Journal of the Formosan Medical Association (2020) **119**, 1343–1352

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com

Practice Guideline

Taiwanese consensus recommendations for acute pancreatitis

Wei-Chih Liao [a,b,1], Tien-Chien Tu [c,1], Kuei-Chuan Lee [d], Jseng-Hwei Tseng [e], Ming-Jen Chen [f], Cheuk-Kay Sun [g], Shang-Yu Wang [h], Wei-Kuo Chang [i], Pi-Yi Chang [j], Ming-Shun Wu [k], Tsung-Jung Lin [l], Hsiang-Lin Lee [m], Jiann-Hwa Chen [n], Kuo-Ching Yuan [o], Nai-Jen Liu [p], Hsing-Chien Wu [q], Po-Chin Liang [r], Hsiu-Po Wang [a,b], Tsann-Long Hwang [s], Chia-Long Lee [c,*]

[a] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan*
[b] *Internal Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan*
[c] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, Cathay General Hospital, Taipei, Taiwan*
[d] *Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[e] *Department of Imaging & Intervention, Chang Gung Memorial Hospital, Linkou, Taiwan*
[f] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, MacKay Memorial Hospital, Taipei, Taiwan*
[g] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan*
[h] *Division of Trauma and Emergency Surgery, Department of Surgery, Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[i] *Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, Taiwan*
[j] *Department of Radiology, Taichung Veterans General Hospital, Taiwan*
[k] *Division of Gastroenterology, Department of Internal Medicine, Wan Fang Hospital, College of Medicine, Taipei Medical University, Taipei, Taiwan*
[l] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, Taipei City Hospital, Ren-Ai Branch, Taipei, Taiwan*
[m] *Department of Surgery, Chung Shan Medical University Hospital, Institute of Medicine4, Chung Shan Medical University, Taichung, Taiwan*
[n] *Division of Gastroenterology and Hepatology, Department of Internal Medicine, Taipei Tzu Chi Hospital, Taipei, Taiwan*
[o] *Division of Acute Care Surgery and Trauma, Department of Surgery, Taipei Medical University Hospital, Taiwan*

* Corresponding author. No. 280, Sec. 4, Ren'ai Rd., Da'an Dist., Taipei City, 106, Taiwan.
E-mail address: cghleecl@hotmail.com (C.-L. Lee).
[1] Dr Liao and Dr Tu contributed equally to this article.

https://doi.org/10.1016/j.jfma.2019.07.019

[p] *Department of Gastroenterology and Hepatology, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan*
[q] *Department of Internal Medicine, Taipei Hospital, Ministry of Health and Welfare, Taiwan*
[r] *Department of Medical Imaging, National Taiwan University Hospital, Taiwan*
[s] *Department of Surgery, Chang Gung Memorial Hospital, Chang Gung University, Lin-Kou, Taiwan*

Received 6 May 2019; received in revised form 11 June 2019; accepted 17 July 2019

KEYWORDS
Acute pancreatitis;
Diagnosis;
Management

The incidence of acute pancreatitis and related health care utilization are increasing. Acute pancreatitis may result in organ failure and various local complications with risks of morbidity and even mortality. Recent advances in research have provided novel insights into the assessment and management for acute pancreatitis. This consensus is developed by Taiwan Pancreas Society to provide an updated, evidence-based framework for managing acute pancreatitis.

Contents

Introduction

The incidence of acute pancreatitis (AP) and AP-related admissions are increasing.[1,2] AP may result in transient (lasting $\leq$ 48 h) or persistent (>48 h) organ failure and various local complications, including acute peri-pancreatic fluid collection (APFC), pancreatic necrosis, pseudocyst, and walled-off necrosis with or without infection. These complications may cause significant morbidity and even mortality.

Recent advances in research have led to significant changes and improvements in the assessment and treatment of AP. Taiwan Pancreas Society developed this consensus recommendation with the aim to provide an updated, evidence-based framework for managing AP.

Methods

Based on literature search through MEDLINE, Cochrane Library, and Embase, a planning panel (Kuei-Chuan Lee, Cheuk-Kay Sun, Ming-Jen Chen, Jseng-Hwei Tseng, and Shang-Yu Wang) drafted statements which were then reviewed by panel members. A face-to-face meeting was conducted in August 2018 to review the evidence and revise the statements. The members then independently voted on each statement (A: accept completely; B: accept with some reservation; C: accept with major reservation; D: reject with reservation; E: reject completely). Consensus was considered to be achieved when ≧80% of members voted "accept completely" or "accept with some reservation", whereas statements were rejected if ≧ 80% of voting members "reject completely" or "reject with some reservation". The level of evidence and grade of recommendation were rated according to Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 Levels of Evidence,[3] with level 1 and grade A being the highest level of evidence and strongest recommendation, respectively.

Consensus statements

Statement 1

The diagnosis of acute pancreatitis requires the presence of at least two of the following features: (1) characteristic abdominal pain, (2) serum amylase or lipase greater than three times the upper limit of normal, (3) compatible image findings of pancreatitis in CT, MRI, or ultrasound.

Evidence level: 1. Recommendation: A

A 67% B 33% C 0% D 0% E 0%

Patients with acute pancreatitis (AP) typically present with epigastric or left upper quadrant abdominal pain that sometimes extends to the back. The pain is often constant, severe but may be variable in intensity. The pain may be alleviated by leaning forward and aggravated by eating, especially foods rich in fat.

In patient with AP, serum amylase usually rises within a few hours after the onset of pain and returns to normal range over the next 5—7 days.[4] Serum amylase level may rise in the absence of AP, such as macroamylasemia, disease of the salivary gland, chronic kidney disease, gynecological disease, and extrapancreatic abdominal diseases, including acute appendicitis, acute cholecystitis, peptic ulcer, bowel ischemia or obstruction.[4,5] Serum lipase remains elevated longer than amylase and appears to be more specific,[6] but a variety of non-pancreatic diseases such as acute cholecystitis, bowel obstruction/infarction, duodenal ulceration, and diabetic ketoacidosis may also cause elevated serum lipase levels. Therefore, in patients with elevated serum lipase/amylase it is important to exclude diagnoses that require urgent surgical intervention, such as perforated hallow organ.[7] On the other hand, in approximately a quarter of patients with AP serum lipase/amylase levels do not exceed 3 times the upper limit of normal,[7] and contrast-enhanced abdominal cross-sectional imaging is recommended to confirm the diagnosis.[8]

Statement 2

Transabdominal ultrasound can be used to search for biliary stones and alternative diagnoses when acute pancreatitis is suspected.

Evidence level: 2 Recommendation: A

A 70% B 30% C 0% D 0% E 0%

Biliary stones and alcoholism are the main causes of AP.[9] Transabdominal ultrasound is non-invasive and inexpensive, with sensitivity and specificity greater than 95% in diagnosing gallstones.[10] Transabdominal ultrasound may also detect clues such as dilated bile duct or free air that suggest concomitant or alternative diagnoses[8,9] and the need for cross section imaging.

Statement 3

Computed tomography or magnetic resonance image is needed when (1) the diagnosis is unclear, or (2) local complications are suspected, or (3) the symptoms persist or aggravate after initial 48—72 h since admission.

Evidence level: 2 Recommendation: B

A 50% B 35% C 6% D 9% E 0%

Routine computed tomography (CT) in patients with AP is not recommended when the diagnosis can be established based on non-imaging criteria.[11] However, if the patient fails to improve after 48—72 h (e.g. pain, nausea, fever, intolerance to oral feeding), contrast-enhanced CT or magnetic resonance imaging (MRI) is recommended to evaluate possible local complications.[8] MRI is comparable to contrast-enhanced CT in assessing the severity of pancreatic inflammation and predicting prognosis.[12]

Statement 4

The severity of acute pancreatitis should be categorized into mild, moderately severe or severe.

Evidence level: 2 Recommendation: A

A 56% B 36% C 8% D 0% E 0%

According to revised Atlanta classification, the severity of AP is classified as mild, moderately severe, and severe.[13]

Severe AP (SAP) is as the presence of persistent organ failure (>48 h) according to modified Marshall scoring system, which is the most important risk factors of mortality.[14] Moderately severe AP is defined by any of the following complications: local complications, systematic complications (i.e. exacerbation of pre-existing co-morbidity), and transient organ failure (<48 h). Compared with SAP, moderately severe AP has a much lower mortality rate and is less likely to require ICU admissions and invasive interventions.[15]

Statement 5

Clinical scoring systems, radiological scores, and biochemical markers may help in early prediction of severe acute pancreatitis.

Evidence level: 2 Recommendation: B

A 83% B 17% C 0% D 0% E 0%

Most AP episodes are mild and recover spontaneously in 48 h after adequate hydration and medical support. On the other hand, AP carries a mortality rate of 2%—3%,[16,17] with complications occurring in 30%—40% of patients which may result in ICU admission, invasive interventions, and prolonged admission.[9] Thus, early prediction of the severity of AP may help optimize patient care and disposition. Various predication models have been proposed, including Ranson's criteria, CTSI, APACHE II score, APACHE combined with scoring for obesity (APACHE-O), the Glasgow scoring system, the Harmless Acute Pancreatitis Score (HAPS), PANC 3, the Japanese Severity Score (JSS), Pancreatitis Outcome Prediction (POP), and Bedside Index for Severity of Acute Pancreatitis (BISAP) score, with variable accuracy and low positive predictive values.[17,18] The BISAP score can predict SAP and moderately severe acute pancreatitis (MSAP) within 24 h of admission. By using 5 common clinical parameters, BISAP score $\geq$3 has specificity of 98.9% and 97.6% and specificity of 45.5% and 75.0% for prediction of SAP and mortality respectively. Serum C-reactive protein (CRP) level may also be useful for predicting the severity of AP; a level higher than 15 mg/dl at 48 h has 86% sensitivity for predicting the severity of AP.[19]

Imaging-based prediction methods such as the CT Severity index (CTSI) and modified CTSI (mCTSI) have similar prediction performance to clinical scoring system.[20] Perfusion CT may be useful for predicting severity with a high positive predictive rate (59%—81%) in predicting persistent organ failure based on its power to diagnose pancreatic necrosis.[21]

Statement 6

Adequate resuscitation with optimal fluid administration and careful monitoring is essential in the acute phase of pancreatitis. Lactate Ringer's solution is the preferred crystalloid fluid.

Evidence level: 1 Recommendation: A

A 53% B 39% C 8% D 0% E 0%

Early aggressive hydration hastens clinical improvement in mild acute pancreatitis. In a randomized controlled trial (RCT) comparing aggressive (20 ml/kg bolus followed by 3 ml/kg/h) or standard (10 ml/kg bolus followed by 1.5 mg/kg/h) hydration with Lactated Ringer's solution within 4 h after diagnosis of mild AP, aggressive hydration reduced the rate of persistent systemic inflammatory response syndrome (SIRS) and increased the rate of clinical improvement.[22] Two RCTs showed that lactated Ringer's solution resuscitation reduced levels of SIRS and C-reactive protein after 24—72 h in patients with mild AP compared with saline.[23,24] Taken together, adequate resuscitation with lactated Ringer's solution is recommended in patients with AP.

Statement 7

Opioid may be used for pain management of acute pancreatitis.

Evidence level: 1 Recommendation: A

A 42% B 47% C 11% D 0% E 0%

Achieving adequate pain relief in patients with AP is often challenging. Different opiate agents have varying effects on basal and phasic contractions of Sphincter of Oddi.[25,26] Morphine and codeine increase the pressure of the sphincter, whereas pentazocine increases the duration of sphincter contraction and ductal pressure.[25] However, a meta-analysis of 5 RCTs with 227 patients found no differences in the risk of complications of pancreatitis or serious adverse events between opioids and non-opioid analgesics, and opioids may decrease the need for supplementary analgesia.[27] Therefore, opioid analgesics may be used to relieve pain in AP.

Statement 8

Routine antibiotic prophylaxis for secondary infection is not recommended in acute pancreatitis, unless infection is either proven or highly suspected.

Evidence level: 1 Recommendation: A

A 47% B 45% C 8% D 0% E 0%

Approximately 40%—70% of patients with necrotizing pancreatitis develop pancreatic infection, which carries a significant risk of morbidity and mortality.[28] A meta-analysis of seven RCTs including 404 patients with necrotizing pancreatitis found that antibiotic prophylaxis was not effective in reducing mortality or preventing pancreatic infection, except that imipenem significantly decreased pancreatic infection in subgroup analysis.[29] Another meta-analysis of nine RCTs and 2 cohort studies including 864 patients with necrotizing pancreatitis also found that antibiotic prophylaxis did not reduce the incidence of infected pancreatic necrosis.[30] Most of the studies included in those two meta-analyses were inadequately powered. These evidence supports that routine antibiotic prophylaxis for secondary infection is not recommended. However, antibiotics must be administered promptly in patients who develop signs of sepsis or have a bacteriologically positive aspiration from necrosis. Additionally, antibiotics should also be given in patients with acute cholangitis or other proven extra-pancreatic infection.

Statement 9

Pharmacological agents might have a role in the treatment of acute pancreatitis.

Evidence level: 2 Recommendation: B

A 73% B 17% C 7% D 3% E 0%

Various clinical studies have assessed the effects of pharmacologic therapies that target different aspects of the pathogenesis of AP. In a meta-analysis of 78 trials including 7366 participants that evaluated therapies including antibiotics, antioxidants, aprotinin, atropine, calcitonin, cimetidine, ethylenediaminetetraacetic acid, gabexate, glucagon, iniprol, lexipafant, non-steroidal anti-inflammatory drugs, octreotide, oxyphenonium, probiotics, activated protein C, somatostatin, somatostatin plus omeprazole, somatostatin plus ulinastatin, thymosin, and ulinastatin, none of those agents reduced in-hospital mortality or mortality within 6 months. On the other hand, the results suggest that gabexate mesilate might reduce the need for additional invasive intervention (OR: 0.58, 95% CI: 0.37—0.90; N = 426; 3 studies), octreotide might reduce organ failure (OR: 0.51, 95% CI: 0.27—0.97; N = 430; 3 studies), and lexipafant might reduce the risk of sepsis (OR: 0.26, 95% CI: 0.08—0.83; N = 290; 1 study). While these results suggest pharmacologic agents might play a role in the treatment of AP, more research is warranted.[31]

Statement 10

Early ERCP is not needed in gallstone pancreatitis patients without obstructive jaundice or acute cholangitis.

Evidence level: 1 Recommendation: A

A 85% B 15% C 0% D 0% E 0%

A multicenter RCT comparing conservative treatment and early endoscopic retrograde cholangiopancreatography (ERCP) (i.e., within 72 h after symptom onset) for endoscopic papillotomy and removal of common bile duct stones showed that overall complication rates were similar, but complications were more severe in patients randomized to early ERCP.[32] Another RCT comparing conservative treatment and early ERCP in patients with acute biliary pancreatitis without coexisting acute cholangitis found no significant differences between the two groups in CT severity index, organ failure score, rate of local complications, and overall mortality and morbidity.[33] These findings support that early ERCP is not beneficial in patients who have acute biliary pancreatitis without concomitant acute cholangitis. Other systemic review/meta-analyses also showed that early ERCP does not provide benefit over conservative treatment for biliary pancreatitis in the absence of acute cholangitis, regardless of the predicted severity of AP.[34—36]

Statement 11

EUS or MRI/MRCP is preferred over ERCP for excluding bile duct stone and evaluation of acute pancreatitis with indeterminate etiology.

Evidence level: 2 Recommendation: C

A 85% B 15% C 0% D 0% E 0%

ERCP carries a risk of complications including post ERCP pancreatitis (PEP); therefore, magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) are preferred over ERCP for confirming the presence of bile duct stones. EUS can detect choledocholiathiasis with a sensitivity and specificity of approximately 95% and a positive predictive value of 91%—100%.[37—39] In a systematic review including 545 patients with AP of suspected biliary origin, EUS resulted in the avoidance of ERCP in 71.2% of cases.[40] In another meta-analysis including 213 patients randomized to EUS-guided ERCP and 210 patients to ERCP, ERCP was avoided in 143 patients (67.1%) in the EUS-first group because of the lack of choledocholithiasis on EUS. The use of EUS significantly reduced the risk of overall complications (relative risk 0.35 (95% confidence interval (C.I.) 0.20 to 0.62); $P < 0.001$) and PEP (relative risk 0.21 (95% C.I. 0.06 to 0.83); $P = 0.03$).[41] MRCP is also highly accurate in diagnosing choledocholithiasis, with sensitivities of 92%—94% and a specificity of 99% in a meta-analysis.[42] A systematic review showed a similar diagnostic value for prospective studies that compared MRCP and EUS for the detection of CBD stones.[43] About 20% of cases with AP remain idiopathic even after complete serum biochemistry, ultrasound and CT evaluations.[44] In a systematic review, EUS identified additional diagnostic information in 61% of patients with idiopathic pancreatitis.[45] Given that microlithiasis/biliary sludge is a common cause of idiopathic pancreatitis, EUS should be considered the first diagnostic modality for evaluation of idiopathic pancreatitis if cross-sectional imaging fails to reveal the etiology.

Statement 12

Per-rectal NSAIDs, pancreatic stent placement, or Lactated Ringer's solution infusion can reduce the risk of post-ERCP pancreatitis.

Evidence level: 1 Recommendation: A

A 76% B 12% C 0% D 9% E 3%

Post-ERCP pancreatitis (PEP) occurs in 3%—15% of ERCPs. A prior history of PEP, a normal serum bilirubin level and procedural factors such as difficult cannulation and repeated pancreatography/pancreatic cannulation are predictive of a high risk of PEP. Two meta-analyses showed that pancreatic duct stent placement effectively reduce the risk of PEP by 61% and 78%, respectively.[46,47] In a double-blinded RCT in patients at high risk of PEP, rectal indomethacin immediately after ERCP reduced the risk of PEP by 46%.[48] Subsequent studies and meta-analysis also demonstrated that peri-ERCP rectal diclofenac or indomethacin reduced the risk of PEP in both high-risk and average-risk patients.[49—52] European Society of Gastrointestinal Endoscopy (ESGE) recommends rectal administration of 100 mg of diclofenac or indomethacin immediately before or after ERCP in all patients without contraindication, with pancreatic stent placement in high-risk patients.[53]

Recent evidence reveals that peri-procedural aggressive Lactated Ringer's (LR) solution infusion also reduces the risk of PEP.[54,55] Another RCT also demonstrates reduced rate of PEP when both LR solution and rectal indomethacin are used compared with normal saline and placebo.[56] A

meta-analyses of 3 RCTs shows that aggressive LR hydration reduces the overall incidence of PEP by 71%.[57]

Statement 13

Gabexate mesilate may be considered for prophylaxis of PEP in selected patients.

Evidence level: 2 Recommendation: B

A 44% B 41% C 9% D 3% E 3%

Gabexate mesylate (GM), a protease inhibitor, has been assessed for prophylaxis of PEP. In a multicenter double-blind RCT comparing 1 g GM intravenous infusion from 30 to 90 min before ERCP till 12 h after the procedure and placebo, patients randomized to GM had a lower rate of abdominal pain (6% vs 14%, $p = 0.009$) and PEP (2% vs 8%, $p = 0.03$).[58] Another double-blind study recruiting 193 patients randomized into GM group receiving 300 mg GM dissolved in 500 mL Ringer's solution via continuous intravenous infusion at 111 mL/h (starting 30 min before endoscopic procedures and continuing up to 4 h afterwards), whereas placebo group was given Ringer's solution only in the same manner. Three and 10 patients experienced post-ERCP pancreatitis in the GM group and the placebo group, respectively (3.1% vs. 10.5%, $p = 0.040$), while hyperamylasemia was noted in 33 and 42 patients in the GM group and the placebo group, respectively (33.7% vs. 43.7%, $p = 0.133$). Pancreatic pain occurred in 15 and 28 patients in the GM group and the placebo group, respectively (15.3% vs. 29.5%, $p = 0.018$). The findings suggest that intravenous infusion of 300 mg GM for 4.5 h could be an effective precaution against post-ERCP pancreatitis and pancreatic pain.[59] However, a meta-analysis including 5 RCTs comparing GM vs placebo showed no significant differences in the incidence of PEP (4.8% vs 5.7%, $p = 0.34$).[60] Taken together, evidence for GM is inconsistent and more research is needed. GM might be considered for prophylaxis of PEP where rectal NSAID, pancreatic stent placement, and aggressive hydration with LR solution are contraindicated.

Statement 14

Early cholecystectomy is recommended to prevent recurrent gallstone pancreatitis. ERCP with sphincterotomy may be an alternative method if cholecystectomy is not feasible.

Evidence level: 2 Recommendation: B

A 82% B 12% C 6% D 0% E 0%

Cholecystectomy is the most effective method to prevent recurrent acute gallstone pancreatitis. In an RCT, same-admission cholecystectomy reduces the risk of gallstone-related complications compared with interval cholecystectomy (risk ratio 0.28).[61] In a prospective observational study, recurrent gallstone pancreatitis is rare after endoscopic sphincterotomy (ES), and the rate of recurrent pancreatitis was comparable between ES alone and ES with cholecystectomy (2.9% vs. 2.4%).[62] A national database analysis showed that among patients without cholecystectomy, ERCP was associated with a lower rate of recurrent pancreatitis and severe pancreatitis. Therefore, ES may be an acceptable alternative to cholecystectomy for preventing recurrent gallstone pancreatitis if cholecystectomy is not feasible.[63]

Statement 15

Percutaneous drainage or early surgical decompression is indicated for patients with abdominal compartment syndrome and failed medical treatments.

Evidence level: 2 Recommendation: B

A 87% B 13% C 0% D 0% E 0%

Abdominal compartment syndrome (ACS), characterized by intra-abdominal pressure (IAP) $>$ 20 mmHg and new-onset organ dysfunction,[64] is a severe complication of severe acute pancreatitis (SAP). The reported incidence of ACS in SAP patients is around 12%–39%,[65] with a mortality rate of 49%[66] and it may be an exceptional condition for early surgical intervention for acute pancreatitis. Regardless of etiologies of ACS, progress of this condition should be terminated as soon as possible otherwise.

Medical treatments including decompression of gastrointestinal content, and optimization of fluid resuscitation and systemic perfusion are recommended to prevent progression from intra-abdominal hypertension (IAH, IAP $>$ 12 mmHg) to ACS.[64] Decompressive laparotomy is indicated if IAH/ACS is refractory to medical management to prevent further deterioration and serious adverse outcomes.[64,67]

Statement 16

Infected pancreatic necrosis should be suspected when clinical conditions deteriorate and/or imaging findings support.

Evidence level: 3 Recommendation: B

A 77% B 19% C 4% D 0% E 0%

Pancreatic parenchymal and/or peripancreatic tissue necrosis occurs in approximately 15% of patients with AP with a mortality rate of approximately 15%. Infected pancreatic necrosis (IPN) carries a 30% mortality rate and must be timely treated,[68–71] preferably in tertiary medical centers by multidisciplinary teams including gastroenterologists/endoscopists, surgeons, and radiologists. IPN usually occurs 1–2 weeks after onset and manifests as fever, leukocytosis, and deteriorating clinical condition, and CT may show the presence of air in the necrosis. A meta-analysis of 8 studies/324 patients with IPN showed that 64% of the patients could be treated by antibiotic alone without requiring drainage.[72] Therefore, broad-spectrum antibiotics that can penetrate the necrosis should be started when IPN is suspected, and aspiration and culture of necrotic material is not routinely required.[8,73–75] Patients who fail to improve or deteriorate with antibiotic treatment require additional interventions such as drainage or necrosectomy. Under those circumstances, microbiological diagnosis may be helpful to dictate later treatment plan.

Statement 17

If the patient's condition allowed, therapeutic interventions for infected pancreatic necrosis should be delayed until 4 weeks after onset.

Evidence level: 2 Recommendation: B
A 76% B 18% C 3% D 3% E 0%

In a multicenter prospective study, patients who had longer time between admission and intervention for IPN had lower mortality (<14 days, 56%; 14–29 days, 26%; >29 days, 15%; P < 0.001).[71] A delay of at least 4 weeks allows for wall-off of the necrotic collection, which makes drainage and necrosectomy easier and reduces the risk of complications after interventions.

Statement 18

Infected pancreatic necrosis should be managed in a step-up approach, starting with percutaneous or endoscopic drainage followed by minimally invasive necrosectomy.

Evidence level: 2 Recommendation: B
A 81% B 19% C 0% D 0% E 0%

The PANTER trial randomly assigned patients with IPN to primary open necrosectomy or step-up approach starting with percutaneously drainage, followed by minimally invasive necrosectomy if necessary.[76] Patients randomized to step-up approach had lower rates of major complications or death (40% vs 69%, P = 0.006) and new-onset multiorgan failure (12% vs 40%, p = 0.002), and 35% of those patients required only percutaneous drainage.

Necrosectomy can be achieved by either surgical or endoscopic necrosectomy. A multicenter RCT showed that endoscopic had a lower rate of major complications or death compared with surgical necrosectomy (20% vs 80%, p = 0.003), and also reduced the risk of new-onset multiple organ failure and pancreatic fistula.[77]

Statement 19

Surgical necrosectomy should be considered only after other treatments failed.

Evidence level: 2 Recommendation: B
A 71% B 29% C 0% D 0% E 0%

As discussed in the above, step-up approach is the current standard of care for IPN. Surgical necrosectomy should be reserved as the last resort. Compared with open laparotomy, minimally invasive necrosectomy with video-assisted or small incision-based left retroperitoneal debridement is associated with lower rates of morbidity and mortality.[78,79]

Statement 20

Nutritional therapy should be based on the severity of disease and clinical assessment.

Evidence level: 3 Recommendation: B
A 69% B 28% C 0% D 0% E 3%

Emergent evidence supports early oral feeding for patients with AP.[80] However, patients may be intolerant of early oral feeding due to pain, vomiting, or ileus and require enteral tube feeding for nutritional support. The goals of nutrition therapy are to prevent malnutritional risk from the time of diagnosis and reduce treatment-related morbidity and mortality.

Statement 21

For patients with mild acute pancreatitis, oral feeding should be started as early as tolerated.

Evidence level: 1 Recommendation: A
A 79% B 21% C 0% D 0% E 0%

In a meta-analysis including 5 RCTs, early oral refeeding decreased the length of hospital stay compared with standard oral refeeding (weighted mean difference −2.22, 95% CI −3.37 to −1.08, *P* = 0.0001) in patients with AP, without significant differences in abdominal pain or abdominal distension.[81] Another systematic review including 11 RCTs also showed that early feeding may reduce length of stay in mild to moderately severe AP without an increase in adverse events.[82]

Statement 22

For moderate to severe diseases, oral or enteral tube feeding is the preferred route nutrition. Parenteral nutrition can be used when nutrition requirements are not met by oral or enteral feeding.

Evidence level: 1 Recommendation: A
A 72% B 28% C 0% D 0% E 0%

A meta-analysis of 8 RCTs demonstrated that compared with total parenteral nutrition (TPN), enteral nutrition significantly reduced mortality (OR 0.37, 95%CI 0.21–0.68, *P* = 0.001), infectious complications (OR 0.46, 95%CI 0.27–0.78, *P* = 0.004), organ failure (OR 0.44, 95%CI 0.44 0.22–0.88, *P* = 0.02), and need for surgical intervention (OR 0.41, 95%CI 0.23–0.74, *P* = 0.003).[83] A review of 12 RCTs also concluded that enteral nutrition reduced the risk of infected peripancreatic necrosis, single organ failure, and multiple organ failure.[80]

Statement 23

Both nasogastric and nasoenteral tubes can be used for enteral feeding with similar outcomes.

Evidence level: 2 Recommendation: B
A 86% B 14% C 0% D 0% E 0%

In a meta-analyses including 3 RCTs (157 patients) comparing nasogastric tubes with nasoenteral tubes in patients with predicted severe AP found no significant differences between the two modalities in mortality (RR 0.69, 95% CI 0.37–1.29, p = 0.25), tracheal aspiration (RR 0.46, 95% CI 0.14–1.53, p = 0.20), diarrhea (RR 1.43, 95% CI 0.59–3.45, p = 0.43), exacerbation of pain (RR 0.94, 95% CI 0.32–2.70, p = 0.90) and ability to achieve energy balance.[84] However, the overall sample size was limited, and the risk of aspiration with nasogastric feeding had not been adequately assessed in those trials. Future large-scale trials are warranted.

Statement 24

For enteral tube feeding, elemental and polymeric formulae are comparable in efficacies.

Evidence level: 1 Recommendation: A
A 73% B 27% C 0% D 0% E 0%

A meta-analysis of 10 RCTs comparing (semi)elemental and polymeric diets for enteral feeding in patients with AP found no significant differences in terms of feeding intolerance, infectious complications, and mortality.[85] Supplementation of enteral nutrition with probiotics or the use of immunonutrition have not been shown to improve clinical outcomes.[85,86]

Conflict of interest

No conflict of interest exist for all the authors.

Funding

The meeting for voting of the statements were supported by Chunghwa Yuming Healthcare Co., Ltd, which played no role in the drafting and approval of the consensus statements.

Acknowledgement

The authors would like to thank the following experts (listed in alphabetical order) who participated in the voting for the statements: Chun-Chao Chang, Taipei Medical University Hospital; Chien-Lin Chen, Buddhist Tzu Chi Medical Center; Kuan-Yang Chen, Taipei City Hospital-Renai Branch; Wen-Chi Chen, Kaohsiung Veterans General Hospital; Yi-Chun Chiu, Kaohsiung Chang Gung Memorial Hospital; Jun-Te Hsu, Chang Gung Memorial Hospital; Jee-Fu Huang, Kaohsiung Medical University Hospital; Wen-Hsin Huang, China Medical University Hospital; Yi-Yin Jan, Chang Gung Memorial Hospital; Cheng-Kuan Lin, Far Eastern Memorial Hospital; Jaw-Town Lin, Fu Jen Catholic University Hospital; Lein-Ray Mo, Show Chwan Memorial Hospital; Ming-Jen Sheu, Chi Mei Hospital.

Cheng-Hsi Su, Taipei Veterans General Hospital; Wei-Wen Su, Changhua Christian Hospital; Chung-Kwe Wang, Taipei City Hospital-Renai Branch; Yao-Sheng Wang, National Cheng Kung University Hospital; Cheng-Chung Wu, Taichung Veterans General Hospital; Hong-Zen Yeh, Taichung Veterans General Hospital; Ta-Sen Yeh, Chang Gung Memorial Hospital.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2019.07.019.

References

1. Xiao AY, Tan ML, Wu LM, Asrani VM, Windsor JA, Yadav D, et al. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. *Lancet Gastroenterol Hepatol* 2016;**1**(1):45—55.
2. Krishna SG, Kamboj AK, Hart PA, Hinton A, Conwell DL. The changing epidemiology of acute pancreatitis hospitalizations: a decade of trends and the impact of chronic pancreatitis. *Pancreas* 2017;**46**(4):482—8.
3. OCEBM Levels of Evidence Working Group. The Oxford 2011 Levels of Evidence. Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653.
4. Vissers RJ, Abu-Laban RB, McHugh DF. Amylase and lipase in the emergency department evaluation of acute pancreatitis. *J Emerg Med* 1999;**17**:1027—37.
5. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. *Am J Gastroenterol* 2002;**97**:1309—18.
6. Treacy J, Williams A, Bais R, Willson K, Worthley C, Reece J, et al. Evaluation of amylase and lipase in the diagnosis of acute pancreatitis. *ANZ J Surg* 2001;**71**:577—82.
7. Rompianesi G, Hann A, Komolafe O, Pereira SP, Davidson BR, Gurusamy KS. Serum amylase and lipase and urinary trypsinogen and amylase for diagnosis of acute pancreatitis. *Cochrane Database Syst Rev* 2017;**4**:CD012010.
8. Tenner S, Baillie J, DeWitt J, Vege SS. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013 Sep;**108**:1400—15. 1416.
9. Forsmark CE, Vege SS, Wilcox CM. Acute pancreatitis. *N Engl J Med* 2016;**375**:1972—81.
10. Greenberg JA, Hsu J, Bawazeer M, Marshall J, Friedrich JO, Nathens A, et al. Clinical practice guideline: management of acute pancreatitis. *Can J Surg* 2016;**59**:128—40.
11. Shinagare AB, Ip IK, Raja AS, Sahni VA, Banks P, Khorasani R. Use of CT and MRI in emergency department patients with acute pancreatitis. *Abdom Imag* 2015;**40**:272—7.
12. Arvanitakis M, Koustiani G, Gantzarou A, Grollios G, Tsitouridis I, Haritandi-Kouridou A, et al. Staging of severity and prognosis of acute pancreatitis by computed tomography and magnetic resonance imaging-a comparative study. *Dig Liver Dis* 2007;**39**:473—82.
13. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102—11.
14. Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. *Gut* 2004;**53**:1340—4.
15. Talukdar R, Clemens M, Vege SS. Moderately severe acute pancreatitis: prospective validation of this new subgroup of acute pancreatitis. *Pancreas* 2012;**41**:306—9.
16. Elizabeth Dong M, Jonathan I, Chang MD, Verma Dhruv, Batech Michael, Villarin Cecia, Karl K, Kwok MD, Chen WanSu, Bechien U, Wu MD. Temporal trends in incidence and outcomes of acute pancreatitis in hospitalized patients in the United States [abstract]. In: *The 82nd annual scientific meeting of the American college of gastroenterology*. Orlando, FL: Orange County Convention Center; 2017.
17. Valverde-Lopez F, Matas-Cobos AM, Alegria-Motte C, Jimenez-Rosales R, Ubeda-Munoz M, Redondo-Cerezo E. BISAP, RANSON, lactate and others biomarkers in prediction of severe acute pancreatitis in a European cohort. *J Gastroenterol Hepatol* 2017;**32**:1649—56.
18. Papachristou GI, Muddana V, Yadav D, O'Connell M, Sanders MK, Slivka A, et al. Comparison of BISAP, Ranson's, Apache-II, and CTSI scores in predicting organ failure, complications, and mortality in acute pancreatitis. *Am J Gastroenterol* 2010;**105**:435—41. quiz 442.
19. Zuleta Martín Gómez, Lobo Xiomara Ruiz, Regino William Otero. A quick and simple set of indicators for predicting the severity of acute pancreatitis. *Rev Colomb Gastroenterol* 2010;**25**:115—24.
20. Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, et al. A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis. *Am J Gastroenterol* 2012;**107**:612—9.

21. Tsuji Y, Takahashi N, Isoda H, Koizumi K, Koyasu S, Sekimoto M, et al. Early diagnosis of pancreatic necrosis based on perfusion CT to predict the severity of acute pancreatitis. *J Gastroenterol* 2017;**52**:1130–9.
22. Buxbaum JL, Quezada M, Da B, Jani N, Lane C, Mwengela D, et al. Early aggressive hydration hastens clinical improvement in mild acute pancreatitis. *Am J Gastroenterol* 2017;**112**:797–803.
23. Wu BU, Hwang JQ, Gardner TH, Repas K, Delee R, Yu S, et al. Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. *Clin Gastroenterol Hepatol* 2011;**9**:710–717 e711.
24. de-Madaria E, Herrera-Marante I, Gonzalez-Camacho V, Bonjoch L, Quesada-Vazquez N, Almenta-Saavedra I, et al. Fluid resuscitation with lactated Ringer's solution vs normal saline in acute pancreatitis: a triple-blind, randomized, controlled trial. *U Eur Gastroenterol J* 2018;**6**:63–72.
25. Staritz M, Poralla T, Manns M, Meyer Zum Buschenfelde KH. Effect of modern analgesic drugs (tramadol, pentazocine, and buprenorphine) on the bile duct sphincter in man. *Gut* 1986;**27**:567–9.
26. Sherman S, Gottlieb K, Uzer MF, Smith MT, Khusro QE, Earle DT, et al. Effects of meperidine on the pancreatic and biliary sphincter. *Gastrointest Endosc* 1996;**44**:239–42.
27. Basurto Ona X, Rigau Comas D, Urrutia G. Opioids for acute pancreatitis pain. *Cochrane Database Syst Rev* 2013:CD009179.
28. Schmid SW, Uhl W, Friess H, Malfertheiner P, Buchler MW. The role of infection in acute pancreatitis. *Gut* 1999;**45**:311–6.
29. Villatoro E, Mulla M, Larvin M. Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. *Cochrane Database Syst Rev* 2010:CD002941.
30. Lim CL, Lee W, Liew YX, Tang SS, Chlebicki MP, Kwa AL. Role of antibiotic prophylaxis in necrotizing pancreatitis: a meta-analysis. *J Gastrointest Surg* 2015;**19**:480–91.
31. Moggia E, Koti R, Belgaumkar AP, Fazio F, Pereira SP, Davidson BR, et al. Pharmacological interventions for acute pancreatitis. *Cochrane Database Syst Rev* 2017;**4**:Cd011384.
32. Folsch UR, Nitsche R, Ludtke R, Hilgers RA, Creutzfeldt W, The German Study Group on Acute Biliary Pancreatitis. 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**(4):237–42.
33. Oria A, Cimmino D, Ocampo C, Silva W, Kohan G, Zandalazini H, 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**(1):10–7.
34. Petrov MS, Uchugina AF, Kukosh MV. Does endoscopic retrograde cholangiopancreatography reduce the risk of local pancreatic complications in acute pancreatitis? A systematic review and metaanalysis. *Surg Endosc* 2008;**22**(11):2338–43.
35. Petrov MS, van Santvoort HC, Besselink MG, van der Heijden GJ, van Erpecum KJ, Gooszen HG. Early endoscopic retrograde cholangiopancreatography versus conservative management in acute biliary pancreatitis without cholangitis: a meta-analysis of randomized trials. *Ann Surg* 2008;**247**(2):250–7.
36. Tse F, Yuan Y. Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. *Cochrane Database Syst Rev* 2012;(5):CD009779.
37. Amouyal P, Amouyal G, Lévy P, Tuzet S, Palazzo L, Vilgrain V, et al. Diagnosis of choledocholithiasis by endoscopic ultrasonography. *Gastroenterology* 1994;**106**:1062–7.
38. Prat F, Amouyal G, Amouyal P, Pelletier G, Fritsch J, Choury AD, et al. Prospective controlled study of endoscopic ultrasonography and endoscopic retrograde cholangiography in patients with suspected common-bile duct lithiasis. *Lancet* 1996;**347**:75–9.
39. Canto MI, Chak A, Stellato T, Sivak Jr MV. Endoscopic ultrasonography versus cholangiography for the diagnosis of choledocholithiasis. *Gastrointest Endosc* 1998;**47**:439–48.
40. De Lisi S, Leandro G, Buscarini E. Endoscopic ultrasonography versus endoscopic retrograde cholangiopancreatography in acute biliary pancreatitis: a systematic review. *Eur J Gastroenterol Hepatol* 2011 May;**23**(5):367–74.
41. Petrov MS, Savides TJ. Systematic review of endoscopic ultrasonography versus endoscopic retrograde cholangiopancreatography for suspected choledocholithiasis. *Br J Surg* 2009 Sep;**96**(9):967–74.
42. Romagnuolo J, Bardou M, Barkun AN. Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. *Ann Intern Med* 2003;**139**:547–57.
43. Ledro-Cano D. Suspected choledocholithiasis: endoscopic ultrasound or magnetic resonance cholangio-pancreatography? A systematic review. *Eur J Gastroenterol Hepatol* 2007;**19**:1007–11.
44. Şurlin V, Săftoiu A, Dumitrescu D. Imaging tests for accurate diagnosis of acute biliary Pancreatitis. *World J Gastroenterol* 2014 November 28;**20**(44):16544–9.
45. Smith I, Ramesh J, Kyanam Kabir Baig KR, Mönkemüller K, Wilcox CM. Emerging role of endoscopic ultrasound in the diagnostic evaluation of idiopathic pancreatitis. *Am J Med Sci* 2015 Sep;**350**(3):229–34.
46. Choudhary A, Bechtold ML, Arif M, Szary NM, Puli SR, Othman MO, et al. Pancreatic stents for prophylaxis against post-ERCP pancreatitis: a meta-analysis and systematic review. *Gastrointest Endosc* 2011;**73**(2):275–82.
47. Mazaki T, Mado K, Masuda H, Shiono M. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: an updated meta-analysis. *J Gastroenterol* 2014;**49**(2):343–55.
48. Elmunzer BJ, Scheiman JM, Lehman GA, Chak A, Mosler P, Higgins PD, et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N Engl J Med* 2012;**366**(15):1414–22.
49. Patil S, Pandey V, Pandav N, Ingle M, Phadke A, Sawant P, et al. Role of rectal diclofenac suppository for prevention and its impact on severity of post-endoscopic retrograde cholangiopancreatography pancreatitis in high-risk patients. *Gastroenterol Res* 2016;**9**(2–3):47–52.
50. Luo H, Zhao L, Leung J, Zhang R, Liu Z, Wang X, et al. Routine pre-procedural rectal indometacin versus selective post-procedural rectal indometacin to prevent pancreatitis in patients undergoing endoscopic retrograde cholangiopancreatography: a multicentre, single-blinded, randomised controlled trial. *Lancet* 2016;**387**(10035):2293–301.
51. He X, Zheng W, Ding Y, Tang X, Si J, Sun L. Rectal indomethacin is protective against pancreatitis after Endoscopic Retrograde Cholangiopancreatography: systematic review and meta-analysis. *Gastroenterol Res Pract* 2018;**2018**:9784841.
52. Yu LM, Zhao KJ, Lu B. Use of NSAIDs via the rectal route for the prevention of pancreatitis after ERCP in all-risk patients: an updated meta-analysis. *Gastroenterol Res Pract* 2018;**2018**:1027530.
53. Dumonceau JM, Andriulli A, Elmunzer BJ, Mariani A, Meister T, Deviere J, et al. Prophylaxis of post-ERCP pancreatitis: European society of gastrointestinal endoscopy (ESGE) guideline. *Endoscopy* 2014;**46**(09):799–815.
54. Buxbaum J, Yan A, Yeh K, Lane C, Nguyen N, Laine L. Aggressive hydration with lactated Ringer's solution reduces pancreatitis after endoscopic retrograde cholangiopancreatography. *Clin Gastroenterol Hepatol* 2014;**12**(2):303–7.
55. Choi JH, Kim HJ, Lee BU, Kim TH, Song IH. Vigorous periprocedural hydration with lactated Ringer's solution reduces

the risk of pancreatitis after retrograde cholangiopancreatography in hospitalized patients. *Clin Gastroenterol Hepatol* 2017;**15**(1):86—92.
56. Mok SRS, Ho HC, Shah P, Patel M, Gaughan JP, Elfant AB. Lactated Ringer's solution in combination with rectal indomethacin for prevention of post-ERCP pancreatitis and readmission: a prospective randomized, double-blinded, placebo-controlled trial. *Gastrointest Endosc* 2017;**85**(5):1005—13.
57. Wu D, Wan J, Xia L, Chen J, Zhu Y, Lu N. The efficiency of aggressive hydration with Lactated Ringer solution for prevention of post-ERCP pancreatitis: a systemic review and meta-analysis. *J Clin Gastroenterol* 2017;**51**(8):e68—76.
58. Cavallini G, Tittobello A, Frulloni L, Masci E, Mariana A, Di Francesco V. Gabexate for the prevention of pancreatic damage related to endoscopic retrograde cholangiopancreatography. Gabexate in digestive endoscopy—Italian Group. *N Engl J Med* 1996;**335**(13):919—23.
59. Xiong GS, Wu SM, Zhang XW, Ge ZZ. Clinical trial of gabexate in the prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis. *Braz J Med Biol Res* 2006;**39**(1):85—90.
60. Andriulli A, Leandro G, Federici T, Ippolito A, Forlano R, Iacobellis A, et al. Prophylactic administration of somatostatin or gabexate does not prevent pancreatitis after ERCP: an updated meta-analysis. *Gastrointest Endosc* 2007;**65**(4):624—32.
61. da Costa DW, Bouwense SA, Schepers NJ, Besselink MG, van Santvoort HC, van Brunschot S, et al. Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial. *Lancet* 2015;**386**(10000):1261—8.
62. Kaw M, Al-Antably Y, Kaw P. Management of gallstone pancreatitis: cholecystectomy or ERCP and endoscopic sphincterotomy. *Gastrointest Endosc* 2002;**56**(1):61—5.
63. Qayed E, Shah R, Haddad YK. Endoscopic retrograde cholangiopancreatography decreases all-cause and pancreatitis readmissions in patients with acute gallstone pancreatitis who do not undergo cholecystectomy: a nationwide 5-year analysis. *Pancreas* 2018;**47**(4):425—35.
64. Kirkpatrick AW, Roberts DJ, De Waele J, Jaeschke R, Malbrain MLNG, De Keulenaer B, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med* 2013 Jul;**39**(7):1190—206.
65. De Waele JJ, Ejike JC, Leppaniemi A, De Keulenaer BL, De laet I, Kirkpatrick AW, et al. Intra-abdominal hypertension and abdominal compartment syndrome in pancreatitis, paediatrics, and trauma. *Anaesthesiol Intensive Ther* 2015 Jul 10;**47**(3):219—27.
66. Chen H, Li F, Sun J-B, Jia J-G. Abdominal compartment syndrome in patients with severe acute pancreatitis in early stage. *World J Gastroenterol* 2008 Jun;**14**(22):3541—8.
67. van Brunschot S, Schut AJ, Bouwense SA, Besselink MG, Bakker OJ, van Goor H, et al. Abdominal compartment syndrome in acute pancreatitis: a systematic review. *Pancreas* 2014 Jul;**43**(5):665—74.
68. Petrov MS, Shanbhag S, Chakraborty M, Phillips AR, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology* 2010;**139**:813—20.
69. Banks PA, Freeman ML, Practice Parameters Committee of the American college of G. Practice guidelines in acute pancreatitis. *Am J Gastroenterol* 2006;**101**:2379—400.
70. Uhl W, Warshaw A, Imrie C, Bassi C, McKay CJ, Lankisch PG, et al. IAP guidelines for the surgical management of acute pancreatitis. *Pancreatology* 2002;**2**:565—73.
71. van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology* 2011;**141**:1254—63.
72. Mouli VP, Sreenivas V, Garg PK. Efficacy of conservative treatment, without necrosectomy, for infected pancreatic necrosis: a systematic review and meta-analysis. *Gastroenterology* 2013 Feb;**144**(2):333—40.
73. Yokoe M, Takada T, Mayumi T, Yoshida M, Isaji S, Wada K, et al. Japanese guidelines for the management of acute pancreatitis: Japanese Guidelines 2015. *J Hepatobiliary Pancreat Sci* 2015 May 13;**22**(6):405—32.
74. Arvanitakis M, Dumonceau J-M, Albert J, Badaoui A, Bali M, Barthet M, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. *Endoscopy* 2018 Apr 9;**50**(05):1—23.
75. Freeman ML, Werner J, van Santvoort HC, Baron TH, Besselink MG, Windsor JA, et al. *Interventions for necrotizing pancreatitis: summary of a multidisciplinary consensus conference*. 2012. p. 1176—94.
76. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al., Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Eng J Med* 2010;**362**:1491—502.
77. Bakker OJ, Van Santvoort HC, van BS, Geskus RB, Besselink MG, Bollen TL, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *J Am Med Assoc* 2012;**307**:1053e61.
78. Raraty MGT, Halloran CM, Dodd S, Ghaneh P, Connor S, Evans J, et al. Minimal access retroperitoneal pancreatic necrosectomy. *Ann Surg* 2010 May;**251**(5):787—93.
79. Rasch S, Phillip V, Reichel S, Rau B, Zapf C, Rosendahl J, et al. Open surgical versus minimal invasive necrosectomy of the pancreas—a retrospective multicenter analysis of the German pancreatitis study group. Lau WYJ, editor. *PLoS One* 2016 Sep 26;**11**(9). e0163651—12.
80. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN. American gastroenterological association institute clinical guidelines committee. American gastroenterological association institute guideline on initial management of acute pancreatitis. *Gastroenterology* 2018 Mar;**154**(4):1096—101.
81. Horibe M, Nishizawa T, Suzuki H, Minami K, Yahagi N, Iwasaki E, et al. Timing of oral refeeding in acute pancreatitis: a systematic review and meta-analysis. *U Eur Gastroenterol J* 2016 Dec;**4**(6):725—32.
82. Vaughn VM, Shuster D, Rogers MAM, Mann J, Conte ML, Saint S, et al. Early versus delayed feeding in patients with acute pancreatitis: a systematic review. *Ann Intern Med* 2017;**166**(12):883—92.
83. Yi F, Ge L, Zhao J, Lei Y, Zhou F, Chen Z, et al. Meta-analysis: total parenteral nutrition versus total enteral nutrition in predicted severe acute pancreatitis. *Intern Med* 2012;**51**(6):523—30.
84. Chang YS, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a meta-analysis. *Crit Care* 2013;**17**(3):R118.
85. Petrov MS, Loveday BP, Pylypchuk RD, McIlroy K, Phillips AR, Windsor JA. Systematic review and meta-analysis of enteral nutrition formulations in acute pancreatitis. *Br J Surg* 2009;**96**:1243—52.
86. Poropat G, Giljaca V, Hauser G, Štimac D. Enteral nutrition formulations for acute pancreatitis. *Cochrane Database Syst Rev* 2015 Mar 23;(3):CD010605.