occur. The development of cardiovascular, renal, and/or hepatic failure often leads to worsening of visceral edema. Such edema in concert with retraction of the fascia and loss of domain may render primary fascial closure impossible. When fascial closure is no longer possible, alternative long-term wound management strategies must be considered. These include split-thickness skin grafting of the exposed abdominal contents, closure of cutaneous advancement flaps over the viscera, fascial closure via component separation, and fascial replacement with one of the many types of commercially available biological mesh materials. Although each technique is well described in the literature, no comparative studies exist that would favor any one approach over the others. In practice, most surgeons use a variety of techniques depending on the specific situation.

Recommendation: No predictable timeframe or preferred technique for definitive abdominal closure is favored by the existing medical literature, and therefore no recommendation can be made.

IS THERE A ROLE FOR ABDOMINAL DECOMPRESSION IN THE MANAGEMENT OF INTRACRANIAL HYPERTENSION?

Increases in intrathoracic or intra-abdominal pressure are transmitted cephalad through the venous system resulting in increases in intracranial pressure (ICP) and decreases in cerebral perfusion pressure (35). This physiologic relationship forms the basis for the so-called multiple compartment syndrome and is the main justification for the use of decompressive laparotomy as a means for treating refractory intracranial hypertension (36). The first case of successful reduction in ICP accompanying abdominal decompression was reported by Bloomfield et al. (37). The trauma group at the University of Maryland has used decompressive laparotomy as a therapeutic modality for treating intractable intracranial hypertension since 2000. An early retrospective

analysis of their experience demonstrated a reduction in ICP in all 17 patients treated by decompressive laparotomy (38). In six of these patients, the decrease was only transient, and all six individuals subsequently expired. The remaining 11 patients all experienced sustained reductions in ICP, and all survived. A subsequent retrospective review by the same group demonstrated that both decompressive craniectomy and decompressive laparotomy effectively lower ICP and suggested that the two procedures could be performed in sequence (36). Despite the findings of these two studies, the role of decompressive laparotomy in the treatment of intracranial hypertension remains unclear. Further studies are needed to more clearly define the specific indications for its use in traumatic brain injury.

Recommendation: Decompressive laparotomy should be considered in patients with intracranial hypertension refractory to conventional medical and/or surgical therapy (Grade B recommendation).

REFERENCES

- Kron IL, Harman PK, Nolan SP. The measurement of intra-abdominal pressure as a criterion for abdominal re-exploration. *Ann Surg* 1984; 199: 28–30.
- Malbrain ML, Cheatham ML, Sugrue M, et al. Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. I. Definitions. *Intensive Care Med* 2006; 32: 1722–32.
- Cheatham MI, Malbrain ML, Kirkpatrick A, et al. Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. II. Recommendations. *Intensive Care Med* 2007; 33: 951–62.
- Meldrum DR, Moore FA, Moore EE, et al. Prospective characterization and selective management of the abdominal compartment syndrome. *Am J Surg* 1997; 174: 667–72.
- Ertel W, Oberholzer A, Platz A, et al. Incidence and clinical pattern of the abdominal compartment syndrome after “damage control” laparotomy in 311 patients with severe abdominal and/or pelvic trauma. *Crit Care Med* 2000; 28: 1747–53.
- Hong JJ, Cohn SM, Perez JM, et al. Prospective study of the incidence and outcome of intra-abdominal hypertension and the abdominal compartment syndrome. *Br J Surg* 2002; 89: 591–6.
- Malbrain ML, Chiumello D, Pelosi P, et al. Incidence and prognosis of intra-abdominal hypertension in a mixed population of critically ill patients: a multiple-center epidemiological study. *Crit Care Med* 2005; 33: 315–22.
- Balogh Z, McKinley BA, Holcomb JB, et al. Both primary and secondary abdominal compartment syndrome can be predicted early and are harbingers of multiple organ failure. *J Trauma* 2003; 54: 848–59.
- Kirkpatrick AW, Brenneman FD, McLean RF, et al. Is clinical examination an accurate indicator of raised intra-abdominal pressure in critically injured patients? *Can J Surg* 2000; 43: 207–11.
- Sugrue M, Bauman A, Jones F, et al. Clinical examination is an inaccurate predictor of intraabdominal pressure. *World J Surg* 2002; 26: 1428–31.
- Cheatham ML, Safcsak K. Intraabdominal pressure: a revised method for measurement. *J Am Coll Surg* 1998; 186: 594–5.
- Gudmundsson FF, Viste A, Gislason H, et al. Comparison of different methods for measuring intra-abdominal pressure. *Intensive Care Med* 2002; 28: 509–14.
- Malbrain ML. Different techniques to measure intra-abdominal pressure (IAP): time for a critical re-appraisal. *Intensive Care Med* 2004; 30: 357–71.
- Zengerink I, McBeth PB, Zygun DA, et al. Validation and experience with a simple continuous intra-abdominal pressure measurement technique in a multidisciplinary medical/surgical critical care unit. *J Trauma* 2008; 64: 1159–64.
- Cheatham ML, White MW, Sagraves SG, et al. Abdominal perfusion pressure: a superior parameter in the assessment of intra-abdominal hypertension. *J Trauma* 2000; 49: 621–6.
- Malbrain ML. Abdominal perfusion pressure as a prognostic marker in intra-abdominal hypertension. In: Vincent JL, ed., *Yearbook of Intensive Care and Emergency Medicine*. New York: Springer, 2002: 792–814.
- Cheatham ML, Malbrain ML. Abdominal perfusion pressure. In: Ivatury RR, Cheatham ML, Malbrain ML, et al., eds., *Abdominal Compartment Syndrome*. Georgetown: Landes Biomedical, 2006: 69–81.
- De Waele J, Delaet I, Hoste E, et al. The effect of neuromuscular blockers on intraabdominal pressure. *Crit Care Med* 2006; 34: A70.
- Balogh Z, McKinley BA, Cocanour CS, et al. Secondary abdominal compartment syndrome is an elusive early complication of traumatic shock resuscitation. *Am J Surg* 2002; 184: 538–43.
- Balogh Z, McKinley BA, Cocanour CS, et al. Supranormal trauma resuscitation causes more cases of abdominal compartment syndrome. *Arch Surg* 2003; 138: 637–42.
- O’Mara MS, Slater H, Goldfarb IW, et al. A prospective, randomized evaluation of intra-abdominal pressures with crystalloid and colloid resuscitation in burn patients. *J Trauma* 2005; 58: 1011–18.
- Oda J, Ueyama M, Yamashita K, et al. Hypertonic lactated saline resuscitation reduces the risk of abdominal compartment syndrome in severely burned patients. *J Trauma* 2006; 60: 64–71.
- Corcos AC, Sherman HF. Percutaneous treatment of secondary abdominal compartment syndrome. *J Trauma* 2001; 51: 1062–4.
- Sharpe RP, Pryor JP, Ghandi RR, et al. Abdominal compartment syndrome in the pediatric blunt trauma patient treated with paracentesis: report of two cases. *J Trauma* 2002; 53: 380–2.
- Latenser BA, Kowal-Vern A, Kimball D, et al. A pilot study comparing percutaneous decompression with decompressive laparotomy for acute abdominal compartment syndrome in thermal injury. *J Burn Care Rehab* 2002; 23: 190–5.
- Reckard JM, Chung MH, Varma MK, et al. Management of intraabdominal hypertension by percutaneous catheter drainage. *J Vasc Interv Radiol* 2005; 16: 1019–21.
- Parra MW, Al-Khayat H, Smith HG, et al. Paracentesis for resuscitation-induced abdominal compartment syndrome: an alternative to decompressive laparotomy in the burn patient. *J Trauma* 2006; 60: 1119–21.
- Gotlieb WH, Feldman B, Feldman-Moran O, et al. Intra-peritoneal pressures and clinical parameters of total paracentesis for palliation of symptomatic ascites in ovarian cancer. *Gynecol Oncol* 1998; 71: 381–5.
- Reed SF, Britt RC, Collins J, et al. Aggressive surveillance and early catheter-directed therapy in the management of intra-abdominal hypertension. *J Trauma* 2006; 61: 1359–65.
- Wittmann DH, Aprahamian C, Bergstein JM, et al. A burr-like device to facilitate temporary abdominal closure in planned multiple laparotomies. *Eur J Surg* 1993; 159: 75–9.
- Brock WB, Barker DE, Burns RP. Temporary closure of open abdominal wounds: the vacuum pack. *Am Surg* 1995; 61: 30–5.
- Barker DE, Kaufman HJ, Smith LA, et al. Vacuum pack technique of temporary abdominal closure: a 7 year experience with 112 patients. *J Trauma* 2000; 48: 201–6.

33. Barker DE, Green JM, Maxwell RA, et al. Experience with vacuum-pack temporary abdominal wound closure in 258 trauma and general and vascular surgical patients. *J Am Coll Surg* 2007; 204: 784–93.
34. Perez D, Wildi S, Demartines N, et al. Prospective evaluation of vacuum-assisted closure in abdominal compartment syndrome and severe abdominal sepsis. *J Am Coll Surg* 2007; 205: 586–92.
35. Bloomfield GL, Ridings PC, Blocher CR, et al. A proposed relationship between increased intra-abdominal, intrathoracic, and intracranial pressure. *Crit Care Med* 1997; 25: 496–503.
36. Scalea TM, Bochicchio GV, Habashi N, et al. Increased intra-abdominal, intrathoracic, and intracranial pressure after severe brain injury: multiple compartment syndrome. *J Trauma* 2007; 62: 647–56.
37. Bloomfield GL, Dalton JM, Sugerman HJ, et al. Treatment of increasing intracranial pressure secondary to the acute abdominal compartment syndrome in a patient with combined abdominal and head trauma. *J Trauma* 1995; 39: 1168–70.
38. Joseph DK, Dutton RP, Aarabi B, et al. Decompressive laparotomy to treat intractable intracranial hypertension after traumatic brain injury. *J Trauma* 2004; 57: 687–95.

Agitation and Delirium in the ICU

Robert Chen

Question Summary		
Question	Answer	Grade
How can sedation needs be assessed?	Sedation requirements should be reexamined frequently using a sedation scale.	A
How should sedation in the ICU be managed?	The use of a sedation protocol or daily interruption of sedation should be considered.	A
What is the evidence for short-acting and non-GABA drugs for ICU sedation?	Propofol and dexmedetomidine should be reserved for ICU sedation where the duration is thought to be no more than 24–48 hours, propofol should be given at an infusion rate of no more than 4–5 mg/kg/hour.	C
What is the impact of delirium in ICU?	Delirium is common. It increases length and cost of stay and may lead to long-term cognitive dysfunction.	
How is delirium identified?	The rate of delirium is high and underdiagnosed. Screen for delirium with a standardized exam or scale.	A
How should delirium be treated?	Treat delirium with environmental changes (risk factor reduction or elimination), then haloperidol.	A
What is the impact of alcohol and trauma?	There is an association with alcohol and trauma. All trauma admissions should be screened for alcohol and alcoholism. If alcoholism is identified, brief intervention is warranted.	A
Should benzodiazepines be given as prophylaxis for alcohol withdrawal?	No! Alcohol withdrawal should be treated with benzodiazepines in a symptom-driven approach.	A
Is processed EEG an equivalent to the qualitative clinical assessment of sedation?	Processed EEG is not ready for sedation assessment.	D
Abbreviations: EEG, electroencephalogram; GABA, gamma-aminobutyric acid; ICU, intensive care unit.		

The intensive care unit (ICU) is a stressful environment for those who care for patients. Similar to the emergency room, it functions 24 hours a day. For the patients, the days and nights are filled with bright illumination, noises of medical devices and alarms, and pain. Like commercial casinos, the ICU robs those within of time cues: there seem to be no chronologic landmarks of sleeping or eating. Activity seems continuous; the stimulation from sound, sight, and touch never stops, nor does it seem predictable. ICUs caring for trauma patients are additionally challenging in that admissions may be polarized toward evenings and weekends, further disrupting a patient's usual daily rhythm. Surgical ICU patients may have pain from surgical disease preoperatively. Trauma patients suffer pain associated with injury. Postoperatively, the patient will have incisional pain and perhaps new pain from reperfusion, drains, or other implanted equipment. Patients may have been taking drugs, recreational or prescribed, prior to admission. Withdrawal from any of those medications can lead to mental and physical stress. Necessary medications may have important central nervous system (CNS) side effects, such as the sedation of seizure prophylaxis or the dysphoria

of systemic steroids. Paralytic medications (1) or medical conditions can rob the patient's ability to communicate and advocate. The patient may also manifest expected CNS changes associated with brain injury or disease. Awake and alert patients have often expressed fear, panic, and helplessness in such a surreal environment (2). Patients have described confusional states, delusions, and hallucinations (3).

Clinically, these stressors can lead to the subjective diagnosis of agitation or unpleasant psychomotor arousal. Agitation and delirium in the ICU are part of the same spectrum that was called ICU-itis, ICU syndrome, or ICU psychosis in the past. This chapter offers an evidence-based approach to agitation and delirium in the ICU.

Clearly, the intensivist must provide comfort to patients in the ICU. Drug therapy is almost universally given. The Society of Critical Care Medicine (SCCM) published guidelines for analgesia, sedation, and treatment of delirium in 2002 (4). In summary, they recommended that sedation be offered after appropriate analgesia. A sedation scale should be used and sedation goals reevaluated regularly. Delirium was to be screened for regularly and treated

with haloperidol. Sleep promotion was felt to be helpful in preventing or treating delirium. In a survey of Canadian intensivists conducted months after the publication of these guidelines, a huge variety in the prescribing practices was seen (5). Half of the respondents did not use a sedation scale, and over 95% did not use formalized delirium screening tools. This result is similar to another survey that described the sizable disconnect between knowledge and practice (6) with only 16% of respondents using a delirium assessment tool. These results would be analogous to drug therapy for hypertension titrated against myocardial infarction or stroke rather than blood pressure measurements.

Analgesia must be the first priority in the surgical ICU. Poor pain control unleashes a neuron-hormonal cascade that can lead to cardiovascular complications, such as dysrhythmias, congestive heart failure, myocardial ischemia, and infarction. A patient's unwillingness to participate in physiotherapy and deep breathing exercises secondary to pain can cause respiratory complications. Unfortunately, it is not uncommon for postoperative ICU patients to be receiving sedative agents alone without accompanying analgesia. With the notable exceptions of some anticonvulsants [gabapentin, pregabalin (7–9)] and central acting alpha 2 agonists (clonidine and dexmedetomidine) (10,11), no other sedating medications have analgesia effects. Avoiding opiates has been proposed as a strategy to reduce delirium, particularly in the elderly. Local or regional anesthetic techniques have in some series reduced postoperative and ICU delirium (12,13). Recent reviews of the literature, however, have demonstrated less favorable conclusions (14,15). Given its lengthy history and wealth of experience, opiates are still the mainstay of an analgesic regime for surgical or trauma pain.

HOW CAN SEDATION NEEDS BE ASSESSED?

Oversedation leads to longer intervals on mechanical ventilation and its expected complications such as ventilation-associated pneumonia (VAP), increased length of stay (LOS) in the ICU, as well as those associated financial costs. Two relatively separate bodies of literature have examined daily interruption of sedation (sedation vacation or drug holiday) and protocol-driven sedation using sedation scales.

Critical care resuscitation is guided by measurable values in almost every domain: cerebral perfusion pressure, alveolar-arterial gradient, cardiac index, serum lactate, blood urea nitrogen, and so on. The clinical evidence continues to suggest that most patients are treated for agitation with medication using informal criteria.

De Jonghe et al. in 2000 published a comprehensive review of sedation scales in the ICU (16). The exhaustive literature search revealed 25 different methods starting with Ramsey in 1974. Ramsey's study was a prospective observational study using alphadolone infusions to achieve sedation in the ICU (17). The outcome was measured by a 6-point scale created empirically where 1 represented agitation and 6 oversedation. The scale has since been validated for reliability and validity. Only three other scales met criteria for reliability and validity: the Comfort scale (18), Sedation Agitation Scale (SAS) (19), and Motor

Activity Assessment Scale (MAAS) (20). The Comfort scale was a multidimensional examination in the pediatric ICU setting that naturally did not include the ability to obey commands. The SAS, in some ways like the Ramsey, began empirically to study haloperidol infusions in critical care. The MAAS was designed and validated in a surgical ICU setting. A rapid-to-administer 7-point scale (0–6) included elements of patient safety, when agitated.

Since De Jonghe and colleagues' review, several more scales have been published meeting criteria for reliability and validity, including the Richmond Agitation Sedation Scale (RASS) (21) and De Jonghe's own group's Adaptation to the Intensive Care Environment (ATICE) (22). ATICE is a multidimensional scale that assesses the domains of consciousness and tolerance to the ICU environment with subscales within each domain. The awakeness and calmness scales (two of five in the ATICE) are represented in Table 84.1 as a single dimension for ease of comparison to the previously described sedation scores. The table demonstrates that any of the aforementioned scales could be easily used to evaluate the clinical spectrum of sedation requirement. Ramsey's scale is polarized toward the description of sedation, while more recent scales have further subdivided ranges of agitation.

Answer: Sedation requirements should be reexamined frequently using a sedation scale. Grade A, Level of evidence Ib.

HOW SHOULD SEDATION IN THE ICU BE MANAGED?

Jean-Louis Vincent published his famous FASTHUG paper in 2005. His synthesis of ICU care called for an assessment of feeding, analgesia, sedation, thrombosis prophylaxis, elevation of the head of the bed, upper gastrointestinal bleeding prophylaxis, and glycemic control. He wondered in terms of analgesia and sedation assessment whether the assessment scales were "so simple that one may wonder if they are necessary" (23). Dr. Papadimos's group applied the FASTHUG idea, which included a twice daily assessment of sedation in a surgical ICU. They were able to halve the rate of ventilator associated pneumonia against historical controls (24). These results were particularly significant as the severity of illness index that was calculated was higher in the intervention group. It is interesting to note that despite a higher index of severity of illness, there was a trend toward a shorter length of stay for those patients who were FASTHUGed.

By instituting a sedation guideline, Adam et al. in a mixed medical and surgical ICU were able to halve the cost of their sedative medications versus historical controls. Unfortunately, LOS calculations were only done on half of the sample due to a change in patient bed utilization for cardiac surgery patients before and after the guideline implementation. Interestingly, the LOS was similar before and after the guideline implementation (25). In using their own ATICE scale as part of a sedative algorithm in a prospective cohort trial, De Jonghe's group was able to demonstrate faster arousal from sedation and thus shorter ventilated times in a medical ICU. Statistically, the reduction was in the order of five days (26). Marshall's institution in Boston instituted a sedation guideline that followed those published by the SCCM (27). An audit the following

Table 84.1 Comparison of Sedation Scales

Ramsay:	6 No response to noise or glabellar tap	4 Brisk response to noise or glabellar tap	3 Responds to oral commands only	2 Cooperative, oriented, tranquil				1 Anxious, agitated, restless		
		5 Sluggish response to noise or glabellar tap								
SAS:	1 Unarousable	2 Very Sedated, arouses but does not communicate or follow commands	3 Sedated, awakens to verbal stimuli or gentle shaking	4 Calm and Cooperative				5 Agitated, anxious or physically agitated, calms to verbal instructions	6 Very Agitated, requiring restraint, verbal reminding, biting ETT	7 Dangerous agitation, Pulling at ET tube, catheters, climbing, striking
Motor activity assessment scale (MAAS)	0 Unresponsive	1 Responsive only to noxious stimuli (opens eyes, raises eyebrows or turns head)	2 Responsive to name or touch	3 Calm, cooperative	4 Restless, cooperative (picking at sheets, tubes)	5 Agitated (does not consistently follow commands)			6 Dangerously agitated	
Richmond agitation sedation scale	−5 Unarousable	−4 No response to voice, responds to physical stimuli	−3 Moderate sedation −2 Awakens to voice for less than 10s −1 Awakens to voice for more than 10s	0 Alert, calm	+1 Anxious	+2 Frequent non-purposeful movements, ventilator dyssynchrony		+3 Pulls or removes tubes	+4 Combative, dangerous	
Adaptation to intensive care environment	0 No eye opening	1 Facial movement to strong stimuli	3 Eyes open to light stimuli	1 Eyes open spontaneously		2 Agitated but responds to verbal order		1 Agitated, does not respond to verbal order		0 Life threatening agitation
Awake 0–5 Calm 0–3		2 Eyes open to strong stimuli	4 Eyes open to voice	3 Calm						

Table 84.2 Partial List of Risk Factors for Delirium**Predisposing Patient factors:**

Advanced age
 Dementia
 CNS and psychiatric disease
 Medical comorbidities: renal, hepatic, etc diseases
 Drug or alcohol dependence
 Vision or hearing impairment

Medical factors:

Trauma
 Severe illness
 Sleep deprivation
 Polypharmacy
 Psychotropic Rx (including opiates)

year demonstrated surprisingly poor compliance. By charging a clinical pharmacist with the daily role of ensuring adherence to the already established protocol, the ventilated days and ICU LOS were almost halved. Despite Dr. Vincent's lack of enthusiasm for sedation scales, even if only included in a protocol, studies would suggest that they are very necessary if for nothing else than to ensure proper assessment of the patient.

Kress et al.'s paper in 2000 was very important in introducing the concept of a daily sedation interruption (28). In a prospective, randomized fashion, patients admitted to a medical ICU were chosen to have infusions of midazolam or propofol interrupted daily or receive routine care. Clearly, blinding would be challenging. Both groups

received morphine analgesia. The duration of mechanical ventilation and LOS in the ICU was a third lower in the intervention group. Two groups have since demonstrated a 50% reduction in VAP when they reinterpreted FASTHUG to include daily sedation interruption (29,30). Although by definition the measured reductions are from multifactorial manipulation, it is plausible that daily interruption of sedation was important.

A very recent study by de Wit and colleagues randomized patients in a closed ICU to receive sedation (and analgesia) driven by protocol or receive daily sedation interruption where the sedation regime was chosen ad hoc by the ICU team. Powered to detect a difference in time to extubation, 268 patients were to be enrolled. The study was stopped by the Data Safety Monitoring Board due to a higher rate of deaths in the daily interruption group. Nevertheless, the duration of mechanical ventilation in the groups differed significantly (6.7 days in the daily interruption versus 3.9 days in the sedation protocol) (31). There are many variables to examine in sedation research. Clearly, following a protocol with a defined sedative goal will prevent oversedation. Whether stopping appropriate sedation can confer additional benefit to the patient is clearly still in question.

Answer: The use of a sedation protocol or daily interruption of sedation should be considered. Grade A, Level of evidence Ib.

WHAT IS THE EVIDENCE FOR SHORT-ACTING AND NON-GABA DRUGS FOR ICU SEDATION?

Propofol, the polysubstituted benzene IV anesthetic was first introduced as an anesthetic induction agent in the early 1980s (32–34). Its pharmacologic properties of relatively quick redistribution and metabolism made it an ideal agent titrating intravenous sedation in the critical care setting. Studies comparing propofol to other medications consistently show the superiority of propofol in ICU for its titratability (35,36). Unfortunately, the “propofol infusion syndrome” first reported in the pediatric literature (37) followed by reports in the adult population make it unsuitable for prolonged use. Patients who had prolonged high-dose sedation succumbed to hemodynamic failure with progressive acidosis, rhabdomyolysis, hyperlipidemia, and liver changes on various imaging modalities. The syndrome and its possible pathophysiology has been well reviewed in the anesthetic and critical care literature (38–40). The American College of Critical Care Medicine in their 2002 clinical practice guidelines (4) advocates caution in the use of propofol particularly in the setting of raised intracranial pressure. In addition, as a Class B recommendation, the guidelines suggest lipid monitoring and inclusion of propofol’s lipid carrier as parenteral nutrition content. As the body of case literature has increased, North American health care agencies have issued warnings against prolonged infusion. A North American manufacturer has contraindicated propofol as an ICU sedative in patients under 18 years of age (41).

As alluded to previously, dexmedetomidine has several advantages as an ICU sedative. As opposed to the gamma-aminobutyric acid (GABA) agonists (benzodiazepines, barbiturates, propofol) it is a centrally acting alpha

2 agonist. It is analgesic at the spinal level while simultaneously providing sedation through central down-regulation of norepinephrine release (42). Given its utility as a coanalgesic, it has been studied more often in the postoperative setting (43,44). In the ICU, its sedative quality is reputed at least as good as propofol yet allows for a qualitative ease in arousal (45). Due to its relatively recent introduction and limited long-term experience, its indication is for sedation duration of less than 24 hours. There are however, studies in the ICU setting where infusions up to a week’s duration have not demonstrated negative effects (46,47).

Answer: Propofol and dexmedetomidine should be reserved for ICU sedation where the duration is thought to be no more than 24–48 hours, propofol should be given at an infusion rate of no more than 4–5 mg/kg/hour. Grade C, Level of evidence IV.

WHAT IS THE IMPACT OF DELIRIUM IN ICU?

The incidence of delirium in the general hospital population is reported to be from 1 in 10 patients to more than 50% in the elderly population. Delirium in critical care units has been suggested in up to 80% of patients (48). The true incidence in the ICU is impossible to quantify as patients receiving necessary sedation makes the assessment difficult. Although there are postulated biologic mechanisms, there is no consensus for a final common pathway. Like acute respiratory distress syndrome, the risk factors are numerous and common to almost all patients in the ICU (49). Because delirium can appear as agitation from insufficient sedation, the intensivist must be aware that prescribed benzodiazepines may be causal, particularly in the elderly (50). Similar to the complications associated with postoperative pain, delirium can increase the patient’s metabolic demands, leading to cardiac decompensation, particularly in patients with cardiac disease and limited physiologic reserve. Failure to participate in respiratory physiotherapy due to delirium could lead to pulmonary complications, such as atelectasis, failure of secretion clearance, and subsequent infection. Delirium has been shown to be an independent risk factor for prolonged ICU stay (51). The diagnosis increased ICU and hospital costs by 39% and 31%, respectively, in one prospective study (48). The effects of delirium in the ICU may persist well after discharge as a risk factor for longer term cognitive dysfunction (52). Because the syndrome is believed to be preventable by some authors, it has been used as a quality of care marker (53). In terms of costs, Inouye estimates that as a potentially preventable adverse event, delirium costs \$4–7 billion to the American health care system (54). Assessing and treating delirium is now slowly being recognized as an important part of ICU care.

Answer: Delirium is common. It increases LOS and cost of stay and may lead to long-term cognitive dysfunction.

HOW IS DELIRIUM IDENTIFIED?

The *Diagnostic and Statistical Manual* (4th edition text revision; DSM-IV TR) defines delirium as being characterized “by a disturbance of consciousness and a change in

cognition that develop over a short period of time" (55). Delirium is differentiated from other steadily dementing illness by its acute onset. As with all psychiatric disease, the diagnosis of delirium is based on clinical criteria. The American Psychiatric Association issues a cautionary statement: "The proper use of these criteria requires specialized clinical training that provides both a body of knowledge and clinical skills."

Using a psychiatrist and a geriatrician following the DSM-IV-TR definition of delirium, Ely et al. were able to demonstrate that nurses and physicians were able to use a screening test with high sensitivity and specificity in the ICU (56). The Confusion Assessment Method (CAM) test was developed and tested in nonintubated patients previously. Four features of delirium were examined: acute onset, inattention, disorganized thinking, and altered level of consciousness. The inattention test, the Attention Screening Examinations, was modified to allow nonverbal answers. Patients nodded or squeezed the examiners hands to answer questions. In 1996, nursing research led to the creation and validation of the NEECHAM confusion scale (57). Without formally addressing acuity, the NEECHAM index also examined inattention, level of consciousness, and disorganization but included a subjective examination of the patient's motoric behavior. Vital signs including oxygen saturation and urinary continence along with vital sign stability were also included in the NEECHAM scale. The NEECHAM scale returns a range of possibilities including normal, at risk, early, or mild delirium and moderate to severe delirium.

When compared side by side (58) in nonintubated patients, the two screening tools resulted in identical abilities to identify a severely delirious patient. As expected there were no mild or at risk patients identified by the CAM ICU. The CAM ICU rating has been shown to be reliable in trauma patients in a study that documented the implementation and subsequent compliance with the scale (59). The postimplementation follow-up was particularly telling. Almost half of the nurses felt the scale did not enhance patient care because the physicians did not modify treatment based on the results!

Answer: The rate of delirium is high and underdiagnosed. Screen for delirium with a standardized exam or scale. Grade A, Level of evidence Ib.

HOW SHOULD DELIRIUM BE TREATED?

Treatment of delirium is based initially at reducing or modifying any of the existing risk factors. The American Psychological Association in their guidelines in 1999 (60) and updated in 2004 (61) describe addressing the somatic risk factors: orienting the patients after providing hearing and visual aids and reestablishing a normal sleep/wake cycle. Inouye had studied prospectively in a nonrandomized fashion the usual care of geriatric patients and care in a specialized unit where particular efforts were made to reorient patients, reduce visual and hearing impairment, reestablish a normal sleep/wake cycle, and aggressively treat dehydration (62). The intervention patients had a relative reduction of approximately 30% of the development of delirium, the number of days with delirium, and the total number of episodes. The guidelines suggest that if

delirium cannot be treated nonpharmacologically, then haloperidol is indicated. One retrospective chart analysis found the administration of haloperidol in critical care patients to be associated with reduced mortality (63). A postulated mechanism was the early treatment of delirium reduced the associated morbidity and mortality. In a prospective, randomized, and blinded study, Kalisvaart's group gave hip surgery patients low-dose haloperidol or placebo (64). Although no change in the incidence of delirium was observed, the duration of delirium was halved, possibly contributing to significant reduction in LOS.

WHAT IS THE IMPACT OF ALCOHOL AND TRAUMA?

In their 2007 report, the World Health Organization suggested that just under half of adults globally used alcohol. This amounts to approximately 2 billion adults worldwide. In addition, since in many developing and developed countries alcohol is produced by individuals on a "home or craft" basis, the foregoing statistic may be an important underestimate (65). The same report recommends a strategy of early intervention and treatment. A patient's decompensation secondary to alcohol withdrawal may be the first presentation of alcohol-related disease and thus an opportunity for the intensivist as a public health advocate.

Studies have shown alcohol to be an important factor in motor vehicle accidents and in nearly half of blunt head and spine injuries (66,67) and more than half of trauma patients (68). Alcohol in the trauma patient is associated with delirium and longer ICU and hospital stays (68). High consumption of alcohol in surgical patients is associated with higher rates of ICU admission as well as mortality (69).

In 2006 the American College of Surgery's Committee on Trauma suggested that all trauma centers screen for alcohol use and alcoholism through questionnaires or toxicological testing. In addition, Level I trauma hospitals are to offer brief intervention and treatment (76). These interventions can be as simple as a "motivational interview" on discharge, identifying the patient's alcohol consumption compared to norms as well as alcohol as a risk factor for trauma. Access to follow-up alcohol abuse counseling is offered. There is evidence that these interventions are cost-effective (77) and reduce alcohol use through follow-up surveys as well as trauma recidivism (78,79).

Answer: There is an association with alcohol and trauma. All trauma admissions should be screened for alcohol and alcoholism. Grade A, Level of evidence Ib. If alcoholism is identified, brief intervention is warranted. Grade A, Level of evidence Ib.

SHOULD BENZODIAZEPINES BE GIVEN AS PROPHYLAXIS FOR ALCOHOL WITHDRAWAL?

Benzodiazepines have been the standard of care for alcohol withdrawal. Kahan et al.'s retrospective chart review, comparing benzodiazepine use in the emergency room in two Canadian urban hospitals for alcohol withdrawal patients, noted that one hospital administered a three times higher dose of benzodiazepines. Patients who received the higher doses had significantly lower number of seizures without a statistically significantly longer LOS (70). A more formal

though still retrospective study by Gold et al. examined the total drug doses and effects before and after the implementation of guidelines for escalating doses of benzodiazepines (71). Despite having received twice the amount of benzodiazepines than historical controls, patients treated with the new protocol were less likely to be intubated and thus less likely to suffer the complications of intubation and ventilation. Stated differently, individualized symptom based management using more benzodiazepines is more effective than the common practice of pretreating withdrawal without a firm diagnosis. Prospective randomized control trials have supported the same conclusions (72,73). The most commonly studied tool for the diagnosis and monitoring of withdrawal is the well-validated Clinical Institute Withdrawal Assessment for Alcohol (revised) or CIWA-Ar (74). It is a multidimensional scale that rates 10 objective and subjective symptoms of withdrawal. With a total possible score of 67, many centers continue to dose benzodiazepines hourly until the score falls under 10–15 for patients at risk of withdrawal seizures.

When the topic was reviewed by the Cochrane group, benzodiazepines, not surprisingly, were found to be superior to placebo. Using the narrow assessment of seizure control in withdrawal benzodiazepines were not necessarily superior to other treatments, such as anticonvulsants (75). However, because benzodiazepines provide more than seizure control, they are more effective than anticonvulsants in treating alcohol withdrawal.

Answer: There is no evidence for the prophylactic treatment of alcohol withdrawal. Alcohol withdrawal should be treated with benzodiazepines in a symptom-driven approach. Grade A, Level of evidence IIb.

Answer: Treat delirium with environmental changes (risk factor reduction or elimination) then haloperidol. Grade A, Level of evidence Ib.

IS PROCESSED EEG AN EQUIVALENT TO THE QUALITATIVE CLINICAL ASSESSMENT OF SEDATION?

Researchers, particularly in anesthesia, have attempted to use the electroencephalogram (EEG) as a monitor of drug-induced sedation (80). A very large amount of information is returned from formal EEG studies. The waveform interpretations at the bedside are complex and time-consuming. The bispectral index (BIS) presents EEG signals from a single pair of electrodes on the forehead. Using a proprietary Fourier-type analysis of the waveform (much like spectral edge technology that preceded it) (81), a highly processed value is returned to the clinician. The BIS scale ranges from 0 to 100, where 0 is coma and 100 is awake (82). There is substantial discussion in the anesthesia literature linking monitoring of intraoperative sedation and patient safety.

The Cochrane anesthesia database suggests a BIS level of 40–60 should be maintained in the setting of surgical anesthesia (83). This author's enthusiasm, however, is tempered by a study in fully conscious volunteers who were pharmacologically paralyzed. Simultaneous monitoring with BIS suggested that the patients were actually under deep general anesthesia (84). A small inpatient study of bilateral BIS monitoring revealed a regression coefficient of only 0.65. During 10% of anesthetic time, the

device suggested different anesthetic depths bilaterally (85). An anesthetic study enrolling 2,000 patients prospectively randomized patients to receive BIS-guided anesthetic care or standard care. Although well powered to detect a difference in anesthesia awareness, no differences were found between groups (86).

Some authors have applied the same technology in the ICU because many of those patients essentially receive IV general anesthesia. BIS was seen to correlate to RASS and SAS scores in brain-injured patients (87). However, traumatic brain injury, metabolic brain injury, and seizures all have EEG sequelae, a theoretical problem in sedation titrated by processed EEG. As evidence, study of BIS as an outcome measure for brain injury demonstrated that its value predicts recovery (88). Another study in mild to moderate brain injury demonstrated a correlation between the Glasgow Coma Score and BIS (89). Particularly in the trauma population where head injury is not uncommon, the additional value of BIS as a sedative guide is then suspect.

Answer: Processed EEG is not ready for sedation assessment. Grade D, Level of Evidence Ib.

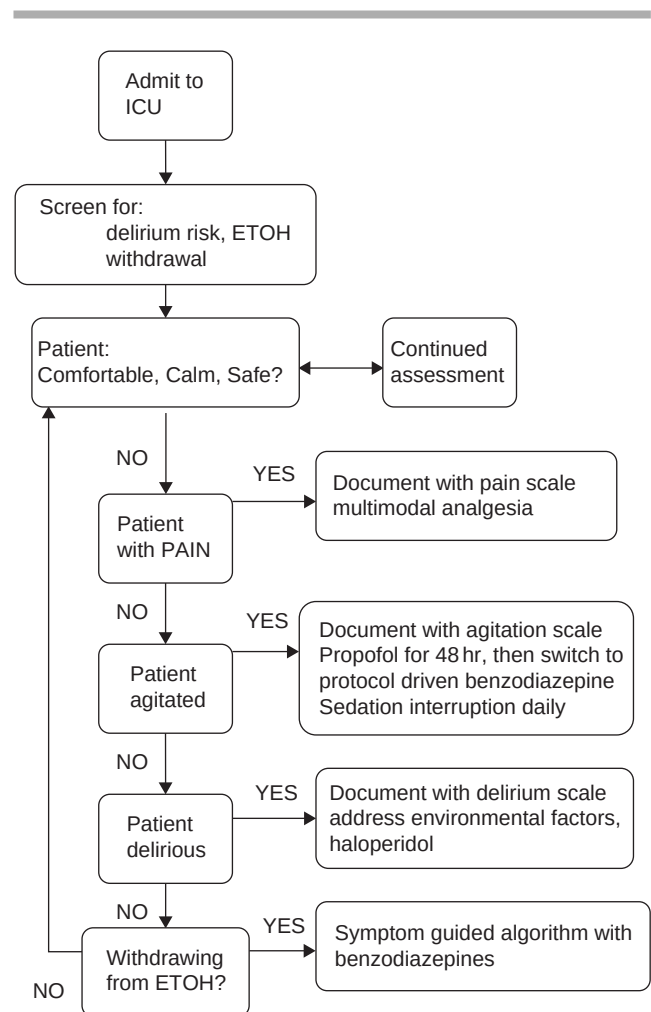


Figure 84.1

CONCLUSION

The appropriate treatment of agitation and delirium in the ICU decrease ICU-related complications. Many still sedate patients using informal measures, which may lead to over-sedation. Many more ignore delirium as a preventable illness. Admission to the ICU following trauma may be the

first opportunity to diagnose alcoholism. In the same way that resuscitation of sepsis, myocardial infarction, and stroke have benefited from evidence-based protocol, sedation in the ICU should follow the same model. One may consider a recursive loop as a model for treating the psychiatric and (Fig. 84.1) CNS ramifications of critical care.

Evidence Summary

Question	Answer	Level of evidence	Grade	Refs.
How can sedation needs be assessed?	Sedation requirements should be reexamined frequently using a sedation scale.	Ib	A	16, 21, 22
How should sedation in the ICU be managed?	The use of a sedation protocol or daily interruption of sedation should be considered.	Ib	A	26, 27, 28, 31
What is the evidence for short-acting and non-GABA drugs for ICU sedation?	Propofol and dexmedetomidine should be reserved for ICU sedation where the duration is thought to be no more than 24–48 hours, propofol should be given at an infusion rate of no more than 4–5 mg/kg/hour.	IV	C	4, 38, 46, 47
What is the impact of delirium in ICU?	Delirium is common. It increases length of stay and may lead to long-term cognitive dysfunction.			48, 51
How is delirium identified?	The rate of delirium is high and underdiagnosed. Screen for delirium with a standardized exam or scale.	Ib	A	57, 58
How should delirium be treated?	Treat delirium with environmental changes (risk factor reduction or elimination), then haloperidol.	Ib	A	62, 63, 64
What is the impact of alcohol and trauma?	There is an association with alcohol and trauma. All trauma admissions should be screened for alcohol and alcoholism. If alcoholism is identified, brief intervention is warranted.	Ib	A	68, 77, 78
Should benzodiazepines be given as prophylaxis for alcohol withdrawal?	No! Alcohol withdrawal should be treated with benzodiazepines in a symptom-driven approach.	IIb	A	72, 73
Is processed EEG an equivalent to the qualitative clinical assessment of sedation?	Processed EEG is not ready for sedation assessment.	Ib	D	84, 87, 88

Abbreviations: EEG, electroencephalogram; GABA, gamma-aminobutyric acid; ICU, intensive care unit.

REFERENCES

- Ballard N, Robley L, Barrett D, et al. Patients' recollections of therapeutic paralysis in the intensive care unit. *Am J Crit Care* 2006n; 15: 86–94.
- Magarey JM, McCutcheon HH. "Fishing with the dead"—recall of memories from the ICU. *Intensive Crit Care Nurs* 2005; 21: 344–54.
- Granberg A, Engberg IB, Lundberg D. Acute confusion and unreal experiences in intensive care patients in relation to the ICU syndrome. Part II. *Intensive Crit Care Nurs* 1999; 15: 19–33.
- Jacobi J, Fraser GL, Coursin DB, et al; Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists (ASHP), American College of Chest Physicians. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med* 2002; 30: 119–41; erratum: *Crit Care Med* 2002; 30: 726.
- Mehta S, Burry L, Fischer S, et al; Canadian Critical Care Trials Group. Canadian survey of the use of sedatives, analgesics, and neuromuscular blocking agents in critically ill patients. *Crit Care Med* 2006; 34: 374–80.
- Ely EW, Stephens RK, Jackson JC, et al. Current opinions regarding the importance, diagnosis, and management of delirium in the intensive care unit: a survey of 912 healthcare professionals. *Crit Care Med* 2004; 32: 106–12.
- Gilron I. Gabapentin and pregabalin for chronic neuropathic and early postsurgical pain: current evidence and future directions. *Curr Opin Anaesthesiol* 2007; 20: 456–72.
- Tiippana EM, Hamunen K, Kontinen VK, et al. Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. *Anesth Analg* 2007; 104: 1545–56.
- Peng PW, Wijesundera DN, Li CC. Use of gabapentin for perioperative pain control—a meta-analysis. *Pain Res Manag* 2007; 12: 85–92.
- Smith H, Elliott J. Alpha(2) receptors and agonists in pain management. *Curr Opin Anaesthesiol* 2001; 14: 513–18.
- Martin E, Ramsay G, Mantz J, et al. The role of the alpha2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. *J Intensive Care Med* 2003; 18: 29–41.
- Bracco D, Noiseux N, Dubois MJ, et al; PeriCARG Group, Montréal. Epidural anesthesia improves outcome and resource use in cardiac surgery: a single-center study of a 1293-patient cohort. *Heart Surg Forum* 2007; 10: E449–E458.
- Papaioannou A, Fraidakis O, Michaloudis D, et al. The impact of the type of anaesthesia on cognitive status and delirium during the first postoperative days in elderly patients. *Eur J Anaesthesiol* 2005; 22: 492–9.

14. Bryson GL, Wyand A. Evidence-based clinical update: general anesthesia and the risk of delirium and postoperative cognitive dysfunction. *Can J Anaesth* 2006; 53: 669–77.
15. Wu CL, Hsu W, Richman JM, et al. Postoperative cognitive function as an outcome of regional anesthesia and analgesia. *Reg Anesth Pain Med* 2004; 29: 257–68.
16. De Jonghe B, Cook D, Appere-De-Vecchi C, et al. Using and understanding sedation scoring systems: a systematic review. *Intensive Care Med* 2000; 26: 275–85.
17. Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone-alphadolone. *Br Med J* 1974; 2: 656–9.
18. Ambuel B, Hamlett KW, Marx CM, et al. Assessing distress in pediatric intensive care environments: The COMFORT scale. *J Pediatr Psychol* 1992; 17: 95–109.
19. Riker RR, Fraser GL, Cox PM. Continuous infusion of haloperidol controls agitation in critically ill patients. *Crit Care Med* 1994; 22: 433–40.
20. Devlin JW, Boleski G, Mlynarek M, et al. Motor Activity Assessment Scale: a valid and reliable sedation scale for use with mechanically ventilated patients in an adult surgical intensive care unit. *Crit Care Med* 1999; 27: 1271–5.
21. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002; 166: 1338–44.
22. De Jonghe B, Cook D, Griffith L, et al. Adaptation to the Intensive Care Environment (ATICE): development and validation of a new sedation assessment instrument. *Crit Care Med* 2003; 31: 2344–54.
23. Vincent JL. Give you patient a fast hug (at least) once a day. *Crit Care Med* 2005; 33: 1225–9.
24. Papadimos TJ, Hensley SJ, Duggan JM, et al. Implementation of the “FASTHUG” concept decreases the incidence of ventilator-associated pneumonia in a surgical intensive care unit. *Patient Saf Surg* 2008; 2: 3.
25. Adam C, Rosser D, Manji M. Impact of introducing a sedation management guideline in intensive care. *Anaesthesia* 2006; 61: 260–3.
26. De Jonghe B, Bastuji-Garin S, Fangio P, et al. Sedation algorithm in critically ill patients without acute brain injury. *Crit Care Med* 2005; 33: 120–7.
27. Marshall J, Finn CA, Theodore AC. Impact of a clinical pharmacist-enforced intensive care unit sedation protocol on duration of mechanical ventilation and hospital stay. *Crit Care Med* 2008; 36: 427–33.
28. Kress JP, Pohlman AS, O'Connor MF, et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000; 342: 1471–7.
29. Resar R, Pronovost P, Haraden C, et al. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf* 2005; 31: 243–8.
30. Youngquist P, Carroll M, Farber M, et al. Implementing a ventilator bundle in a community hospital. *Jt Comm J Qual Patient Saf* 2007; 33: 219–25.
31. de Wit M, Gennings C, Jenvey WL, et al. Randomized trial comparing daily interruption of sedation and nursing implemented sedation algorithm in medical intensive care unit patients. *Crit Care* 2008; 12: R70.
32. Dundee JW. New i.v. anaesthetics. *Br J Anaesth* 1979; 51: 641–8.
33. Rogers KM, Dewar KM, McCubbin TD, et al. Preliminary experience with ICI 35 868 as an i.v. induction agent: comparison with althesin. *Br J Anaesth* 1980; 52: 807–10.
34. Rutter DV, Morgan M, Lumley J, et al. ICI 35868 (Diprivan): a new intravenous induction agent. A comparison with methohexitone. *Anaesthesia* 1980; 35: 1188–92.
35. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): A randomised controlled trial. *Lancet* 2008; 371: 126–34.
36. Fong JJ, Kanji S, Dasta JF, et al. Propofol associated with a shorter duration of mechanical ventilation than scheduled intermittent lorazepam: a database analysis using Project IMPACT. *Ann Pharmacother* 2007; 41: 1986–91.
37. Parke TJ, Stevens JE, Rice AS, et al. Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports. *Br Med J* 1992; 305: 613–16.
38. Wysowski DK, Pollock ML. Reports of death with use of propofol (Diprivan) for nonprocedural (long-term) sedation and literature review. *Anesthesiology* 2006; 105: 1047–51.
39. Kam PC, Cardone D. Propofol infusion syndrome. *Anaesthesia* 2007; 62: 690–701.
40. Vasile B, Rasulo F, Candiani A, Latronico N. The pathophysiology of propofol infusion syndrome: a simple name for a complex syndrome. *Intensive Care Med* 2003; 29: 1417–25.
41. Diprivan 1% (Propofol injection 10mg/mL) drug monograph. AstraZenica Canada, Mississauga, 2004.
42. Coursin DB, Coursin DB, Maccioli GA. Dexmedetomidine. *Curr Opin Crit Care* 2001; 7: 221–6.
43. Vandermeulen E. Systemic analgesia and co-analgesia. *Acta Anaesthesiol Belg* 2006; 57: 113–20.
44. Weinbroum AA, Ben-Abraham R. Dextromethorphan and dexmedetomidine: New agents for the control of perioperative pain. *Eur J Surg* 2001; 167: 563–9.
45. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perceptions. *Br J Anaesth* 2001; 87: 684–90.
46. Venn M, Newman J, Grounds M. A phase II study to evaluate the efficacy of dexmedetomidine for sedation in the medical intensive care unit. *Intensive Care Med* 2003; 29: 201–7.
47. Shehabi Y, Ruettimann U, Adamson H, et al. Dexmedetomidine infusion for more than 24 hours in critically ill patients: sedative and cardiovascular effects. *Intensive Care Med* 2004; 30: 2188–96.
48. Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med* 2004; 32: 955–62.
49. Dasgupta M, Dumbrell AC. Preoperative risk assessment for delirium after noncardiac surgery: a systematic review. *J Am Geriatr Soc* 2006; 54: 1578–89.
50. Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006; 104: 21–6.
51. Thomason JW, Shintani A, Peterson JF, et al. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. *Crit Care* 2005; 9: R375–R381.
52. Jackson JC, Gordon SM, Hart RP, et al. The association between delirium and cognitive decline: a review of the empirical literature. *Neuropsychol Rev* 2004; 14: 87–98.
53. Arora VM, Johnson M, Olson J, et al. Using assessing care of vulnerable elders quality indicators to measure quality of hospital care for vulnerable elders. *J Am Geriatr Soc* 2007; 55: 1705–11.
54. Inouye SK. Delirium in older persons. *N Engl J Med* 2006; 354: 1157–65.
55. Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision. Washington, DC: American Psychiatric Association, 2000.

56. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA* 2001; 286: 2703–10.
57. Neelon VJ, Champagne MT, Carlson JR, et al. The NEECHAM Confusion Scale: Construction, validation, and clinical testing. *Nurs Res* 1996; 45: 324–30.
58. Van Rompaey B, Schuurmans MJ, Shortridge-Baggett LM, et al. A comparison of the CAM-ICU and the NEECHAM Confusion Scale in intensive care delirium assessment: An observational study in non-intubated patients. *Crit Care* 2008; 12: R16.
59. Soja SL, Pandharipande PP, Fleming SB, et al. Implementation, reliability testing, and compliance monitoring of the Confusion Assessment Method for the Intensive Care Unit in trauma patients. *Intensive Care Med* 2008.
60. American Psychological Association. Practice guideline for the treatment of patients with delirium. *Am J Psych* 1999; 156 (5 Suppl): 1–20.
61. Cook IA. Guideline Watch: Practice Guideline for the Treatment of Patients with Delirium. Arlington, VA: American Psychiatric Association, 2004.
62. Inouye SK, Bogardus ST Jr., Charpentier PA, et al. A multi-component intervention to prevent delirium in hospitalized older patients. *N Engl J Med* 1999; 340: 669–76.
63. Milbrandt EB, Kersten A, Kong L, et al. Haloperidol use is associated with lower hospital mortality in mechanically ventilated patients. *Crit Care Med* 2005; 33: 226–9.
64. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: A randomized placebo-controlled study. *J Am Geriatr Soc* 2005; 53: 1658–66.
65. WHO Expert Committee on Problems Related to Alcohol Consumption. Second report. Geneva, World Health Organization, 2007 (WHO Technical Report Series 944).
66. Golan JD, Marcoux J, Golan E, et al. Traumatic brain injury in intoxicated patients. *J Trauma* 2007; 63: 365–9.
67. Kluger Y, Jarosz D, Paul DB, et al. Diving injuries: a preventable catastrophe. *J Trauma* 1994; 36: 349–51.
68. Blondell RD, Powell GE, Dodds HN, et al. Admission characteristics of trauma patients in whom delirium develops. *Am J Surg* 2004; 187: 332–7.
69. Delgado-Rodríguez M, Gómez-Ortega A, Mariscal-Ortiz M, et al. Alcohol drinking as a predictor of intensive care and hospital mortality in general surgery: a prospective study. *Addiction* 2003; 98: 611–16.
70. Kahan M, Borgundvaag B, Borsoi D, et al. Treatment variability and outcome differences in the emergency department management of alcohol withdrawal. *Can J Emerg Med* 2005; 7: 87–92.
71. Gold JA, Rimal B, Nolan A, et al. A strategy of escalating doses of benzodiazepines and phenobarbital administration reduces the need for mechanical ventilation in delirium tremens. *Crit Care Med* 2007; 35: 724–30.
72. Saitz R, Mayo-Smith MF, Roberts MS, et al. Individualized treatment for alcohol withdrawal. A randomized double-blind controlled trial. *JAMA* 1994; 272: 519–23.
73. Daeppen JB, Gache P, Landry U, et al. Symptom-triggered vs fixed-schedule doses of benzodiazepine for alcohol withdrawal: A randomized treatment trial. *Arch Intern Med* 2002; 162: 1117–21.
74. Sullivan JT, Sykora K, Schneiderman J, et al. Assessment of alcohol withdrawal: The revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict* 1989; 84: 1353–7.
75. Ntais C, Pakos E, Kyzas P, et al. Benzodiazepines for alcohol withdrawal. *Cochrane Database Syst Rev* 2005;3.
76. Gentilello LM. Alcohol and injury: American College of Surgeons Committee on trauma requirements for trauma center intervention. *J Trauma* 2007; 62(6 Suppl): S44–S45.
77. Gentilello LM, Ebel BE, Wickizer TM, et al. Alcohol interventions for trauma patients treated in emergency departments and hospitals: a cost benefit analysis. *Ann Surg* 2005; 241: 541–50.
78. Gentilello LM, Rivara FP, Donovan DM, et al. Alcohol interventions in a trauma center as a means of reducing the risk of injury recurrence. *Ann Surg* 1999; 230: 473–80.
79. Soderstrom CA, DiClemente CC, Dischinger PC, et al. A controlled trial of brief intervention versus brief advice for at-risk drinking trauma center patients. *J Trauma* 2007; 62: 1102–11.
80. Bowdle TA. Depth of anesthesia monitoring. *Anesthesiol Clin* 2006; 24: 793–822.
81. Tonner PH, Bein B. Classic electroencephalographic parameters: Median frequency, spectral edge frequency etc. *Best Pract Res Clin Anaesthesiol* 2006; 20: 147–59.
82. Sigl JC, Chamoun NG. An introduction to bispectral analysis for the electroencephalogram. *J Clin Monit* 1994; 10: 392–404.
83. Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A. Bispectral index for improving anaesthetic delivery and postoperative recovery. *Cochrane Database Syst Rev* 2007: 6.
84. Messner M, Beese U, Romstöck J, et al. The bispectral index declines during neuromuscular block in fully awake persons. *Anesth Analg* 2003; 97: 488–91.
85. Niedhart DJ, Kaiser HA, Jacobsohn E, et al. Intrapatient reproducibility of the BISxp monitor. *Anesthesiology* 2006; 104: 242–8.
86. Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med* 2008; 358: 1097–108.
87. Deogaonkar A, Gupta R, DeGeorgia M, et al. Bispectral index monitoring correlates with sedation scales in brain-injured patients. *Crit Care Med* 2004; 32: 2403–6.
88. Dunham CM, Ransom KJ, McAuley CE, et al. Severe brain injury ICU outcomes are associated with cranial-arterial pressure index and noninvasive bispectral index and transcranial oxygen saturation: a prospective, preliminary study. *Crit Care* 2006; 10: R159.
89. Paul DB, Umamaheswara Rao GS. Correlation of bispectral index with Glasgow Coma Score in mild and moderate head injuries. *J Clin Monit Comput* 2006; 20: 399–404.

Malignant Hypertension: An Evidence-based Surgery Review

David S. Owens and Marshall A. Corson

Summary of Grade of Recommendations for Questions Regarding Malignant Hypertension		
Question	Summary recommendation	Grade
What is the optimal target BP for chronic therapy?	Care guidelines recommend SBP <140 and DBP <90 mmHg in the general population and <130/<80 in those with diabetes or chronic kidney disease.	B
How should preexisting hypertension be managed in the perioperative setting?	Antihypertensive therapies should be continued throughout the perioperative period when possible; with SBP >180 or DBP >110 mmHg, nonemergency surgeries should be deferred.	B
What is the threshold for pharmacologic treatment of high BP acutely in ambulatory individuals?	SBP >180, DBP >120 mmHg, or lower pressures with target organ dysfunction, should be treated aggressively to lower SBP to <160 mmHg, DBP to <110 mmHg, or by ~20% overall.	C
What are the clinical implications of APH?	APH may follow cardiovascular, neurological, or head and neck surgeries and is associated with adverse clinical outcomes. Pharmacologic therapy is indicated at SBP >160 or DBP >110 mmHg for noncardiac surgeries and SBP >140 or DBP >90 mmHg following cardiac surgeries.	C
What are the best therapies for APH?	Agents shown to be most effective include sodium nitroprusside, nitroglycerin, labetalol, nicardipine, and fenoldopam.	C
What signs and symptoms suggest end organ compromise due to malignant hypertension?	Encephalopathy, hemorrhagic or ischemic CVA, myocardial ischemia and infarction, acute pulmonary edema, aortic dissection, acute renal failure, or anastomotic complications; these signs may be masked in the perioperative period and should be aggressively sought in patients with severe hypertension.	B
What are the best pharmacologic therapies for acute management of hypertension in the presence of complicating conditions?	No pharmacologic agents have been shown to improve morbidity and mortality in hypertensive emergencies, but appear to be equally efficacious at lowering BP acutely. Choice of therapy should be tailored to clinical context and patient condition.	C
Abbreviations: APH, acute postoperative hypertension; BP, blood pressure; CVA, cerebrovascular accident; DBP, diastolic blood pressure; SBP, systolic blood pressure.		

INTRODUCTION

Hypertension is a common but incompletely understood disorder that may result in damage, either acute or chronic, to the end organs exposed to elevated blood pressure (BP). It is a particularly menacing problem in the perioperative period due to increased catecholamine states related to anxiety or pain, the frequent inability to take oral medications, and the potential effects of anesthetic agents. Preexisting hypertension is the largest risk factor for postoperative hypertension (1,2), and long-standing preexisting hypertension can complicate perioperative clinical management due to left ventricular hypertrophy, diastolic heart failure, chronic kidney disease, and cerebrovascular or coronary vascular stenoses. In this chapter, we provide an evidence-based review of the management of hypertension in the perioperative period, with particular attention to the management of malignant hypertension, in which an acute

elevation in BP raises the risk of life-threatening end organ damage. The management of intraoperative hypertension is not addressed.

WHAT IS THE OPTIMAL TARGET BP FOR CHRONIC THERAPY?

There is now a vast body of literature informing the management of chronic hypertension, which has been summarized in detail in the most recent Seventh Report of the Joint National Committee (JNC 7) on the Prevention, Evaluation and Treatment of High Blood Pressure (3). Epidemiologic studies have shown that in general, the risk of clinical events increases when the BP is above 115/75 mmHg. This association is continuous, with a doubling of risk for every ~20/10 mmHg increase in BP (3,4).

Based on this finding, the JNC 7 guidelines developed a new classification of prehypertension for systolic BP of 120–139 mmHg or diastolic BP of 80–89 mmHg. Patients with prehypertension are at increased risk of clinical events and should be counseled on lifestyle modifications such as lowering dietary salt intake, proper exercise, avoiding excessive alcohol intake, and weight loss. Whether *normalization* of BP with treatment to systolic BP <120 mmHg will reduce end organ complications of hypertension is currently under study in clinical trials (5). However, hypertension is just one risk factor for clinical events, and the need for and intensity of therapy should be put into the context of the patient's entire risk profile.

The initiation of pharmacologic therapy should be considered when the patient is unable to reach target BP after a trial of lifestyle interventions. In patients without other cardiovascular risk factors, the target BP should be less than 140/90 mmHg (3). In patients with diabetes, chronic kidney disease, or prior cardiovascular events, the target BP should be less than 130/80 mmHg. The choice of pharmacologic therapy is dependent on the patient's other risk factors and comorbidities and is beyond the scope of this text, but patients often need multidrug therapy for optimal BP control. Many randomized controlled trials of specific agents have been performed. Beta-blockers may be particularly useful in the perioperative setting but appear to be less effective for chronic BP control. Dihydropyridine calcium channel blockers, thiazide diuretics, and angiotensin converting enzyme (ACE) inhibitors are often good initial agents of choice.

Summary/Recommendations: Blood pressure above 115/75 mmHg is associated with increased clinical events. Pharmacologic therapy is generally initiated when BP remains above 130/80 mmHg in patients with concurrent diabetes, chronic kidney disease, or prior cardiovascular events or if BP remains above 140/90 mmHg in patients with no other risk factors (Grade B recommendation).

HOW SHOULD PREEXISTING HYPERTENSION BE MANAGED IN THE PERIOPERATIVE SETTING?

Preexisting hypertension raises the risk for intraoperative hemodynamic instability (6,7) and perioperative clinical events (8,9) and is one of the most common reasons for canceling or postponing surgery (10). This may be especially true of untreated, severe hypertension (2,6,11). However, in a series of 676 patients, Goldman and Caldera found that inadequately treated hypertension did not pose an increased risk compared to adequately treated hypertension (11), likely because of the skill of anesthesiologists to control BP intraoperatively. In a meta-analysis of 30 trials, Howell et al. found that the odds ratio for the association between hypertensive disease and perioperative cardiac outcomes was 1.35 (95% confidence interval [CI] 1.17–1.56), a finding the authors felt was more statistically than clinically meaningful (7). Accordingly, the current American Heart Association guidelines on preoperative risk stratification for noncardiac surgeries no longer categorize hypertension as a clinical risk factor for perioperative cardiac events (12). It is currently recommended that for patients with stage 3 hypertension (BP greater than 180/110 mmHg),

the risk of perioperative clinical events should be weighed against the risks in delaying surgery, and the surgery should be potentially postponed to allow more optimal BP control (12).

In patients with preexisting hypertension, antihypertensive therapy should be continued throughout the perioperative period if possible. This is especially important for beta-blockers and alpha-blockers (e.g., clonidine), for which abrupt discontinuation can cause rebound tachycardia and hypertension. Although the benefits of routine preoperative use of beta-blockers for high-risk patients has recently been called into question (13–18), discontinuation of beta-blockers has been shown to significantly increase perioperative cardiovascular events and one-year mortality (19–21). If the patient is unable to take oral medications, similar-acting parental or transcutaneous alternatives are available. Data from observational studies and a single randomized trial suggest ACE inhibitor or angiotensin-blocking agents are associated with intraoperative hypotension (22,23), leading some authors to recommend they be held prior to surgery and restarted postoperatively (22,24). However, holding these medications has not been shown to improve clinical outcomes.

Summary/Recommendations: Antihypertensive therapy should be continued preoperatively and throughout the perioperative period using parenteral or transcutaneous alternatives if needed. This recommendation is strongest for patients on beta-blockers. In patients with BP greater than 180/110 mmHg, postponement of elective surgeries should be considered after weighing competing risks (Grade B recommendation).

WHAT IS THE THRESHOLD FOR PHARMACOLOGIC TREATMENT OF HIGH BP ACUTELY?

Severely elevated systolic or diastolic BP can cause a variety of acute end organ complications, including effects on the brain (encephalopathy, hemorrhage, or stroke), heart (myocardial infarction or heart failure), kidneys (acute renal failure), or vasculature (aortic dissection). Severe hypertension with the presence of any of these signs or symptoms is referred to as *hypertensive emergency* (25), requires prompt therapy, and is discussed in more detail below.

Hypertensive urgency is defined as a resting systolic BP above 180 mmHg systolic or 120 mmHg diastolic in the absence of signs or symptoms of end organ damage (25). BPs of this magnitude should be repeated and verified, ideally in a quiet room with the patient at rest, making sure to use a properly sized BP cuff (26). If the patient is having symptoms of chest discomfort, BP should be measured in both arms and both legs as an initial screening for aortic dissection.

Patients with hypertensive urgency merit pharmacologic intervention. However, chronic hypertension can perturb normal cerebral or coronary arterial autoregulation, and rapid reduction in BP may precipitate ischemic events. Thus in the absence of signs or symptoms of end organ damage, the goal of pharmacologic therapy should not be to normalize BP quickly but to reduce BP 20%, or below 160/100 mmHg, over several hours to days (27). This

recommendation is not based on clinical trial data per se but on expert consensus and physiologic considerations. In contrast, if patients have signs or symptoms of end organ compromise, more immediate therapy is justified. The therapies of choice and the aggressiveness of therapy depend on the clinical context and are outlined further shortly.

Summary/Recommendations: Hypertensive urgency, defined as a systolic BP greater than 180mmHg or a diastolic BP greater than 120mmHg in the absence of symptoms, merits pharmacologic intervention. Blood pressure should be lowered ~20% over the course of hours to days, with a target of less than 160/100mmHg (Grade C recommendation).

WHAT ARE THE CLINICAL IMPLICATIONS OF ACUTE POSTOPERATIVE HYPERTENSION?

Acute postoperative hypertension (APH) is broadly defined as a significant elevation in BP in the immediate postoperative period and can be associated with severe clinical sequelae, including strokes, intracranial hemorrhage, myocardial ischemia, heart failure, acute renal failure, and surgical anastomotic or site complications (28). BP typically becomes elevated less than 2 hours postoperatively, remaining elevated for several hours, although persistent BP elevation for up to 48 hours has been reported. APH is believed to be caused by adrenergic stimulation, vasoconstriction, and resultant elevation in systemic vascular resistance, and significant elevations in plasma catecholamine levels have been observed (29–31). Anesthetic and procedural factors may influence the incidence of APH, which appears to be most common following cardiovascular, neurosurgical, and head and neck surgeries. APH is especially common following carotid endarterectomy, which may be due to stimulation of baroreceptors (32,33).

Despite being a well-recognized disorder, there is debate surrounding many important features of APH, including a strict definition, its clinical importance, the proper threshold for initiation of therapy, and the appropriate aggressiveness of therapy. Although there are few prospective studies showing clinical benefit of therapy, especially following noncardiac surgery, postoperative hypertension is associated with increased morbidity and mortality (1,2), and it seems intuitive that treatment of severe hypertension may improve clinical outcomes. Thus, therapeutic decisions are often made on an individual basis, with consideration of the patient's current and preoperative blood pressures, the presence and severity of comorbidities, the type of surgery performed, and an evaluation of the risk of surgical complications.

Although no studies have examined the optimal threshold for initiation of therapy, a BP of 160/90mmHg, a mean arterial pressure of >110mmHg, or a relative 20% increase in systolic or diastolic BP compared to preoperative levels have all been used in clinical trials as thresholds for intervention. In contrast, the link between APH and postoperative complications has been more clearly defined for cardiovascular surgeries, and a threshold BP of 140/90mmHg or a mean arterial BP of 105mmHg are often used for initiation of therapy.

Summary/Recommendations: APH following cardiac surgery is associated with adverse clinical outcomes, and hypertension should be treated if the BP is >140/90mmHg. The benefits of treating APH following noncardiac surgeries is less well established, but therapy is generally recommended for BPs >160/110mmHg, although treatment of less severe hypertension may be justified in high-risk patients (Grade C recommendation).

WHAT ARE THE BEST THERAPIES FOR APH?

After verification that the BP is elevated, the next step is the identification of potentially reversible causes of hypertension. Pain, anxiety, agitation (e.g., emergence from anesthesia), hypercarbia, hypoxia, hypovolemia or hypervolemia, and other irritants (e.g., bladder distention) can all increase sympathetic tone and are frequent causes of perioperative hypertension (34). These causes should be considered and addressed prior to the initiation of antihypertensive therapy.

Because APH is a short-lived process with often rapidly fluctuating BPs, the ideal pharmacologic treatments would be fast-acting and possess short half-lives to allow rapid titration to effect. Because all parenteral, vasoactive medications have the potential for adverse effects, the choice of specific agents often depends on the type of surgery, the patient's comorbidities, and the clinical context. Currently, there are no randomized trials demonstrating improvement in clinical outcomes and only limited data comparing the effectiveness of different agents in lowering BP. Evidence supporting the use of specific agents for the treatment of APH are provided here and summarized.

Sodium Nitroprusside

Sodium nitroprusside is a nitric oxide donor, which causes relaxation of vascular smooth muscles via cyclic guanosine monophosphate (GMP)-dependent pathways, thus serving as a very potent, direct arterial vasodilator. Advantages of sodium nitroprusside include its quick onset, rapid metabolism, and lack of direct cardiotoxicity. Potential major adverse effects include hypotension, reflex tachycardia, myocardial ischemia, intrapulmonary shunting (from reversal of physiologic hypoxic vasoconstriction), decreased cerebral blood flow with increased intracerebral pressures, and the potential for cyanide toxicity. It is contraindicated in patients with myocardial ischemia, encephalopathy, acute cerebrovascular accident, and liver or renal failure. When sodium nitroprusside is used, intra-arterial BP monitoring and thiocyanate surveillance are recommended.

Sodium nitroprusside has been shown to be effective in treating APH following both cardiovascular (35–37) and noncardiac surgeries (37), with the vast majority of patients achieving target BPs. It has been shown to be equally effective as nitroglycerin (36,38), labetalol (39,40), esmolol (41), fenoldopam (42), and nicardipine (37). However, because of its potential for serious side effects, the use of sodium nitroprusside should be limited to situations where these risks are justified, such as the treatment of hypertension

following cardiac surgery. Additionally, because nitroprusside may raise intracranial pressure, it should generally be avoided for the treatment of APH following neurologic surgeries.

Nitroglycerin

Intravenous nitroglycerin is predominantly a venodilator, which results in a reduction in myocardial preload; it produces limited direct arterial or coronary vasodilation. Advantages of using nitroglycerin include a quick onset of action, a short half-life, a reduction in pulmonary vascular resistance, and a reduction in myocardial oxygen demands. Potential disadvantages include tachyphylaxis (occurs after 48–72 hours, not usually limiting in APH treatment), reflex tachycardia, headaches (which often limit dosing), and a reduction in cardiac output in patients that are preload-dependent.

Intravenous nitroglycerin has been shown to be effective in treating APH following cardiac surgery (35,36,38), but has not been specifically investigated after neurosurgical, head and neck, or other noncardiac procedures. Several trials have compared its efficacy against sodium nitroprusside and suggest equivalent BP control, albeit through quite distinct mechanisms.

Labetalol

Labetalol is a nonselective beta-adrenergic receptor antagonist that also offers partial antagonism of alpha-adrenergic receptors. It thus acts as a myocardial depressant, with both negative inotropic and chronotropic effects, and as a direct vasodilator. It is available in both oral and intravenous formulations. Given parenterally, it has a short onset of action but a longer half-life than either sodium nitroprusside or nitroglycerin. Advantages of labetalol include reducing myocardial oxygen demands and lack of effect on cerebral perfusion and intracerebral pressures. It is therefore a good treatment option for patients with myocardial ischemia or following neurosurgical procedures. It is contraindicated in patients with heart failure, low cardiac output, severe bronchospasm, bradycardia, or impaired atrioventricular nodal conduction.

Because APH appears to be mediated by elevated plasma catecholamine levels, labetalol would appear to have theoretical advantages. It is one of the most widely studied treatments for APH and has proven efficacy following cardiovascular (39), neurologic (43), carotid endarterectomies (40), and other general surgeries (44). It has been tested against sodium nitroprusside and esmolol and found to be equally efficacious.

Esmolol

Esmolol is another beta-adrenergic antagonist, but it has more beta-1 receptor selectivity and is thus more cardioselective. It lowers BP by decreasing heart rate and myocardial contractility but has little effect on systemic vascular resistance. Its main advantage over labetalol is pharmacokinetic; it has a very rapid onset of action and a

very short half-life because it is metabolized intravascularly by erythrocyte (RBC) esterase. Advantages and contraindications for esmolol are similar to labetalol, although theoretically with less potential for pulmonary bronchospasm and with more rapid clearance.

Although esmolol would appear to be the ideal agent for the management of APH, there are few studies documenting its efficacy. It has been studied following cardiac (41) and neurologic (45,46) surgeries and following repair of aortic coarctations (47). Muzzi et al. found esmolol to be equally effective as labetalol following neurologic surgeries, and Gray et al. found it to be equally effective as sodium nitroprusside following cardiac surgeries, with less deterioration in oxygenation.

Nicardipine

Nicardipine is a parenteral dihydropyridine calcium channel blocker whose primary mechanism of action is arterial vasodilation with limited direct effects on cardiac function. Importantly, it has direct coronary and cerebral vasodilating effects and results in an improvement in myocardial perfusion and metabolism. Potential adverse effects include reflex tachycardia, hypotension, nausea, and vomiting (48).

Nicardipine is reasonably well studied for the treatment of APH, including randomized, placebo-controlled trials (48,49), and this agent has proven efficacy following cardiovascular (50,51) and noncardiac procedures (37,48), although its efficacy following neurosurgical procedures has not been demonstrated.

Fenoldopam

Fenoldopam is among a newer class of vasodilators that acts as an agonist of peripheral dopamine type-1 receptors and is FDA-approved for the treatment of acute hypertension. Its quick onset of action, short half-life, and potential for increasing renal perfusion and glomerular filtration rate make it an attractive choice in the treatment of APH (52). Dopamine type-1 receptors are especially concentrated on the renal and splanchnic arterioles, and thus fenoldopam can increase renal perfusion and the glomerular filtration rate, resulting in net natriuresis. Potential adverse effects of fenoldopam include hypotension, tachycardia, headache, and dizziness. Fenoldopam has been shown to be an effective treatment of severe hypertension (53–58) with improved renal perfusion compared to nitroprusside, but it is less well studied in the postoperative setting with only a few small observational trials.

Nifedipine

Although nifedipine is available in sublingual formulation, there is limited drug bioavailability with this approach. Alternatively, crushing the tablet allows for rapid gastric absorption. However, this delivery method has been shown to result in unpredictable BP responses and has been associated with severe hypotension (59). Because of this, nifedipine is no longer recommended as a treatment for APH.

Summary/Recommendations: Sodium nitroprusside, nitroglycerin, labetalol, esmolol, nicardipine, and fenoldopam

Table 85.1 Levels of Evidence for the use of Specific Pharmacologic Agents in the Treatment of Acute Postoperative Hypertension

	Type of Surgery			
	Cardiovascular	Neurologic	Head and Neck	General
Nitroprusside	IIa	V*	IIb	IIb
Nitroglycerin	IIa	IIa	IIa	IIa
Labetalol	IIa	IIa	IIb	IIb
Esmolol	IIb	Ib	V	V
Nicardipine	Ib	Ib	Ib	Ib
Fenoldopam	IIb	V	V	Ib

*May cause potential harm.

have been shown to be effective in the treatment of postoperative hypertension (Table 85.1). The choice of pharmacologic agents should be primarily guided by consideration of patient comorbidities and physiologic conditions (Grade C recommendation).

WHAT SIGNS AND SYMPTOMS SUGGEST END ORGAN COMPROMISE DUE TO ACUTE HYPERTENSION?

Severe hypertension can result in rapid end organ deterioration, especially when the hypertension develops acutely. APH has been associated with adverse clinical events, including encephalopathy, hemorrhagic and ischemic cerebrovascular accidents, myocardial ischemia and infarction, congestive heart failure, aortic dissection, acute renal failure, and surgical site or anastomotic complications. Symptoms of end organ damage are often masked in the postoperative period due to sedation, analgesia, and impaired levels of consciousness, and severe hypertension may be a physiologic response to myocardial ischemia, stroke, or increased intracranial pressure. Thus, it is imperative that all patients with significant postoperative hypertension undergo a complete physical examination aimed at determining whether there is impairment in end organ function.

Although hypertensive urgencies in the nonsurgical setting are infrequent when the diastolic BP is <130 mmHg (27), the rate of change in BP is an important factor in the development of end organ damage due to limits of autoregulation. Thus, hypertensive urgencies may be more common perioperatively, when hypertensive stimuli are frequently present. In nonsurgical settings, the most common symptoms of end organ damage include chest pain, dyspnea, impaired cognition, and headache (60). Focal stroke-like symptoms cannot be singly attributed to hypertension, and a complete neurologic evaluation is warranted. Signs of end organ damage may include pulmonary rales, cardiac murmurs or gallops, ischemic electrocardiogram (ECG) changes, impaired cognition, decreased urine output with hematuria or proteinuria, or papillary edema on fundoscopic examination.

Summary/Recommendation: Patients with APH merit full evaluation, with attention to signs and symptoms of end organ (i.e., brain, heart, lung, kidney, and vasculature)

involvement. Patients with end organ involvement should receive prompt therapy targeted at relieving and preventing further end organ damage (Grade B recommendation).

WHAT ARE THE BEST PHARMACOLOGIC THERAPIES FOR ACUTE MANAGEMENT OF HYPERTENSION IN THE SETTING OF COMPLICATING CONDITIONS?

When signs or symptoms of end organ involvement are present, prompt treatment of severe hypertension is necessary and should be dictated by the clinical syndrome. There is limited clinical trial evidence for the utility of particular pharmacologic agents in given clinical circumstances, especially in the postoperative setting. Indeed, a recent Cochrane review by Perez et al. concluded that there was insufficient randomized controlled data showing that treatment of hypertensive emergencies resulted in improvement in clinical outcomes (61). This is in part due to the ethics of performing placebo-controlled trials in this setting. Perez et al. further concluded that although there were minor differences in BP effects of different pharmacologic agents, the clinical significance of these differences is unknown. Thus, the following recommendations are based primarily on knowledge regarding the physiologic effects of the medications and, when available, studies of hypertensive emergency in the nonperioperative setting.

Encephalopathy

Hypertensive encephalopathy is generally due to the development of cerebral edema (62) and is generally manifest as symptoms of nausea, vomiting, headache, or impairment in cognition, although more severe symptoms such as seizure and coma can occur if untreated. If encephalopathy is suspected, computed tomography should be performed to exclude hemorrhage or stroke, as aggressive BP lowering is contraindicated in these situations. The goal of therapy should be to reduce BP by less than 25% within the first two to six hours, aiming for a diastolic BP of 100–105 mmHg (63). There is no particular agent of choice for the treatment of hypertensive encephalopathy, although sodium nitroprusside should be avoided due to the possibility of increased cerebral pressure and decreased cerebral perfusion.

Stroke

Cerebrovascular accidents (CVAs) often cause a severe reflex elevation in BP, making it difficult to determine if the CVA or the hypertension is the primary inciting event. This hypertension generally declines within 24 hours of the inciting event. The proper management of hypertension in the setting of an ischemic CVA is controversial, and there are some data suggesting that aggressive treatment of hypertension may result in worse clinical outcomes (64–66). The current American Stroke Association and American Heart Association guidelines recommend therapy only if thrombolysis is planned, if the hypertension is causing other organ impairment, or if the BP is severely elevated (systolic BP >220 or diastolic BP >120mmHg) (67). In these situations, BP should be lowered slowly, aiming for a 15% reduction in BP over the initial 24 hours (67). The recommended pharmacologic treatment options include beta-blockers or nicardipine, which has been shown to be effective following both ischemia and hemorrhagic CVAs (68). The treatment of hypertension following hemorrhagic CVA is slightly more complex and dependent on whether intracerebral pressure is elevated (69). It is recommended that neurologic or neurosurgical consultation be obtained for all suspected CVAs.

Myocardial Ischemia

Severe hypertension results in an increase in myocardial wall stress, the principal determinant of myocardial oxygen consumption. In the presence of fixed obstructive lesions in the coronary arteries, this increase in oxygen demand may outstretch the supply of oxygen, resulting in subendocardial ischemia, which manifests as ST segment depression on ECG. If untreated, this may result in a non-ST segment elevation myocardial infarction. Beta-blockers and nitroglycerin (sublingual or intravenous) are the cornerstones of therapy in this situation, because they reduce myocardial oxygen demands by decreasing heart rate, contractility, and preload (thus reducing wall stress).

It is crucially important that all patients with perioperative chest pain have an ECG to exclude the presence of ST segment elevation, which indicates a distinct pathologic mechanism of coronary plaque rupture and *in situ* thrombosis that requires localized treatment with percutaneous intervention and stenting. The increased catecholamines and inflammation seen postoperatively predisposes to plaque rupture, which in turn may cause reflex hypertension. Importantly, the majority of plaques causing ST segment elevation myocardial infarctions are initially nonobstructive and would not be identified on preoperative stress testing.

Acute Pulmonary Edema

Severe hypertension can cause an increase in intracardiac pressures, which are then transmitted back into the

pulmonary vasculature, resulting in acute pulmonary edema. This may be due to myocardial ischemia, resulting in impaired cardiac systolic function, but may also be seen in the absence of ischemia in patients with impaired baseline systolic function, diastolic dysfunction, or valvular regurgitation. Transthoracic echocardiography can identify contributing factors and guide therapy. The treatment of systolic heart failure primarily involves a reduction of systemic vascular resistance using vasodilators (70); beta-blockers and calcium channel blockers are contraindicated in the absence of myocardial ischemia due to their cardiosuppressive effects. Nitroprusside is a good initial treatment option that can interrupt the cycle of hypertension, heart failure, and pulmonary edema, which then further increases catecholamines and BP. Nitroglycerin may also be beneficial because it can increase venous capacitance and reduce preload. ACE inhibitors and angiotensin receptor blockers are the preferred options for maintenance therapy. If the primary mechanism of heart failure is diastolic dysfunction, treatment should be directed at reducing BP and slowing heart rate to allow increased diastolic filling. Together with diuretics, beta-blockers and/or calcium channel blockers are the preferred agents of choice in this setting.

Aortic Dissection

Aortic dissection should be considered in all patients with chest discomfort, especially if they have a prior history of hypertension, aortic valve pathology, or Marfan syndrome. Given the high early mortality associated with aortic dissection, prompt diagnosis and treatment can be life-saving (71,72). Medical therapy, primarily involving BP control, is the recommended treatment for Type B (descending aorta) and in the acute, preoperative management of Type A (ascending aorta) dissections. The aim of medical therapy is to reduce aortic wall stress and thus minimize further dissection. In this setting, the treatment of choice is beta-blockers, which lower shear stress by reducing both stroke volume and the force of cardiac ejection. Vasodilators such as sodium nitroprusside are not the preferred agents (but can be used in beta-blocker intolerant patients), because they may cause reflex tachycardia and a compensatory increase in cardiac contractility (73). Esmolol is recommended as the initial pharmacologic therapy, due to its rapid pharmacokinetics, although treatment with other parenteral or oral beta-blockers may be substituted as clinical condition stabilizes. The target of therapy should be a systolic blood pressure of 100–120mmHg and a heart rate of <60 beats per minute (71,73).

Summary/Recommendations: The treatment of hypertensive emergencies should be guided by symptoms rather than absolute BP. The choice of pharmacologic therapy depends on the clinical context, patient condition and comorbidities, and urgency of therapy (Grade C recommendation).

Evidence Supporting the use of Specific Pharmacologic Therapies in Acute Postoperative Hypertension

Ref.	Year	Surgery	Study design	Size (n)	Endpoint	Comparison drug	Comments
<i>Sodium nitroprusside</i>							
31	1977	Cardiac	Observational		BP	—	
38	1980	Cardiac	Observational	77	BP, hemodynamics	Nitroglycerin	Effective at lowering BP.
35	1982	Cardiac	Crossover	17	BP	Nitroglycerin	Equally effective, but worse pulmonary gas exchange.
36	1985	Cardiac	Crossover	33	BP	Nitroglycerin	Equally effective; no change in myocardial metabolism.
41	1987	Cardiac	Crossover	20	BP	Esmolol	Equally effective; opposite effects on CI and SV.
39	1989	Cardiac	RCT	91	BP	Labetalol	Equally effective; opposite effects on CI.
40	1990	CEA	RCT	19	BP	Labetalol	Equally effective
50	1991	Cardiac	RCT	74	BP	Nicardipine	No difference in MAP.
37	1992	Cardiac/noncardiac	RCT	139	BP	Nicardipine	Equally effective, but more side effects than nicardipine
74	1993	Cardiac	Crossover	12	Hemodynamics	Nitroglycerin, prostacyclin	Equally effective at reaching target BP.
42	1993	Cardiac	RCT	20	Hemodynamics	Fenoldopam	Equally effective at reaching target BP; lower SV, CI, urine output.
75	1994	Cardiac	RCT	177	BP	Isradipine	Equally effective; slower control with more lability.
76	1996	Cardiac	Observational	12	BP	—	Improved splanchnic perfusion.
77	2003	Cardiac	RCT	30	BP	Clevidipine	Equally effective; fewer hemodynamic changes with clevidipine.
<i>Labetalol</i>							
78	1987	Vascular	Observational	6	Hemodynamics	—	Reduced MAP, HR, and CI.
79	1987	Noncardiac	Observational	15	Hemodynamics	—	Reduced BP and HR.
43	1988	Neurologic	Observational	15	BP, ICP	—	Enrolled those who failed SNP; lowered ICP compared with SNP alone
80	1989	Neurologic	Observational	9	BP, safety	—	Effective, no major side effects.
81	1989	Vascular	Observational	12	Hemodynamics	—	Lowered BP, improved CI.
86	1990	Cardiac	Observational	65	BP, hemodynamics	—	APH defined as SBP >140 mmHg; LV dysfunction excluded.
46	1990	Neurologic	RCT	—	BP	Esmolol	Equally effective, less bradycardia with esmolol.
44	1991	General	Observational	495	BP	—	Retrospective and prospective analyses.
<i>Esmolol</i>							
45	1988	Neurologic	RCT	40	BP	Placebo	Effective BP control following neurosurgery.
46	1990	Neurologic	RCT	—	BP	Labetalol	Equally effective, less bradycardia with esmolol.
<i>Nicardipine</i>							
82	1990	ENT	RCT	14	BP	Placebo	Effective at treating APH.
49	1990	Noncardiac	RCT	30	BP	Placebo	Effective at treating APH.
50	1991	Cardiac	RCT	74	BP	Nitroprusside	Equally effective.
48	1991	Cardiac/noncardiac	RCT	122	BP	Placebo	APH defined as SBP >140 mmHg.
37	1992	Cardiac/noncardiac	RCT	139	BP	Nitroprusside	Equally effective, fewer side effects with nicardipine
51	1997	AAA repair	Observational	16	BP	—	Enrolled APH after failing fixed-dose nitroprusside
<i>Fenoldopam</i>							
83	1993	Noncardiac	RCT	16	BP	Placebo	Effective at lowering BP
84	1998	Cardiac	RCT	—	BP, hemodynamics	Nifedipine	Equally effective; faster reduction in BP. Excluded patients with ischemia.

Abbreviations: AAA, abdominal aortic aneurysm; APH, acute postoperative hypertension; BP, blood pressure; CEA, carotid endarterectomy; CI, cardiac index; DBP, diastolic blood pressure; ENT, ear, nose, throat; HR, heart rate; ICP, intracranial pressure; LV, left ventricle; MAP, mean arterial pressure; RCT, randomized controlled trial; SBP, systolic blood pressure; SNP, sodium nitroprusside; SV, stroke volume.

REFERENCES

- Gal TJ, Cooperman LH. Hypertension in the immediate post-operative period. *Br J Anaesth* 1975; 47: 70-4.
- Towne JB, Bernhard VM. The relationship of postoperative hypertension to complications following carotid endarterectomy. *Surgery* 1980; 88: 575-80.
- Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 report. *JAMA* 2003; 289: 2560-72.
- Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360: 1903-13.
- Cushman WC, Grimm RH Jr., Cutler JA, et al. Rationale and design for the blood pressure intervention of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007; 99(12A): 44i-55i.
- Prys-Roberts C, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension. I. Cardiovascular responses of treated and untreated patients. *Br J Anaesth* 1971; 43: 122-37.
- Howell SJ, Sear JW, Foex P. Hypertension, hypertensive heart disease and perioperative cardiac risk. *Br J Anaesth* 2004; 92: 570-83.
- Aronson S, Boisvert D, Lapp W. Isolated systolic hypertension is associated with adverse outcomes from coronary artery bypass grafting surgery. *Anesth Analg* 2002; 94: 1079-84.
- Howell SJ, Sear YM, Yeates D, et al. Hypertension, admission blood pressure and perioperative cardiovascular risk. *Anaesthesia* 1996; 51: 1000-4.
- Dix P, Howell S. Survey of cancellation rate of hypertensive patients undergoing anaesthesia and elective surgery. *Br J Anaesth* 2001; 86: 789-93.
- Goldman L, Caldera DL. Risks of general anesthesia and elective operation in the hypertensive patient. *Anesthesiology* 1979; 50: 285-92.
- Fleisher LA, Beckman JA, Brown KA, et al. ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery: Executive Summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): Developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. *Circulation* 2007; 116: 1971-96.
- Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. *N Eng J Med* 1999; 341: 1789-94.
- Mangano DT, Layug EL, Wallace A, et al. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. *N Eng J Med* 1996; 335: 1713-20.
- Devereaux PJ, Yang H, Guyatt GH, et al. Rationale, design, and organization of the PeriOperative ISchemic Evaluation (POISE) trial: a randomized controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. *Am Heart J* 2006; 152: 223-30.
- Yang H, Raymer K, Butler R, et al. The effects of perioperative beta-blockade: results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. *Am Heart J* 2006; 152: 983-90.
- Juul AB, Wetterslev J, Gluud C, et al. Effect of perioperative beta blockade in patients with diabetes undergoing major non-cardiac surgery: randomised placebo controlled, blinded multicentre trial. *Br Med J* 2006; 332: 1482.
- Devereaux PJ, Yang H, Yusuf S, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008; 371: 1839-47.
- Shammash JB, Trost JC, Gold JM, et al. Perioperative beta-blocker withdrawal and mortality in vascular surgical patients. *Am Heart J* 2001; 141: 148-53.
- Goldman L. Noncardiac surgery in patients receiving propranolol. Case reports and recommended approach. *Arch Intern Med* 1981; 141: 193-6.
- Hoeks SE, Scholte Op Reimer WJ, van Urk H, et al. Increase of 1-year mortality after perioperative beta-blocker withdrawal in endovascular and vascular surgery patients. *Eur J Vasc Endovasc Surg* 2007; 33: 13-19.
- Bertrand M, Godet G, Meersschaert K, et al. Should the angiotensin II antagonists be discontinued before surgery? *Anesth Analg* 2001; 92: 26-30.
- Coriat P, Richer C, Douraki T, et al. Influence of chronic angiotensin-converting enzyme inhibition on anesthetic induction. *Anesthesiology* 1994; 81: 299-307.
- Comfere T, Sprung J, Kumar MM, et al. Angiotensin system inhibitors in a general surgical population. *Anesth Analg* 2005; 100: 636-44.
- The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). *Arch Intern Med* 1993; 153: 154-83.
- Linforts EW, Feussner JR, Blessing CL, et al. Spurious hypertension in the obese patient. Effect of sphygmomanometer cuff size on prevalence of hypertension. *Arch Intern Med* 1984; 144: 1482-85.
- Marik PE, Varon J. Hypertensive crises: challenges and management. *Chest* 2007; 131: 1949-62.
- Haas CE, LeBlanc JM. Acute postoperative hypertension: a review of therapeutic options. *Am J Health Syst Pharm* 2004; 61: 1661-73; quiz 1674-75.
- Wallach R, Karp RB, Reves JG, et al. Pathogenesis of paroxysmal hypertension developing during and after coronary bypass surgery: A study of hemodynamic and humoral factors. *A J Cardiol* 1980; 46: 559-65.
- Breslow MJ, Jordan DA, Christopherson R, et al. Epidural morphine decreases postoperative hypertension by attenuating sympathetic nervous system hyperactivity. *JAMA* 1989; 261: 3577-81.
- Roberts AJ, Niarchos AP, Subramanian VA, et al. Systemic hypertension associated with coronary artery bypass surgery. Predisposing factors, hemodynamic characteristics, humoral profile, and treatment. *J Thor Cardiovasc Surg* 1977; 74: 846-59.
- Bove EL, Fry WJ, Gross WS, et al. Hypotension and hypertension as consequences of baroreceptor dysfunction following carotid endarterectomy. *Surgery* 1979; 85: 633-7.
- Hirschl M, Kundi M, Hirschl MM, et al. Blood pressure responses after carotid surgery: Relationship to postoperative baroreceptor sensitivity. *Am J Med* 1993; 94: 463-8.
- Hogenson KD. Acute postoperative hypertension in the hypertensive patient. *J Post Anesth Nursing* 1992; 7: 38-44.
- Flaherty JT, Magee PA, Gardner TL, et al. Comparison of intravenous nitroglycerin and sodium nitroprusside for treatment of acute hypertension developing after coronary artery bypass surgery. *Circulation* 1982; 65: 1072-7.
- Fremes SE, Weisel RD, Mickle DA, et al. A comparison of nitroglycerin and nitroprusside. I. Treatment of postoperative hypertension. *Ann Thoracic Surg* 1985; 39: 53-60.
- Halpern NA, Goldberg M, Neely C, et al. Postoperative hypertension: a multicenter, prospective, randomized comparison

- between intravenous nicardipine and sodium nitroprusside. *Crit Care Med* 1992; 20: 1637–43.
38. Kaplan JA, Finlayson DC, Woodward S. Vasodilator therapy after cardiac surgery: a review of the efficacy and toxicity of nitroglycerin and nitroprusside. *Can Anaesthet Soc J* 1980; 27: 254–9.
39. Cruise CJ, Skrobik Y, Webster RE, et al. Intravenous labetalol versus sodium nitroprusside for treatment of hypertension postcoronary bypass surgery. *Anesthesiology* 1989; 71: 835–9.
40. Geniton DJ. A comparison of the hemodynamic effects of labetalol and sodium nitroprusside in patients undergoing carotid endarterectomy. *AANA J* 1990; 58: 281–7.
41. Gray RJ, Bateman TM, Czer LS, et al. Comparison of esmolol and nitroprusside for acute post-cardiac surgical hypertension. *Am J Cardiol* 1987; 59: 887–91.
42. Hill AJ, Feneck RO, Walesby RK. A comparison of fenoldopam and nitroprusside in the control of hypertension following coronary artery surgery. *J Cardiothor Vasc Anesth* 1993; 7: 279–84.
43. Orlowski JP, Shiesley D, Vidt DG, et al. Labetalol to control blood pressure after cerebrovascular surgery. *Crit Care Med* 1988; 16: 765–8.
44. Malsch E, Katonah J, Gratz I, et al. The effectiveness of labetalol in treating postoperative hypertension. *Nurse Anesth* 1991; 2: 65–71.
45. Gibson BE, Black S, Maass L, et al. Esmolol for the control of hypertension after neurologic surgery. *Clin Pharmacol Therap* 1988; 44: 650–3.
46. Muzzi DA, Black S, Losasso TJ, et al. Labetalol and esmolol in the control of hypertension after intracranial surgery. *Anesth Analg* 1990; 70: 68–71.
47. Smerling A, Gersony WM. Esmolol for severe hypertension following repair of aortic coarctation. *Crit Care Med* 1990; 18: 1288–90.
48. Efficacy and safety of intravenous nicardipine in the control of postoperative hypertension. IV Nicardipine Study Group. *Chest* 1991; 99: 393–8.
49. Goldberg ME, Clark S, Joseph J, et al. Nicardipine versus placebo for the treatment of postoperative hypertension. *Am Heart J* 1990; 119: 446–50.
50. David D, Dubois C, Loria Y. Comparison of nicardipine and sodium nitroprusside in the treatment of paroxysmal hypertension following aortocoronary bypass surgery. *J Cardiothor Vasc Anesth* 1991; 5: 357–61.
51. Vincent JL, Berlot G, Preiser JC, et al. Intravenous nicardipine in the treatment of postoperative arterial hypertension. *J Cardiothor Vasc Anesth* 1997; 11: 160–4.
52. Murphy MB, Murray C, Shorten GD. Fenoldopam: A selective peripheral dopamine-receptor agonist for the treatment of severe hypertension. *N Eng J Med* 2001; 345: 1548–57.
53. Shusterman NH, Elliott WJ, White WB. Fenoldopam, but not nitroprusside, improves renal function in severely hypertensive patients with impaired renal function. *Am J Med* 1993; 95: 161–8.
54. Elliott WJ, Weber RR, Nelson KS, et al. Renal and hemodynamic effects of intravenous fenoldopam versus nitroprusside in severe hypertension. *Circulation* 1990; 81: 970–7.
55. White WB, Halley SE. Comparative renal effects of intravenous administration of fenoldopam mesylate and sodium nitroprusside in patients with severe hypertension. *Arch Int Med* 1989; 149: 870–4.
56. Bednarczyk EM, White WB, Munger MA, et al. Comparative acute blood pressure reduction from intravenous fenoldopam mesylate versus sodium nitroprusside in severe systemic hypertension. *Am J Cardiol* 1989; 63: 993–6.
57. Munger MA, Rutherford WE, Anderson L, et al. Assessment of intravenous fenoldopam mesylate in the management of severe systemic hypertension. *Crit Care Med* 1990; 18: 502–4.
58. Tumlin JA, Dunbar LM, Oparil S, et al. Fenoldopam, a dopamine agonist, for hypertensive emergency: A multicenter randomized trial. Fenoldopam Study Group. *Acad Emerg Med* 2000; 7: 653–62.
59. Grossman E, Messerli FH, Grodzicki T, et al. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? *JAMA* 1996; 276: 1328–31.
60. Zampaglione B, Pascale C, Marchisio M, et al. Hypertensive urgencies and emergencies. Prevalence and clinical presentation. *Hypertension* 1996; 27: 144–7.
61. Perez MI, Musini VM. Pharmacological interventions for hypertensive emergencies: a Cochrane systematic review. *J Human Hypertens* 2008; 22: 596–607.
62. Strandgaard S, Paulson OB. Cerebral blood flow and its pathophysiology in hypertension. *Am J Hypertens* 1989; 2: 486–92.
63. Vaughan CJ, Delanty N. Hypertensive emergencies. *Lancet* 2000; 356: 411–17.
64. Ahmed N, Nasman P, Wahlgren NG. Effect of intravenous nimodipine on blood pressure and outcome after acute stroke. *Stroke J Cereb Circ* 2000; 31: 1250–5.
65. Semplicini A, Maresca A, Boscolo G, et al. Hypertension in acute ischemic stroke: A compensatory mechanism or an additional damaging factor? *Arch Int Med* 2003; 163: 211–16.
66. Castillo J, Leira R, Garcia MM, et al. Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. *Stroke J Cereb Circ* 2004; 35: 520–6.
67. Adams HP Jr., del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: A guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke J Cereb Circ* 2007; 38: 1655–711.
68. Qureshi AI, Harris-Lane P, Kirmani JF, et al. Treatment of acute hypertension in patients with intracerebral hemorrhage using American Heart Association guidelines. *Crit Care Med* 2006; 34: 1975–80.
69. Broderick J, Connolly S, Feldmann E, et al. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: A guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group. *Stroke J Cereb Circ* 2007; 38: 2001–23.
70. Elkayam U, Janmohamed M, Habib M, et al. Vasodilators in the management of acute heart failure. *Crit Care Med* 2008; 36(1 Suppl): S95–S105.
71. Ince H, Nienaber CA. Diagnosis and management of patients with aortic dissection. *Heart (Br Card Soc)* 2007; 93: 266–70.
72. Nienaber CA, Eagle KA. Aortic dissection: New frontiers in diagnosis and management: Part I: From etiology to diagnostic strategies. *Circulation* 2003; 108: 628–35.
73. Nienaber CA, Eagle KA. Aortic dissection: New frontiers in diagnosis and management: Part II: Therapeutic management and follow-up. *Circulation* 2003; 108: 772–78.
74. Kieler-Jensen N, Houltz E, Milocco I, et al. Central hemodynamics and right ventricular function after coronary artery bypass surgery. A comparison of prostacyclin, sodium nitroprusside, and nitroglycerin for treatment of postcardiac surgical hypertension. *J Cardiothor Vasc Anesth* 1993; 7: 555–9.
75. Leslie J, Brister N, Levy JH, et al. Treatment of postoperative hypertension after coronary artery bypass surgery. Double-blind

- comparison of intravenous isradipine and sodium nitroprusside. *Circulation* 1994; 90: II256–61.
76. Parviainen I, Ruokonen E, Takala J. Sodium nitroprusside after cardiac surgery: Systemic and splanchnic blood flow and oxygen transport. *Acta Anaesthesiol Scand* 1996; 40: 606–11.
77. Powroznik AV, Vuylsteke A, Naughton C, et al. Comparison of clevidipine with sodium nitroprusside in the control of blood pressure after coronary artery surgery. *Eur J Anaesthesiol* 2003; 20: 697–703.
78. Chauvin M, Deriaz H, Viars P. Continuous i.v. infusion of labetalol for postoperative hypertension. Haemodynamic effects and plasma kinetics. *Br J Anaesth* 1987; 59: 1250–6.
79. Leslie JB, Kalayjian RW, Sirgo MA, et al. Intravenous labetalol for treatment of postoperative hypertension. *Anesthesiology* 1987; 67: 413–16.
80. Cosentino F, Vidt DG, Orlowski JP, et al. The safety of cumulative doses of labetalol in perioperative hypertension. *Cleve Clin J Med* 1989; 56: 371–6.
81. Orlowski JP, Vidt DG, Walker S, et al. The hemodynamic effects of intravenous labetalol for postoperative hypertension. *Cleve Clin J Med* 1989; 56: 29–34.
82. Halpern NA, Sladen RN, Goldberg JS, et al. Nicardipine infusion for postoperative hypertension after surgery of the head and neck. *Crit Care Med* 1990; 18: 950–5.
83. Goldberg ME, Cantillo J, Nemiroff MS, et al. Fenoldopam infusion for the treatment of postoperative hypertension. *J Clin Anesth* 1993; 5: 386–91.
84. Gombotz H, Plaza J, Mahla E, et al. DA1-receptor stimulation by fenoldopam in the treatment of postcardiac surgical hypertension. *Acta Anaesthesiol Scand* 1998; 42: 834–40.
85. Varon J. Diagnosis and management of labile blood pressure during acute cerebrovascular accidents and other hypertensive crises. *Am J Emerg Med* 2007; 25: 949–59.
86. Sladen RN, Klamerus KJ, Swafford MW, et al. Labetalol for the control of elevated blood pressure following coronary artery bypass grafting. *J Cardiothorac Anesth* 1990; 4: 210–21.

Appendix

Evidence-Based Injury Prevention Summary		
Question	Answer	Grade
What is the estimated number of lives saved by the implementation of primary safety belt laws in the United States?	Evidence supports the benefit of primary belt laws in reducing injuries and fatalities.	A
What evidence exists on the effectiveness of SBI for alcohol problems for reducing subsequent injury among emergency room patients?	Evidence supports SBI to reduce short-term recidivism, but additional research on long-term effects is needed.	A
What are the applications of preventive medicine to the control of domestic violence?	Screening programs increase victim identification; however, evidence on intervention effectiveness is limited.	B
What is the evidence for the effectiveness of clinician counseling regarding firearm safety?	Evaluation of gun safety programs in primary care settings have resulted in inconsistent outcomes.	B
What is the effectiveness of injury prevention counseling delivered by a health care provider in improving safety practices among pediatric patients?	There is sufficient evidence to suggest that injury prevention counseling improves safety practices among the pediatric population.	A

Summary of Evidence on Aspects of Trauma Systems and Corresponding Recommendations			
Question	Statement	Evidence	Recommendation
Can surgeons play an important role in public health?	Surgeons have a important role in public health	IIa	B
Can trauma systems prevent injury?	Trauma systems prevent injury recidivism associated with alcohol abuse	IIb	A
	Trauma system implementation has been associated with reductions in mortality from motor vehicle crashes	IIc	B
	Trauma systems should play a more active role in injury prevention	IIc	B
Once a severe injury occurs, how long do we have?	Prompt intervention after major trauma is a first principle of trauma systems	V	D
Prehospital care: Scoop and run or stay and play?	Prehospital intubation in traumatic brain injury should be selective and attempted with care when necessary	IIb	B
	Prehospital fluid resuscitation should be limited in patients with penetrating mechanisms in urban environments	1b	B
	Scene time and interventions in trauma should be minimized if possible until more is known about the effects of specific interventions	IIa	B
	Local analyses should be done to determine trauma center catchments that may be more rapidly served by air medical transport	IIb	B
Are trauma centers accessible?	Trauma systems must be made more accessible in rural environments, where injury severity adjusted mortality is high	IIc	B
Do trauma systems save lives?	Trauma systems increase survival	IIc	B
What features of trauma systems make a difference?	Specific structural and process factors influence trauma system performance	IIb	—
	Trauma center volume influences outcome	IIc	B
	Trauma center designation influences outcome	IIc	B
What are the long-term outcomes of trauma systems?	Further optimization or trauma system performance will depend on the collection and analysis of data on injury-related disability	IIb	—
Can trauma systems help build safer societies, and at what cost?	A systematic approach to trauma care improves survival	IIa	B
	Inclusive trauma systems improve survival	IIc	B
	Inclusive trauma systems may improve survival in mass casualty and multicaseualty situations	Needed	
	Trauma systems are cost-effective	IIb	B
Can trauma systems save lives in low-resource settings?	Trauma systems have the potential to reduce morbidity and mortality in low-income settings	Needed	

Clinical Questions			
Question	Answer	Level	Grade of recommendation
Can the principles of EBM be used to assess trauma outcomes?	Yes	I II III	B
Can application of the concepts of EBM actually improve outcome?	Yes	I II III	B
Can application of the concepts of EBM be applied to specifically improve trauma outcome?	Yes	I II III	B

Clinical Questions		
Issue	Recommendation	Strength of recommendation
What is the role of a trauma system in combat injury outcomes?	Trauma systems are responsible for improvements in outcome after combat injury and should be a key element of the battlefield medical system.	C
What are the impact damage control measures on the morbidity and mortality of combat injury?	1. Damage control resuscitation should be considered for combat injury requiring massive transfusion.	B
	2. Damage control surgery techniques, including extraabdominal procedures, should be entertained for severe battlefield injury with unstable physiology.	C
	3. The indication for resuscitative thoracotomy should be considered in all patients in extremis, excluding isolated brain injury.	B
What are the contemporary techniques and outcomes of colon surgery performed on the battlefield?	Colon diversion should be performed in patients with high-energy colon injury patients that would not tolerate complications.	C
What are the contemporary techniques and outcomes of vascular surgery performed on the battlefield?	1. Damage control techniques, including shunting, should be utilized to optimize revascularization outcomes.	B
	2. In the combat environment, arterial reconstruction should be performed with autogenous material.	B
	3. In the context of battlefield venous injury, venous ligation is safe and effective option for the management of venous vascular injury.	B
	4. Proximity extremity injury should be evaluated by angiography to mitigate the risk of occult vascular injury.	B
What are the contemporary techniques and outcomes of burn surgery performed on the battlefield?	Burn casualties should be resuscitated based on urine output.	B

Clinical Questions		
Question	Answer	Grade
What are the LeFort fractures?	To ensure a positive outcome, a strong degree of suspicion based on mechanism of injury is mandated.	B
How would you secure the airway after a penetrating injury to the airway?	Avoid blind nasal intubation in facial trauma. Early oral intubation or tracheostomy.	B
Define neck injuries	Penetrating injuries are usually described according to the entrance site as one of three zones of the neck. An additional classification system divides the neck into anterolateral or posterior portions, divided by the sternocleidomastoid muscle.	B
How do you evaluate and diagnose penetrating neck injuries?	Following brief training (e.g., the Advanced Trauma Life Support course) physicians are capable of performing emergency cricothyroidotomy in the field with a high success rate and minimal complications, regardless of medical specialty.	B
What is the optimal management of the airway in someone with penetrating neck injury?	Concomitant cervical spine injury should not delay appropriate and timely treatment of facial fractures because adequate means of intraoperative stabilization are readily available. LMA have been shown to be effective in the management of difficult airway.	B

Clinical Questions		
Question	Answer	Grade of recommendation
Are HR and BP adequate indicators of shock?	Trauma patients who have suffered significant blood loss may present in compensated shock with normal vital signs, therefore, HR and BP are not adequate indicators of shock.	B
Is there a biochemical parameter that best identifies shock and guides resuscitation?	Serum lactate, arterial base deficit, arterial pH, and bicarbonate can help identify occult hypoperfusion. Lactate may be the best biochemical parameter to follow over time. Therapy aimed at normalizing a biochemical parameter as a single endpoint of resuscitation has not been studied prospectively.	B
Does hemodynamic monitoring with a pulmonary artery catheter improve outcomes?	The use of pulmonary artery catheters does not improve outcomes. Pulmonary artery catheters may offer a benefit in severely injured patients or elderly trauma patients.	A C
Do local tissue perfusion measures improve our ability to diagnose shock? Does their use improve outcomes?	There is no evidence that using local tissue perfusion as a guide for therapy improves outcomes.	A
Should the geriatric trauma patient have more invasive monitoring?	Elderly patients with severe injuries may benefit from invasive hemodynamic monitoring.	C
<i>Abbreviations:</i> BP, blood pressure; HR, heart rate.		

Questions Summary		
Question	Answer	Grade of recommendation
What type of fluid should be used for acute resuscitation of the trauma patient?	Isotonic crystalloid	A
How does one determine whether a traumatized patient requires fluid resuscitation?	Blood pressure less than 110 mmHg on presentation	C
What are the endpoints for termination of fluid resuscitation?	Clinical judgment	B
Does the concept of hypotensive (delayed) resuscitation have a role in trauma care?	Yes	A
Should blood or blood products be used as an initial resuscitation fluid, when available?	No	C
Do vasoactive drugs play a role in early resuscitation of the trauma patient?	No	C

Summary of Clinical Questions		
Question	Answer	Grade of recommendation
1 What is the role of FAST in the initial assessment of hemodynamically stable blunt trauma patients?	As a result of its low sensitivity and negative predictive value for intraperitoneal free fluid and intra-abdominal injuries, FAST should not be used as the only diagnostic modality to exclude significant intra-abdominal injury in the initial assessment of the blunt trauma patient.	B
	Patients with suspected intra-abdominal injury should undergo clinical observation or further investigation, irrespective of the ultrasound findings.	B
2 What is the role of FAST in the initial assessment of hemodynamically unstable blunt trauma patients?	FAST is specific and has a high positive predictive value for the presence of hemoperitoneum.	B
	A positive FAST warrants laparotomy in hemodynamically unstable patients.	B
	Hemodynamically unstable patients with a negative FAST may benefit from diagnostic peritoneal aspirate to rule out an intra-abdominal source of bleeding.	C
3 What is the role of ultrasound in the initial assessment of penetrating trauma patients: cardiac view and abdominal view?	Ultrasound should be the initial diagnostic modality for patients with penetrating precordial wounds.	A
	A positive ultrasound for fluid in the pericardial sac warrants immediate surgical intervention.	B
	The FAST is not a reliable imaging modality in penetrating trauma for ruling out significant intra-abdominal injury.	B
	Patients with penetrating injuries to the abdomen with a negative FAST require further investigation.	C
4 What is the current evidence to support the use of US for the diagnosis of pneumothorax in the resuscitation area?	Ultrasound is as or more sensitive than plain chest radiography and can be utilized to diagnose pneumothorax in injured patients.	A
5 Routine AP pelvis plain radiographs: are these mandatory?	Clinical assessment is sensitive for the identification of significant pelvic fractures in hemodynamically stable, evaluable trauma patients and routine pelvic plain films are unnecessary in this population.	B
6 What is the role of CT angiography in peripheral vascular injuries?	Multidetector helical CT angiography is sensitive for the identification of peripheral vascular injuries and can be used as the initial diagnostic modality for the assessment of suspected vascular injuries in the extremities.	B
Abbreviations: AP, ATLS protocol; CT, computed tomography; FAST, focused abdominal sonography for trauma; US, ultrasonography.		

Question Summary		
Question	Answer	Grade
Does a damage control approach improve mortality?	The application of damage control techniques does appear to have decreased mortality rates, although the absolute mortality reduction is difficult to quantify, due to improvements in critical care and resuscitation.	C
How do we preoperatively identify the damage control patient?	A damage control approach should be taken with any patient in the ED who has any of the following characteristics: 1. An RTS ≤ 5 2. Patients who require $\geq 2,000$ ml of crystalloids for resuscitation in the ED 3. Patients who require ≥ 2 units of PRBCs for resuscitation in the ED 3. Patients who have a pH ≤ 7.2	C
How do we intraoperatively identify the damage control patient?	In the operating room, a damage control technique should be employed when and if the following criteria apply: Patients who require $\geq 4,000$ ml of PRBCs for their resuscitation Patients who have had an ED or OR thoracotomy Patients who have a pH ≤ 7.2 Patients who have a temperature of $\leq 34^{\circ}\text{C}$ If the patient has an inaccessible major venous injury If the surgeon cannot achieve hemostasis owing to a recalcitrant coagulopathy If the definitive operative repair is a time-consuming procedure in the patient with suboptimal response to resuscitation If the patient requires the management of an extra-abdominal life-threatening injury If the patient will require a reassessment of intra-abdominal contents If the surgeon cannot reapproximate the abdominal fascia due to splanchnic reperfusion-induced visceral edema.	D
When should we terminate an initial damage control operation?	Damage control operations should be rapidly terminated, and the patient should be transferred to the intensive care unit, when the patient meets any of the following criteria: Core temperature $\leq 34^{\circ}\text{C}$ pH ≤ 7.2 PT $\geq$ twice normal PTT $\geq$ twice normal	B
What is the best method to temporarily close the abdomen that prevents long-term morbidity?	Temporary closure of the open abdomen is best accomplished with a combination of a vacuum type device and a fascial tensioning system. Abdominal closure is best accomplished by hospital day 8 to reduce morbidity.	C
What is the morbidity rate from a damage control approach?	Expected complication rate from damage control ranges from 25% to 40% of patients, with the most common complications being intra-abdominal abscesses and enterocutaneous fistulae. Methods to avoid these complications are unclear from the literature.	C
Abbreviations: ED, emergency department; OR, operating room; PRBCs, packed red blood cells; PT, prothrombin time; PTT, partial thromboplastin time; RTS.		

Clinical Questions		
Question	Answer	Grade of recommendation
Do massive transfusion protocols work?	Protocols improve blood product utilization and outcomes	B
Is there an ideal FFP:PRBCs ratio for administration of FFP?	Early empiric use of FFP at ratios of 1:1 or 1:2 are beneficial	B
Is there a role for whole blood transfusion in trauma?	Whole blood transfusion may be life-saving in austere settings	C
Is factor VIIa a useful adjunct to massive transfusion in trauma?	The role of rFVIIa remains not well defined. The largest PRCT on the topic has been closed due to futility. Until the full report from this study is release, the off-label use of this adjunct for trauma should be considered carefully	B
What is the best tool to determine coagulopathy associated with trauma and guide therapy?	No Level I, II, or III evidence exists. Traditional laboratory parameters remain standard. Thromboelastography use is under investigation	C
Abbreviations: FFP, fresh frozen plasma; PRBCs, packed red blood cells; PRCT, prospective randomized control trial; rFVIIa, recombinant factor VIIa.		

Clinical Questions		
Question	Answer	Grade of recommendation
Do evidence-based guidelines improve outcome?	Yes, outcomes and mortality may be improved.	B
Does repeat head CT determine the need for intervention?	Only patients with deteriorating exam or severe injury require repeat CT.	B
Does progesterone improve outcome?	Yes, it improves both mortality and functional outcome.	A
When and how should DVT prophylaxis be utilized?	LMWH, VCF, and SCDs are all effective in TBI patients. Timing of LMWH is unknown.	B
Is seizure prophylaxis beneficial?	Yes, up to 7 days after TBI. It is not beneficial after 7 days.	B
What is the optimal transfusion trigger?	Transfusion triggers should be the same as other ICU patients.	C
Abbreviations: CT, computed tomography; DVT, deep vein thrombosis; ICU, intensive care unit; LMWH, low molecular weight heparin; SCD, sequential compression device; TBI, traumatic brain injury; VCF: vena cava filter.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the impact of airway maneuvers on cervical spine movement?	Relative segmental spine movement might happen, and can be minimized with in-line immobilization	B
What is the preferred way to achieve tracheal intubation in patients with suspected CSI?	Both direct oral and fiber optic awaked nasotracheal intubation are safe and effective. Oral intubation is preferred in emergency situations	B C
What criteria should be used to clear the cervical spine in a trauma patient?	The Nexus or the Canadian c-spine criteria can be used for clinical clearance of the spine	B
What is the imaging modality of choice for evaluation of the spine?	CT	B
Should high-dose corticosteroids be used in trauma patients with SCI?	No	B
What is the optimal timing to operate a patient with spinal injury?	No advantage for early operation except for decompression in evolving neurological deterioration	D
Abbreviations: CSI, cervical spinal cord injury; CT: computed tomography; SCI, spinal cord injury.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the proper method and timing of closing and caring for facial lacerations and injuries after closure?	Repair should be performed within 6 hours with either absorbable or nonabsorbable sutures. Postoperative care with polyurethane dressing and botulinum toxin improve outcome.	A
What is the proper timing of repair of facial fractures, especially in the setting of neurologic trauma/other injuries?	Early repair in the neurologically stable patient appear to outweigh any possible issues related to delay.	B
Are antibiotics indicated in the management of facial lacerations or facial fractures and if so, when?	Prophylactic antibiotics in nonbite wounds is not necessary. In fractures, perioperative antibiotic use reduces the incidence of infection. Postoperative antibiotic do not seem to reduce infection rate.	A
Which treatment is better for mandible fractures: closed or open reductions?	Performance of open reduction and internal fixation with appropriate size fixation is critical in the development of the best possible result and patient outcome.	A

Question Summary for Ocular Trauma		
Question	Answer	Grade
Do steroids or orbital surgery improve visual outcomes in traumatic optic neuropathy?	Retrospective case series do not support the use of steroids or orbital surgery.	C
Does enucleation have a role in the prevention or treatment of sympathetic ophthalmia?	Case series do not support the use of enucleation solely to prevent or treat SO.	C
Does patching speed resolution of simple corneal abrasions?	Several randomized clinical trials showed no benefit from patching.	A
Do topical NSAIDs provide pain control in simple corneal abrasions?	Topical NSAIDs reduce pain without affecting time to heal.	A
What medications prevent rebleeds in traumatic hyphemas?	Steroids and antifibrinolytics decrease rebleeds.	A
When is surgical intervention indicated after traumatic hyphema?	In non-sickle cell patients, 60 mmHg for 2 days, any corneal blood staining.	D
Do prophylactic intravitreal antibiotics reduce post-traumatic endophthalmitis?	In cases of intraocular foreign bodies.	B
Can CT accurately detect clinically occult ruptured globes?	No, but certain findings may heighten clinical suspicion.	B
Abbreviations: CT, computed tomography; NSAIDs, nonsteroidal anti-inflammatory drugs; SO, sympathetic ophthalmia.		

Summary of Key Questions and Answers		
Question	Answer	Grade
Is physical exam adequate to rule out significant aerodigestive or vascular injury in penetrating trauma?	Physical exam is adequate to rule out significant airway and vascular injuries. Caution is required when ruling out a digestive tract injury based on physical exam, and observation may be warranted.	B
Are both esophagoscopy and fluoroscopic studies required to rule out esophageal injuries?	Contrast esophagography, if completely negative, may effectively rule out an esophageal injury; however, esophagoscopy should be added in those cases that the esophagography is equivocal.	C
How reliable is CT scan for ruling out a vascular or aerodigestive tract injury?	16-slice CT scan can accurately identify vascular injuries and trajectory of bullets.	B
	Reformatted images are helpful in detecting tracheobronchial injuries.	C
	CT scan cannot be used to rule out an esophageal injury.	C
Can color flow Doppler rule out a vascular injury?	Duplex ultrasound may be used to rule out an arterial injury in Zone II, however is limited in Zones I or III.	C
What are the risk factors for BCVI?	Cervical spine fractures, carotid canal fractures, seat belt sign, unilateral neurologic deficits, near hanging, LeFort II or III	C
Is selective exploration safe for penetrating neck trauma?	Mandatory exploration and selective explorations have equivalent outcomes.	C
How should BCVI injuries be treated?	Systemic anticoagulation with either IV heparin (PTT 40–50 s) or antiplatelet therapy decreases stroke rate in Grades II, III, IV injuries.	C
Abbreviations: BCVI, blunt carotid/vertebral arterial injury; CT, computed tomography; PTT, partial thromboplastin time.		

Clinical Questions		
Question	Answer	Grade of recommendation
Duration of prehospital CPR for penetrating thoracic injuries after which EDT futile?	According to retrospective data, EDT after more than 15 minutes of prehospital CPR is futile.	C
Should EDT be performed after blunt mechanism of injury in patients requiring prehospital CPR?	Limiting EDT use to patients with penetrating injuries results in better survival rates.	C
Is EDT effective at reducing mortality in patients with extrathoracic injuries?	EDT may facilitate salvage in a very select group of agonal patients with vascular injuries to the abdomen, neck, or extremities.	C
Do protocolized approaches to the performance of EDT influence outcomes?	A protocol confining EDT use to penetrating injuries with signs of life may improve survival rates.	C
Should the pericardium be opened in all cases of emergency thoracotomy?	Pericardiotomy should be performed following penetrating thoracic injury for evacuation of tamponade, direct control of cardiac hemorrhage, and optimal delivery of cardiac compressions.	C
Abbreviations: CPR, cardiopulmonary resuscitation; EDT, emergency department thoracotomy.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the best imaging modality for lung injury?	Although no Level I data exists, chest x-ray remains the initial imaging modality of choice. CT has the greatest sensitivity and specificity for detection of commonly encountered injuries.	C
What is the optimal method for pain control in patients with chest wall trauma?	Thoracic epidural use should be strongly considered in patients with thoracic pain refractory to narcotic-based regimens	B
What is the optimal initial method for control of lung hemorrhage?	No significant level of evidence exists. Familiarity with various techniques is advised.	D
What is the most efficient ventilatory weaning modality after acute lung injury?	Pressure supported or T-tube spontaneous breathing trials are superior to synchronized mechanical ventilation weaning.	A
What is the optimal method of resolving persistent air leaks?	There is an absence of Level I data. The role of VATS has not yet been validated.	D
What is the optimal management of retained hemothorax?	Early VATS may decrease hospital stay and cost. Further examination of VATS and pleural fibrinolytics in the post-traumatic setting is needed.	B
Abbreviations: CT, computed tomography; VATS, video-assisted thoracoscopic surgery.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the ultimate imaging modality for diagnosing blunt thoracic aortic injury?	Angiography is the ultimate modality for making the diagnosis of blunt thoracic aortic injury.	B
What modality should be used to follow minimal aortic injuries from blunt trauma?	TEE appears to be a good modality in following minimal aortic injuries.	B
What medications should we use in the medical management of MAIs and how long should patients be required to take these medications?	Beta-blockade and intravenous vasodilator therapy should be used for the medical management of MAIs. There is no study answering the question as to how long these medications should be used.	B
When is nonoperative management to be considered?	MAIs can be managed nonoperatively with specific medical treatment protocols to control heart rate and blood pressure. Similarly, patients who are poor operative candidates can have their injuries managed nonoperatively with treatment protocols (beta-blockade and intravenous vasodilator). Patients who are initially managed nonoperatively because of concerns of concomitant injuries and whose follow-up studies reveal resolution of the aortic injury can continued to be managed nonoperatively on beta-blockade and intravenous vasodilator.	B
What is the target blood pressure to maintain when nonoperative management or delayed surgical therapy is considered?	Controlling the heart rate and blood pressure (systolic between 100 and 120 mmHg) using beta-blockade and intravenous vasodilator is effective in preventing rupture of blunt thoracic aortic injury.	B
Which operative technique should be used for repair of descending thoracic aortic injuries? Is any technique superior?	Some form of distal perfusion should be used because neurologic complications seem to correlate with ischemia time.	B
Are endovascular stent procedures superior to open vascular procedures?	Endovascular stent grafts are associated with lower mortality, fewer postoperative neurologic complications including paraplegia, and fewer systemic complications than open procedures.	B
Abbreviations: MAI, minimal aortic injury; TEE, transesophageal echocardiography.		

Cardiac Trauma Question Summary		
Question	Answer	Grade
How do you rule out a significant blunt cardiac injury?	The combination of repeated normal cTnI levels with a normal ECG	C+
Who should and should not get a continuous ECG monitoring, and for how long?	Young (<40–50 years) asymptomatic stable patients with a normal ECG do not need further monitoring	C+
Which patients with suspected blunt cardiac injury should undergo echocardiography?	Unstable patients and patients with high suspicion of complications should be subjected to echocardiography dependent on the questionable need for urgent surgery	C
Is there a role for pericardiocentesis in penetrating cardiac trauma?	There is not enough data to support the usage of pericardiocentesis in patients with penetrating cardiac injury	C
How do you manage a foreign body in the heart?	The management of foreign bodies in the heart should be conservative unless the patient has signs of complications	C
Must one use pledgets when suturing the heart?	There is not enough data to show that pledgets must be used in every cardiac trauma surgery	C
Abbreviations: cTnI, cardiac troponin I; ECG, electrocardiogram.		

Clinical Question Summary		
Question	Answer	Grade of recommendation
What are the most common symptoms and signs of tracheobronchial injury?	Respiratory distress and subcutaneous emphysema/crepitus	B
What is the best diagnostic test for tracheobronchial injury?	Bronchoscopy	C
Is there a role for nonoperative management of traumatic tracheobronchial injuries?	Yes in patients with small <2 cm tears and a benign clinical presentation	C
What are the most common symptoms and signs of esophageal injury?	Pain (neck, chest, or on swallowing) and crepitus on physical exam	B
What is the best initial diagnostic test for esophageal injury?	Esophagography or esophagoscopy	C
Is there a role for nonoperative management of traumatic esophageal injury?	Not enough evidence to recommend for traumatic injuries at this time	D

Clinical Questions			
Questions	Answers	Level of evidence	Grade of recommendation
What is the role of nonoperative management in penetrating spleen injury?	Very little. Has 93% failure rate.		No recommendation
Which patients are candidates for nonoperative management of blunt spleen injury, and who is likely to fail?	- Hemodynamically stable patient with reliable abdominal examination is standard.	IIA	B
	- SAE can augment nonoperative management.	IIA	B
	- Age should not exclude a patient from nonoperative management. Older patients' increased mortality is a function of their decreased overall reserve.	IIC	No recommendation
	- >2 units PRBCs greatly increase chance of nonoperative management failure.	IIA	B
	- Evidence of contrast extravasation or other vascular injury increases chance of failure.		B
Which patients are angiography candidates, and who fail embolization?	- SAE can improve nonoperative management in stable patients with CT scans showing	IIA	B
	1. Grade III–V injury	IIA	B
	2. Contrast extravasation		No recommendation
What radiologic studies should be obtained in patients with splenic injuries?	3. Concern for pseudo-aneurysm or arteriovenous fistula		
	- There are conflicting data concerning factors indicative of embolization failure.		
	- Patients should undergo FAST exam in trauma room.	IIA	B
	- Stable patients with blunt mechanism should undergo abdomen/pelvis CT scan.	IIA	B
	- Imaging has highest yield when clinical symptoms of failure are present.	IIA	B
	- There is conflicting evidence about inpatient imaging studies.		No recommendation
What are the steps to prevent OPSS?	- Outpatient imaging is of little use in asymptomatic patients.		B
	- Intact, functional spleen is best defense against OPSS,	IIA	B
	- Up-to-date immunization recommendations can be found on the CDC Web site,	IIA	B
	- Pneumococcus, meningococcus, and Hib vaccine should be given >14 days postsplenectomy, may not be feasible in trauma population,	IIA	B
When is it safe to resume activities after splenic injuries?	- Refer to APSA's 2000 recommendations	IC	B
	- Graduated return based on injury severity, both inpatient and outpatient		
	- Reimaging as outpatient unnecessary without clinical indicators		
How are patients with special circumstances managed nonoperatively?	- Pediatric patients should be managed according to AAPSA 2000 guidelines for splenic injuries.	IIA	B
	- Cirrhotics do much worse. Carries 50% overall mortality.		No recommendation
	- Anticoagulation administration has few data.		No recommendation
Abbreviations: APSA, American Pediatric Surgical Association; CDC, Centers for Disease Control and Prevention; CT, computed tomography; FAST, focused abdominal sonography for trauma; Hib, Haemophilus influenza B; OPSS, overwhelming postsplenectomy sepsis; PRBCs, packed red blood cells; SAE, splenic artery aneurysm.			

Clinical Questions		
Question	Answer	Grade of recommendation
What criteria best defined the optimal candidate for non operative management of hepatic trauma?	Hemodynamic stability regardless of CT findings or amount of hemoperitoneum.	B
Are serial CTs useful for follow-up?	No. Routine CT studies are not indicated.	C
When are drains indicated in hepatic trauma, and what kind should be used?	The systematic use of drainage of the biliary tract does not benefit hepatic trauma patients and T-tube choledocostomy increases the risk of intra-abdominal infection and mechanical complications. The use of open drainages is not warranted as they may increase the risk of intra-abdominal infection after surgical treatment of liver trauma.	B
Is CT useful in the assessment of GSW to the liver?	CT with IV contrast and in some cases with oral and rectal contrast discriminates stable GSW patients who do not need to be operated. NOM based on clinical evaluation and evolution, complemented with early IV contrast CT, can be implemented safely for abdominal solid organ injury secondary to GSW.	C
Is hepatic angio-embolization effective in controlling hemorrhage in liver trauma?	With a multidisciplinary approach, arterial embolization is safe and effective in the management of severe hepatic trauma and can be safely performed as an adjunct to the principles of damage control.	C
Abbreviations: CT, computed tomography; GSW, gunshot wound; NOM, nonoperative management.		

Levels of Evidence				
Question	Answer	Level of evidence	Grade of recommendation	
Anastomosis or ostomy after colon resection for trauma?	Anastomosis, except in selected patients	2A	B	
Is it safe to perform colon anastomosis after damage control laparotomy?	Yes, in selected patients	4	C	
Stapled or hand-sewn anastomosis after hollow viscus injury for trauma?	Either, although handsewn may be better in better in patients with edematous bowel	4	D	
Should the skin be closed after laparotomy for colon trauma?	No	1B	B	
How long should antibiotics be continued after repair of hollow viscus injury?	No more than 24 hours	1A	A	
Should presacral drains be used in the management of rectal trauma?	No, except in selected cases	2A	D	

Question summary		
Question	Answer	Grade of recommendation
What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in blunt trauma?	There is no single diagnostic modality of choice. The optimal approach is to use the cited studies in a sequential manner until the diagnosis has either been suspected to a degree where operative intervention is warranted or excluded beyond reasonable doubt.	C
What is the optimal diagnostic modality for the diagnosis of diaphragmatic injury in penetrating trauma?	In unstable patients, diagnosis is established at operation. In stable patients, obtain a chest x-ray and CT scan. If equivocal, proceed with laparoscopy or thoracoscopy.	C
What is a clinically useful classification system that guides operative management?	Diaphragmatic injuries are best classified as contusions requiring no intervention, lacerations that can be primarily repaired, avulsions that can be reattached, or associated with significant tissue loss where prosthetics have to be used for adequate repair.	D
What is the optimal approach to the operative management of diaphragmatic injuries?	In the acute phase, approach the injury abdominally. In the latent phase, use a thoracic approach. In the obstructive phase, use an abdominal approach for the left side; a combined approach for the right side is preferred.	C
What is the ideal suture material/prosthesis for repair of diaphragmatic injuries?	Nonabsorbable material applied as simple interrupted, continuous, or horizontal mattress sutures is appropriate. Prosthetics, possibly biologics, should be used when the defect cannot be closed primarily.	C
What are the differences in the approach to left versus right-sided injuries?	On the left side, repair all injuries irrespective of the mechanism. On the right, repair those due to blunt trauma and due to penetrating trauma only if large.	C
What are the consequences of missed injuries?	A wide spectrum of often dramatic consequences may result. These make early diagnosis and repair desirable.	C
Abbreviation: CT, computed tomography.		

Questions		
Question	Recommendation	Grade
1. Is serum amylase a reliable indicator of pancreatic injury?	No. Although the majority of patients with pancreatic injury will present with an elevated serum amylase, its specificity is unknown, and therefore it should not be used to diagnose pancreatic injury.	B
2. Is CT reliable in detecting pancreatic injuries? When should pancreatography be used?	CT is accurate in detecting abnormalities suggesting pancreatic injury. There is conflicting evidence as to its reliability in predicting ductal injury. There is insufficient evidence to recommend either routine or selective use of ERCP.	C
3. Is MRCP reliable for the evaluation of pancreatic injuries?	There is insufficient evidence to assess the reliability of MRCP in the evaluation of pancreatic injury.	N/A
4. Is NOM of adult blunt pancreatic injuries feasible?	NOM of hemodynamically stable adult patients with blunt pancreatic injuries lacking other associated injuries requiring laparotomy may succeed if there is no pancreatic duct injury. Endoscopic stenting of patients with known ductal injuries may avert surgical therapy in selected cases.	C
5. Is NOM of pediatric blunt pancreatic injuries feasible?	NOM of hemodynamically stable pediatric patients with blunt pancreatic injuries lacking other associated injuries requiring laparotomy is feasible, and is more likely to succeed if the pancreatic ductal status is normal. Selected patients with known ductal injuries may be managed nonoperatively.	B
6. Does octreotide lower the likelihood of developing a pancreatic fistula after surgery for pancreatic trauma?	There is insufficient evidence for or against the prophylactic use of octreotide to reduce postoperative pancreatic-related complications.	N/A
7. Is drainage alone a sufficient operative treatment for pancreatic ductal injuries?	Pancreatic ductal injuries except for those in the pancreatic head should be managed with resection rather than drainage.	C
8. Is CT reliable to diagnose duodenal perforation after blunt trauma? Is oral contrast necessary? Is fluoroscopic duodenography useful?	In patients with duodenal perforation, CT will reliably show a constellation of abnormalities. There is insufficient evidence to recommend the use of oral contrast or duodenography.	C
9. Does pyloric exclusion decrease the likelihood of a duodenal leak after primary repair of a duodenal perforation?	Pyloric exclusion does not decrease the likelihood of duodenal leak after primary repair of a duodenal perforation.	C
Abbreviations: CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; NOM, nonoperative management.		

Clinical Questions		
Question	Answer	Grade
Is color duplex doppler a good diagnostic tool for abdominal vascular trauma?	Not enough evidence	Not enough evidence
Is CTA a good diagnostic tool for abdominal vascular trauma?	Yes	B
Is MRA a good diagnostic tool for abdominal vascular trauma?	Not enough evidence	Not enough evidence
Is there a role for thoracotomy to control the aorta in abdominal vascular exsanguinations?	No for EDT; possible yes for prelaparotomy thoracotomy	C
Under what circumstances are interventional and endovascular techniques superior to open vascular repair?	Angioembolization for hemodynamically stable active bleed; stent indication not detailed in abdominal vascular trauma literature	C
Regarding optimal control of aorta, is there a role for intraoperative placement of an endovascular balloon?	Not enough evidence	Not applicable
Should SMV injuries be ligated or repaired?	Ligate hemodynamically unstable patients; repair hemodynamically stable patients	C
In difficult vascular repairs, should anticoagulation be used postoperatively? If so, for how long?	Not enough evidence	Not applicable
How should vascular repairs of large vessels be followed: ultrasonography or CT scan?	Extrapolate from vascular surgery literature	Not enough evidence
What are the outcomes of abdominal vascular surgery?	Mortality rate ranging from 39–54%	C
Abbreviations: CT, computed tomography; CTA, computed tomography angiography; EDT, emergency department thoracotomy; MRA, magnetic resonance angiography; SMV, superior mesenteric vein.		

Question Summary		
Question	Answer	Grade
What is appropriate time for fetal monitoring after trauma?	All pregnant trauma patients >20 weeks of gestation should have fetal monitoring for at least 6 hours.	C
Should KB test be performed in pregnant trauma patient?	KB test should be performed in all pregnant patients >12 weeks of gestation.	B
Should FAST be performed in every pregnant patient with suspected abdominal trauma?	FAST should be performed in every pregnant trauma patient with suspected intrabdominal injury.	C
Should diagnostic radiologic studies be withheld in pregnant trauma patient?	Radiologic studies necessary for maternal evaluation should not be withheld on the basis of its potential danger to the fetus. Unnecessary duplication of studies should be avoided, and appropriate mandatory shielding should be used whenever possible.	C
What is the role of CS section and when it should be performed?	Perimortem CS should be considered in moribund pregnant patient after 24 weeks of gestation. Delivery must occur in 20 minutes of maternal death, but should ideally begin within 4 minutes of maternal arrest.	C
Abbreviations: CS, cesarean section; FAST, focused abdominal sonography for trauma; KB, kleihauer-betke.		

Summary of Evidence and Recommendations			
Question	Answer	Level of evidence	Grade of recommendation
When is pelvic angiography and embolization indicated?	Contrast extravasation on CT. Hypotension with pelvic fracture and absence of extrapelvic injury.	IIb	B
Does extraperitoneal pelvic packing aid in hemostasis?	Probably, in selected cases	IV	C
Should rFVIIa be given routinely to facilitate hemostasis?	No, there is inadequate evidence to support routine use. Prophylactic use in the elective setting does not diminish blood loss.	IV IIb	D B
Is fecal diversion mandatory in all patients with open pelvic fractures?	No. Fecal diversion should be considered in patients with rectal or perineal wounds.	IIa	B
Is plain radiography of the pelvis necessary in all blunt trauma patients?	No. In stable patients undergoing CT scanning, plain pelvic x-ray adds little information.	IIIb	B
What is the optimal timing for operative pelvic fixation?	3–7 days postinjury	IIc	B
Abbreviation: CT, computed tomography.			

Summary of Clinical Scenarios and Evidence-Based Recommendations		
Question	Answer	Grade
Can a diagnosis of vascular injury be adequately made by physical exam supplemented with ABI?	Physical exam with ABI is more than 90% sensitive for the presence of vascular injury.	B
Is CTA adequate for diagnosis of vascular injury or is invasive angiography always required?	In centers with the technical expertise, CTA is comparable to conventional angiography.	B
Should knee dislocation still be treated as a special circumstance—is routine angiography necessary?	Routine investigation is not required following knee dislocation in the presence of a normal exam.	B
Is there a role for the nonoperative management of vascular injuries?	Minor abnormalities, e.g., intimal flaps, may be safely observed with a low risk of complications.	C
What is the role of endovascular treatment (stenting) in the management of acute vascular injuries?	Although stenting is technically feasible, there is insufficient evidence to recommend this approach due to the lack of long-term follow-up.	C
What role should intravascular shunting for damage control vascular surgery play in the management scheme for vascular injuries?	Evidence suggests that shunting may improve outcomes in damage control vascular surgery.	C
Should the ATLS recommendations for the use of tourniquets be revised?	There is insufficient evidence from civilian studies at this time to change the current ATLS recommendations.	D
Following repair of an acute vascular injury should fasciotomies be performed prophylactically or should we measure compartment pressures?	There is insufficient evidence to recommend either prophylactic fasciotomies in all patients or to recommend specific screening protocols.	C
Abbreviations: ABI, ankle-brachial index; ATLS, Advanced Trauma Life Support; CTA, computed tomography angiography.		

Clinical Questions		
Question	Answer	Strength
How are common soft tissue infections, such as human or animal bites, flexor tenosynovitis, and hand abscess, treated and are the current empiric antibiotic used based on clinical evidence?	Bacteriology of animals and humans are studied and general guidance is given regarding antibiotic coverage however this may miss a significant amount of organism.	B
When is it appropriate to operate on scaphoid fractures and what are the diagnostic techniques employed?	No significant improvement of operative treatment over nonoperative treatment but may have decreased time to return to work. No significant improvement of MRI over CT currently in the diagnosis of scaphoid fractures.	B
What are the indications for replantation of digits and extremities?	Large retrospective reviews confirming successful outcomes in 70–87% of patients	C
What are the indications for release of forearm compartment syndrome, hand compartment syndrome, and acute carpal tunnel syndrome?	Pressure within 20 mmHg of diastolic cause ischemic muscle necrosis, and success of treatment is both time and pressure dependent.	C
What are the current options to treat flexor and extensor tendon injuries?	Most hand surgeons would operate when laceration is >50% of flexor tendon. Early improved function with dynamic splinting up to 6 months, then no difference.	C
How are common fractures of the hand, such as phalanx fractures, boxer's fractures, bennett fractures, Rolando fractures, treated?	Closed reduction or open reduction of fractures may be attempted, the technique must be adjusted for the individual fracture with the goal of preservation of function through stabilizing an adequate reduction.	C
What do you do with a fingertip amputation that is too distal for replantation?	Defects smaller than 1 cm ² can be allowed to heal by secondary intent, otherwise, a composite graft or local flap can be used instead.	C
Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.		

Grade Recommendation		
Subject	Findings	Grade recommendation
How well do clinical findings aid in the diagnosis of CS of the lower extremity?	Clinical findings are poor predictors of compartmental for the diagnosis of lower extremity have to be defined.	C
Which compartmental pressure measurement method is optimal method for diagnosis of acute lower leg CS?	It is unclear what the value of optimal method of measuring compartmental syndrome.	C
The optimal method for screening and diagnosing CS.	No recommendation on this subject.	C
Is it safe to use tourniquets in major lower extremity trauma?	Tourniquet use appears indicated on the battlefield when required for hemorrhage control for limited time intervals. Civilian use of tourniquets is not generally recommended.	C
Is damage control justified for the orthopedic care of multiple trauma patients?	Damage control orthopedic is recommended in severely injured multiple trauma patients.	B
When should antibiotics be used in the setting of open lower extremity fracture?	No prophylactic antibiotics are required for open fractures resulting from low-velocity civilian gunshot wounds that do not require open reduction and internal fixation. In the setting of open extremity fractures, no more than 24 hours are required postoperatively.	B
What is the optimal time from injury to long bone fracture stabilization in the multiple trauma patient?	There is no difference in survival in polytrauma patients who undergo early or late long bone fracture stabilization. It is unclear whether timing of bone fracture stabilization impacts outcome in the setting of chest or brain injury.	C
What is the best method for prediction of amputation after severe lower extremity injuries?	There is no predictive scale that can be used with confidence to determine whether to amputate or attempt to salvage a mangled lower extremity. Scoring systems should be used only as guides to supplement the surgeon's clinical judgment and experience.	C
Abbreviation: CS, compartment syndrome.		

Summary of Recommendations			
Question	Answer	Level of evidence	Grade
Which management strategies improve ischemia and reperfusion injury following traumatic extremity injury?	1. Damage control techniques aid in limb salvage after life-threatening trauma.	IIIb	C
	2. Large vessel venous injuries should be repaired when feasible.	IIIb	C
	3. Temporary vascular shunts are safe and fewer amputations are performed in patients with severely mangled extremities.	IIb	B
Is there a difference in limb salvage strategies in the setting of upper versus lower extremity injury?	1. Limb salvage rate exceeds 90% in upper extremities, but poor functional outcomes	IV	D
	2. The rate of upper extremity amputation is higher in the setting of complex wartime injury.	IV	D
What prehospital adjuncts are available that impact limb salvage following traumatic extremity injury?	1. Tourniquets are life-saving when placed appropriately and do not adversely impact limb salvage.	IIb	B
	2. Hemostatic agents effectively control hemorrhage.	*	*
What contemporary strategies in skeletal reconstruction impact limb salvage following traumatic injury?	1. Definitive stabilization (intramedullary nail) within 24 hours of injury in stable patients.	Ib	A
	2. Early external fixation followed by intramedullary nail in unstable patients.	Ib	A
	3. Early antibiotic coverage continued for 3 days from time of injury.	Ib	A
How do advances in soft tissue wound management strategies impact limb salvage following traumatic injury?	1. Frequent and adequate debridement is a critical component of soft tissue wound closure.	IIb	B
	2. Negative-pressure wound therapy decreases infection rates and hastens time to wound closure.	IIIb	C
	3. Complex reconstruction of soft tissue defects should occur within 72 hours of injury and by experienced subspecialists.		
How do injury patterns impact decision making regarding extremity salvage?	1. Severe soft tissue injuries, nerve injuries and vascular injuries influence decision to amputate but no difference in functional outcome	Ib	A
	2. Limb salvage rates associated with wartime extremity injuries are comparable to that reported in civilian literature	IIIb	C
Which extremity severity scores predict limb salvage and functional outcome?	1. No scoring system accurately predicts limb salvage or functional outcome	Ib	A
What are the costs of reconstruction and quality of life?	1. There is no significant difference in functional outcome between limb salvage and amputation.	Ib	A
	2. Limb salvage is associated with more operations, longer recovery time, and more than twice the cost than amputation.	Ib	A

Clinical Questions and Recommendations		
Question	Answer	Recommendation grade
What is the optimal resuscitation method following severe burn?	Parkland or modified Brooke formula with isotonic crystalloid	C
How is burn depth best determined?	Laser Doppler imaging	B
When is the optimal time for burn wound excision?	First 48 hours after injury	B
How is blood loss best minimized during burn excision procedures?	Tourniquets, topical thrombin, and fibrin sealant	B
How is burn wound infection effectively minimised?	Early excision and grafting, topical antimicrobials	B
What is the best method of ventilation after smoke inhalation injury to minimize lung complications?	High-frequency percussive ventilation	C

Clinical Questions		
Question	Answer	Grade of recommendation
What substance is the most useful agent for fluid resuscitation in the patient with the acute burn and how should it be administered?	Crystalloid: Parkland formula	A
What, if any, are the indications for the use of the antibiotics in burn patients?	Systemic: none Topical: yes; silver sulfadiazene, mafenide	A
When and what form of initial debridement is necessary? What is the best method of burn wound excision?	Early excision and grafting (excluding inhalational injury)	A
What is the best choice of definitive treatment: Autograft? Allograft? Integra?	Autograft; select skin replacements depending on clinical indication	B
What is the best ancillary treatment to prevent scar contracture or keloids?	Silicone sheeting, pressure garments (15 mmHg)	B

Clinical Questions: Inhalation Injury		
Question	Answer	Recommendation grade
What are the indications for endotracheal intubation?	Early prophylactic airway control is indicated for most symptomatic patients with II and for patients with extensive burns during initial resuscitation.	C
What are the indications for tracheostomy?	Tracheostomy is an option for long-term airway management and may facilitate pulmonary toilet.	C
What diagnostic procedures should be performed?	A presumptive diagnosis can be made on clinical grounds, supplemented by fiber optic laryngoscopy. Definitive diagnosis requires bronchoscopy.	B
What mode of mechanical ventilation is most effective?	High-frequency percussive ventilation improves ventilation and oxygenation and may reduce pneumonia and mortality.	C
What IV fluid strategies improve outcome?	Avoid under- or over-resuscitation. II patients frequently require larger volumes for burn shock resuscitation, but no evidence supports initiation of resuscitation at higher infusion rates.	C
What drugs improve outcome?	Inhaled heparin may prevent obstructing clots and casts.	C
How is CO poisoning diagnosed?	Cooximetry (measurement of COHb and Methb levels) should be performed in patients with II.	D
What treatment is safe and effective for CO poisoning?	100% oxygen should be given to all patients with CO poisoning until the COHb is normal (<5%).	D
What is the role for HBOT?	HBOT is an option for patients with CO poisoning to prevent delayed neurocognitive syndrome.	C
What treatments are safe and effective for cyanide?	Hydroxocobalamin should be considered for patients with known or suspected cyanide poisoning.	C
Should II patients be transferred to a burn center?	Consultation with the regional burn center should be performed on admission.	D
Note: The reader is cautioned that, for example, recommendations concerning airway management, treatment of CO poisoning, and burn center referral are considered standard of care in the United States despite the cited levels of evidence. Abbreviations: CO, carbon monoxide; COHb, carboxyhemoglobin; HBOT, hyperbaric oxygen therapy; II, inhalation injury; Methb, methemoglobin.		

Evidence Based Data for Electrical, Cold and Thermal Injuries		
Question	Answer	Grade of recommendation
Do all patients with electrical injury require continuous cardiac monitoring?	Patients with high-voltage injuries or a history of loss of consciousness, arrhythmia, or abnormal electrocardiogram at admission require monitoring.	B
What are the key prompts for upper arm fasciotomy after electrical injury?	Neurovascular compromise, increased compartment pressures, and persistent myonecrosis are indications for decompression.	C
What is the most effective method of rewarming following cold injury?	Rewarming should wait until there is no further risk of freezing, and rate depends on severity of injury.	C
What role do thrombolytics play in salvaging tissues damaged by the cold?	Thrombolytics should be reserved for those with a poor response to rewarming and evidence of diminished perfusion.	C
What is the role of endoscopy in managing patients with caustic ingestion?	Endoscopy should be reserved for symptomatic patients or those attempting suicide.	C
Is there any role for exogenous agents to prevent esophageal stricture after caustic ingestion?	Data on steroids are mixed; other agents may be useful but require more study.	B

Clinical Questions in Wound Care Management		
Question	Answer	Grade of recommendation
Factors affecting wound healing?	Infection, hypoxemia, foreign body, radiation	B
Does preoperative smoking affect wound healing?	Yes, it increases risk of infection and ischemia	B
What is mechanism of accelerated wound healing in NPWT?	Decrease edema, increase blood flow, micromechanical forces, removal of effluent and bacteria	B
Does NPWT affect healing time or cost?	It appear to affect healing time, but no strong evidence for cost	B
How does acellular dermal replacement affect wounds in burn and reconstructive surgery?	Acellular dermal replacement decreases hypertrophic scars and contracture. It also reduces donor site morbidity.	B
Is HBO beneficial to ischemic or irradiated flaps?	Although intuitive, there is no convincing evidence that HBO improves survival of ischemic or irradiated flaps	C
What are effective treatments against keloid and hypertrophic scar?	Excision and intralesional triamcinolone injection. Radiation for refractory and selected cases.	B
Abbreviations: HBO, hyperbaric oxygen therapy; NPWT, negative-pressure wound therapy.		

Clinical Questions		
Question	Answer	Grade of recommendation
First aid after pit viper snakebite?	Extremity/patient immobilization and immediate transport to a medical facility.	C
Should snake antivenin be administered?	1. Early/immediate administration of antivenom for symptomatic snakebite victims. 2. Asymptomatic patients may undergo a trial of initial observation. 3. Minimally symptomatic patients who suffered a confirmed copperhead envenomation may not require antivenom.	B
What antivenin should be used for pit viper snakebite?	Crotalidae polyvalent immune Fab (ovine) (CroFab; FabAV)	B
What is the dosing regimen for FabAV?	Initial dosing of six vials, repeated until control of venom effects then maintenance with two vials at 6, 12, and 18 hours. Redosing with six vials if worsening occurs during this 24-hour observation period.	C
When is surgical debridement indicated and are fasciotomies still needed after pit viper snake envenomation?	Early surgical debridement has no role in the treatment of envenomation. Debridement of necrotic tissue may be required after medical therapy. Fasciotomy should be performed for documented elevations in compartment pressures refractory to antivenom and conservative therapy.	C
Should antibiotics be administered after pit viper snake envenomation?	No	A

Question Summary		
Question	Answer	Grade
Should tourniquets be used prehospital with exsanguinating extremity trauma?	Tourniquets are the most important prehospital life-saving maneuver for combat-injured patients.	B
What is the optimal work-up for abdominal, flank, and back fragmentation wounds from explosions?	CT scan should be used to evaluate for intraperitoneal penetration in hemodynamically stable patients.	C
Should hemostatic dressing be used on combat wounds?	Hemostatic agents, including HEMCON dressings, may provide additional benefit for hemostasis compared to cloth bandages.	C
How can large soft tissue injuries from explosions be treated?	After initial irrigation and debridement, Wound VAC negative-pressure dressings can be applied safely.	C
How should combat injured patients undergoing a massive blood transfusion be resuscitated?	FFP and PRBCs should be administered in a 1:1.4 ratio. This is clinically given as a simple 1:1 ratio.	B
How is a major vessel injury treated in an austere surgical environment?	Major vascular injuries are treated with a temporary shunt and fasciotomy prior to transfer to a higher level of care.	B
How can "over-resuscitation" be avoided in combat wounded undergoing global transport?	A simple burn flowsheet, documenting intravenous fluid rate and urine output can decrease over-resuscitation in burn patients	C
Abbreviations: CT, computed tomography; FFP, fresh frozen plasma; PRBCs, packed red blood cells.		

Question Summary		
Question	Answer	Grade
When is a CT scan of the head indicated in pediatric head trauma?	If one of the referenced decision tools are used. In general, if one of the following are present: GCS < 15, evidence of skull fracture, headache, vomiting, coagulopathy, or seizure.	B
Is there a role for hypertonic saline in pediatric head injury?	There is no evidence to support a reduction in mortality or even severe morbidity with hypertonic saline. There is limited evidence for its role in lowering refractory intracranial hypertension with limited side effects.	C
When is clinical clearance of the cervical spine appropriate in children?	If there is no neck pain, midline tenderness, neurological deficit, or painful distracting injury in a child older than seven. Not enough evidence in younger patients to support application of clinical clearance except in unusually mature children.	B
How should femur fractures be managed in children?	Excluding patients under five and those with very proximal or distal fractures, significant contamination, or gross comminution, intramedullary rod placement results in shorter recovery time at a cost comparable to other methods.	B
How should blunt pancreatic transection be managed in children?	There is insufficient evidence to support the superiority of early pancreatectomy or nonoperative management of pancreatic transection. The incidence of this injury is likely too low to permit a large, randomized controlled trial.	C
Abbreviations: CT, computed tomography; GCS, Glasgow Coma Score.		

Question Summary		
Question	Answer	Grade
Are there any patient characteristics or pre-morbid conditions that are known to increase mortality and/or require specialized treatment?	The current evidence points to worse outcomes for geriatric patients with preexisting chronic disease. There are no recommendations, however, for how this information can be used to improve care.	C
What is the impact on treatment and outcome for patients on warfarin?	Geriatric patients with warfarin use, elevated international normalized ratio, and intracranial hemorrhage have worse outcomes. Again, no interventions have been proven beneficial to reduce mortality in this cohort.	C
What is the impact on treatment and outcome for patients on beta-blockers, and when should they be used?	No specific recommendation can be made as to the use or timing of beta-blockers in the geriatric trauma patient. Further research is definitely needed.	C
What are the optimal triage guidelines for the geriatric trauma patient?	There is insufficient evidence to make any evidence-based conclusions on the optimal triage guidelines for the geriatric trauma patient. The current recommendations from the American College of Surgeons Committee on Trauma are similarly based and will remain the standard until better studies are performed.	D
What are the optimal strategies for resuscitation and monitoring of the geriatric trauma patient?	It appears that aggressive therapy and monitoring improves outcomes in a very select subset of geriatric trauma patients. Identifying these patients and the exact intervention remains in need of further high-quality studies.	B
Are there any injury-prevention programs that have been shown to work for geriatric patients?	Regular strength and balance exercises are effective at preventing falls and injuries in elderly people. Hip protectors can be considered in high-risk groups.	A
Are there any circumstances where withholding/withdrawing care is appropriate?	Current recommendations cannot be made at this time. The existing data, however, can be used to aide physicians in their conversations with patients and families about end-of-life decisions.	C

Rural Trauma Question Summary		
Question	Answer	Grade of support
Does mode of transportation impact mortality?	Unclear	D
Are mortality rates higher for patients injured in rural areas?	Yes	C; there is inconsistency
What are the roles of rural physicians?	Assess, resuscitate, perform initial stabilizing procedures	B
Has rural trauma system development impacted care?	Yes	B

Clinical Questions		
Question	Answer	Grade
Are there other agents and/or techniques that can be used to improve the duration of POI?	Minimally invasive surgical techniques, local epidural anesthetics, avoidance of NGT, and early enteric feedings.	A
Does chewing gum shorten the duration of POI?	Yes, chewing gum has been shown to decrease length of POI and LOS.	A
Does the use of selective opiate receptor inhibitors decrease duration of POI?	Yes, it has an impact of both the duration of POI, tolerance of solid diet, and LOS, but unclear on cost/benefit ratio.	A
Are there any techniques/agents that have been shown to decrease intra-abdominal adhesion formation following laparotomy?	Sharp dissection, minimizing tissue trauma, decreasing foreign bodies in surgical field, barrier devices.	A
What does the use of water-soluble contrast do?	Causes an osmosis of water into the bowel lumen and decreases edema of the bowel wall, which promotes proximal bowel distention and increases the pressure gradient across an obstructing region.	
Is the early use of water soluble contrast indicated in the diagnosis/management of SBO?	The use of water-soluble contrast has shown to predict the success of conservative management, but has not been shown to decrease the need for operation.	A
Can CT predict the need for operation in patients with incomplete SBO?	CT scan can diagnose SBO and SBO causing ischemia and the requirement for surgical intervention.	A
Is there any difference between stapled or handsewn techniques for bowel anastomosis?	There has been no difference shown between the two, however, stapled anastomoses have a higher rate of stricture.	A
Abbreviations: CT, computed tomography; LOS, length of stay; NGT, nasogastric tube; POI, postoperative ileus; SBO, small bowel obstruction.		

UGI Bleeds: Question Summary		
Question	Answer	Grade
What is the role of medical therapy in prevention of UGI bleeds?	PPI should be used as stress ulcer prophylaxis in critically ill patients. Risk of ulcer formation is significantly reduced with maintenance PPI or H2RA for patients who take NSAIDs regularly.	A A B
What is the role of medical therapy in treating active UGI bleeds?	Beta-blockers can be used safely for primary prophylaxis of variceal bleeding. PPI should be preferentially used over H2RAs to reduce bleeding episodes after successful endoscopy. Octreotide should be used to slow the rate of variceal bleeding until definitive endoscopy is performed.	A B
What is the role of endoscopy for treating or preventing UGI bleeds?	Endoscopy should be used as first-line treatment for actively bleeding ulcers as it provides additional prevention of rebleeding compared to medical therapy. Endoscopic banding ligation is the treatment of choice for acute variceal bleeding and should be undertaken as soon as possible. Banding ligation is effective for preventing variceal bleeding and should be used when medical prophylaxis cannot be tolerated.	A A B
What is the role for interventional radiology in treating UGI bleeds?	Angiography is safe and should be used in patients with massive UGI bleeding who are too ill to undergo an operation.	C
Abbreviations: H2RA, histamine-2 receptor antagonist; NSAIDs, nonsteroidal anti-inflammatory drugs; PPI, proton pump inhibitor; UGI, upper gastrointestinal.		

Clinical Questions		
Questions	Answers	Grade
How has the surgery of PUD changed over time?	The number of operations performed for PUD has declined by >80% over the past two decades. The most common indications are perforation and bleeding. Operations for intractability are rare. Patients are generally older, sicker, and more often female.	B
What are the major risk factors for PUD?	In Western countries, PUD is primarily caused by <i>Helicobacter pylori</i> infection and NSAID use. Idiopathic causes include ZES, G-cell hyperplasia, Crohn's disease, cocaine abuse, and systemic mastocytosis.	A
What is the appropriate therapy for <i>Helicobacter pylori</i> -positive PUD?	First-line therapy combines PPI + clarithromycin + amoxicillin or metronidazole and has a successful eradication rate of 78–90%. Rescue therapies are available for nonresponders.	A
How can the risk of PUD be minimized in patients requiring regular NSAID therapy?	If found, <i>H. pylori</i> should be eradicated before NSAID therapy is initiated. Misoprostol, PPI therapy, and double-dose H2RA therapy are all effective in reducing the risk of NSAID-induced GI complications.	A
In a patient suspected of having a bleeding peptic ulcer, what should the initial approach be?	A rapid and accurate diagnosis and aggressive resuscitation should proceed simultaneously in patients thought to be bleeding from an UGI source.	A
In patients with bleeding ulcers, what is the current role of endoscopy?	Endoscopy is the definitive diagnostic and prognostic study. It is also an effective therapeutic tool with initial hemostasis rates of 85–100%.	A
What is the role of pharmacotherapy in the management of a bleeding peptic ulcer?	When used as an adjunct to endoscopic therapy, PPIs reduce the risk of further bleeding and the need for surgery.	A
Under what circumstances is an operation indicated for a bleeding peptic ulcer?	Surgery is indicated for peptic ulcer hemorrhage that is not controlled by endoscopic therapy or recurs following apparently successful endoscopic therapy (5–20%).	A
What surgical techniques are associated with the lowest rate of UGI rebleeding?	When used for peptic ulcer bleeding, combined partial gastric resection and vagotomy is associated with the lowest recurrence rate. However, this approach also has a higher rate of short-term and long-term postoperative complications. Vagotomy with oversewing of the ulcer is effective when combined with anti- <i>H. pylori</i> therapy in <i>H. pylori</i> + patients.	A
What approach is preferred for the management of perforated PUD?	Nonoperative therapy can be used in selected patients who are found to have a sealed perforation on contrast study. Patch closure is indicated in most patients. <i>H. pylori</i> should be eradicated when infection is present. The laparoscopic approach is being used with increased frequency.	B
Abbreviations: GI, gastrointestinal; H2RA, histamine-2 receptor antagonist; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; PUD, peptic ulcer disease; UGI, upper gastrointestinal.		

Clinical Questions and Grades		
Question	Answer	Grade of recommendation
What factors predict mortality in ECF?	A model incorporating APACHE II scoring and serum albumin is highly accurate in predicting mortality.	A
Do VTACs increase the risk of fistula formation?	In trauma patients, probably not. In patients with abdominal sepsis, caution is advised until better studies are obtained.	C
What is the optimal nutritional strategy in ECF?	TPN not only can provide complete nutritional support to patients but may also increase rates of closure.	C
What is the role of somatostatin or octreotide in the management of ECF?	Enteral nutrition should be considered on a selective basis.	C
	Somatostatin and octreotide do not significantly increase the frequency of spontaneous ECF closure.	A
What is the optimal timing for elective surgical intervention for ECF?	Somatostatin may decrease both fistula output and time to spontaneous closure.	B
	Octreotide is inconsistently demonstrated to decrease fistula output.	D
	Avoid elective surgery until at least six weeks, preferably several months, after diagnosis, and only after stabilization of nutritional status and resolution of sepsis.	D
Is surgical closure of the fistula best accomplished by resectional or nonresectional approaches?	Resection of the involved segment of bowel is preferred when possible.	C
Abbreviations: ECF, enterocutaneous fistula; TPN, total parenteral nutrition; VTAC, vacuum-based temporary abdominal closure.		

Clinical Questions		
Question	Answer	Grade of recommendation
Should all PEHs be repaired?	Yes	B and C
Surgical repair of asymptomatic PEH in high-risk or elderly patient?	Yes No	B and C B
What is the natural history of PEHs?	—	—
What is the recurrence rate of surgically repaired PEH?	0–42%	A, B, C
Is laparoscopic repair indicated in all PEH patients?	Yes	B and C
Abbreviation: PEH, paraesophageal hernia.		

Clinical Questions		
Question	Answer	Grade of recommendation
What are the most reliable clinical findings on history and physical examination to rule in or out appendicitis?	Abdominal pain often localized to the epigastrium or periumbilical area followed by anorexia and nausea are the most reliable diagnostic findings on history and physical exam.	C
What is the best laboratory test to make the diagnosis of appendicitis?	Overall laboratory markers of acute inflammation in acute appendicitis remain highly sensitive but relatively nonspecific when it comes to making the diagnosis of appendicitis. No one test has been found to be both highly sensitive and specific for acute appendicitis.	B
Does giving a patient with suspected appendicitis pain medicine decrease the ability to make the diagnosis of appendicitis?	Giving pain medicine to adults and children suspected of acute appendicitis prior to surgical evaluation does not seem to affect diagnostic accuracy or outcomes.	B
What operation is better for treating acute appendicitis?	Data support the use of performing laparoscopic appendectomy for patients with acute appendicitis if the surgical expertise and equipment are available.	B
Does giving prophylactic antibiotics to patients with appendicitis who undergo appendectomy decrease infectious complications?	Antibiotic prophylaxis is effective in preventing postoperative wound infections and intra-abdominal abscesses. The type of antibiotic and preferred time and duration of antibiotic administration needs to be evaluated.	B
What is the best diagnostic imaging modality to diagnose acute appendicitis?	The most accurate imaging modality for making the diagnosis of appendicitis is computed tomography. The routine use of performing CT on all patients suspected to have appendicitis cannot be recommended at this time.	B
Is interval appendectomy necessary?	The routine performance of interval appendectomy after nonoperative treatment of complicated acute appendicitis is not supported. Routine interval appendectomy is not a cost-effective intervention.	C
Should antibiotic treatment alone replace appendectomy for acute appendicitis?	Antibiotics should not be used routinely as the primary treatment of acute appendicitis. Surgery continues to remain the primary option for the treatment of acute appendicitis.	B
Abbreviation: CT, computed tomography.		

Key Issues in the Management of Lower Gastrointestinal Bleeding		
Question	Answer	Grade of recommendation
What is the diagnostics accuracy of Tc-99 sulfur colloid injection versus Tc-99-tagged red cells?	Tc-99-labeled RBCs appears superior to Tc-99 sulfur colloid injection. For all comers, about half of the scans will be positive. Angiography is not indicated when scintigraphy is negative. Positive scans should be followed up with further localization studies to improve anatomic accuracy.	B C
What is the diagnostic accuracy of colonoscopy, radionuclide scanning, and angiography in the setting of LGIB?	Colonoscopy when available is the most accurate method of diagnosing LGIB and is the gold standard against which other studies are measured offering control of some lesions as well. Scintigraphy may offer valuable information for angiographic screening but is insufficient for operative planning alone. MDCT is emerging as a valuable noninvasive modality but has not been sufficiently studied to determine whether it can be used as a sole modality for operative planning.	C C C
What is the ideal order of diagnostic test in the setting of LGIB?	Colonoscopy is the ideal single test in the face of LGIB. In the event this is not available and an intervention is required, scintigraphy or MDCT should be performed to rule out proximal sources in the small bowel prior to angiographic embolization/vasopressin or surgical resection.	C C
What is the clinical effectiveness intra-arterial vasopressin infusion versus transcatheter embolization?	The major drawbacks of vasopressin therapy are coronary ischemia and rebleeding after cessation of therapy. Cessation of bleeding occurs in up to 90% of patients. Some studies have shown significant rebleeding after therapy is stopped. On the other hand, embolic therapy shows a similar rate of initial hemorrhage control with less early rebleeding, however, there is at about a 10% risk of significant colon ischemia. Super-selective embolism has not eliminated ischemia as a risk. The late rebleeding risk is 10–15% with either techniques.	No recommendations
What are the criteria for surgical intervention in LGIB and what operation should be done?	Patients who bleed 2 or more units of blood should receive an evaluation to localize the source of bleeding expeditiously. Clinical stability and available testing options will determine to what extent localization studies can be performed so that excessive transfusion is avoided (>10 units). Persistent bleeding with true anatomic localization may allow for segmental resection otherwise subtotal colectomy with ileorectostomy should be performed.	C C C
Abbreviations: LGIB, lower gastrointestinal bleeding; MDCT, multidetector computed tomography; RBCs, red blood cells.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the appropriate indication for elective sigmoid resection after uncomplicated diverticulitis?	A case-by-case determination of the need for operative management is necessary.	C
Should younger patients (<40–50 years) undergo elective sigmoid colon resection after a single attack of acute diverticulitis?	Individualized decisions based on patients circumstance will need to be made prior to proceeding with surgery.	C
Are there any evidence-based dietary recommendations to prevent the recurrence of acute uncomplicated diverticulitis?	Dietary fiber can play a role in both the prevention of initial and recurrent attacks of uncomplicated diverticulitis.	A
What is the optimal operation for patients requiring surgery for complicated acute diverticulitis?	Primary resection of the inflamed colon (with or without primary anastomosis).	A
Is performing a primary anastomosis an option?	Primary anastomosis of the colon at the initial operation can be considered in Hinchey stage I and II patients.	B
Is laparoscopic colectomy equivalent or superior to open colectomy for diverticular disease? Is the overall cost different?	Laparoscopic colon resection is a safe and effective approach for the elective treatment of patients with diverticular disease.	B

Clinical Questions		
Question	Answer	Grade
What is the clinical presentation?	Absence of passage of flatus (90%) and/or feces (80.6%) and abdominal distension (65.3%) were the most common symptoms and physical finding, respectively.	C
What is the differential diagnosis?	Large bowel cancer, adhesions, retroperitoneal tumors, and hernias were the most common causes of large bowel obstruction. Hernias, adhesions, strictures, endometriosis, ingested foreign bodies, phytobezoars, gallstones, and rectal foreign bodies have all been found to cause large bowel obstruction.	C
What is the proper diagnostic evaluation?	CT imaging is more accurate in making the diagnosis of large bowel obstruction than was contrast enema. CT imaging also allows for the evaluation of other disease processes and is more readily available. CT imaging in conjunction with contrast enema may yield superior results.	C
What is the preferred operative approach?	Stomas are preferred for patients with recurrent disease or for palliative resections. A primary anastomosis can be safely performed for obstructing colon lesions.	B
What are the nonoperative approaches?	Colonic stenting can be used as a bridge to surgery or as a palliative option. The success rate for relieving obstruction is around 90%. Three-quarters of patients in which colonic stents are used as a bridge to surgery go on to elective resection.	B
What are the outcomes?	Mortality rates for patients presenting with large bowel obstruction are 20–25%. If colonic stenting is available, the mortality rate can be significantly reduced.	B
Abbreviation: CT, computed tomography.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the ideal mode of imaging in CMI and AMI?	AMI: angio or CTA CMI: duplex, angio, CTA, MRA	B
Endovascular therapy for AMI?	Selective thrombolysis in early AMI	C
Open or endovascular treatment for CMI?	Open has better patency, both may be offered safely	B
Single- or multivessel open reconstruction?	Equivalent, may be tailored to patient	C
How to treat mesenteric venous thrombosis?	Anticoagulation +/- surgery for peritonitis; catheter-directed thrombolysis may be safe	C
How to treat NOMI?	Catheter-directed vasodilators +/- surgery for peritonitis	C
Abbreviations: AMI, acute mesenteric ischemia; CMI, chronic mesenteric ischemia; CTA, computed tomography angiography; MRA, magnetic resonance angiography; NOMI, nonocclusive mesenteric ischemia.		

Clinical Questions		
Question	Answer	Grade of recommendation
Is observation alone a viable option?	No. Clear benefit with intervention for grade II and greater hemorrhoids.	A
Is there a clear advantage of one nonoperative management strategy over the others?	Yes. Rubber band ligation is superior to anal dilation, sclerotherapy, and infrared photocoagulation.	A
Is one operative strategy superior to the others?	Yes. Conventional hemorrhoidectomy is superior to procedure for prolapse and hemorrhoids but no significant difference between Milligan Morgan (open) hemorrhoidectomy and Ferguson hemorrhoidectomy.	B
What is the best management strategy for symptomatic external hemorrhoids?	Excision over topical agents and incision.	B

Anorectal Fissure, Fistula, and Abscess: Question Summary		
Question	Answer	Grade
How do nonoperative medical therapies (nitroglycerin, calcium channel blockers, and botulinum toxin) compare with placebo and lateral internal sphincterotomy in the treatment of anal fissures?	Nonsurgical therapies are superior to placebo but inferior to lateral internal sphincterotomy for healing anal fissures.	A
What is the impact of technique on the outcomes of patients undergoing surgery for anal fissure?	Lateral internal sphincterotomy (open or closed) is the surgical treatment of choice for chronic anal fissures.	A
What is the healing and incontinence rate for fistulotomy for simple fistula-in-ano?	Fistulotomy is appropriate for simple fistula-in-ano with high rates of healing and low rates of incontinence.	B
What is the healing and incontinence rate for more complex fistulas treated with fibrin glue, fistula plug, or a seton?	Complex fistulas-in-ano may be successfully treated with fibrin glue, fistula plug, or a seton. Success and incontinence rates vary widely.	C
What is the healing and incontinence rate for more complex fistulas treated with an endorectal advancement flap?	Complex fistulas-in-ano may be successfully treated with an endorectal advancement flap. Success rates vary widely, but incontinence is infrequent.	C
Are antibiotics unnecessary for most patients undergoing routine incision and drainage of perirectal abscesses?	Antibiotics are unnecessary for most patients following adequate abscess drainage.	B

Pilonidal Disease: Question Summary		
Question	Answer	Grade
What is the optimal treatment of acute pilonidal disease?	Incision and drainage of abscess only	B
Do antibiotics have a role in the treatment of pilonidal disease?	Only with significant cellulitis or special situations (i.e., immunosuppressed)	D
How does gluteal cleft shaving influence pilonidal disease recurrence?	Evidence supports its use in sinus disease with limited downside	C
What is the expected outcome with respect to wound healing and recurrence of excision of pilonidal cyst/sinus with primary closure versus healing by secondary intention versus excision with marsupialization?	Excision with primary closure is associated with faster healing and higher recurrence. Secondary intention closures are associated with delayed healing but lower recurrence rates	B
Should a flap be required, what is the optimal type of flap reconstruction following excision?	There is insufficient evidence to support one flap over another. They do have a role in complex or recurrent disease	C
What is the optimal strategy for the treatment of recurrent pilonidal disease?	There is insufficient evidence to support one strategy. Surgeon comfort and ability may guide the use of flaps versus more conservative strategies. Recurrent abscesses should be drained	C
What is the role of nonoperative management of chronic pilonidal disease	Phenol injection has shown some success with limited data. Local care including is an adjunctive measure for this strategy	C

Rectal Prolapse: Question Summary		
Question	Answer	Grade
What is the optimal preoperative evaluation for those patients with rectal prolapse—i.e., what are the data on colonoscopy, anorectal physiology studies, manometry, transit studies, and defecography?	Anorectal physiology studies have little correlation with postoperative outcomes and rarely impact operative management. Colonoscopy should be performed on those at-risk patients by current screening/surveillance recommendations for colorectal cancer.	C, B
What is associated with better perioperative outcomes: abdominal or perineal approaches?	There is insufficient evidence to support one approach over the other due to significant selection bias. In general, perineal approaches are associated with higher recurrence.	I, B
When considering abdominal approaches, which technique is associated with improved outcomes: mobilization with suture rectopexy, suture rectopexy with the addition of mesh, or resection rectopexy?	Results for all abdominal procedures are comparable in terms of postoperative morbidity and recurrence. Resection rectopexy is associated with less postoperative constipation.	B, B
Does laparoscopy provide superior outcomes to open repair?	Laparoscopy has equivalent morbidity, mortality, and recurrence rates, with similar postoperative functional outcomes as open surgery. Laparoscopy is associated with decreased length of stay and longer operative times.	B
How does rectal prolapse surgery affect postoperative function in those patients with preoperative fecal incontinence?	Repair via either the perineal or abdominal approach, regardless of method, is associated with improved continence and a smaller degree of complete resolution.	B
How does rectal prolapse surgery affect postoperative function in those patients with preoperative constipation?	Repair via either the perineal or abdominal approach is associated with improved constipation, though rates widely vary. Patients with significant preoperative constipation should avoid a Ripstein procedure and likely benefit more from addition of a sigmoid resection.	B, B
What is the optimal treatment for recurrence?	The abdominal approach is associated with lower subsequent recurrence rates when compared to the perineal approach, and should be considered when the patient's risk profile permits it.	B

Acute Cholecystitis: Question Summary		
Question	Answer	Grade
Should laparoscopic or open cholecystectomy be performed in acute and complicated acute cholecystitis?	Laparoscopic attempt is preferred.	C
What should the timing of surgical intervention be?	Early cholecystectomy preferred to delayed cholecystectomy.	B
What are the indications and outcomes for nonsurgical intervention?	Unclear.	D
Indications for drain placement?	Drains may harm the patient, does not confer benefit.	B
Which antibiotic therapy is warranted?	Several are appropriate.	B
Which perioperative pain therapy is effective?	Stepwise multimodality approach.	A

Questions to be Addressed	
Question	Recommendation
What is the optimal antibiotic strategy for acute cholangitis?	Antibiotics should be initiated early (Grade A). Blood and bile cultures should be routinely obtained to guide therapy (Grade B). There is insufficient evidence to recommend a specific antibiotic regimen or duration of therapy. Duration of therapy should be guided by clinical response and disease severity (Grade B). There is insufficient evidence that biliary penetration is a factor that influences clinical outcome. However, antibiotic therapy should be used in conjunction with expeditious clearance of obstructed bile ducts to derive maximum benefit (Grade C).
What is the preferred mode of biliary decompression for cholangitis due to biliary stones? What is the optimal timing for biliary decompression?	Endoscopic biliary decompression is preferred over surgery (Grade A). Percutaneous transhepatic biliary drainage is an alternative where endoscopic decompression is not possible (Grade C). Patients who do not respond to medical management after 6–24 hours should undergo urgent drainage (Grade C). Certain patients are at high risk for failure of medical therapy and should undergo urgent drainage even before clinical deterioration (Grade C).
Is cholecystectomy warranted after ES and clearance of bile duct stones with or without cholangitis? If so, when should it be performed?	Prophylactic cholecystectomy should be offered to patients after ES unless prohibited by patient-related factors, in patients with proven gallbladder stones (Grade A). The optimal time after ES for cholecystectomy is unclear but earlier LC may be associated with a lower conversion rate to open cholecystectomy (Grade C). In patients with no gallbladder stones, cholecystectomy may not be necessary (Grade B).
Does MRCP play a role in the management of acute cholangitis due to biliary stones?	There is insufficient evidence to support the use of MRCP in the management of acute cholangitis due to bile duct stones (Grade D).
<i>Abbreviations:</i> ES, endoscopic sphincterotomy; LC, laparoscopic cholecystectomy; MRCP, magnetic resonance cholangiopancreatography.	

Clinical Questions		
Question	Answer	Grade
Scoring systems: is one superior to another in predicting the clinical course of AP?	No. Systems are complimentary not mutually exclusive.	B
What is the role of ERCP in acute biliary pancreatitis?	Only if evidence of cholangitis or biliary obstruction exists.	A
What is the role of prophylactic antibiotics in severe AP?	Studies do not show a benefit. May be reasonable in severe AP.	B
Is EN safe and superior to TPN in AP?	Safe and less expensive but clinical benefit unclear.	B
Is gastric feeding safe and equivalent to jejunal feeding in AP?	Safe in hemodynamically stable patients if tolerated.	B
Can the inflammatory cascade of AP be alleviated?	Not with current drug regimens.	A
<i>Abbreviations:</i> AP, acute pancreatitis; EN, enteral nutrition; ERCP, endoscopic retrograde cholangiopancreatography; TPN, total parenteral nutrition.		

Clinical Questions		
Question	Answer	Grade of recommendation
What is the definition of a pancreatic pseudo-cyst?	The Atlanta classification system provides a definition for pancreatic pseudo-cyst. However, this system has been recently criticized.	C
What is the incidence of pancreatic pseudo-cysts?	The true incidence of pancreatic pseudo-cyst is unknown.	C
What is the incidence of complicated pancreatic pseudo-cysts?	The true incidence of complicated pancreatic pseudo-cyst is unknown.	C
What is the optimal time for intervention once the diagnosis of pancreatic pseudo-cyst has been confirmed?	The optimal time of intervention for pancreatic pseudo-cysts is unknown.	C
What are the optimal imaging modalities for diagnosis of a pancreatic pseudo-cyst?	Contrast-enhanced computed tomography is the imaging modality of choice.	C
What is the optimal method of therapeutic intervention?	The optimal approach to pancreatic pseudo-cyst drainage remains controversial.	C
Do delays in surgical intervention affect outcome?	Yes.	C

Clinical Questions		
Question	Answer	Grade of recommendation
How can liver abscess be defined?	Two types; pyogenic, caused by bacteria, and amebic, caused by <i>Entamoeba histolytica</i> .	B
Which are the epidemiologic facts for liver abscess?	Variable depending on the population and the time period. Patients with pyogenic liver abscess are more likely to be older, to be female, and to have a biliary cause and an underlying malignant disease. Amebic liver abscess (and other extraintestinal disease) is 7–10 times more common in adult men.	B
Which is the etiology of liver abscess, and which pathogens are more common ?	The causes are divided into six categories, based on the route of extension of infection: biliary, portal vein, hepatic artery, direct extension, traumatic, and cryptogenic. Virtually any organism is capable of causing liver abscess.	B
Which are the symptoms of liver abscess?	Patients with an amebic liver abscess are more likely than those with a pyogenic abscess to present with pain and diarrhea and to have hepatomegaly and a tender liver on physical examination. Fever is present in most patients, occurring in approximately 90% of them with either type of liver abscess; high, spiking fevers associated with chills are seen most frequently with pyogenic hepatic abscesses.	A,B
How can the diagnosis be achieved in patients with liver abscess?	Demonstration of <i>E. histolytica</i> in the stool is still the only definitive proof of intestinal amebiasis.	B
What is the differential diagnosis for liver abscess?	A simple cyst, malignancy, and amebic abscess.	
Which are the treatment modalities for liver abscess?	For pyogenic liver abscess, usually both antibiotic therapy and drainage for successful treatment. Medical management alone gains growing interest.	A, B
What is the prognosis for the patients with liver abscess?	Mortality mainly from associated underlying disease rather than the abscess itself.	B

Questions Regarding Diagnosis and Treatment of Variceal Hemorrhage		
Question	Answer	Level of evidence/Grade of recommendation
In cirrhotic patients, what is the most reliable predictor of variceal development?	Measurement of the HVPG is the preferred method to assess portal pressure and is predictive of variceal development.	Ib/A
What is the best diagnostic test to identify esophageal and gastric varices?	Upper endoscopy is the best diagnostic test to detect the presence of esophageal and gastric varices.	V/D
In cirrhotic patients who have no varices by upper endoscopy, what is the best treatment to prevent development of varices?	When screening upper endoscopy reveals no varices, β -blockers are not helpful to prevent formation of varices. Instead, these patients should undergo regular surveillance upper endoscopy.	Range from Ib/A to V/D
In cirrhotic patients who have small varices, what is the best treatment to prevent first variceal hemorrhage?	Patients with small varices—especially those with increased risk of gastrointestinal hemorrhage—should receive nonselective β -blockers to prevent growth to large varices.	IIb/C
In cirrhotic patients who have large varices, what is the best treatment to prevent first variceal hemorrhage?	Nonselective β -blockers reduce the risk of first variceal hemorrhage in patients with large varices. EBL is probably more effective than nonselective β -blockers to reduce the risk of first variceal hemorrhage in these patients, but EBL may not improve survival. EBL should be recommended when these patients have contraindications or intolerance to β -blocker therapy.	Range from Ia/A to V/D
In cirrhotic patients who have acute variceal hemorrhage, what specific resuscitative fluids should be given?	Prompt but careful resuscitation of blood loss due to acute variceal hemorrhage should occur with colloid solution to maintain hemodynamic stability and with packed red cells to maintain hemoglobin near 8 g/dl.	Ib/A
In cirrhotic patients who have acute variceal hemorrhage, what is the role of prophylactic antibiotics, if any?	Prophylactic antibiotics should begin at hospital admission for all patients who present with acute variceal hemorrhage, because they decrease bacterial infections, improve failure to control acute variceal hemorrhage, prevent recurrent variceal hemorrhage, and decrease mortality.	Ia/A
In cirrhotic patients who have acute variceal hemorrhage, what is the best treatment to control hemorrhage?	When acute variceal hemorrhage is suspected, pharmacologic intervention should begin immediately, even before variceal hemorrhage is confirmed by upper endoscopy. Upper endoscopy should be performed as soon as possible, and, if variceal hemorrhage is confirmed, endoscopic therapy (preferably with EBL) should be used to control hemorrhage. Failure to control acute variceal hemorrhage should prompt a second endoscopic attempt before considering rescue therapy with TIPSS or surgical shunt. Balloon tamponade should be considered as a temporizing measure only if definitive therapy is planned.	Range from Ia/A to IIb/B
In cirrhotic patients who recover from acute variceal hemorrhage, what is the best treatment to prevent further variceal hemorrhage?	Data support combined β -blocker and endoscopic therapy, even though a recent consensus conference recommends EBL or β -blocker + nitrate. Patients who develop recurrent variceal hemorrhage on EBL or β -blocker therapy alone should receive combined therapy. Patients who fail combined therapy should be considered for TIPSS or surgical shunt. TIPSS can be used as a bridge to transplantation, and suitable candidates should be referred to specialized liver transplant centers early.	Range from Ia/A to IV/C
Abbreviations: EBL, endoscopic band ligation; HVPG, hepatic vein pressure gradient; TIPSS, transjugular intrahepatic portosystemic shunt.		

Gangrene of the Foot: Question Summary		
Question	Answer	Grade of recommendation
What imaging or testing is best?	ABI and TBI for screening MRA, CTA, duplex for operative planning.	B
Is cardiac work-up necessary?	No. Maximize medical management.	A, C
Is endovascular or open revascularization best?	Endovascular first approach is reasonable in most patients.	B
Is primary amputation best for some patients?	Yes, in select patients.	C
Abbreviations: ABI, ankle-brachial index; CTA, computed tomography angiography; MRA, magnetic resonance arteriography; TBI, toe-brachial index.		

Clinical Questions		
Question	Answer	Grade of recommendation
Can embolic ischemia be distinguished from thrombotic ischemia based on clinical findings alone?	Yes, but expect a subgroup that defies accurate diagnosis.	C
Is perioperative anticoagulation necessary in treatment of acute limb ischemia?	No conclusive evidence is available to support administration or withholding of anticoagulation.	C
Should initial thrombolysis be performed over surgical revascularization?	No. Selected patients receiving thrombolysis may avoid surgical intervention or undergo a procedure of decreased magnitude, but higher risks of bleeding, embolization, and stroke are expected.	B

Clinical Questions		
Question	Answer	Grade of recommendation
What are the optimal resuscitation goals?	Low-grade hypotension is acceptable.	C
What are the preferred resuscitation fluids?	Blood products are preferred.	B
Should a CT scan be obtained in patients with suspected rAAA?	Yes, except in most extreme cases.	B
Can EVAR be used in patients with rAAA?	Yes.	B
What can be done to avoid paraplegia and/or ischemic colitis?	Try to maintain flow to at least one hypogastric artery.	B
Abbreviations: CT, computed tomography; EVAR, endovascular repair; rAAA, ruptured abdominal aortic aneurysm.		

Clinical Questions		
Question	Answer	Grade of recommendation
What are the two basic categories of aortic dissection?	Ascending (type A), descending (type B)	N/A
What is the optimal imaging modality for aortic dissections?	CT scanning with and without contrast using multidetector array technology; MRI and TEE may be useful adjuncts	A
When is further or different modality of imaging indicated?		
Should D-dimer levels be measured?	Yes	A
What is the appropriate role and timing of operative intervention for each type of AAD?	Immediate open surgery for type A; initial med Rx for type B	A
What is the role of blood pressure management during the acute and subacute phase of the injury? What is the role of long-term blood pressure management?	Beta-blocker is crucial for early management, lifelong blood pressure monitoring and treatment is necessary	A
What is the role of endovascular stent graft repair for type B dissections? What are the data?	Limited role for stent graft repair and no long-term data	C
What follow-up is required post-stent graft placement?	Serial CTs of the treated aorta for at least 5 years	A
Abbreviations: AAD, acute aortic dissection; CT, computed tomography; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography.		

Summary of Clinical Questions		
Question	Answer	Grade
What is the best initial treatment for venous thromboembolism?	LMWH is the preferred initial treatment for DVT compared to unfractionated heparin in most patients.	A
Is home therapy for venous thromboembolism safe and effective compared to inpatient care?	Home therapy for DVT with LMWH is safe and cost-effective in carefully chosen patients.	A
What is the optimal oral starting dose of vitamin K antagonists?	There is no consensus on the optimal starting dose of warfarin. Clinicians should consider patient-specific factors for determining a warfarin dose. Patients at low risk for bleeding may safely tolerate a 10 mg loading dose.	B
What is the optimal length of oral vitamin K antagonist treatment for DVT?	Extended therapy with vitamin K antagonists is warranted to prevent recurrent venous thromboembolism. Risks of bleeding versus recurrence of venous thromboembolism for individual patients may alter the optimal duration of therapy.	A
	DVT associated with a transient event maybe effectively treated with 3 months of vitamin K antagonists.	B
Does catheter-directed thrombolysis decrease DVT recurrences and incidence of post-thrombotic syndrome?	Though catheter-directed thrombolysis results in increased venous patency and decreased incidence of post-thrombotic syndrome, bleeding complications limit the routine use of this technology.	B
Do compression stockings reduce the long-term complication of post-thrombotic syndrome?	Graded compression stockings reduce the incidence of post-thrombotic syndrome when used early after the diagnosis of DVT.	A
Abbreviations: DVT, deep venous thrombosis; LMWH, low molecular weight heparin. DVT, deep venous thrombosis.		

Clinical Questions		
Question	Answer	Grade of recommendation
Who is at risk for PE?	Patients with spinal injuries, older age, major surgery or trauma, previous history of thromboembolism, and cancer.	B
What is the optimal diagnostic test for PE?	CT angiography	A
Are heparin and compression devices adequate for PE prophylaxis?	The effectiveness of heparin and compression devices in trauma and emergency surgery patients is unclear. LMWH seems to perform better than UFH.	B
Is PE and mortality from PE reduced by IVC filters?	The effectiveness of IVC filters in reducing PE and mortality from PE in trauma and emergency surgery patients is unclear.	C
Is LMWH as safe and effective as UFH for the treatment of PE?	Yes	A
Abbreviations: CT, computed tomography; IVC, inferior vena cava; LMWH, low-molecular weight heparin; PE, pulmonary embolism; UFH, unfractionated heparin.		

Clinical Questions		
Question	Answer	Grade
What is the standard for diagnosis in NSTIs?	Clinical; confirmation by open biopsy.	C
What is the best approach to initial resection?	As complete as the patient will tolerate.	C
Should hyperbaric oxygen be part of the standard treatment for NSTIs?	No. More rigorous trials are needed.	C
Should intravenous immunoglobulin be part of the standard treatment for NSTIs?	No; although it may be helpful, it has not been proven to improve outcomes.	C
Abbreviations: NSTI, necrotizing soft tissue infection.		

Key Issues in the Management of Incarcerated Hernias			
Question	Answer	Grade of recommendation	Level of evidence
What are the appropriate physical examination and imaging evaluations necessary to diagnose incarcerated hernia?	Physical examination is acceptable for diagnosis of most incarcerated hernias. CT imaging or ultrasound are acceptable adjunctive modalities in specific clinical scenarios.	C C	V IV
What are the technical considerations for treating incarcerated hernia that influence choice of repair?	Laparoscopic and open repairs with mesh are acceptable forms of hernia repair in the presence of incarceration. Experience with laparoscopic technique influences outcome.	B B	IIB IIB
What are the repair options in the face of GI contamination or infection?	The use of biologic/synthetic prostheses are well documented for use in contaminated/infected hernias. Higher complication rates are expected.	B	IIIB, IV IIIB
What are the characteristics of incarceration/strangulation that impact mortality/morbidity?	Mortality correlates with severity scoring in general; however, delay in treatment and the need for bowel resection have additional implications for subsequent mortality.		IIB, IIIB
What are the most effective intraoperative evaluation tools to assess bowel viability?	Objective techniques are superior to clinical evaluation. Laser Doppler flowmetry may be most sensitive technique; however, Doppler ultrasound and/or fluorescein dye are more readily available. Laparoscopy transabdominally or through the hernia sac is useful technique for assessing intestinal viability in selected cases.	B C	IIB, IIIB IV
Should hernias be repaired to prevent incarceration and strangulation?	Authors continue to cite the need for elective hernia repair to avoid morbidity and mortality. Watchful waiting of its small hernias in healthy patients can be recommended.	B	IB, IIB, IIIB
Abbreviations: CT, computed tomography; GI, gastrointestinal.			

Clinical Questions		
Question	Answer	Grade of recommendation
What is the protocol for diagnosis of bacteremia?	Blood cultures remain the gold standard. Multiple PCR methods can be used as an adjunct.	B
What is the best way to diagnose catheter-related bacteremia when the catheter is removed?	We recommend a semiquantitative or preferentially quantitative culture of the catheter segment in addition to two blood cultures obtained percutaneously from a peripheral vein and from a suspected intravascular device.	B
What is the significance of empiric therapy in the patient with bacteremia?	Early administration of effective empiric antimicrobial treatment leads to a decrease in the mortality rate, duration of hospital stay, and hospital costs.	B
How can we prevent the occurrence of catheter-related bloodstream infections?	Recommended preventive strategies with the strongest supportive evidence are: - Education and training of health care providers - Maximal sterile barrier precaution - Use of a 2% chlorhexidine preparation for skin antisepsis - Use of antiseptic/antibiotic impregnated catheter if rate of infection is high despite adherence to other strategies	B A A A
Abbreviations: PCR, polymerase chain reaction.		

Strategies to Reduce Catheter Infections		
Question	Answer	Grade
What is the best method and site to insert intravascular catheters?	Use of the subclavian site, chlorhexidine skin prep solutions, and maximum barrier precautions.	B, A, A
Is education useful in preventing CRBSI?	Education programs reduce the risk of CRBSI.	B
What other behavioral interventions are helpful in preventing or reducing CRBSI?	Multimodal intervention programs that encompass education and process reduce the incidence of CRBSI.	B
How long should catheters remain <i>in situ</i> ?	Catheters should not be changed on a scheduled basis but should be removed when no longer needed, when they are suspected of causing infection, or when they are not functional.	B
Should anti-infective catheters be used?	Anti-infective catheters should be used if the rate of CRBSI remains high despite the use of best practices to prevent CRBSI.	A
Do anti-infective catheters promote antibiotic resistance?	Anti-infective catheters do not promote antibiotic resistance.	B
Abbreviations: CRBSI, catheter-related bloodstream infection.		

Clinical Questions		
Question	Answer	Grade of recommendation
Are invasive methods better for diagnosing VAP?	Invasive methods of diagnosing VAP are no better than noninvasive methods and are much less expensive.	A
What are the modifiable risk factors for VAP?	The use of closed suction systems, ETT with subglottic suctioning ports, PUC and silver coating, new water bath-type humidifiers, and the semi-recumbent position all decrease the rates of VAP.	A
How should antibiotics be used to treat VAP?	Empiric coverage should be broad and nearly always includes more than one drug. Studies have not demonstrated any advantage to double-covering any microbe after speciation including <i>Pseudomonas</i> . Vancomycin is as effective as linezolid. Antibiotics should be given for no more than 8 days.	A
Does timing of tracheotomy change outcomes in patients with VAP?	Yes, early tracheostomy should be performed.	B
What is the epidemiology of VAP?	Rates of VAP are between 20% and 71% with wide variability based on patient population. Rates of VAP increase as time of intubation accumulates.	B
What is the best method to assess and tailor treatment for VAP?	Antibiotics can be stopped when clinical signs of infection have resolved.	B
Abbreviations: ETT, endotracheal tube; PUC, polyurethane cuff; VAP, ventilator-associated pneumonia.		

Question Summary		
Question	Answer	Grade
What is the optimal time from door to PCI that reduces mortality?	90 minutes is the optimal time from door to PCI. Patients who received an intervention within this timeframe experienced a reduction in mortality.	A
What beta-blocker is recommended for management of an acute MI, and is an IV dose superior?	Early initiation of low-dose beta-blocker therapy and careful titration should be the goal until rate control has been achieved.	A
Is a baby aspirin (81 mg) adequate for management of an acute MI?	A minimum of 162 mg aspirin should be administered within 10 minutes of recognizing that the patient is experiencing an acute MI.	A
Is clopidogrel indicated in the management of an acute MI?	Adding clopidogrel to aspirin does improve outcome in non-ST-elevation MI and should be considered. However, caution should be taken in postoperative patients.	A
What ACE-I is indicated for the management of an acute MI, and is an IV dose superior?	The current ACC/AHA recommendations suggest that an oral dose of ACE-I therapy is the optimal treatment. On review of IV ACE-I therapy, mortality is not affected when compared to oral ACE-I therapy, which improved mortality. For LVEF < 40%, it is a class I level A recommendation. For low-risk patients > 40% LVEF, it is IIa level B recommendation.	A
Does the addition of an ARB improve the benefit of an ACE-I?	Addition of an ARB does not improve the outcome of the patient and was noted to introduce more adverse effects. ARBs are as effective as ACE-Is and can be used when ACE-Is are not tolerated by the patient due to adverse reactions.	A
Abbreviations: ACC, American College of Cardiology; ACE-I, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous intervention.		

Clinical Questions		
Question	Answer	Grade of recommendation
What are effective and safe pharmacologic strategies for prevention of postoperative atrial fibrillation after coronary artery bypass surgery?	Beta-blockers Amiodarone	A B
Are there intraoperative strategies to consider that may reduce incident atrial fibrillation after cardiothoracic surgery?	Applying mild hypothermia, performing a posterior pericardiotomy, and by using heparin-coated bypass circuits	C
What drugs should be avoided in patients with atrial fibrillation with underlying Wolff-Parkinson-White syndrome?	Adenosine, beta-blockers, and calcium channel blockers	A
Is elective cardioversion, chemically or by direct current, a reasonable option in the postoperative atrial fibrillation patient?	Yes. It may reduce length of hospital stay and prolong duration in normal sinus rhythm.	B
Should warfarin be given in postoperative atrial fibrillation that is recurrent or persists for more than 24 hours?	Warfarin anticoagulation should be initiated for at least 4 weeks to mitigate the risk of stroke.	B

Clinical Questions		
Question	Answer	Grade of recommendation
Is TPN or tube feedings better for the patient?	Enteral feeds have fewer and less severe infective complications and faster return of bowel function.	A
What is the safest and most effective, feeding the stomach or the small bowel?	Complication rates are the same for both methods. Gastric feeds have faster onset of goal feeds.	A
Does immunonutrition improve outcome?	Yes, immunonutrition is linked to shorter hospital stay and vent days as well as overall infection. Mortality unchanged.	A
What's the best way to start and advance postoperative patients on a diet?	Give them a diet of choice as soon as possible. Waiting for flatus and physician-dictated diets drag things out longer with no decrease in complications.	A
Is glutamine a beneficial additive to feedings?	Yes, glutamine is readily available and relatively cheap. Multiple studies link glutamine to lower infections and decreased morbidity.	A
How early can tube feeds be safely started?	Enteral feeds can be safely started within 12–24 hours. Early tube feeds are linked to lower septic morbidity.	A
Abbreviations: TPN, total parenteral nutrition.		

Clinical Questions		
Question	Answer	Grade of recommendation
What are risk factors for development of ALI/ARDS?	Risk factors for ARDS/ALI include severe sepsis, multiple system trauma, massive blood transfusion, aspiration, and others	B
What is appropriate ventilator management in ALI/ARDS?	Low tidal volume ventilation (V_T <8 ml/kg predicted body weight) PEEP/ FiO_2 titrated to adequate oxygenation (SpO_2 88–95%)	A
What are common causes of poor outcome in ALI/ARDS?	Age, immunocompromise, severity of illness, organ failure	B
Is there a risk of PEEP >10, FiO_2 >0.5?	Major risk of PEEP is barotrauma (hazard ratio of 1.67 for every 5 cm H_2O PEEP) Risk of higher percentage of FiO_2 not well characterized Titration of PEEP/ FiO_2 should be carried out in graded fashion	A D
Salvage therapies for severe hypoxemia?	No significant outcome benefit for salvage therapies in patients with severe ARDS	A
How should I wean my patient from the ventilator?	Daily SBT in appropriate patients Method of SBT: Pressure support, continuous positive airway pressure, T-piece all equivalent Daily interruption of sedation decreased time on ventilator, ICU, hospital	A
Abbreviations: ALI, acute lung injury; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; PEEP, positive end-expiratory pressure; SBT, spontaneous breathing trial.		

Question Summary		
Question	Answer	Grade of recommendation
Which surgical patients are at higher risk of developing ARF?	Cardiac, vascular, transplant, and multiple-trauma patients are the higher risk surgical patients. Patients with preexistent morbidities, diabetes, or renal dysfunction consider as higher risk.	C
Which are the signs for early recognition of AKI or ARF?	The first signs of ARF are decrease urine output and elevation of BUN and creatinine.	C
Diuretics, dopamine, fenoldopam, and others: Do they play any role in preventing ARF?	Dopamine should not be used. Diuretics and fenoldopam can be use in the early stages, the data are clear for the need of more multicenter randomized controlled trials.	C
ARF in surgical patients: What are the treatment modalities?	Current modalities include IHD and CRRT. The new techniques SLED and CRRT with high volumes, but there is the need of more prospective randomized trials.	C
Is CRRT better than IHD in patients with ARF after surgery?	No significant difference in the mortality rate or the progression to ESRD in patients with ARF treated with IHD or CRRT. CRRT has shown advantages in patients with low blood pressure.	B
Does CRRT has a role in the critical ill trauma patient without ARF?	Has shown some benefits in the critically ill patient without evidence of ARF, specially in sepsis and ARDS, but there isn't enough data to support its use.	C
How does ARF impact the morbidity and mortality of surgical patients?	ARF has a tremendous impact in the morbidity and mortality not only in surgical patients.	C
Abbreviations: AKI, acute kidney injury; ARF, acute renal failure; BUN, blood urea nitrogen; CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; IHD, intermittent hemodialysis; SLED, slow extended daily dialysis.		

Evidence-Based Practice of Tight Glucose Control in the Perioperative Setting		
Issues	Answers	Recommendation grade
TGC in the cardiac and neurosurgical ICU	It is beneficial.	A
TGC in the general surgical ICU	It is beneficial.	B
TGC in medical surgical ICU	It is beneficial after 3 days of ICU stay.	B
TGC in the cardiac surgical OR	It is beneficial with a target blood sugar around 150 mg/dl.	B
TGC in the noncardiac surgical OR	It may be beneficial in critically ill.	C
Target glucose level in diabetics and nondiabetics	No difference in their target glucose values.	C
Prevention of glucose toxicity or insulin	Both play a role in providing TGC benefits.	B
Optimum target blood glucose value with least adverse effects	TGC 80–110 mg/dl may not be the same in all surgical settings to provide maximum benefits with least adverse effects.	B
Blood glucose variability and outcome	Decreasing variability by continuous insulin infusion increases good outcome.	B
Cost savings	TGC decreases cost and health care utilization.	B
Abbreviations: ICU, intensive care unit; OR, operating room; TGC, tight glucose control.		

Clinical Questions		
Question	Answer	Grade of recommendation
Are there risk factors that can be used to identify patients at-risk for ACS/IAH ?	Abdominal surgery; ileus; pulmonary, hepatic, or renal dysfunction; >3.5 L/24 hour resuscitation, hypothermia, oliguria, anemia, base deficit, high GAP CO ₂	B
How should patients be screened for ACS/IAH?	Intermittent IAP measurement via urinary bladder (B) with repeat measurements if IAH is present (C)	B, C
Is there a threshold level of IAP that mandates intervention?	There appears to be benefit in keeping APP ≥50–60 mmHg	C
Are there any effective nonsurgical strategies for treating ACS/IAH?	Decompressive laparotomy (B), neuromuscular blockade (C), supine positioning (C), avoid overly zealous fluids (B), colloid or hypertonic crystalloid (C), percutaneous catheter drainage (C)	B, C
Is there a preferred technique for temporary abdominal closure?	No	N/A
Is there a predictable time frame or preferred technique for definitive abdominal closure?	No	N/A
Is there a role for abdominal decompression in the management of intracranial hypertension	Decompressive laparotomy should be considered in cases of refractory intracranial hypertension	B
Abbreviations: ACS, abdominal compartment syndrome; APP, abdominal perfusion pressure; GAP CO ₂ , gastric-to-arterial PCO ₂ difference IAH, intra-abdominal hypertension; IAP, intra-abdominal pressure; N/A, not available.		

Question Summary		
Question	Answer	Grade
How can sedation needs be assessed?	Sedation requirements should be reexamined frequently using a sedation scale.	A
How should sedation in the ICU be managed?	The use of a sedation protocol or daily interruption of sedation should be considered.	A
What is the evidence for short-acting and non-GABA drugs for ICU sedation?	Propofol and dexmedetomidine should be reserved for ICU sedation where the duration is thought to be no more than 24–48 hours, propofol should be given at an infusion rate of no more than 4–5 mg/kg/hour.	C
What is the impact of delirium in ICU?	Delirium is common. It increases length and cost of stay and may lead to long-term cognitive dysfunction.	
How is delirium identified?	The rate of delirium is high and underdiagnosed. Screen for delirium with a standardized exam or scale.	A
How should delirium be treated?	Treat delirium with environmental changes (risk factor reduction or elimination), then haloperidol.	A
What is the impact of alcohol and trauma?	There is an association with alcohol and trauma. All trauma admissions should be screened for alcohol and alcoholism. If alcoholism is identified, brief intervention is warranted.	A
Should benzodiazepines be given as prophylaxis for alcohol withdrawal?	No! Alcohol withdrawal should be treated with benzodiazepines in a symptom-driven approach.	A
Is processed EEG an equivalent to the qualitative clinical assessment of sedation?	Processed EEG is not ready for sedation assessment.	D
Abbreviations: EEG, electroencephalogram; GABA, gamma-aminobutyric acid; ICU, intensive care unit.		

Summary of Grade of Recommendations for Questions Regarding Malignant Hypertension		
Question	Summary recommendation	Grade
What is the optimal target BP for chronic therapy?	Care guidelines recommend SBP <140 and DBP <90 mmHg in the general population and <130/<80 in those with diabetes or chronic kidney disease.	B
How should preexisting hypertension be managed in the perioperative setting?	Antihypertensive therapies should be continued throughout the perioperative period when possible; with SBP >180 or DBP >110 mmHg, nonemergency surgeries should be deferred.	B
What is the threshold for pharmacologic treatment of high BP acutely in ambulatory individuals?	SBP >180, DBP >120 mmHg, or lower pressures with target organ dysfunction, should be treated aggressively to lower SBP to <160 mmHg, DBP to <110 mmHg, or by ~20% overall.	C
What are the clinical implications of APH?	APH may follow cardiovascular, neurological, or head and neck surgeries and is associated with adverse clinical outcomes. Pharmacologic therapy is indicated at SBP >160 or DBP >110 mmHg for noncardiac surgeries and SBP >140 or DBP >90 mmHg following cardiac surgeries.	C
What are the best therapies for APH?	Agents shown to be most effective include sodium nitroprusside, nitroglycerin, labetalol, nicardipine, and fenoldopam.	C
What signs and symptoms suggest end organ compromise due to malignant hypertension?	Encephalopathy, hemorrhagic or ischemic CVA, myocardial ischemia and infarction, acute pulmonary edema, aortic dissection, acute renal failure, or anastomotic complications; these signs may be masked in the perioperative period and should be aggressively sought in patients with severe hypertension.	B
What are the best pharmacologic therapies for acute management of hypertension in the presence of complicating conditions?	No pharmacologic agents have been shown to improve morbidity and mortality in hypertensive emergencies, but appear to be equally efficacious at lowering BP acutely. Choice of therapy should be tailored to clinical context and patient condition.	C
Abbreviations: APH, acute postoperative hypertension; BP, blood pressure; CVA, cerebrovascular accident; DBP, diastolic blood pressure; SBP, systolic blood pressure.		

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