

Endoscopic retrograde cholangiopancreatography

Mustafa A. Arain and Martin L. Freeman

University of Minnesota, Minneapolis, MN, USA

Chapter menu

Introduction, 2582	Endoscopic retrograde cholangiopancreatography in pancreatic disease, 2605
Indications for endoscopic retrograde cholangiopancreatography, 2582	Endoscopic retrograde cholangiopancreatography in surgically altered upper gastrointestinal anatomy, 2610
Complications of endoscopic retrograde cholangiopancreatography, 2583	Further reading, 2611
Therapeutic and diagnostic techniques, 2587	
Biliary diseases, 2591	

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a specialized endoscopic procedure for the management of pancreatic and biliary diseases, in which the common bile duct and/or the pancreatic duct are accessed via papillary orifices or surgical anastomoses. Cannulation is achieved using a variety of catheter devices, typically via the accessory channel of a specialized side-viewing endoscope (also known as a duodenoscope), in order to access the biliary or pancreatic ducts. Contrast injection allows radiographic opacification of the ducts followed by therapeutic and diagnostic interventions.

Diagnostic ERCP using a specialized fiberoptic duodenoscope was first described in 1968, and biliary sphincterotomy to facilitate bile duct stone removal in 1973 [1,2]. ERCP offered a less invasive means of evaluation and management of pancreaticobiliary disorders than open surgery. Over the ensuing four decades, improvement in techniques and accessories has made ERCP the preferred modality for management of these conditions. However, ERCP is an invasive procedure that may result in localized or systemic complications with potentially significant risk of morbidity and even mortality. There has been a concerted effort to identify and understand risk factors associated with complications, and implementation of measures to minimize these complications. Simultaneously, there

have been advances in noninvasive imaging modalities, including magnetic resonance imaging (MRI)/ magnetic resonance cholangiopancreatography (MRCP), and contrast-enhanced computed tomography (CT) and endoscopic ultrasonography (EUS), allowing detailed and high-resolution evaluation of the biliary tree and its surrounding structures, as well as the pancreatic duct and pancreatic parenchyma. In the current era, ERCP is primarily a therapeutic procedure used in conditions requiring drainage of the biliary and pancreatic ducts (e.g., stone or strictures, or leaks). In addition, ERCP plays a therapeutic role in the excisional or ablative management of tumors of the major or minor papilla and selected intraductal tumors. Diagnostic ERCP is now reserved for diseases in which a diagnosis remains unclear despite noninvasive imaging modalities, such as in the evaluation of indeterminate strictures of the bile duct.

Indications for endoscopic retrograde cholangiopancreatography

ERCP is now primarily a therapeutic modality for biliary and pancreatic disorders [3,4]. While there are several specific disorders that lead to the need for ERCP, the primary goal of therapeutic ERCP is to reestablish drainage of the biliary and

pancreatic ducts into the duodenum or surgically anastomosed lumen. Conditions requiring therapeutic ERCP can broadly be divided into those in which there is impairment of flow (biliary or pancreatic stones; malignant or benign strictures) and ductal leaks. Leaks may occur as a result of surgery (e.g., cholecystectomy, pancreatic resection, liver transplantation, etc.), trauma, or as a de novo complication of diseases such as necrotizing pancreatitis. Urgent or emergent therapeutic ERCP is indicated when establishing drainage is essential, with or without proven cause of obstruction, such as in the setting of ascending cholangitis. In the past, ERCP was the first-line modality in the management of patients with suspected biliary obstruction. However, the role of ERCP has evolved significantly over the last two decades [5,6].

In some situations the findings from imaging modalities are not conclusive or the exact etiology of an underlying condition may not be clear (e.g., indeterminate nature of a biliary stricture), in which case ERCP with intraductal imaging and biopsy can play an important role in diagnosis. The role of ERCP in pancreatic indications such as idiopathic recurrent acute pancreatitis and chronic pancreatitis is controversial, as the quality of evidence supporting efficacy in these settings is highly variable [7]. The role of ERCP is even more controversial in sphincter of Oddi dysfunction (SOD), a syndrome in which patients, typically young women with upper abdominal pain, with or without pancreatic and liver enzyme abnormalities and/or ductal dilation, may undergo manometry, and/or biliary and pancreatic sphincterotomy. Because SOD is associated with a high risk of ERCP-related complications, and efficacy of interventions such as biliary and/or pancreatic sphincterotomy is under some doubt, the procedure should only be considered after extensive evaluation for other etiologies of pain have been excluded.

Finally, continuing improvements in endoscopic technology and development of specialized accessories has led to the application of access and drainage outside pancreatic and biliary ductal structures. EUS may be used to obtain antegrade access to the bile duct or pancreatic duct and a wire passed through the papillary or anastomotic orifice in order to allow completion of ERCP (rendezvous procedure) when, for example, ERCP access is not possible due to duodenal or ampullary distortion by tumor, intradiverticular papilla, or postsurgical ductal anastomoses. Currently, drainage and debridement of intraabdominal and retroperitoneal collections such as pseudocysts, walled off pancreatic and peripancreatic necroses, and postoperative abscesses are now routinely performed through ERCP, but usually after access is obtained using EUS guidance. Thus, in the modern era, advanced endoscopists are increasingly using therapeutic EUS in combination with ERCP during the same or tandem procedures in the endoscopic management of pancreaticobiliary diseases.

Complications of endoscopic retrograde cholangiopancreatography

Diagnostic and therapeutic ERCP can be associated with a variety of complications, including pancreatitis, hemorrhage, perforation, infection, and cardiopulmonary complications. In prospective series the overall short-term complication rate of ERCP is typically 5%–10% [8–13]. The severity of complications varies from mild (resulting in minimal morbidity) to severe (requiring prolonged hospitalization or additional interventions, or even long-term disability or death). Consensus definitions are widely used to report complications and to standardize outcome assessment across centers and studies (Table 135.1)

Table 135.1 Consensus definitions for the major complications of endoscopic retrograde cholangiopancreatography.

	Mild	Moderate	Severe
Pancreatitis	Clinical pancreatitis, amylase at least 3 times normal at more than 24 h after the procedure, requiring admission or prolongation of planned admission to 2–3 days	Pancreatitis requiring hospitalization of 4–10 days	Hospitalization for more than 10 days, pseudocyst, or intervention (percutaneous drainage or surgery)
Bleeding	Clinical (i.e., not just endoscopic) evidence of bleeding, hemoglobin drop <3 g, no transfusion	Transfusion (4 units or less), no angiographic intervention or surgery	Transfusion 5 units or more, or intervention (angiographic or surgical)
Perforation	Possible or only very slight leak of fluid or contrast, treatable by fluids and suction for ≤3 days	Any definite perforation treated medically 4–10 days	Medical treatment for more than 10 days, or intervention (percutaneous or surgical)
Infection (cholangitis)	>38°C for 24–48 h	Febrile or septic illness requiring more than 3 days of hospital treatment or percutaneous intervention	Septic shock or surgery

Any intensive care unit admission after a procedure grades the complication as severe.
Other rarer complications can be graded by length of needed hospitalization.

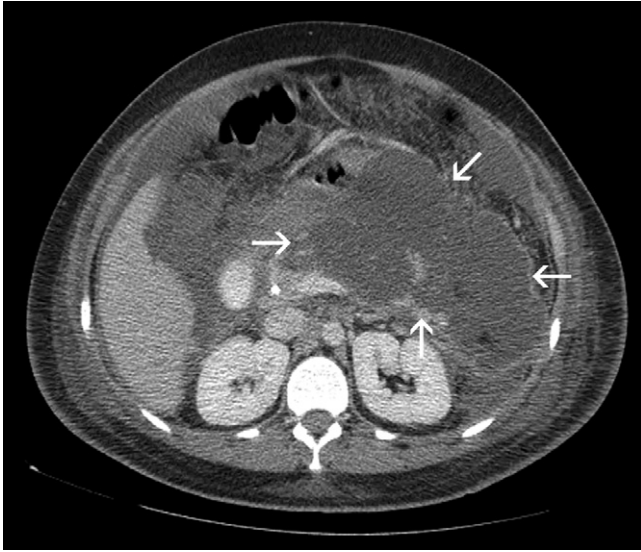


Figure 135.1 Contrast-enhanced computed tomography scan showing extensive pancreatic and peripancreatic necrosis from post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis resulting from an ERCP using needle-knife precut without a protective pancreatic stent.

[14]. Many prospective multicenter studies have been performed to evaluate patient and procedure-related risk factors associated with ERCP complications [8–23]. Better understanding of risk factors, improved techniques, and advances in technology have led to significant advances in prevention and management of complications.

Acute pancreatitis is the most common complication of ERCP, and likely results from multiple factors including injection and manipulation of the pancreatic orifice and pancreatic duct [8–23]. The risk of ERCP-related pancreatitis ranges from 2% to 20%, depending largely on patient and procedural variables, as well as on definitions used. Pancreatitis can range from mild, with pain requiring 1 or 2 days extra hospitalization, to necrotizing (Figure 135.1). Risk is highest in patients with suspected sphincter of Oddi dysfunction, reaching up to 20%, especially when combined with other risk factors, and is much lower in other conditions, for example <5% for bile duct stones. Some of the procedural and operator-related factors that increase the risk of pancreatitis are listed in Table 135.2.

There are many strategies to reduce the risk of post-ERCP pancreatitis (Box 135.1). To summarize, they consist of: (1) recognition of patient-related risk factors, with avoidance of ERCP or modification of other strategies in high-risk patients; (2) recognition and modification of procedure-related risk factors, especially in high-risk patients; (3) placement of prophylactic pancreatic stents in appropriate high-risk patients; and (4) pharmacological prevention.

Technique-related advances include use of guidewire cannulation, which has been shown in metaanalyses to reduce pancreatitis rates and improve cannulation success, presumably by minimizing contrast injection and instrumentation of the pan-

Table 135.2 Risk factors for post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis in multivariate analyses.

Definite ^a	Maybe ^b	No ^c
Suspected SOD	Acinarization	Small CBD diameter
Young age	Female gender	SO manometry
Normal bilirubin	Absence of CBD stone	Biliary sphincterotomy
History of post-ERCP pancreatitis	Lower ERCP case volume	
Difficult or failed cannulation	Trainee involvement	
Pancreatic duct injection		
Pancreatic guidewire placement		
Pancreatic tissue sampling by any method		
Pancreatic sphincterotomy (major or minor papilla)		
Balloon dilation of intact biliary sphincter		
Precut sphincterotomy		

^aSignificant by multivariate analysis in most studies.

^bSignificant by univariate analysis only in most studies.

^cNot significant by multivariate analysis in any study. CBD, common bile duct; SOD, sphincter of Oddi dysfunction; SO, sphincter of Oddi.

Box 135.1 Strategies for prevention of post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis: the four Ps.

Patient selection:

Avoidance of unnecessary or marginally indicated ERCP, especially in higher-risk patients, by using alternative imaging techniques (magnetic resonance cholangiopancreatography, endoscopic ultrasonography, intraoperative cholangiography)

Procedural modification:

Efficient cannulation, minimizing pancreatic injection and instrumentation

Pancreatic stents:

Placement of pancreatic stents in high-risk cases

Pharmacology:

Administration of a prophylactic drug before or after high-risk cases

creas using conventional techniques [15]. The most extensively studied technique for reduction of post-ERCP pancreatitis is placement of protective small-caliber pancreatic stents (Figures 135.2 and 135.3). Pancreatic stent placement has been shown to decrease the risk of post-ERCP pancreatitis of all severities by approximately two-thirds in more than 10 prospective randomized controlled trials and at least five metaanalyses primarily involving high or very high-risk patient groups [16–22].

Pancreatic stent placement is increasingly used as a primary method to reduce risk of post-ERCP pancreatitis in routine practice, and is increasingly considered standard of care in high-risk circumstances [23]. However, pancreatic stent placement itself may be complicated by failed attempts, or may cause complications including migration into the duct, stent-related ductal or parenchymal injury, or duct perforation [24–27]. The optimal techniques and stents for prevention of post-ERCP pancreatitis are undergoing continuing investigation.

Pharmacological prevention of post-ERCP pancreatitis has been a long sought goal, and many agents have been investi-

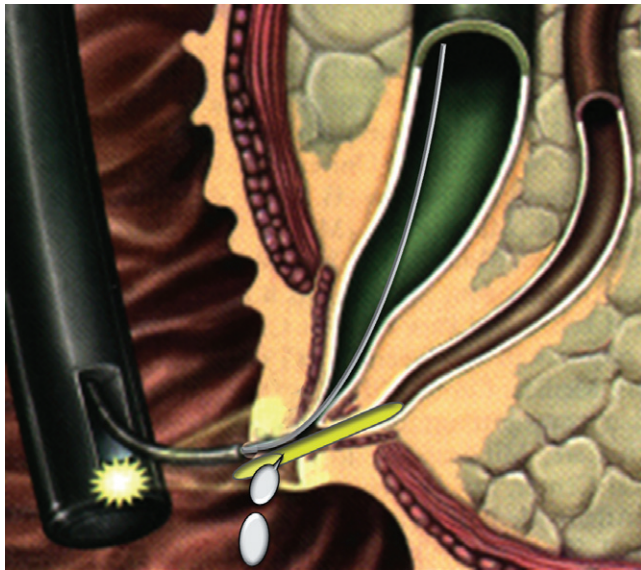


Figure 135.2 Schematic showing the protective effect of a pancreatic stent (yellow) in preserving pancreatic juice drainage during biliary access and endoscopic retrograde cholangiopancreatography.

gated. Most have turned out to be disappointing or unfeasible due to prolonged administration and expense. Nonsteroidal antiinflammatory drugs (NSAIDs) administered by a rectal, but not oral route, have been demonstrated in randomized controlled trials and metaanalyses to reduce risk of post-ERCP pancreatitis by about one-half [28–30]. Excess adverse renal and bleeding events have not been seen in carefully selected patient groups. Because most studies were performed in patients at low or mixed risk of post-ERCP pancreatitis, the relative role of NSAIDs compared to or in addition to pancreatic stents is unclear and is undergoing investigation.

The risk of hemorrhage from ERCP is primarily related to sphincterotomy, and is most significantly increased in patients with ascending cholangitis, presence of coagulopathy, or treatment with an anticoagulant within 3 days of sphincterotomy [8]. Intraoperative bleeding also elevates risk of delayed hemorrhage, but can almost always be controlled during the procedure or at a delayed presentation by the injection of dilute epinephrine, balloon tamponade, placement of clips (Figure 135.4), or placement of a fully covered self-expanding metal biliary stent (FCSEMS) for mechanical tamponade [31].

Perforation is a rare but serious complication of ERCP can occur by several mechanisms: (1) guidewire puncture may happen at any site but is rarely consequential as long as ductal drainage is achieved; (2) at the periampullary region in the setting of sphincterotomy, which is generally more significant; or (3) at the bowel wall, especially in patients with difficult access or altered anatomy, and almost always mandates intervention of some kind. Early recognition is critical (Figures 135.5 and 135.6), and can make it possible to manage the perforation by endoscopic techniques, either closure of sphincterotomy leaks by FCSEMS, clips, or closure of sphincterotomy or bowel perforations using standard or over-the-scope clips [32,33]. Surgery is usually required for large perforations, those that

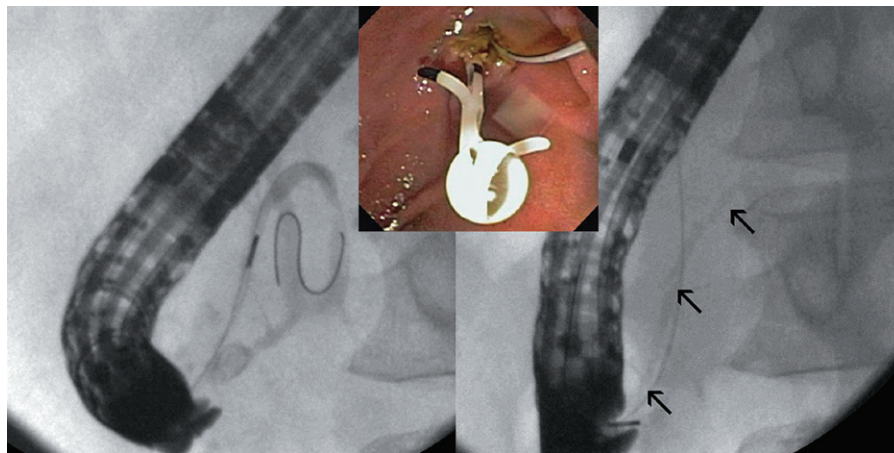


Figure 135.3 Fluoroscopic and endoscopic views of placement of short (2 cm), soft material, inner-flanged 4Fr pancreatic stent to the head of a pancreatic duct with an ansa-loop (360 degree turn in the pancreatic duct), over a knuckled 0.018 inch guidewire passed just into the loop turn of the pancreatic duct, for prevention of post endoscopic retrograde cholangiopancreatography pancreatitis. Such ducts are usually considered difficult to stent.

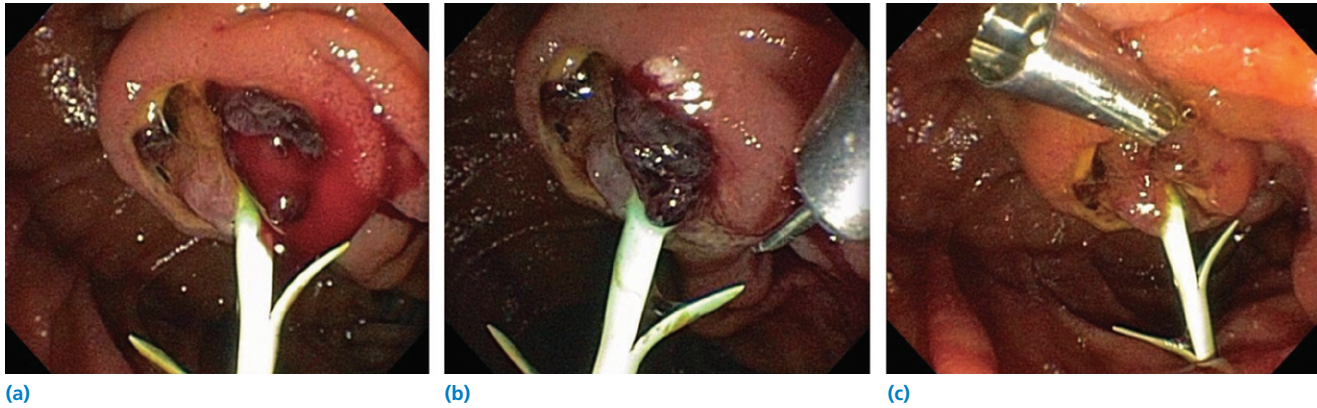


Figure 135.4 Delayed hemorrhage 3 days after biliary sphincterotomy that included a protective pancreatic stent (white): **(a)** fresh bleeding from the cut edge of the sphincterotomy just above the pancreatic stent; **(b)** injection of epinephrine to control the bleeding; **(c)** careful placement of a single endoscopic clip on the bleeding vessel, taking care to avoid the pancreatic orifice as defined by the pancreatic stent.

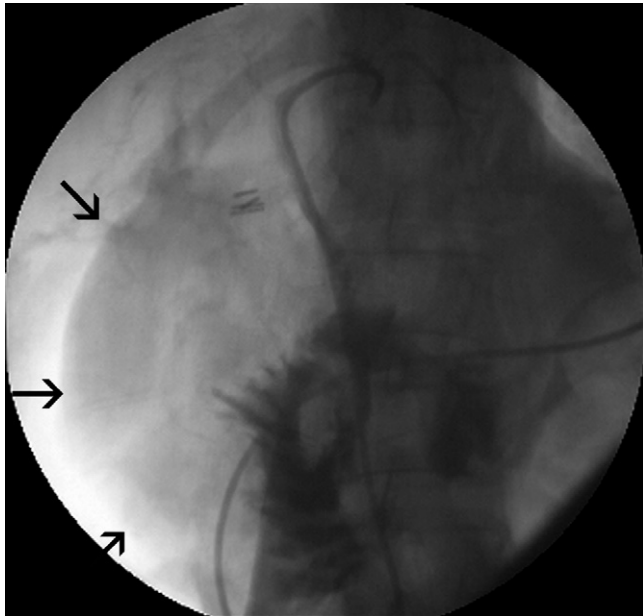


Figure 135.5 Large retroperitoneal perforation recognized during a biliary sphincterotomy. Extensive air can be seen outlining the right kidney, representing a large retroperitoneal leak at the sphincterotomy site. A nasobiliary drain has been placed and contrast fills the bile duct and duodenal sweep.

cannot be controlled by endoscopic or other minimally invasive routes, and those with delayed recognition resulting in large retroperitoneal or intraperitoneal collections.

Overall complications include pancreatitis, hemorrhage, infection, especially from occluded stents (Figure 135.7), perforation, cardiopulmonary, and others. Risk factors for overall complications are shown in Table 135.3. In the past, sedation and analgesia for ERCP was primarily administered by endoscopists or their nurses and assistants. There has been a trend towards the use of monitored anesthesia care or general anesthe-

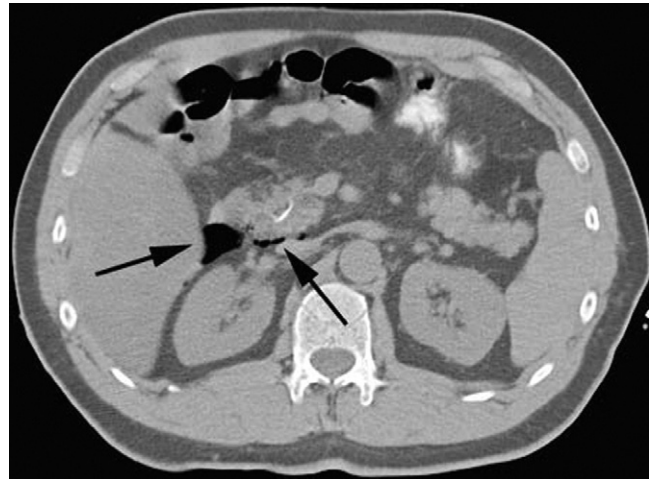


Figure 135.6 Computed tomography scan showing small amount of retroperitoneal air (arrows) immediately after endoscopic ampullectomy, recognized during the procedure and treated by endoscopic clipping, with uneventful recovery.

sia provided by an anesthetist. Anesthesia-related complications are now very rare (less than 0.5%). Death from ERCP complications is rare (<0.5%) and is usually a consequence of cardiopulmonary compromise, either directly from the procedure or indirectly as a result of stress from complications. Acute and chronic comorbid illnesses likely play an important role [8].

The importance of expertise in determining complications and outcomes of ERCP is intuitive and well recognized but has been difficult to demonstrate clearly in the literature. Large regional studies, mostly from European countries with centralized healthcare systems, have shown that higher case volumes are associated with improved technical success and lower complications, while some other studies do not bear out this difference, perhaps because of a different mix of cases and higher success rates at high-volume compared to low-volume centers



Figure 135.7 Cholangitis resulting from an occluded 10Fr plastic biliary stent, with purulent biliary drainage through the stent.

Table 135.3 Risk factors for overall complications of endoscopic retrograde cholangiopancreatography (ERCP) in multivariate analyses.

Definite ^a	Maybe ^b	No ^c
Cirrhosis	Young age	Comorbid illness
Suspected SOD	Pancreatic contrast injection	Small CBD diameter
Difficult cannulation	Failed biliary drainage	Female sex
Precut sphincterotomy	Trainee involvement	Billroth II gastrectomy
Lower ERCP case volume	Periampullary diverticulum	
Percutaneous biliary access		

^aSignificant by multivariate analysis in most studies
^bSignificant by univariate analysis only in most studies
^cNot significant by multivariate analysis in any study
 CBD, common bile duct; SOD, Sphincter of Oddi dysfunction.

[11,34–36]. Complications of sphincterotomy have been shown to correlate with case volume [8]. It is therefore recommended that ERCP be carried out at centers with demonstrated satisfactory outcomes, and that high-risk patients or complex procedures should be performed by expert endoscopists at specialized, high-volume centers [31,37].

Therapeutic and diagnostic techniques

ERCP is usually performed using a dedicated side-viewing endoscope with the patient positioned prone on a fluoroscopic

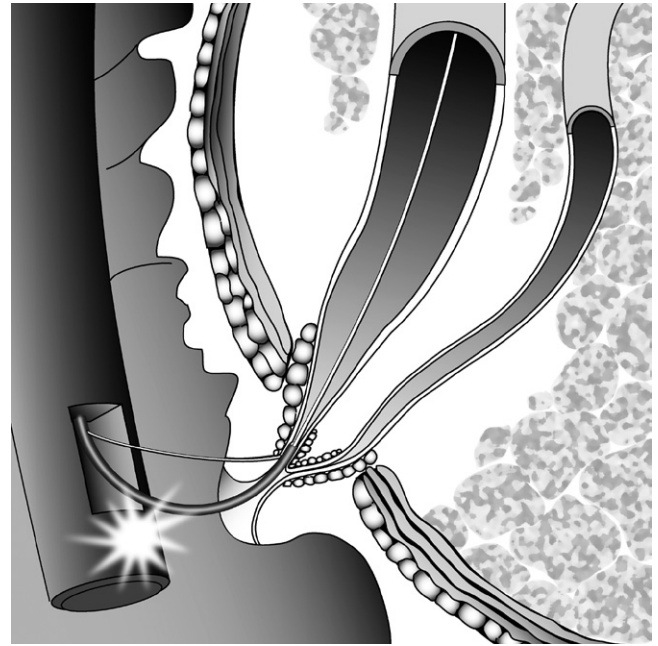


Figure 135.8 Schematic showing wire-guided biliary cannulation via a bowed papillotome.

table. The duodenoscope is advanced to the second portion of the duodenum and aligned with the major papilla (or minor papilla for dorsal pancreatic duct cannulation) in order to achieve access to the biliary and/or pancreatic ducts. Deep cannulation and wire placement are essential for successful completion of diagnostic and therapeutic ERCP. Access can be achieved using several devices, including papillotomes, guidewires, cannulas, and precut papillotomes. Once deep cannulation has been achieved, radiopaque contrast is injected under fluoroscopic visualization to confirm cannulation and to delineate ductal anatomy and abnormalities. Although obtaining biliary or pancreatic access may be straightforward, it can occasionally be challenging for novice and advanced endoscopists alike. Many techniques and devices can facilitate biliary or pancreatic cannulation when standard cannulation technique is unsuccessful (Figures 135.8–135.13). Increasingly, pancreatic ductal access with guidewires and protection with pancreatic stents is used to facilitate biliary access. Precut sphincterotomy refers to an incision made with a papillotome to gain entry into the desired duct, and is generally associated with increased complications, whether due to prior access attempts or the precut itself. No approach is universally superior to another in achieving biliary access and the ideal approach is determined by operator expertise and the clinical situation. When ERCP cannulation fails, in appropriate circumstances, alternative approaches include EUS-guided rendezvous to deliver a transpapillary wire that can be used for retrograde ERCP cannulation [38–41].

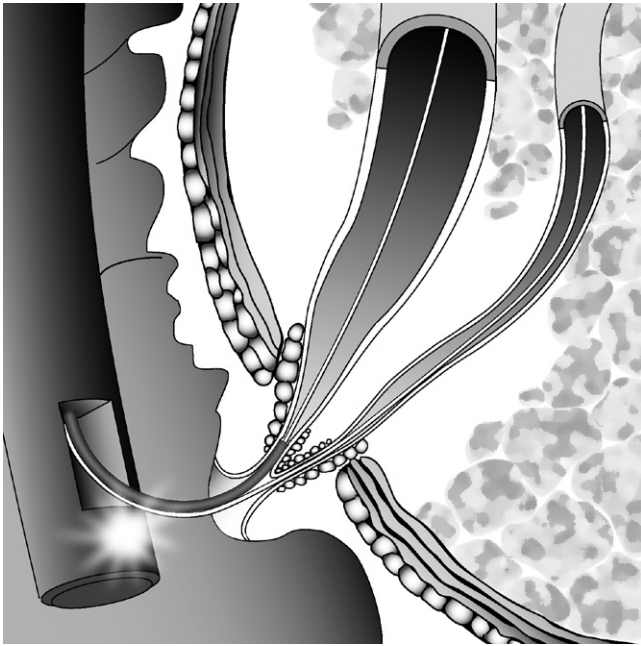


Figure 135.9 Schematic showing “double wire” or “pancreatic guidewire” assisted biliary cannulation, in which a pancreatic guidewire is used to facilitate biliary cannulation. Pancreatic stent placement is recommended when access is achieved.

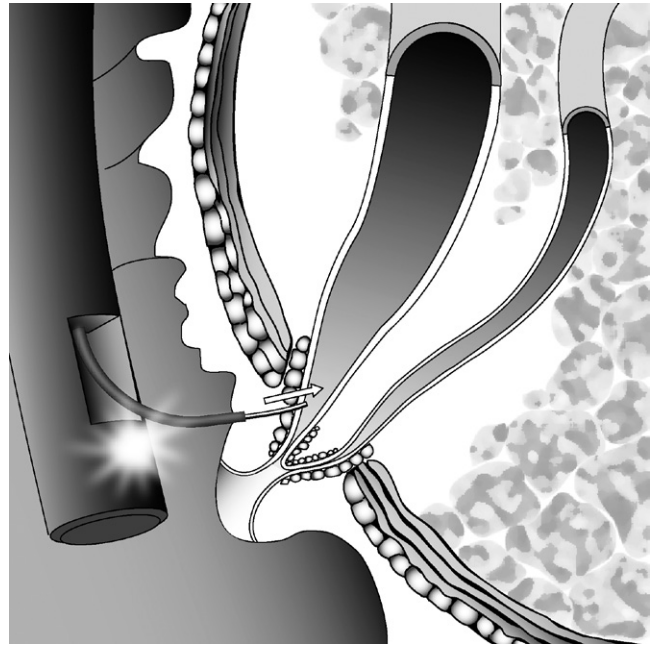


Figure 135.11 Schematic showing needle knife fistulotomy for biliary access in which the roof of the papilla is punctured directly, avoiding the papillary orifice, a technique suitable primarily for patients with prominent papilla and dilated bile duct.

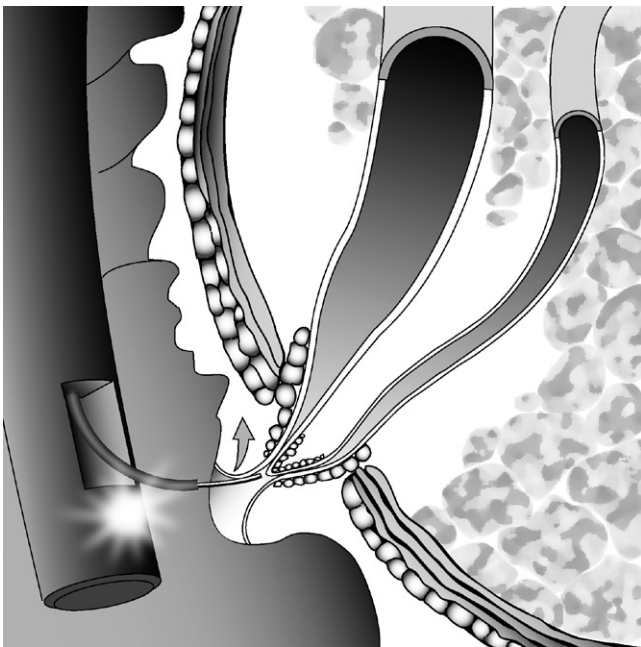


Figure 135.10 Schematic showing needle knife precut for biliary access using a freehand technique starting at the papillary orifice and cutting cephalad, with no protective pancreatic stent.

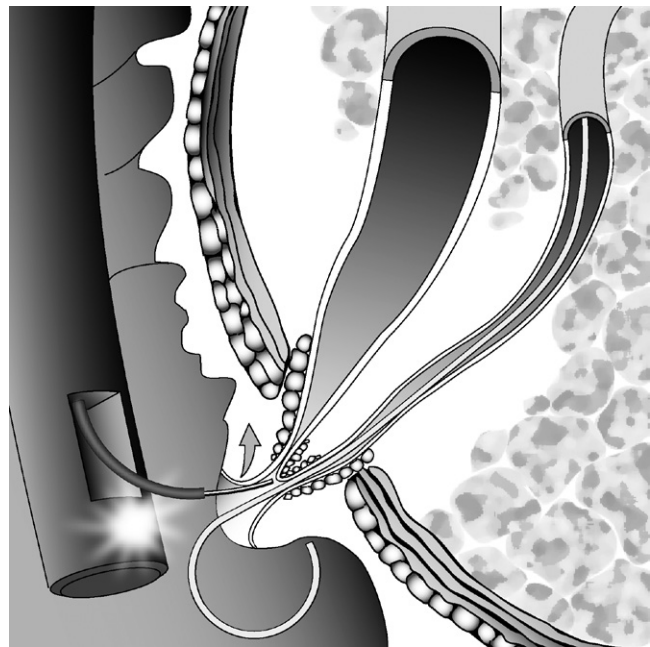


Figure 135.12 Schematic showing needle knife precut for biliary access using a freehand technique starting at the papillary orifice and cutting cephalad, with prior placement of a protective pancreatic stent.

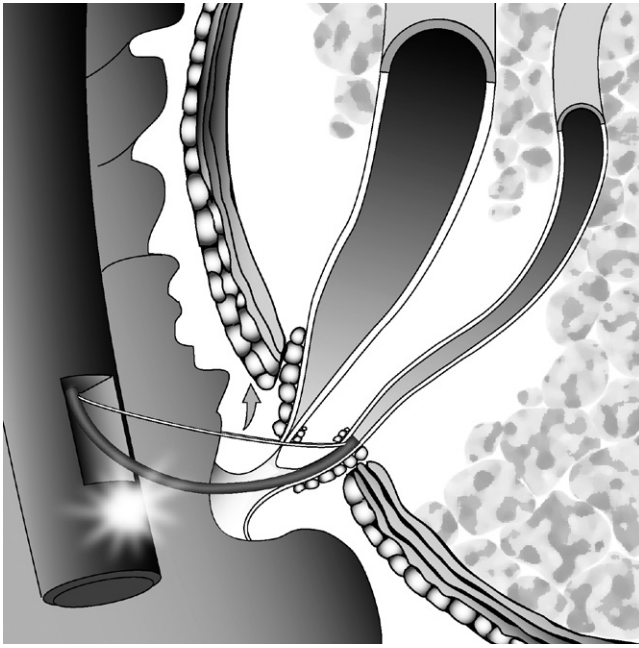


Figure 135.13 Schematic showing transpancreatic precut sphincterotomy for biliary access, in which the papillotomy is intentionally lodged in the pancreatic duct and the septum incised in order to gain biliary access.

Sphincterotomy and balloon dilation

Endoscopic sphincterotomy and endoscopic balloon dilation (EBD) are integral parts of modern ERCP. Widening of the biliary and pancreatic orifices by these techniques allows completion of therapeutic procedures such as removal of stones and placement of prostheses, easier introduction of diagnostic devices such as cytology brushes and biopsy forceps for sampling, completion of more complex procedures such as intraductal cholangioscopy and treatment of conditions in which symptoms, predominantly pain, may be attributable to increased sphincter pressure (sphincter of Oddi dysfunction) or idiopathic benign stenosis of the major or minor papilla.

Biliary sphincterotomy is most commonly performed using a bow-type traction sphincterotome passed over a previously placed guidewire. Angulation of the cutting wire and injection of contrast allow precise control of sphincterotomy [38,42]. Pancreatic sphincterotomy may be performed using a traction sphincterotome, similar to biliary sphincterotomy, or by using a knife papillotomy over a pancreatic stent, cutting freehand with the needle knife along the plane of the stent. Although biliary and pancreatic sphincterotomy are generally well tolerated, as discussed earlier, significant complications can occur [31].

Endoscopic papillary balloon dilation is an alternative or adjunct to sphincterotomy. This technique was first described in 1974 and was performed mostly for common bile duct stones [43]. The risk of post-ERCP bleeding is decreased as there is no need to cut the sphincter muscle [44]. There is debate in the literature regarding the safety of balloon dilation compared to

Box 135.2 Limitations of plastic and metal biliary stents.

Plastic stents

- Excessive length to diameter
- Lack of conformability
- Early occlusion
- Risk of migration
- Bacterial colonization
- Cholangitis from stent occlusion or nondrained segments
- Difficulty in placement of multiple stents

Metal stents

- Placement in patients with benign disease
- Placement in wrong segmental ducts
- Preclude resection
- Tumor ingrowth
- Stone formation
- Reactive hyperplasia
- Cholangitis – early or late
- Erosion into vessels (bleeding)

sphincterotomy with regards to other complications, especially pancreatitis. Balloon dilation of intact biliary sphincter has been associated with a markedly increased risk of pancreatitis in one study from the United States, and a metaanalysis of pooled studies [45,46].

In contrast, studies from Asia report no significant increase in the risk of pancreatitis, especially if balloon dilation is performed for 5 min or longer rather than 1 min, as is widely done elsewhere [47–49].

Prosthetic stent placement

Prosthetic stent placement is an integral part of diagnostic and therapeutic ERCP. Stent placement is intended to optimize drainage of the biliary or pancreatic ducts. Primary indications for biliary stent placement are palliation of malignant and treatment of benign strictures, bile leaks, and to temporize or facilitate bile duct stone removal. Pancreatic stents are also placed for the treatment of recurrent pancreatitis, strictures, duct leaks, to facilitate pancreatic stone removal, and to reduce risk of post-ERCP pancreatitis.

Stents are hollow tubular devices that may broadly be divided into two categories, plastic and metal (Box 135.2). Plastic biliary stents are typically available in diameters ranging from 7 Fr to 11.5 Fr, lengths ranging from 5 to 22 cm, either straight or curved configurations, and with or without flanges or pigtailed anchoring options at either end, and without or without side holes. They may be composed of hard (polyethylene) or soft (polyurethane or derivative) materials (Figure 135.14). There is no clearly demonstrated significant difference in the patency and drainage characteristics of various configurations of plastic biliary stents. However, rigid stents can be more difficult to remove in case they migrate above a stricture or inside the duct, and can result in significant bowel injury if they migrate outwards [50]. Metal biliary stents have a wire mesh design, which is either interwoven or laser cut into metal framework, resulting

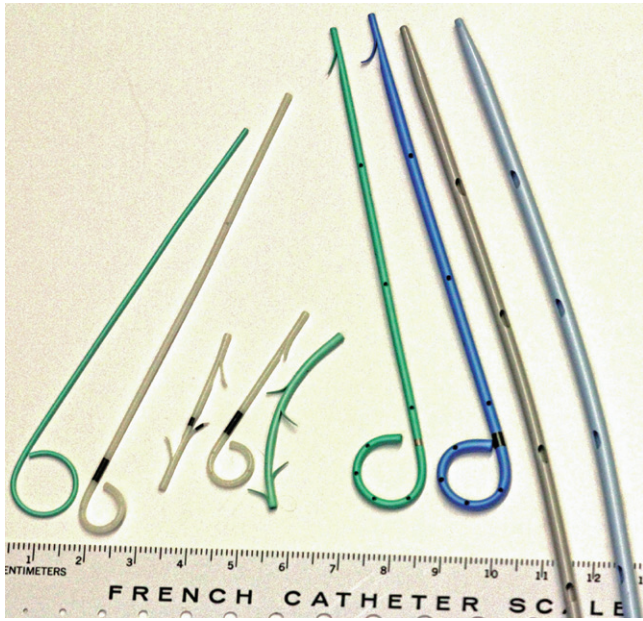


Figure 135.14 A variety of plastic stents used in the pancreatic duct for prophylactic and therapeutic purposes, ranging from 3 Fr on the left to 10 Fr on the right.

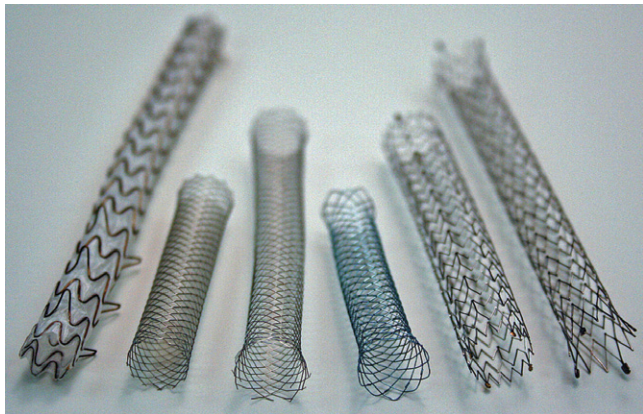


Figure 135.15 A variety of self-expanding metallic biliary stents, both covered (three on the left), and uncovered (three on the right).

in a narrow or open cell mesh design, respectively. These stents have a wider lumen than plastic stents (8 or 10 mm, approximately 24 or 30 Fr) and also come in a variety of lengths (4–10 cm) (Figure 135.15). Uncovered self-expanding metal stents (SEMS) are considered permanent and indicated for unresectable malignant strictures of the biliary tree. FCSEMS have a coating around the inner and outer surface of the stent mesh, which prevents embedding into the tissues [51]. Although only approved for malignant conditions, FCSEMS have the advantage of being easily removable and are therefore increasingly used for benign indications as well. FCSEMS have the advantage of preventing tissue ingrowth, but have the disadvantage of potential migration out of or up into the duct. Metallic

biliary stents are significantly more expensive than plastic biliary stents (approximately \$1000–\$2600 compared to \$35–\$150 US Dollars). However, the cost of the stent may be offset by the need for fewer procedures and reduced procedure-related morbidity in patients who require long-term stenting. The choice of appropriate stent varies by clinical scenario, stent availability, and operator expertise.

Similar to biliary plastic stents, pancreatic stents are made of hard (polyethylene) or more recently of soft (polyurethane or derivatives) plastic and come in a variety of sizes (3 Fr–10 Fr), lengths (2–22 cm), anchoring options (with or without internal and external flanges), and external configuration (straight with dual flanges, or single pigtail) [38]. Longer stents have multiple side holes in order to optimize drainage of pancreatic duct side branches. Techniques and equipment for accessing pancreatic ducts and deep placement of guidewires and stents in pancreatic ducts are quite different from those used for biliary access. The role of pancreatic stents in specific diseases is discussed below.

Cholangioscopy

Cholangioscopes allow direct visualization of the bile duct and directed tissue acquisition as well as directed therapy, for example difficult bile duct stones. There are currently three options for cholangioscopy: (1) mother–daughter scope (Olympus America, Center Valley, PA; Pentax, Orangeburg, NT); (2) Spyglass (Boston Scientific, Natick, MA); or (3) slim or ultraslim upper endoscopes (a variety of manufacturers) [52]. In the mother–daughter system, a small choledochoscope is advanced through the working channel of the duodenoscope. This system is fragile and generally requires two operators. The Spyglass system, also referred to as a single-operator cholangioscope (SOC) system, uses a 10 Fr disposable sheath through which a fiberoptic bundle is advanced into the bile duct. There is a four-way control, as for an endoscope, in order to steer the sheath inside the bile duct. Water irrigation maintains visualization of the duct. There is an additional channel that allows tissue acquisition or advancement of therapeutic devices such as stone lithotripsy probes. Limitations of the Spyglass system are that with each subsequent use, the image quality deteriorates due to breakage of individual fibers of the fiberoptic bundle, the cost of a replacement fiber is high (>\$2000) and there is a 7%–10% risk of cholangitis due to prolonged water irrigation in the bile duct [53–55]. Despite these limitations, Spyglass is increasingly popular because it requires only a single operator and allows intraductal evaluation and therapy with relative ease. The third option for cholangioscopy is the placement of an ultraslim upper endoscope directly into the bile duct. This has the advantage of providing high-quality digital video images and a large endoscope channel for devices. However, the duct may be too small to accommodate the endoscope or the scope may fall out of the ampullary opening as it is advanced due to the formation of a loop in the duodenum [56–58]. The role of cholangioscopy in the management of biliary diseases is discussed later in this chapter.

Biliary diseases

Bile duct stones

The most common indication for ERCP is the removal of bile duct stones. In the past, ERCP was performed in a high proportion of patients suspected of having bile duct stones. Because such patients can now be evaluated with great accuracy using alternative less-invasive modalities, ERCP should only be considered for patients with a high suspicion of, or confirmed, bile duct stones, or in fragile patients in whom sphincterotomy is planned in lieu of cholecystectomy.

Patients with suspected bile duct stones typically present with abdominal pain, elevation of liver enzyme tests, and evidence of gallstones on imaging, for which the first-line modality is typically transabdominal ultrasound of the gallbladder. Intraductal stones cannot be diagnosed in the majority of patients using transabdominal ultrasound as it has a low sensitivity for bile duct stones due to poor visualization of the distal bile duct. Ultrasound is sensitive for detection of dilation of the bile duct due to an obstructing stone in the duct but is a non-specific predictor of bile duct stones [59]. In the past, most such patients would undergo ERCP for diagnostic and therapeutic purposes. However, a significant proportion of patients pass their bile duct stone prior to ERCP and therefore do not need to be exposed to the risks of ERCP for diagnostic purposes alone. MRCP, EUS, and intraoperative cholangiography or ultrasonography offer alternative imaging modalities to evaluate the bile duct without exposing patients to an unnecessary ERCP [60–64]. A risk stratification system based on factors predictive of bile duct stones and an algorithm to categorize patients according to the most appropriate imaging or therapeutic modality has been developed [5].

Biliary stone removal

After biliary access is obtained, in most cases a biliary sphincterotomy is performed over a guidewire to widen the biliary orifice (Box 135.3; Figure 135.16). If sphincterotomy is con-

traindicated (e.g., in the setting of coagulopathy), or when preferred, the biliary orifice can be widened by stretching the biliary orifice using a balloon catheter, a process referred to as endoscopic papillary balloon dilation (EPBD). Once the papillary orifice is enlarged, most small stones can be removed using a stone extraction balloon or a wire basket. A stone extraction balloon has an inflatable balloon that is advanced into the bile duct over a guidewire. The balloon is advanced above the distal-most stone and inflated to the size of the bile duct upstream from the stone. Downward traction of the catheter along the plane of the duct is then used to deliver the stone from the biliary orifice. Contrast injection through the inflated balloon (occlusion cholangiogram) can be performed to confirm that all stones have been removed. In the setting of multiple stones, stone removal is initiated in the distal duct with sequential removal of more proximal stones in order to minimize the risk of stone impaction at the biliary orifice. Stone balloon catheters come in a variety of sizes (5–20 mm) and have the advantage that they are easy to use [65]. Disadvantages are that the inflated balloon can slip past a stone in the duct and the balloon can rupture, especially in the setting of large, hard stones.

Stone retrieval baskets have four or more circumferentially arranged wires and an outer sheath. In the closed position, the basket wires are covered by the sheath. The closed basket device

Box 135.3 Commonly used techniques for removal of bile duct stones.

- Biliary sphincterotomy
- Large (>10 mm) balloon dilation
- Balloon extraction
- Basket extraction
- Mechanical lithotripsy
- Temporary plastic (or metallic) biliary stents
- Intraductal cholangioscopically directed lithotripsy
 - Electrohydraulic lithotripsy
 - Holmium laser lithotripsy

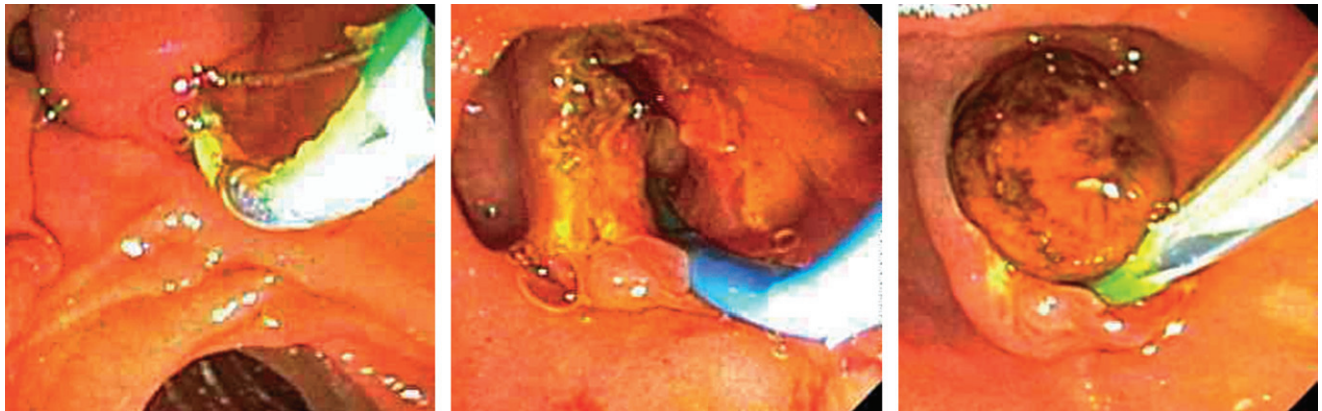


Figure 135.16 Biliary sphincterotomy followed by extraction of a bile duct stone.

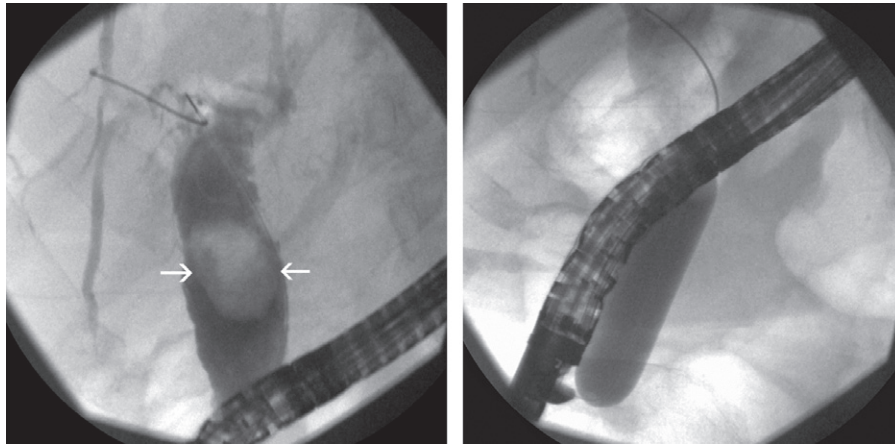


Figure 135.17 Endoscopic papillary large balloon dilation to extract a very large bile duct stone after sphincterotomy but without requiring mechanical lithotripsy: very large stone (arrows), followed by balloon dilation to 15 mm (left to right).

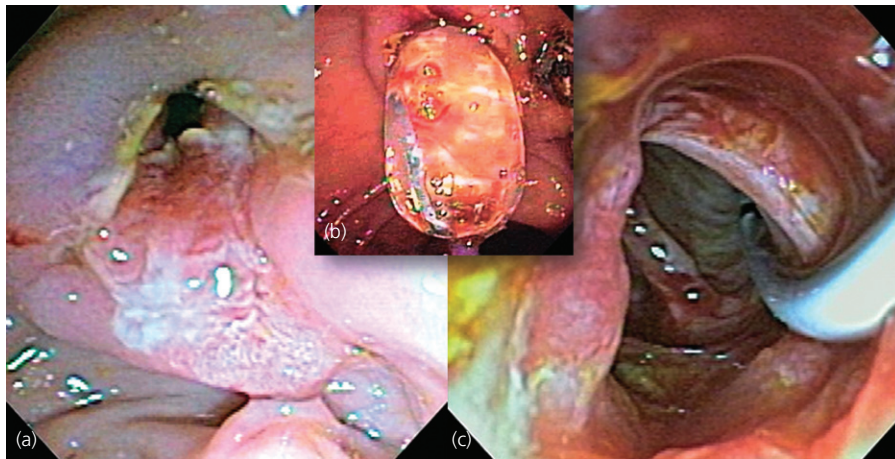


Figure 135.18 Endoscopic papillary large balloon dilation to extract a very large bile duct stone after sphincterotomy, same patient as Figure 135.17, showing postsphincterotomy (a), 15-mm balloon dilation (b), and dramatically enlarged papillary orifice (c) allowing sight up the common bile duct and cystic duct from the duodenum.

may be advanced directly into the bile duct or over a guidewire. Once inside the duct, the basket is opened alongside or just above a stone using an external handle. The basket then is gradually pulled back towards the duodenum with to and fro movements of the basket to “engage” the stone in the basket wires. The open basket can be pulled down or the basket closed to capture the stone to deliver the stone through the biliary orifice. Baskets can become trapped around stones that cannot be delivered, but can be “rescued” by use of a mechanical lithotripsy sheath passed over the cut wires of the basket after the endoscope is removed. There is a wide variety of baskets in various configurations and sizes (up to 3 cm wide). Baskets are useful in patients with large stones, intrahepatic ductal stones, and stones that slip past a balloon catheter.

In most cases, bile duct stones are less than 1 cm in size and can be removed using a stone balloon catheter or basket.

Approximately 10%–15% of patients have “difficult bile stones.” These include single or multiple large bile duct stones (usually >1 cm), stones occurring in the setting of unfavorable ductal anatomy such as a stricture below the stone, or a large stone in a small duct, and stones in patients with altered surgical anatomy. In such situations more advanced techniques are required to remove bile duct stones. Three main approaches may be used in patients with normal anatomy: (1) placement of stent in the bile duct to facilitate stone removal at a later time; (2) lithotripsy to break up stones; and (3) large balloon dilation of the biliary orifice after biliary sphincterotomy to facilitate stone removal (Figures 135.17–135.19). Each of these approaches is discussed further below and although a single technique may be preferable or sufficient to remove stones in some patients, often a combination of techniques is used for very large, multiple, or otherwise difficult stones (Figures 135.20–135.24).

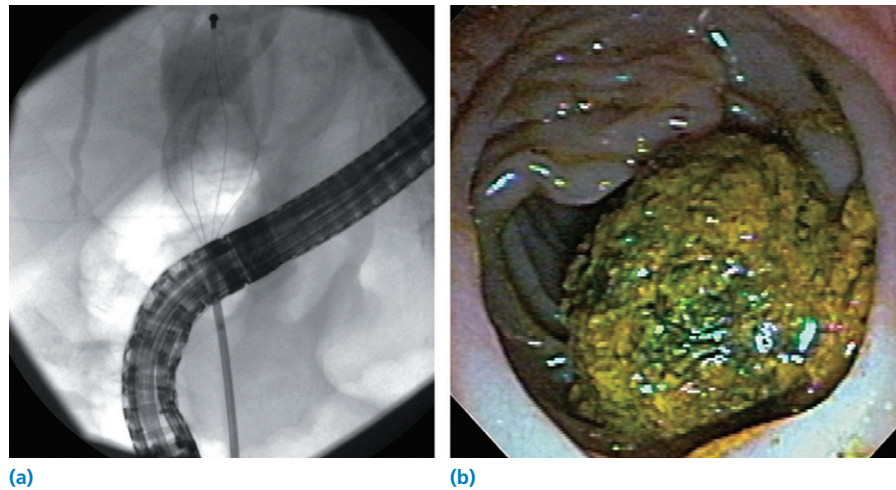


Figure 135.19 Basket extraction of a very large stone using endoscopic papillary large balloon dilation after sphincterotomy, same patient as Figures 135.17 and 135.18. Basket capture (a) followed by delivery of a 2-cm stone intact into duodenum (b).

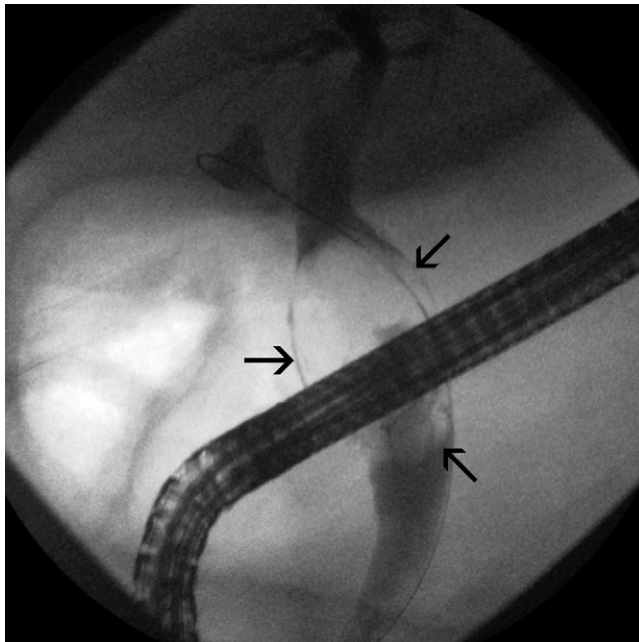


Figure 135.20 Extremely large bile duct stone (3 × 4 cm).

Stent placement

The placement of multiple stents adjacent to large bile duct stones serves three purposes. Firstly, it allows drainage of bile around large stones, thus minimizing the risk of obstruction and cholangitis. Secondly, friction from the stents rubbing against stones facilitates stone breakage and, finally, the presence of multiple stents across the biliary orifice allows dilation of the distal bile duct and orifice to facilitate stone removal in the future (Figure 135.21c). Hard polythene stents with complete internal and external pigtailed are recommended in this

setting to prevent distal migration of the stents into the duodenum and to facilitate stone breakdown. This approach is especially useful in patients considered to be poor candidates for prolonged endoscopic procedures, if additional equipment needed for stone removal is not available, or complete stone removal is not accomplished in a single setting. Depending on the number of stents placed, ERCP can be repeated after a period of weeks to months to remove the remaining stones. The stents may be left indefinitely in elderly patients with a plan to repeat ERCP only if signs of biliary obstruction develop [66–68].

Large balloon dilation of biliary orifice

In endoscopic papillary large balloon dilation (EPLBD) the biliary sphincter is dilated with a large-diameter (12–20 mm) dilation balloon after endoscopic biliary sphincterotomy, resulting in a very large orifice to facilitate removal of large or multiple stones with less chance of impaction in the distal bile duct or papillotomy [43,69] (Figures 135.17–135.19 and 135.23). Controlled radial expansion balloons that deliver stepwise inflation are typically used. The length of the sphincterotomy prior to dilation, size of dilation balloon, and rate and duration of inflation vary by center. It is generally recommended that the dilation should be performed slowly with gradual dilation of the balloon to a maximum and that the balloon size be limited to that of the native distal duct. In a randomized controlled trial, EPLBD with limited sphincterotomy compared to sphincterotomy alone resulted in similar success and complication rates, but significantly less need for mechanical lithotripsy and lower costs [70–74].

Overall, adverse events have been reported to occur in 7.9% of patients (156 of 1984) and included bleeding (which may be delayed) in 3.4%, pancreatitis (mild to moderate with no severe cases) in 2.6%, and perforation in 0.6% of patients in one large

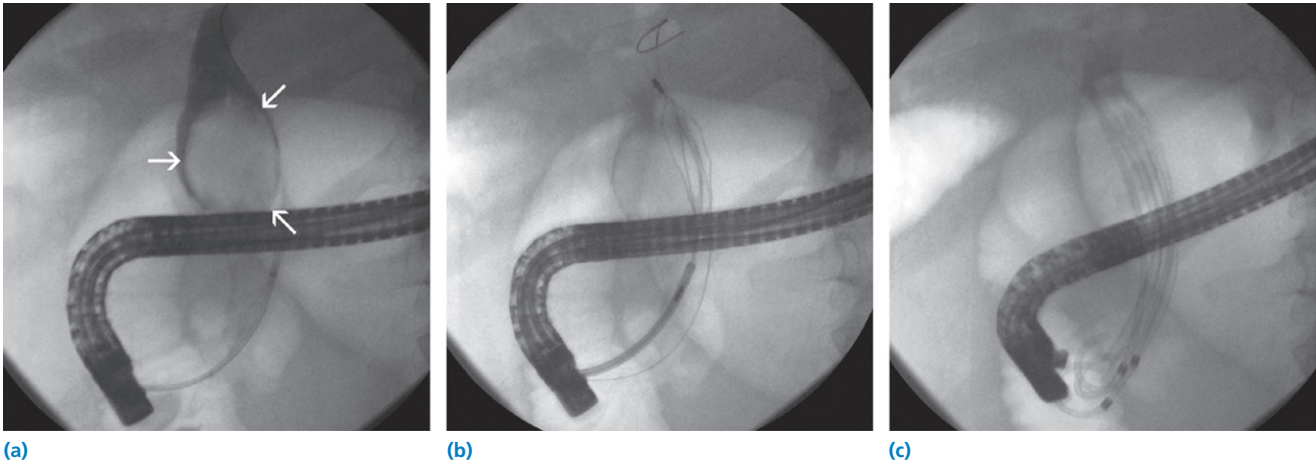


Figure 135.21 Extremely large bile duct stone (3 × 4 cm) **(a)**, failure of mechanical lithotripsy basket to capture stone **(b)**, followed by placement of multiple biliary stents **(c)**. Source: Courtesy of Rajeev Attam, MD.

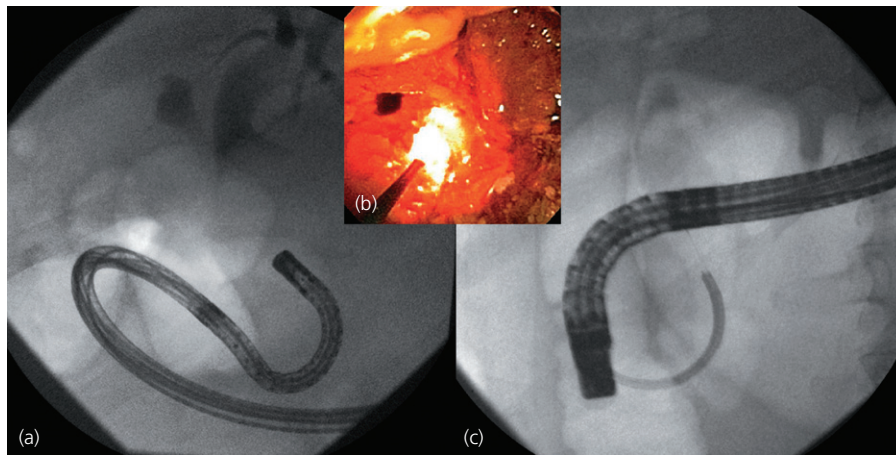


Figure 135.22 Direct cholangioscopy for intraductal lithotripsy of stone in Figures 135.20 and 135.21: using pediatric forward viewing endoscope **(a)**, single operator cholangioscopy through the duodenoscope **(c)**, and holmium laser lithotripsy **(b)** performed through direct peroral cholangioscopy. Source: Courtesy of Rajeev Attam, MD.

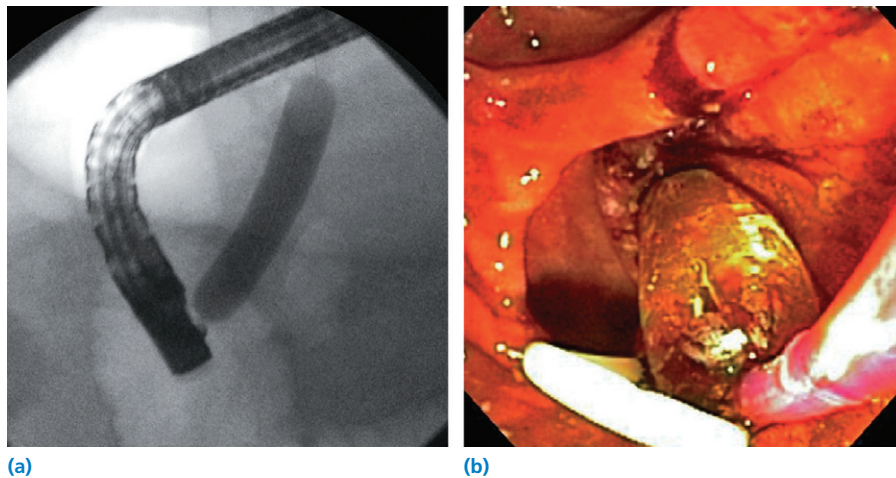


Figure 135.23 Large balloon dilation (12 mm) to facilitate extraction of stone fragments (Figures 135.20–135.22), after placement of a protective pancreatic stent **(b)**.

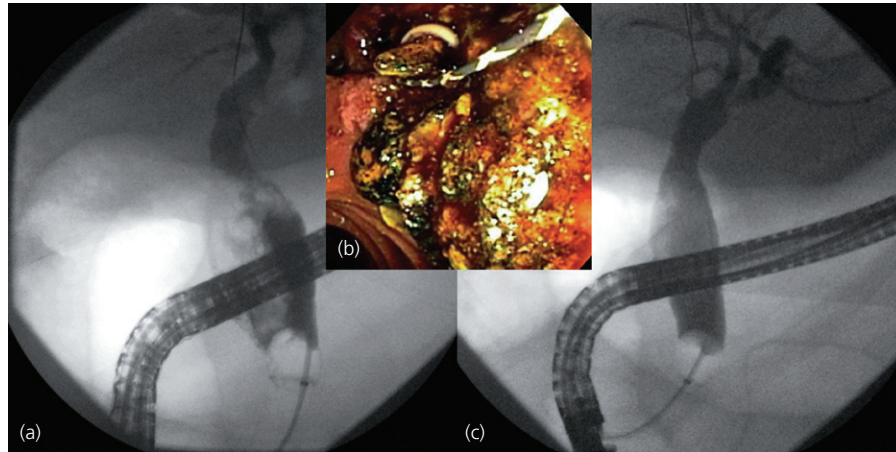


Figure 135.24 Final clearance of all stone fragments after intraductal laser and electrohydraulic lithotripsy, large balloon dilation, and mechanical lithotripsy of stone in Figures 135.20–135.23. Cholangiogram showing fragmented stones (a), endoscopic view of fragments (b), and final cholangiogram showing complete clearance (c).

review [75]. The presence of cirrhosis, a complete sphincterotomy at the time of the large balloon dilation, and presence of a biliary stricture were associated with an increased risk of complications. Careful patient selection, a less than complete sphincterotomy, and minimal balloon dilation in patients with a biliary stricture were recommended [75].

Lithotripsy techniques

Fragmentation of large or difficult stones may be achieved using various approaches including mechanical lithotripsy, intraductal electrohydraulic or laser lithotripsy, and extracorporeal shock wave lithotripsy (ESWL). The specific approach is determined by the nature of the stones and the availability of equipment and expertise.

Mechanical lithotripsy is commonly used due to its relative ease and availability. Mechanical lithotripsy may be performed using standard stone removal baskets that are lithotripsy compatible or dedicated baskets designed for lithotripsy. The procedure involves capturing of a stone in the basket and application of external pressure using a dedicated lithotripsy handle. The stone is thus crushed between the basket wires and outer sheath of the basket. A wide selection of mechanical lithotripsy baskets is available [65]. The basket and stone may occasionally become lodged in the distal bile duct or biliary orifice. Many baskets therefore have a mechanism for the wires to break free if continued pressure is applied using the lithotripsy handle. In rare cases, the basket and stone may still not be removable, in which case the outer sheath of the basket and the duodenoscope are removed from the patient exposing the basket wires through the patient's mouth. A specially designed metallic sheath can then be placed over the wire and the proximal end of the wire connected to a salvage lithotripsy handle. Cranking the handle with the locked wire in place advances the metal sheath against the trapped stone allowing the stone or the wires around it to break. Mechanical lithotripsy is widely used and stone removal can

successfully be achieved in about 90% of patients with difficult stones [76–79]. When mechanical lithotripsy fails this is usually because the stone is wedged, without space in the duct for the basket to expand around the stone (Figure 135.21).

Intraductal electrohydraulic and laser lithotripsy

Intraductal lithotripsy techniques using electrohydraulic or laser have been gained considerable popularity over the last few years, in part due to more widespread availability of intraductal cholangioscopy. In both techniques a small probe is advanced into the bile duct and onto the stone under direct vision, and a dedicated generator provides high-frequency shock waves in a water medium using either electrical or pulsed laser energy (Figure 135.22). Stone fragmentation occurs by transmission of the shock waves from the probe to the stones through the water medium. The water medium also helps absorb the shock waves, thus minimizing the risk of ductal injury. Intraductal lithotripsy techniques are indicated in patients with large stones that are “boxed in” in a small duct, occur above a stricture, or are not amenable to removal by mechanical lithotripsy. The efficacy of both techniques has been demonstrated in several reports [54,80–83]. These technologies have the advantage that stone removal can be accomplished in the same setting as the initial ERCP, using either direct per oral cholangioscopy via a forward-viewing endoscope, or dedicated cholangioscope through the ERCP duodenoscope (Figure 135.22). The main risk with both is that of ductal injury or cholangitis from the infusion of fluid required during cholangioscopy.

Extracorporeal shock wave lithotripsy

In extracorporeal shock wave lithotripsy (ESWL) shock waves are generated outside the body using electrohydraulic or piezoelectric energy generators and are transmitted via a liquid medium, usually in the form of a fluid-filled cushion bath, to the area of interest including kidney, pancreatic, and biliary

stones. The procedure typically requires general anesthesia. Because most bile duct stones are radiolucent, fluoroscopic visualization of bile duct stones may not be possible and alternative methods, such as transabdominal ultrasound imaging or ERCP-guided nasocystic drain placement to inject contrast into the bile duct or stent placement, are needed to target treatment. Although ESWL is used for pancreatic stones commonly, at least in the United States, it is rarely used for bile duct stones, due to the availability of other effective techniques to facilitate bile duct stone removal and the fact that ERCP is still required after ESWL to remove stone fragments from the bile duct.

Role of endoscopic retrograde cholangiopancreatography in disease associated with gallstone disease

Biliary stone disease may be asymptomatic or manifest clinically with pain, ascending cholangitis, acute pancreatitis, acute cholecystitis, or rarer complications such as cholecystoenteric fistula or impacted stone in the terminal ileum.

In general, removal of bile duct stones is recommended whether or not patients are symptomatic, due to the risk of cholangitis, pancreatitis, and other complications. In contrast, gallbladder stones generally only mandate intervention when symptomatic. While cholecystectomy is the preferred approach, patients with acute cholecystitis who are considered to be poor surgical candidates (e.g., terminal disease, in the setting of another severe acute illness, coagulopathy including advanced liver disease, etc.) have traditionally been treated with percutaneous drainage of the gallbladder (cholecystostomy). An alternative approach is to perform ERCP and place a stent through the papillary orifice and cystic duct into the gallbladder thus achieving internal drainage and avoiding the morbidity associated with percutaneous drainage catheters [84,85] (Figure 135.25).

Biliary leaks

Bile duct leaks most commonly result from iatrogenic injury, especially cholecystectomy. Although the incidence of bile duct complications after laparoscopic cholecystectomy has decreased compared to the 1990s when laparoscopic cholecystectomy was first introduced, having plateaued in the 0.2%–0.4% range, similar to that of open cholecystectomy [86–89]. Patients with aberrant intrahepatic anatomy are particularly prone to leaks and injury (Figure 135.26). Any surgical procedure involving the liver or extrahepatic biliary system may result in bile duct leaks. Bile leaks occur in up to 25% of patients after liver transplantation, with the highest incidence after living donor liver transplantation [90].

In the setting of cholecystectomy, the leak may be recognized at the time of surgery, especially if an intraoperative cholangiogram is performed or in the postoperative period, either by the presence of bile in a surgical drain or later based on symptoms and imaging. With nondrained leaks, abdominal pain, fever, and leukocytosis are typical, and some patients progress to frank peritonitis. Although a transabdominal ultrasound or abdominal CT scan may show a fluid collection suggestive of a leak, the diagnosis is most commonly made with a hepatobiliary radionuclide scan.

Optimal management of biliary leaks is determined by the degree of bile duct injury. Simple leaks from the cyst duct or a small aberrant branch of the liver to the gallbladder fossa (duct of Luschka) can be treated endoscopically. The goal of ERCP is to decrease the transpapillary pressure in the biliary system to allow preferential biliary drainage into the duodenum, permitting the leak to heal. This is most commonly achieved by placement of a transpapillary stent (typically up to 10 Fr stent) in the bile duct, with or without sphincterotomy [91]. The most commonly practiced approach, at least in the USA (including the authors), is to perform both. As a general rule, the stent does

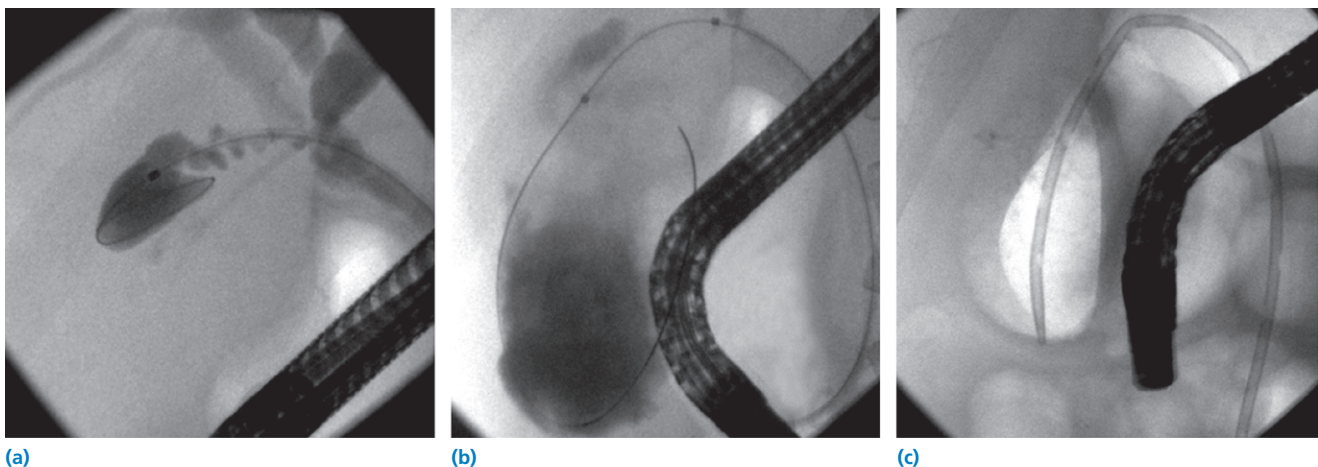


Figure 135.25 Gallbladder stenting to treat acute cholecystitis in a poor surgical candidate. Guidewire passed into cystic duct (a), deep into gallbladder (b), and placement of 20-cm soft fenestrated 10 Fr transpapillary stent into gallbladder (c).

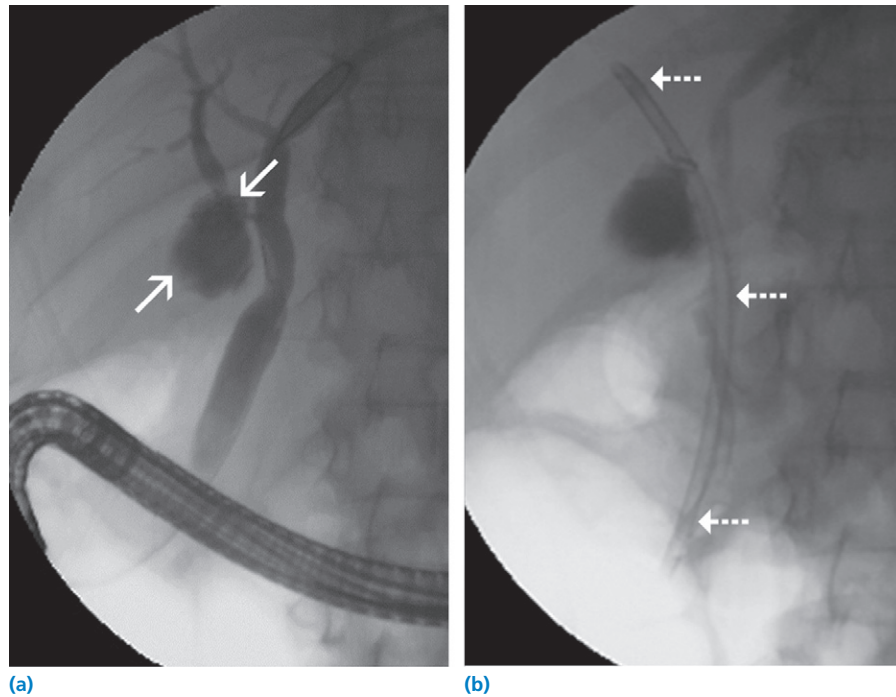


Figure 135.26 Cholangiograms showing a postcholecystectomy leak from an aberrant, low-insertion, right posterior sectoral duct, into which the cyst duct drained and was inadvertently injured during cholecystectomy. Leak shown by arrows (a) and 10Fr stent placed transpapillary into right posterior sectoral duct bridging the leak (b) (arrows).

not need to cross the site of the leak. The leak is typically bridged with a stent if a large sectoral branch, for example the right posterior sectoral duct, or the common hepatic duct, has been injured. The biliary stent is typically left in place for 4–6 weeks, following which the stent is removed at endoscopy unless there is concern for a persistent leak or retained stone, in which case an ERCP can be repeated. FCSEMS may be placed in patients with voluminous leaks, particularly if there is a large defect in the duct [92]. Patients with substantial bilomas often require adjunctive percutaneous drainage, and those with clinical peritonitis may benefit from a washout of the abdominal cavity by laparoscopy or laparotomy.

Leaks occurring in the setting of a significant bile duct injury (e.g., transection or ligation of the common hepatic or bile duct) or an aberrant major sectoral duct (commonly the right posterior sectoral duct) require further evaluation, usually with an MRCP, to determine the site of the injury and intrahepatic ductal anatomy, to assess for a potentially “disconnected duct,” and to plan management accordingly. Most patients in this setting typically require a percutaneous transhepatic catheter (PTC) drainage to divert bile drainage externally in order to allow the leak to heal, and eventually also require a surgical repair such as a Roux-en-Y hepaticojejunostomy, usually at a later date when the peritoneal inflammation has subsided [93,94]. ERCP may be performed to confirm complete transection and exclude the possibility of a small communication with the duct above the level of the injury. Occasionally, the transected

or ligated duct can be crossed using an ERCP, PTC, or even EUS-guided approach, following which it may be possible to treat the ductal injury using a transpapillary approach at ERCP [95].

Biliary strictures

Biliary strictures may be benign, malignant, or indeterminate, implying that a definitive etiology cannot be determined based on initial presentation and evaluation (usually cross-sectional imaging) (Box 135.4 and Table 135.4). The role of ERCP in the management of benign strictures is to establish biliary drainage and to treat the stricture with the aim of achieving complete stricture resolution, whereas in malignant strictures the primary aim is to establish biliary drainage either prior to surgery or for palliative purposes. Evaluation of indeterminate biliary strictures represents one of the few indications for which ERCP is performed for both diagnostic and therapeutic purposes. Several ERCP-guided tissue sampling techniques, as well as intraductal cholangioscopic evaluation, may be indicated.

Benign strictures

Benign strictures of the biliary tree primarily occur in the setting of surgery, typically cholecystectomy, after surgical biliary anastomosis such as after liver transplantation (Figures 135.27 and 135.28), or in the setting of chronic pancreatitis. Other less common etiologies are shown in Box 135.4. Primary sclerosing cholangitis and IgG4 cholangiopathy are

Box 135.4 Etiologies of bile duct strictures.**Benign**

- Surgical
 - Cholecystectomy
 - Biliary anastomosis
 - Liver transplant
 - Bile duct resection
- Pancreatic
 - Chronic pancreatitis
 - Acute pancreatitis
 - Necrosis/pseudocyst
 - Autoimmune pancreatitis
- Autoimmune (IgG4 cholangiopathy)
- Abdominal trauma
- Inflammatory (due to stones, etc.)
- Primary sclerosing cholangitis
- Intraarterial chemotherapy
- Recurrent pyogenic cholangitis
- Choledochal cyst
- Vascular compression
 - Portal hypertensive biliopathy
 - Arterial (pseudoaneurysm, etc.)
- Sarcoidosis

Malignant

- Primary (cholangiocarcinoma, etc.)
- Local extension (pancreas, gallbladder)
- Metastatic (colon, breast, lymphoma, etc.)

also important causes of benign strictures but require an approach somewhat different from other, more focal benign strictures.

Biliary injury with subsequent development of strictures occurs in up to 0.5% of operations involving the biliary tree, most commonly cholecystectomy, and may occur secondary to direct injury with clips, cautery, or transection, or through indirect injury from interruption of the vascular supply to a segment of the biliary tree. Benign anastomotic strictures are discussed below. Distal biliary strictures occur in up to 30% of patients with chronic pancreatitis and may be difficult to treat because of the fibrotic and often calcified pancreatic tissue surrounding the distal bile duct. Symptoms attributable to benign biliary strictures can range from relatively mild abdominal discomfort to symptoms of obstruction with jaundice, pruritus, and even cholangitis. Left untreated, chronic biliary obstruction can ultimately lead to secondary biliary cirrhosis and eventually end-stage liver disease. Stones forming above strictures can be particularly difficult to manage because of the relatively small portal for stone extraction [96].

Prior to endoscopic or surgical therapy, great care must be taken to ensure that the stricture is indeed benign. Comparison of various sampling techniques is shown in Table 135.4. Often, as with cholecystectomy-related injury, the clinical history is sufficient to make a presumptive diagnosis. In ambiguous clinical settings such as chronic pancreatitis where there is a risk of a superimposed malignant stricture, further evaluation with

Table 135.4 Summary of diagnostic performances of various endoscopic methods used to evaluate bile duct strictures. Source: Adapted from Yoon and Brugge 2013 [213]. Reproduced with permission of Elsevier.

Method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Cholangiography	74–85	70–75	74–79	70–82	72–80
Brush cytology	30–57	90–100	94–100	8–62	–
Endobiliary forceps biopsy	43–81	90–100	94–100	31–75	–
FISH	34–48	91–100	100	60–88	70
DIA	38–49	77–98	69–97	50–87	56–64
EUS without FNA	78	84	–	–	–
EUS-guided FNA	43–89	100	100	29–67	80–91
IDUS	83–91	50–92	92–96	67–100	76–90
Cholangioscopy with or without biopsy	89–96	96–100	89–100	91–96	–
SOC impression	78–100	77–82	80–88	80–92	80–89
SOC-guided biopsy	49–82	82–100	100	72–100	75–82
pCLE	83–98	33–88	71–80	80–97	81–86
OCT	79	69	75	73	74

DIA, digital image analysis; EUS, endoscopic ultrasound; FISH, fluorescent in situ hybridization; FNA, fine-needle aspiration; IDUS, intraductal ultrasound; NPV, negative predictive value; OCT, optical coherence tomography; pCLE, probe-based confocal laser endomicroscopy; PPV, positive predictive value; SOC, single operator cholangioscopy.

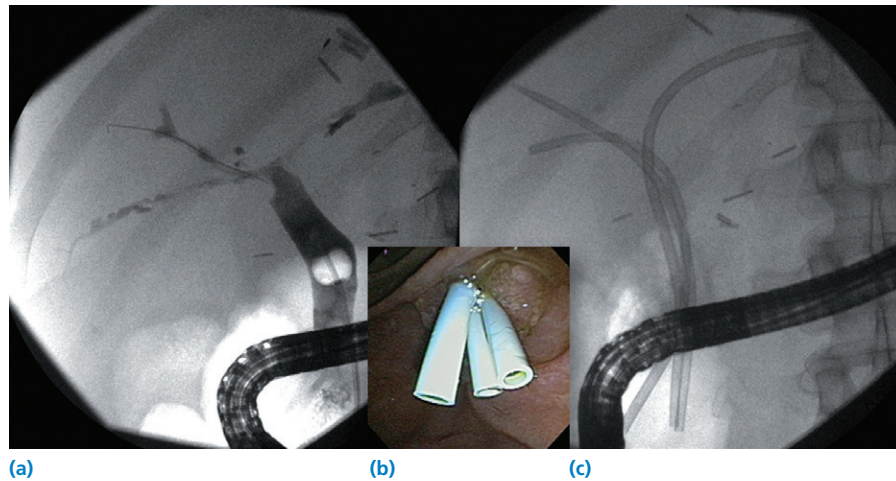


Figure 135.27 Nonanastomotic hilar stricture after liver transplant, at takeoff of right anterior, posterior, and left hepatic sectoral ducts (a); 10 Fr stents placed into each of three sectoral ducts, right anterior, posterior, and left (b, c).

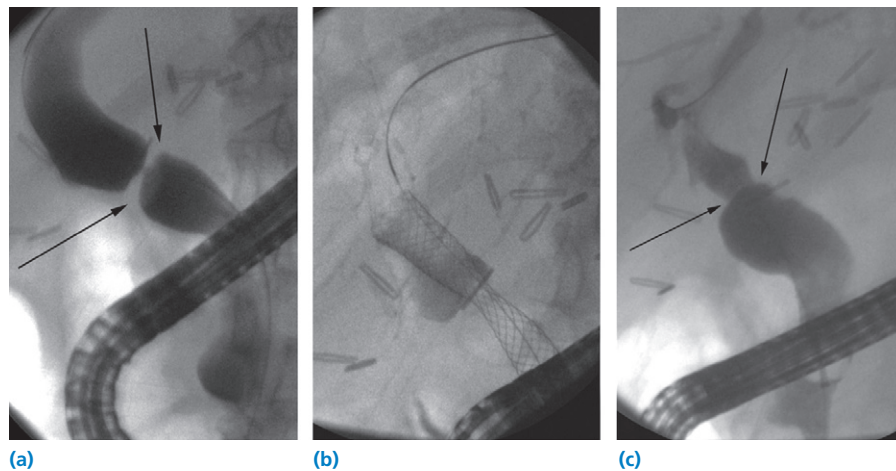


Figure 135.28 Anastomotic stricture after liver transplant (arrows) (a), treated with self-expanding metallic covered stent (b), with complete resolution of stricture after removal of stent (c). Source: Courtesy of Rajeev Attam, MD.

endoscopic ultrasound and fine-needle aspiration may be necessary to exclude malignancy. Proximal strictures should (ideally) be evaluated by MRCP prior to ERCP. MRCP is particularly useful as it is noninvasive, does not require contrast, and allows evaluation of the bile ducts both above and below the level of the stricture. By allowing imaging of the entire biliary tree, MRCP provides a “roadmap” that can be used to plan therapy and target specific ducts at the time of ERCP.

Endoscopic management of benign biliary strictures involves balloon dilation followed by placement of one or more plastic stents to dilate the stricture and “remold” the stenotic part of the duct. This approach has been shown to be effective in multiple studies, with results depending on the location of the stricture. Common bile duct strictures respond better than strictures involving the hilum. The general approach is to place the maximal number of stents that can be accommodated in the

duct(s). Stent exchange and addition of more stents if possible is performed at 3-monthly intervals for up to 1 year; this results in stricture resolution in 74%–90% of patients, with recurrence in 20%–30% of patients in both short and long-term follow-up [97–99]. Benign strictures related to chronic pancreatitis typically occur in the distal bile duct and are usually treated using the same approach involving placement of multiple plastic stents over a prolonged period of time. However, these strictures have a higher relapse rate due to the occurrence of the stricture in the setting of fibrosis and often a calcified and permanently scarred pancreas [98,100,101].

While uncovered metal biliary stents are contraindicated, FCSEMS are increasingly being used for in the management of benign biliary strictures. Early results have been promising, with clinical success in up to 90% of patients. However, long-term efficacy of these stents has not yet been proven. FCSEMS

offer the advantage of a larger lumen and more radial force than plastic stents, although the cumulative diameter of plastic stents can be greater than that of a single 10-mm FCSEMS and provide the additional benefit of biliary drainage in the space between the stents [102–104]. Placement of FCSEMS may lead to the need for fewer ERCPs due to the larger lumen of the stents. Because sludge occlusion occurs fairly frequently, ERCP is typically repeated at 3 to 4-month intervals to minimize the risk of cholangitis due to stent occlusion. Other disadvantages of fully covered stents are considerably higher cost and, depending on the type FCSEM stent used, the risk of stent migration, both into the proximal duct or out into the small intestine with some stents. Stents with antimigratory flanges can minimize the risk of migration. Some benign strictures are refractory to endoscopic therapy regardless of the type and number of stents used to treat them. A multidisciplinary approach, including consultation with an experienced hepatobiliary surgeon, rather than repeated ERCPs is strongly recommended in such patients. A detailed discussion regarding the types of surgery is beyond the scope of this chapter. However, proximal strictures such as those involving the hilum or the extrapancreatic bile duct are usually treated with a bilioenteric bypass (Roux-en-Y hepaticojejunostomy).

Primary sclerosing cholangitis (PSC) is an inflammatory disease associated with scarring of the intra- and extrahepatic biliary system resulting in biliary strictures, secondary biliary stones, and, in some patients, progression to cholangiocarcinoma. The diagnosis of PSC can be made using noninvasive imaging modalities and confirmed by liver biopsy. The primary role of ERCP in patients with PSC is for the removal of stones and treatment of extrahepatic or hilar strictures (also known as dominant strictures) felt to be causing symptoms (e.g., recurrent cholangitis or stone disease) or laboratory abnormalities (e.g., elevation of alkaline phosphatase and bilirubin). Stent placement is associated with an increased risk of recurrent cholangitis in the setting of PSC, so that when possible it is recommended that strictures be treated primarily with balloon dilation [105,106]. Short-term stent placement is reserved for high-grade or recurrent strictures with the goal of removing stents at the earliest opportunity. Cholangiocarcinoma develops in approximately 10%–15% of patients with PSC. ERCP is not recommended for screening purposes due to the poor yield of tissue acquisition techniques (sensitivity of 18%–40%) and the risk of complications, especially cholangitis [107]. However, it has been recommended that brushings and biopsies (for cytological and histological analysis, respectively) be obtained from dominant strictures at the time of the *initial* ERCP. ERCP-guided tissue acquisition is also recommended in patients who develop a new stricture with concern for malignancy or have a deterioration in their clinical condition, for example development of jaundice, worsening liver function, or weight loss [107]. In addition to routine bile duct brushing and biopsies, cells may be collected for molecular analysis techniques, such as fluorescence in situ hybridization (FISH) to evaluate for changes in

DNA, which may be suggestive of malignancy. In the setting of PSC, the addition of FISH analysis has been shown to increase the detection of malignancy but at the expense of specificity [108,109].

Malignant biliary strictures

Malignant strictures of the biliary tree may be divided into two categories: those occurring in the extrahepatic bile duct, such as in the setting of pancreatic cancer, and those occurring more proximally, also referred to as hilar strictures. Either can be due to primary tumors, local extension, or metastases. Patients with malignant biliary obstruction typically present with painless jaundice, pruritus, fatigue, anorexia, and/or weight loss. Pain usually occurs in more advanced disease, and the presentation of pancreatic cancer may be preceded by the onset of diabetes. The presence of a mass lesion in the head or neck of the pancreas resulting in a stricture of the common bile duct and the pancreatic duct, known as the double-duct sign, on cross-sectional imaging such as CT and MRI/MRCP, is highly suspicious for pancreatic cancer, although chronic pancreatitis and autoimmune pancreatic may occasionally present similarly.

Noninvasive imaging, including contrast-enhanced CT scan and in the case of hilar strictures an MRCP, should be performed prior to invasive imaging and procedures. For tissue diagnosis, endoscopic ultrasound with fine-needle aspiration of a mass lesion is the diagnostic study of choice for pancreatic cancers and, to a lesser extent, hilar tumors associated with masses. Local and regional evaluation, including tissue sampling of liver metastases, lymph nodes, and the left adrenal gland, can be done at the same time. EUS-guided sampling of the liver or the bile duct is generally avoided in patients with suspected cholangiocarcinoma who may be potential candidates for resection, or in a few centers liver transplantation, in order to minimize the risk of seeding the needle tract with malignant cells.

Distal malignant obstruction

The primary role of ERCP in the management of patients with pancreatic cancer and other causes of distal malignant obstruction is to relieve jaundice and associated symptoms. There are three main contexts for biliary stenting: prior to surgery in patients considered to have resectable disease, prior to neoadjuvant chemotherapy in patients deemed to have advanced but potentially resectable disease if the tumor is responsive to treatment, and for palliative purposes in patients with advanced disease. There is general consensus that ERCP with biliary stent placement is indicated in the latter two groups to alleviate symptoms associated with biliary obstruction (jaundice, pruritus, malabsorption, and secondary cholangitis) and to allow normalization of liver function prior to chemotherapy (neoadjuvant or palliative) [110–113]. The role of ERCP for stent placement in patients considered to have resectable disease is under scrutiny, with at least one randomized trial suggesting worse outcomes with preoperative stenting than no ERCP at all

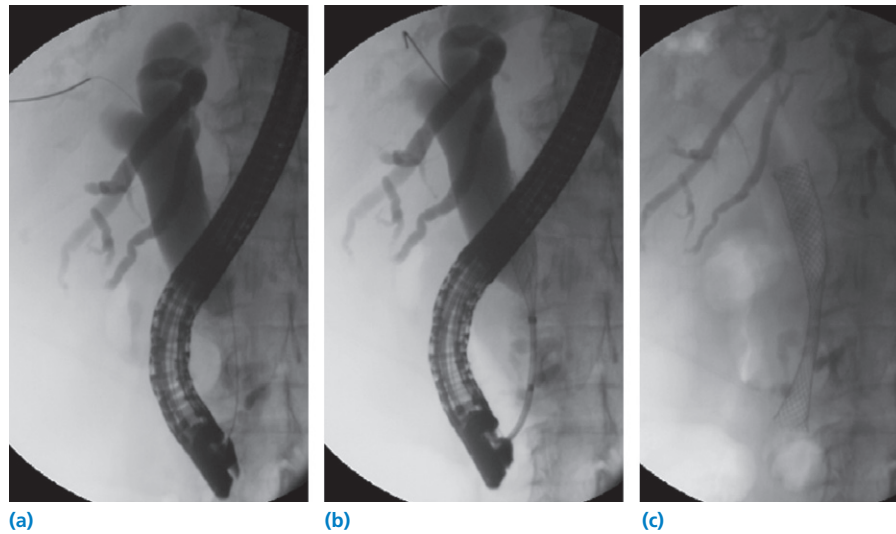


Figure 135.29 Distal malignant biliary stricture caused by pancreatic mass effect from pancreatic ductal adenocarcinoma. Cholangiogram showing stricture (a), placement of metallic stent (b), and complete drainage after deployment of stent (c).

[113–118]. Limitations of the randomized trial [104] included low technical success rates (69%–83%) and use of plastic stents rather than metallic stents, which are currently preferred for neoadjuvant therapy, a strategy not offered in that study (Figure 135.29).

Hilar malignant obstruction

Hilar tumors can be characterized by level of ductal obstruction, commonly referred to as Bismuth–Corlette classification I–IV, depending on the number and extent of foci of obstruction. The Bismuth–Corlette classification has a role in determining the extent of drainage, but its importance may have been overemphasized. Understanding hepatic segmental anatomy and sectoral ductal anatomy with its many variations is a prerequisite for optimal endoscopic drainage. Both CT scan and three-dimensional MRCP greatly facilitate understanding of hepatic segmental and ductal anatomy, and should be performed prior to considering ERCP, as complete injection of all sectors above the hilum poses a very high risk of cholangitis (Figures 135.30–135.33). The segmental ducts typically coalesce to form three main sectoral ducts – the right anterior sectoral duct (draining segments V and VIII), the right posterior sectoral duct (draining segments VI and VII), and the left main hepatic duct (draining segments II–IV). Variations in confluence of these sectors and differing extent of tumors, as well as replacement of sectors by tumor or atrophy, have major implications for the approach to effective and safe drainage. Whether palliative endoscopic stenting should be unilateral (perhaps best referred to as single) or bilateral (perhaps best referred to as multiple) has been debated for many years, with varying opinions based on anecdotal evidence and conflicting data [119–121]. The principle governing drainage had been that approximately 50% or greater of the liver needs to be drained for effective palliation and is associated with improved survival [122]. One study suggested

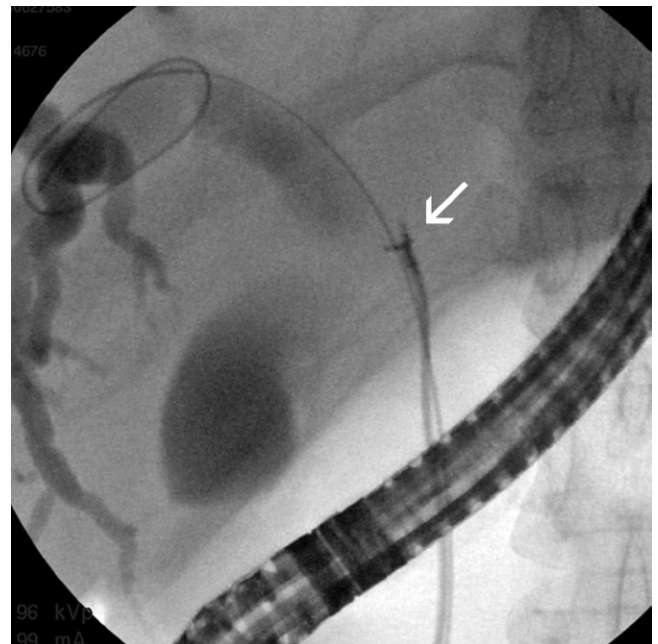


Figure 135.30 Cholangiogram showing intraductal forceps biopsy of hilar malignant biliary stricture (arrow), a technique recommended in addition to brush cytology.

that: (1) more than 50% drainage of liver volume based on hepatic sectors was a strong predictor of drainage effectiveness, especially in Bismuth type three or IV patients; (2) intubating an atrophied sector was ineffective and was associated with increased risk of cholangitis and should thus be avoided; and (3) more than 50% volume drainage is associated with a longer survival. Achieving drainage of more than 50% of liver volume often requires more than one of three sectors to be stented – sometimes on the same lobe, sometimes opposite lobes.

Increasingly, the concept of “unilateral” and “bilateral” drainage is becoming outdated.

Cumulative data, including a randomized comparative trial, support the conclusion that metallic stents are superior to plastic stents for palliation of distal tumors and hilar tumors alike, with respect to early and late complications, stent patencies, need for repeat interventions, and perhaps mortality [123–126]. Placement of a single metal stent is relatively straightforward (Figure 135.32). In contrast, placement of two metal stents can be challenging. The stents may be placed side-by-side or stent-

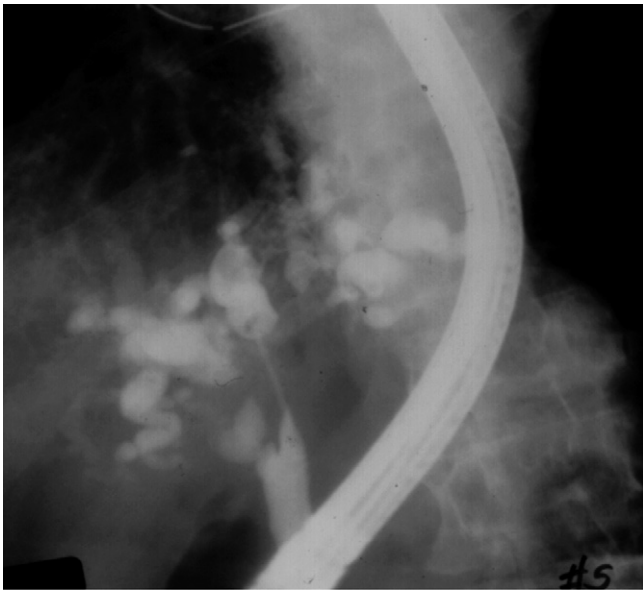


Figure 135.31 Endoscopic retrograde cholangiopancreatography with cholangiogram of complex Bismuth IV hilar tumor, performed many years ago, demonstrating perils of complete retrograde opacification of multiply obstructed segments, posing a risk of cholangitis.

through-stent (Y configuration) (Figure 135.33). While achievable in most cases, placement of multiple metal stents can be challenging even when performed by expert endoscopists in high-volume centers. It is essential that a diagnosis of unresectable malignancy has been firmly established and that the correct sectors and segmental ducts be accessed before placement of a metallic stent. When in doubt, plastic stenting is a reasonable substitute [127].

Localized treatment of malignant hilar strictures, typically for palliative purposes in the setting of unresectable disease, can be performed during ERCP using photodynamic therapy (PDT) or radiofrequency ablation (RFA). PDT involves the systemic administration of a photosensitizing agent, which is activated locally in the region of the tumor using a light emitting probe introduced via ERCP. The main risks associated with PDT are cholangitis (up to 25% of patients) and phototoxicity (in about 10.2% of patients), the latter from exposure of the skin to natural light. PDT has been shown to add survival advantage compared with plastic stents alone in a number of studies [128,129]. Problems with these data are that the control groups received conventional plastic stents, which are known to perform poorly in hilar malignancy.

A more recent development has been the introduction of a bipolar catheter, which uses radio waves to generate heat to destroy tumor cells locally. The Habib EndoHPB (EMcision UK, London, United Kingdom) has been used for both malignant hilar and pancreatic cancer-related strictures [130,131]. Ablation in the region of the cyst duct may lead to cholecystitis due to obstruction of the cystic duct and thermal injury in the hilum predisposes patients to the development of cholangitis as well as localized infections, including abscess formation. Although, preliminary reports using this device described encouraging short-term results with minimal complications, long-term follow-up and large studies demonstrating the efficacy of this device are needed [130,132].

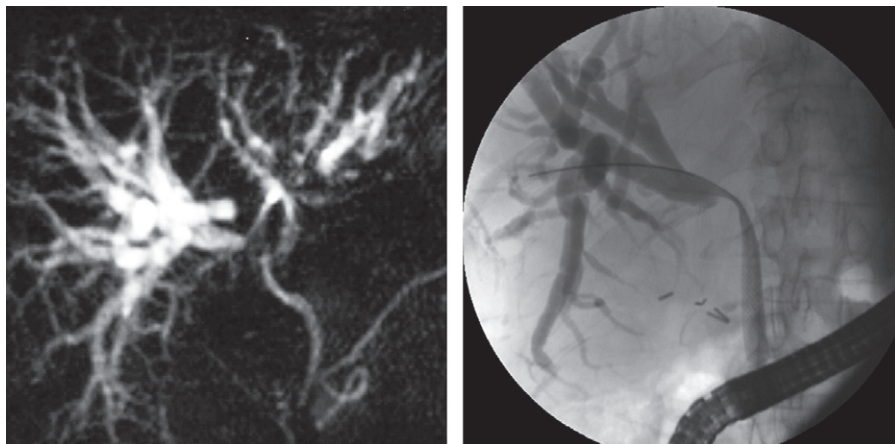


Figure 135.32 MRCP and endoscopic retrograde cholangiopancreatography showing complex Bismuth IV cholangiocarcinoma with selective opacification and metallic stenting into right anterior sector only.

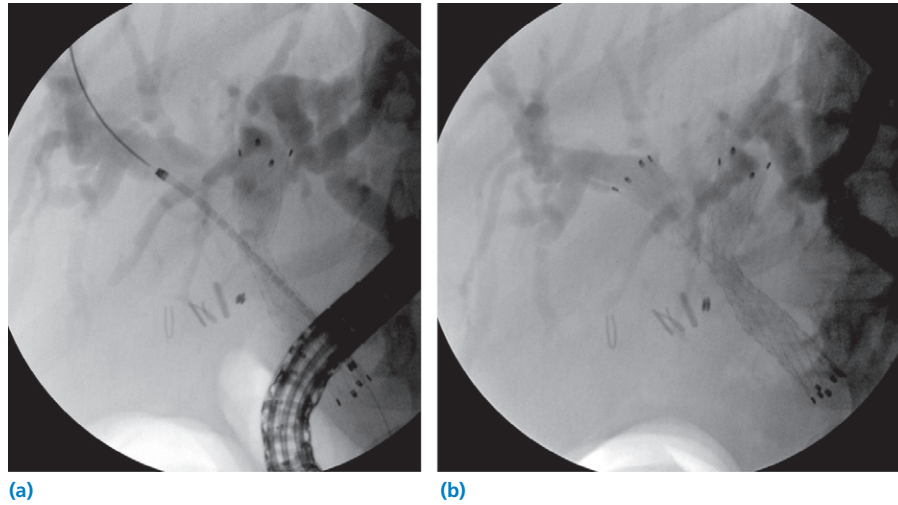


Figure 135.33 Cholangiograms showing placement of dual uncovered metallic stents in a “Y” configuration (stent-through-stent). The first stent has been deployed in the left hepatic duct and a second stent is passed through the lumen of that stent into right anterior sectoral duct (a), followed by deployment showing “Y” configuration (b).

Indeterminate biliary strictures

Determining the etiology of a biliary stricture based on clinical presentation and initial imaging modalities may be challenging. Diagnosis requires a multimodality approach including blood tests and cross sectional radiological studies (CT and MRI/MRCP, and EUS). ERCP should generally be reserved as the last step for tissue acquisition as well as therapy. Several techniques for biliary evaluation and tissue acquisition have been described (Table 135.4) [73]. Tissue sampling at ERCP should almost always include both brush cytology and forceps biopsy (Figure 135.30), due to substantially higher yield than either alone. Tissue obtained from ERCP may be sent for routine cytology, histology, and advanced cytological techniques such as FISH or digital image analysis (DIA) to evaluate for molecular changes in the DNA of biliary epithelial cells that may be suggestive of malignancy. Intraductal assessment may include intraductal ultrasound to assess for duct wall abnormalities and direct visualization by cholangioscopy with or without directed biopsies. The biliary epithelium may be evaluated for visual abnormalities using confocal laser endomicroscopy which allows for high resolution in vivo histological assessment and optical coherence tomography, which uses localized infrared light technology. Currently, the utility of the latter two techniques is limited by high cost, subjectivity, and lack of interobserver agreement [133–135].

The role of direct cholangioscopy in unexplained biliary strictures is not settled at present. While conceptually appealing, direct cholangioscopy in its most widely available form is expensive, leads to cholangitis in 7%–10% of cases due to required infusion of fluid, and allows only limited visualization and subjective diagnosis. Cholangioscopically directed biopsies are currently tiny (1 mm), providing smaller tissue samples and lower yield, and have a lower reported sensitivity of 57% and

accuracy of 78% compared to fluoroscopically directed biopsies, which have a sensitivity of 76% and accuracy of 88% [136]. EUS obviates the need for cholangioscopy in approximately 60% of cases, and the combination of all of the above approaches leads to a tissue diagnosis in over 90% of patients [137]. Direct cholangioscopy may be reserved for a second ERCP if all of the above strategies including EUS fail to yield a diagnosis [138,139].

Cells obtained for cytology may be evaluated for DNA abnormalities using FISH and DIA. FISH is a cytogenetic technique in which fluorescently labeled DNA probes are used to detect the presence or absence of specific DNA sequences. A test of FISH positivity (that is the presence of two or more copies of specific chromosomes, usually 3, 7, 17, and 9p21) has been shown to increase the detection of malignancy [108,109]. In DIA, computer analysis of the nuclear DNA content and nuclear features is performed after digital conversion of images of cells obtained at cytology [140,141]. Both techniques are more sensitive than cytology alone, but at the expense of specificity. Thus the overall advantage of DNA probes in evaluating unexplained biliary strictures is not clear at this point.

Endoscopic retrograde cholangiopancreatography after liver transplantation

Complications of the biliary tract affect approximately one-third of patients after liver transplantation and result in significant patient morbidity and increased patient mortality [90]. The spectrum of biliary complications includes biliary leaks, strictures, choledocholithiasis, cast formation, papillary stenosis, and other less common conditions. An anticipatory approach and a clear understanding of the risk factors for biliary complications following liver transplantation can result in the prompt diagnosis and management of these conditions.

Biliary strictures after liver transplantation are characterized as anastomotic strictures (Figure 135.28) or nonanastomotic strictures (Figure 135.29), which are also called ischemic strictures. Anastomotic strictures are usually short segmental areas of stenosis involving the ductal anastomosis, occur early, and are characterized by the formation of scar tissue at the anastomotic site. Nonanastomotic strictures are long, are thought to be the result of ischemic injury to the duct, and may be associated with obvious vascular compromise (hepatic artery or portal vein occlusion) or secondary causes resulting in vascular injury (cytomegalovirus, ischemia time, ABO incompatibility). Ischemic strictures are more common after donor after cardiac death (DCD) than conventional deceased donor liver transplant (DDLT). The principles of stricture management are similar to those discussed for nontransplant patients.

MRCP is the study of choice in the diagnosis of strictures. ERCP is the first-line treatment modality in the management of biliary complications and is successful in the majority of patients, with PTC reserved for situation in which ERCP is not successful (e.g., a disconnected duct or high-grade stenosis that cannot be traversed at the time of ERCP) or after Roux-en-Y hepaticojejunostomy if the biliary anastomosis cannot be reached despite enteroscopy assistance (Figure 135.34). A clear understanding of the different types of surgical reconstruction during liver transplantation is vital to the appropriate management of biliary complications and, similar to hilar strictures, a thorough understanding of the normal and variant anatomies of the liver segments and their individual and sectoral ducts is

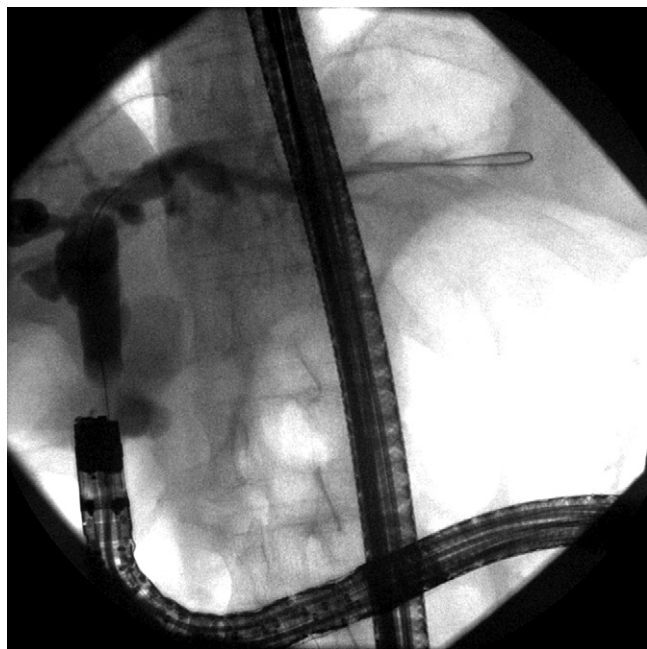


Figure 135.34 Endoscopic retrograde cholangiopancreatography via a forward-viewing endoscope in a patient after liver transplant with Roux-en-Y hepaticojejunostomy.

also essential. Compared to conventional DDLT, the risk of biliary complications is increased in patients who receive a liver from DCD or a living donor (LDLT).

In anastomotic strictures, multiple stents are placed in the bile duct with stent exchange and/or placement of additional stents every few months until the stricture resolves. Alternatively, FCSEMS may be used. Nonanastomotic strictures, like other hilar strictures, are more challenging due to the small size of the intrahepatic ducts and difficulty in the placement of multiple stents. In general, anastomotic strictures resolve within 3–6 months whereas nonanastomotic strictures require a long duration of therapy [99,142–145]. Anastomotic strictures after LDLT require longer stent therapy than in patients with conventional DDLT [146,147].

Biliary stone disease is common after liver transplantation and may occur independently or in the setting of strictures due to impairment in biliary flow. The formation of multiple, long, and diffuse stones, known as biliary casts, is a unique form of stone disease in the setting of liver transplantation. The exact etiology of biliary cast disease is not known but it has been associated with ischemia and strictures. Stone management is similar to that in nontransplant patients with the potential need for cholangioscopy and other advanced techniques for casts or stones occurring above strictures. Rarely, patients with a Roux-en-Y hepaticojejunostomy may require percutaneous cholangioscopy with electrohydraulic or laser lithotripsy for intrahepatic stone removal.

Biliary leaks commonly complicate liver transplantation with a higher incidence in patients with a DCD and LDLT. They usually occur in the early postoperative period. Biliary leaks are typically treated with placement of a biliary stent to bridge the leak, usually with sphincterotomy. If there is an associated biliary stricture, the stricture can be carefully dilated, and one or more stents can be placed beyond both the stricture and the leak though this is usually avoided in the first few weeks following surgery. ERCP results in resolution of >85% of leaks [142,148,149]. FCSEMS have been used in the treatment of biliary leaks considered to be refractory to conventional treatment. Despite improvements in endoscopic techniques, stents, and deep enteroscopy techniques, endoscopic therapy may not be successful or feasible in certain situations. Large anastomotic leaks (e.g., in the setting of hepatic artery compromise) may not heal with endoscopic therapy. Similarly, leaks from a perforation or compromise of a Roux-en-Y anastomosis may require surgery because of an inability to reach the anastomosis for definitive treatment.

Ampullary tumors

A wide variety of benign and malignant tumors involve the major or minor papillas. The most common are ampullary adenomas, which like colonic adenomas have a potential for progression to malignancy. Ampullary adenomas may occur sporadically or in the setting of familial adenomatous polyposis. ERCP allows diagnosis and often removal of ampullary tumors.

Narrow-band imaging or dye-assisted endoscopy may allow more detailed evaluation of the ampullary mucosa, and to obtain repeat biopsies of the ampullary region. EUS, MRI/MRCP, or intraductal ultrasound at ERCP can be used for staging, which is recommended for lesions greater than 2 cm in size and those with features suggestive of malignancy (ulceration, bleeding, induration) [150,151].

Candidates for endoscopic resection are ampullary tumors with: (1) size less than 4–5 cm, (2) benign histology, (3) no endoscopic evidence of malignancy, and (4) no ductal invasion [152,153]. A wide variety of techniques using various devices have been described for the resection of ampullary tumors (ampullectomy). In general, given the higher risk of complications (5%–56%, mean 19%) including retroperitoneal perforation (0%–7%, mean 0.4%), bleeding (0%–17%, mean 4%), and pancreatitis (0%–33%, mean 10%), only endoscopists with extensive expertise should perform endoscopic ampullectomy [153]. Pancreatic stent placement has been shown to decrease the risk of pancreatitis in a randomized controlled trial as well as case–control series [154,155]. Late complications such as papillary stenosis may occur. The reported clinical success of endoscopic ampullectomy varies from 29% to 100%, with an overall success rate of 79% [153]. All patients require surveillance for recurrence of adenomatous tissue even after seemingly complete resection is achieved.

Endoscopic retrograde cholangiopancreatography in pancreatic disease

Over the last two decades, considerable strides have been made in diagnosis and management of pancreatic diseases. Simultaneously, improvements in endoscopic technologies and techniques have enabled ERCP to play an increasingly safe and effective role in the management of pancreatic diseases. ERCP for pancreatic diseases is technically more demanding and riskier than ERCP for most biliary conditions. It should ideally be performed by dedicated endoscopists with advanced endoscopic expertise in a multidisciplinary context, including the disease processes and involvement of specialized surgeons and interventional radiologists as appropriate.

Acute pancreatitis

Several excellent guidelines have been published regarding management of acute pancreatitis, and specifically the role of ERCP in acute biliary pancreatitis [156–158].

ERCP may be indicated early in the course of the disease. However, even in this setting, the obstructing gallstone often passes through the ampullary orifice spontaneously, usually resulting in resolution of biliary and pancreatic obstruction and obviating the need for ERCP. Depending on the clinical picture and laboratory findings, in patients in whom there is a suspicion of a persistent stone in the bile duct an EUS, MRCP, or intra-

operative cholangiography at the time of cholecystectomy should be performed for further evaluation. Pooled data from seven prospective studies, with a total of 757 patients, designed to evaluate the role of early ERCP versus conservative management of patient with acute biliary pancreatitis was reported in a metaanalysis [159]. ERCP was shown to be beneficial in two settings: (1) acute cholangitis, where it was associated with a decreased risk of mortality and local and systemic complications; and (2) persistent biliary obstruction, where it was associated with a decreased risk of complications. Importantly, routine ERCP in all patients with biliary pancreatitis was not found to improve mortality or local and systemic complications regardless of the predicted severity of pancreatitis. Thus, ERCP should be performed urgently (usually within 12 h) in patients with acute biliary pancreatitis with concomitant acute cholangitis and early in the course (usually within 24–72 h) in patients with evidence of persistent biliary obstruction.

Complications of acute pancreatitis

The definitions of localized complications associated with pancreatitis have been updated in order to simplify and standardize terminology and develop evidence based guidelines for their management [160]. According to the revised Atlanta criteria, there are now thought to be only four types of collections associated with pancreatitis: acute peripancreatic fluid collection occur in interstitial edematous pancreatitis; pancreatic pseudocysts are a delayed (usually >4 weeks) complication of interstitial edematous pancreatitis and are rare after acute pancreatitis; and necrosis, which may be an acute necrotic collection (in the early phase and before demarcation), or walled-off necrosis, which is surrounded by a radiologically identifiable capsule (the latter rarely develops before 4 weeks have elapsed from onset of pancreatitis). Indications for intervention include infection, biliary or gastric obstruction, and disconnected pancreatic duct [161]. Interventions for necrotizing pancreatitis have undergone a paradigm shift towards minimally invasive techniques and away from open surgical necrosectomy, with endoscopic necrosectomy emerging as a principle form of treatment. Several multicenter studies, a randomized trial, several evidence-based guidelines, and consensus statements have all endorsed the safety and efficacy of this technique [156,157,161–166]. Endoscopic transluminal drainage and necrosectomy are generally performed using combined endoscopic ultrasound and ERCP techniques. The specific role of ERCP in these settings is to treat associated biliary obstruction, and to evaluate and treat pancreatic duct leaks or disruptions. Side leaks with an intact main pancreatic duct almost always respond to transpapillary pancreatic stenting. In contrast, pancreatic necrosis in the central portion of the pancreas may result in a completely disconnected pancreatic duct proximal and distal to the area of the necrosis. Transpapillary pancreatic stent placement may or may not help in this circumstance, and these patients may be best managed with long-term transmural stents (e.g., cystgastrotomy stents) to rechannel drainage of the disconnected portion

of the pancreas, or by surgery to drain or remove the disconnected portion of the pancreas [161].

Recurrent acute pancreatitis

It is estimated that 20% of patients with acute pancreatitis will have one or more additional episodes of acute pancreatitis during their lifetime. Although there is no universally accepted definition, recurrent acute pancreatitis (RAP) is generally defined as the occurrence of two or more episodes of acute pancreatitis (see Chapter 82). The spectrum of conditions associated with RAP includes biliary disease (often in the form of microlithiasis not visualized by conventional cross-sectional imaging), persistent alcohol use, congenital anomalies of the pancreaticobiliary tract (pancreas divisum, annular pancreas,

anomalous pancreaticobiliary junction) or duodenum (duplication cyst), genetic causes (SPINK1, PRSS1 or CFTR and other mutations), potentially sphincter of Oddi dysfunction (highly controversial), and idiopathic disease. Given the broad range of conditions associated with RAP, it is important to perform a thorough diagnostic evaluation of patients with noninvasive or minimally invasive imaging modalities such as MRCP and EUS and, in selected patients, genetic testing (typically in young patients with or without a family history of pancreatitis or cystic fibrosis).

ERCP is often performed in these patients in the hope that pancreatic sphincterotomy and/or stent placement in the major or minor papilla (Figures 135.35 and 135.36) will interrupt the cycle of recurrent pancreatitis by improving pancreatic drain-

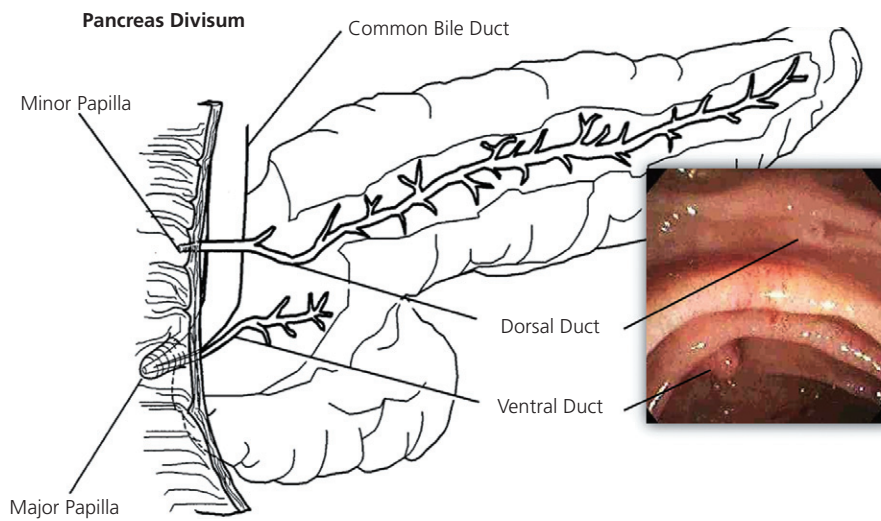


Figure 135.35 Illustration showing anatomy of pancreas divisum.

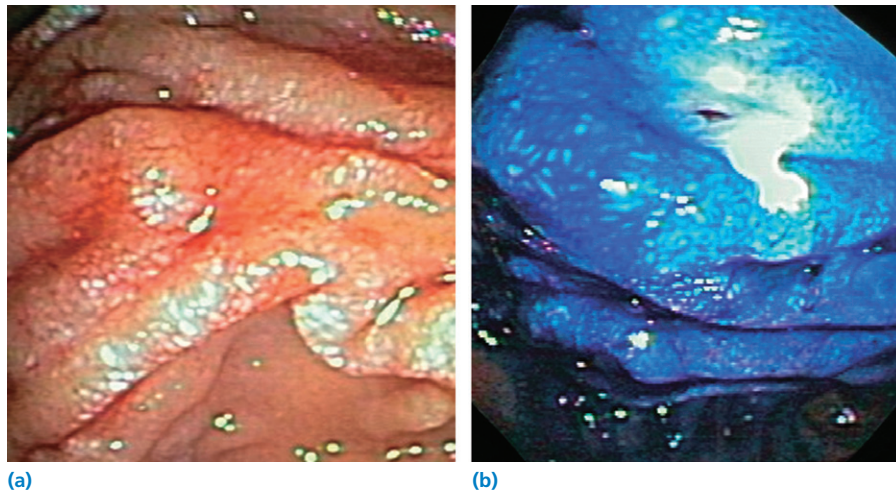


Figure 135.36 Endoscopic view of minor papilla with no visible structure or landmarks (a), and open orifice of minor papilla after spraying methylene blue and intravenous secretin administration (b).

age. Although ERCP may result in an improvement in symptoms and/or RAP episodes in some settings, the response is unpredictable, and evidence supporting efficacy of ERCP for RAP is highly variable, with very few randomized prospective trials, and substantial remaining controversy [167–169]. ERCP for RAP is technically challenging and associated with a high risk of complications, including post-ERCP pancreatitis in up to 20% of patients. Indwelling pancreatic stents may lead to ductal and parenchymal injury, strictures, and subsequent chronic pancreatitis. RAP itself often progresses to chronic pancreatitis (either obvious or subtle) and/or chronic pain irrespective of any endoscopic intervention.

Pancreas divisum is the most common congenital abnormality of the pancreatic ductal system, resulting from failed fusion of the dorsal and ventral anlage in the second month of gestation (Figure 135.35). Pancreas divisum occurs in approximately 7% of the Western population. Although usually asymptomatic, pancreas divisum may be associated with chronic pain, RAP, or chronic pancreatitis. Endoscopic minor papillotomy, intended to relieve intraductal pressure, has gained acceptance as the preferred treatment for clinical manifestations of pancreas divisum (Figure 135.36). Unfortunately, the efficacy of minor papillotomy has not been clearly established, as no randomized controlled trials have been performed. The majority of literature on this topic consists of retrospective case series with outcome measures of varying validity [170–172]. An older randomized trial of routine minor papilla stent exchange without papillotomy suggested significant improvement [167]. Most problematic in the literature regarding pancreas divisum is failure to measure quality-of-life and chronic pain burden, which are often substantially impaired in patients with pancreas divisum and recurrent pancreatitis, whether or not there is obvious morphological evidence of chronic pancreatitis. The response rate to ERCP with minor papillotomy and stent placement varies considerably by study and indication with poorest response for pain alone (25%–44%) and a slightly better response reported in the setting of chronic pancreatitis (45%–55%) [173]. An NIH-funded multicenter, pilot study evaluated the role of ERCP in patients with RAP (two or more episodes) in the setting of pancreas divisum [169]. In this study, pain and disability were measured using a validated instrument: at 6-month follow-up, only 8.3% of patients had recurrence of pancreatitis and the overall pain score was reduced from 4 to 1, including a significant decrease in the number of days associated with pain disability. In this study, the risk of ERCP-related pancreatitis was relatively low (5.6%) compared to more typical rates of 8%–11.2%. ERCP for pancreas divisum should be performed at expert centers and preferably in the context of prospective studies.

Congenital conditions such as annular pancreas, anomalous pancreaticobiliary junction, and duodenal duplication cysts are all conditions that may be associated with RAP. Annular pancreas may be associated with pancreatitis or gastric outlet obstruction. ERCP may be performed for RAP to ensure ade-

quate pancreatic drainage. However, ERCP has no beneficial role in patients with chronic pancreatitis or duodenal stenosis related to annular pancreas. Anomalous pancreaticobiliary junction is defined as the presence of a common biliary and pancreatic duct channel measuring more than 15 mm in length, and may be associated with a congenital dilation of the biliary tree referred to as choledochal cysts, which are classified according to their location along the biliary tree (see Chapter 91). The risk of cholangiocarcinoma and gallbladder cancer is increased in the presence of choledochal cysts. ERCP with sphincterotomy may be beneficial for RAP but in order to minimize the risk of malignancy cholecystectomy, surgical excision of the choledochal cyst is recommended [174,175]. In patients with choledochal cysts involving the main bile duct (type I and IV), a pancreatic stent can be placed prior to surgery to allow identification of the pancreatic duct at the time of the surgery and enable the surgeon to excise the bile duct as close to the pancreatic duct as possible in order to minimize the risk of malignancy and recurrent pain or infection from the retained biliary stump.

The role of ERCP in diagnosis and treatment of sphincter of Oddi dysfunction is highly controversial, and is addressed in detail elsewhere (see Chapter 93) [151,156].

Autoimmune pancreatitis

Autoimmune pancreatitis (AIP) is an inflammatory condition of the pancreas mediated by the autoimmune system associated with characteristic findings on imaging and histological assessment of the pancreas and characterized by being responsive to corticosteroid therapy (see Chapter 83). AIP has been subdivided into two types. Type 1 AIP is a manifestation of IgG4 disease, is often associated with serum IgG4 elevation, presence of IgG4 cells in pancreatic parenchyma, a characteristic pancreatic histological pattern known as lymphoplasmacytic sclerosing pancreatitis, and is often associated with involvement of other organs including salivary glands, retroperitoneal fat, and the intra- and extrahepatic biliary tree. Type 2 AIP is associated with normal IgG4 levels in the serum and pancreatic tissue, typically does not involve additional organs, and is associated with a histological pattern of neutrophils in the pancreas with characteristic granulocyte–epithelial lesions. Type 2 AIP is more common in the United States and Europe and rare in East Asia, typically occurs in younger patients, may be associated with inflammatory bowel disease, and may present with acute pancreatitis [176–183]. ERCP findings suggestive of AIP include a long (more than one-third the length of the pancreatic duct) stricture, multifocal strictures of the pancreatic duct, and mild dilation of the pancreatic duct upstream from strictures (<5 mm), whereas a focal stricture with marked dilation of the upstream pancreatic duct is more consistent with pancreatic malignancy [183]. A concomitant biliary stricture may be present in both conditions. ERCP has a reported sensitivity and specificity of 33%–91% and 80%–90%, respectively, for differentiating AIP from pancreatic cancer [184]. ERCP is

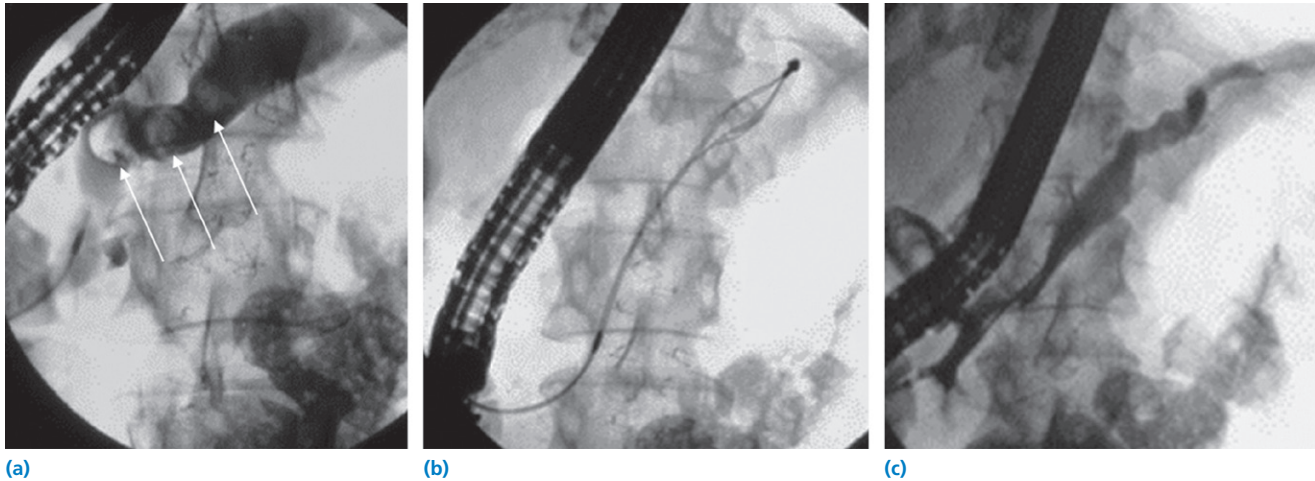


Figure 135.37 Fluoroscopy showing large pancreatic stones (a), basket extraction (b), and complete clearance (c).

increasingly replaced by EUS and ERCP for the diagnosis of AIP. Biopsies of the major papilla (also known as ampullary biopsies) can be obtained at the time of EUS or ERCP and immunostained for the presence of IgG4 cells. An increase in the number of IgG4-positive cells (>10 per high power field) in ampullary biopsies can be seen in type 1 AIP and has been used a diagnostic feature for this entity. However, this finding is not entirely specific for AIP and has been described in other conditions including pancreatobiliary malignancies [185,186].

Chronic pancreatitis

Chronic pancreatitis may be defined as a progressive inflammatory condition of the pancreas, which may lead to development of chronic abdominal pain, progressive loss of exocrine and exocrine function, and increased risk of pancreatic cancer [187] (see Chapter 84). The development of upper abdominal pain is the most debilitating symptom associated with chronic pancreatitis, the severity of which varies widely and does not correlate well with the severity of abnormalities on imaging.

ERCP offers a minimally invasive approach to treatment of chronic pancreatitis, including pancreatic sphincterotomy, stone removal, stricture dilation and stenting, and closure of duct leaks with or without associated pseudocysts [173]. Patients should be managed using a multidisciplinary approach, and the risks and benefits of all options, including surgical management, should be considered. The management of chronic pancreatitis has been addressed in two randomized prospective trials [188,189]. Both studies found significantly superior results with drainage or resection operations than with endoscopic therapy, but were limited by including only patients with very advanced disease with markedly dilated pancreatic ducts, often with a very large stone burden, and utilizing suboptimal techniques for endoscopic management. In clinical practice, such patients represent a small fraction of patients with painful chronic pancrea-

titis, many of whom have smaller ducts, less stone burden, and/or comorbid disease, rendering them more suitable to endoscopic than surgical therapy. In addition, drainage operations impair islet yield should the patient fail to respond and ultimately be considered for total pancreatectomy with islet autotransplantation [190].

Pancreatic duct stones

Obstructing pancreatic duct stones may result in pain or disruption of the upstream duct and a pseudocyst. Stone removal can be accomplished using ERCP alone (Figure 135.37), ESWL alone, or a combination of the two. The exact approach is determined by the size and location of stones, the overall stone burden, and local expertise. Small pancreatic stones can be removed at ERCP using a stone removal basket after a pancreatic sphincterotomy. Unlike biliary stones, pancreatic stones are usually calcified and obstructing stones are typically significantly large relative to the size of the downstream duct and pancreatic orifice even after pancreatic sphincterotomy and balloon dilation of the pancreatic orifice. Therefore, the preferred approach for large stones is to perform ESWL to fragment stones in conjunction with ERCP. The success of ESWL for pancreatic stones is dependent on the equipment and operator technique, with greater success in achieving stone fragmentation reported in high-volume centers. ESWL alone has been shown to be as effective as ESWL with ERCP in removal of stones and pain relief and has been shown to be associated with shorter hospital stay and decreased cost [191]. ESWL has been reported to be effective in achieving pain relief and stone removal in a large metaanalysis, with correlation coefficients of 0.62 and 0.74, respectively (a correlation coefficient of greater than 0.5 is indicative of a large effect) and subsequently in large individual studies as well [192–194]. On the basis of these findings, European guidelines for the management of pancreatic duct stones recommend the use of ESWL as a first step in

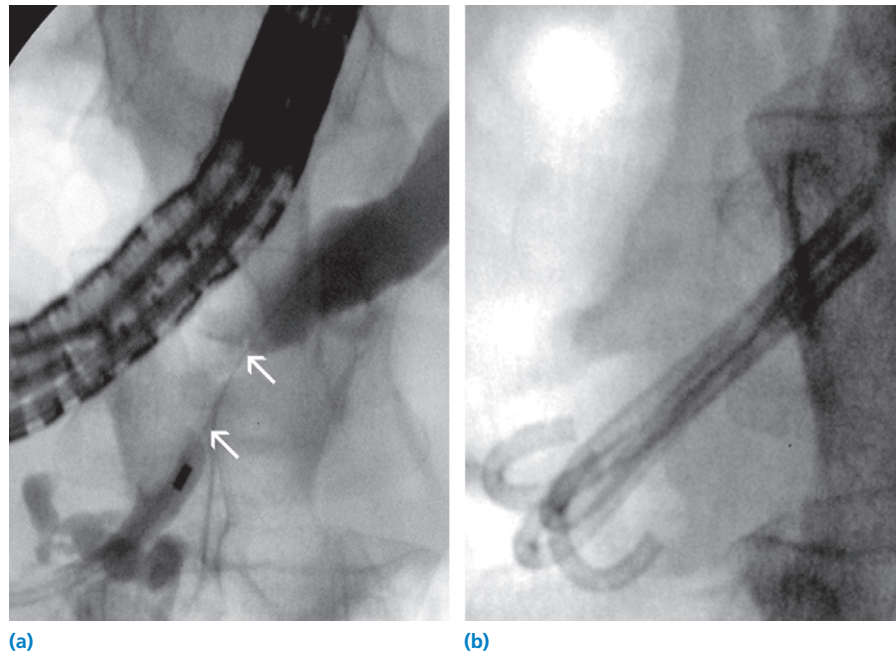


Figure 135.38 Distal main pancreatic duct stricture in patient with hereditary pancreatitis (a), and placement of four 7Fr pancreatic stents (b).

centers with considerable experience with ESWL [195]. ESWL is not as widely established for pancreatic stones in the USA and therefore in most centers, if available, ESWL is combined with ERCP. Difficult pancreatic stones not completely fragmented or removed may be removed using intraductal lithotripsy techniques such as electrohydraulic and laser lithotripsy, similar to bile duct stones.

Pancreatic stricture

The principles of pancreatic stricture treatment are similar to those of biliary stricture treatment, usually involving pancreatic sphincterotomy, balloon dilation, and stent placement. Depending on the degree of stricture, a stent as small as 3 Fr in size may initially be placed with subsequent upsizing to as many stents (Figure 135.38) or as large a stent as can be accommodated in the upstream duct. Practices regarding the size and number of stents placed, timing of ERCP for stent exchange, and duration of therapy vary significantly. European guidelines recommend placement of a 10Fr stent with stent exchange planned at an interval close to a year later or sooner if there is concern for stent occlusion [195]. However, in the USA, the practice is to exchange stents more frequently [196]. Pancreatic stent placement has been shown to achieve immediate pain relief in 65%–95% of patients and sustained relief in 32%–68% of patients (up to 48-month follow-up) [197]. Stents may need to be exchanged no less than every 2–3 months to minimize stent occlusion and related complications. The use of FCSEMS to treat refractory pancreatic duct strictures has been reported [198,199]. These stents may be associated with spontaneous

migration and stent-induced injury of the pancreatic duct and they should therefore be used with caution, ideally in the setting of clinical trials. Patients with refractory strictures or with minimal relief of symptoms despite stent placement should be considered for surgical treatment modalities rather than repeated ERCP procedures.

Pancreatic duct leaks and disruptions

Pancreatic duct leaks or disruptions may result from acute or chronic pancreatitis, surgery involving the pancreas (e.g., after distal pancreatectomy), trauma, iatrogenic (e.g., from ductal injury during ERCP), or other causes. The injury may range from mild to complete transection resulting in a disconnected pancreatic duct. Pancreatic duct leaks can result in pancreatic ascites, pleural effusion, or early (acute fluid or necrotic collections) or late complications (pseudocyst or walled off necrosis). Management differs significantly between pseudocysts and walled off necrosis. Small pseudocysts may be treated with a transpapillary stent to drain the cyst and close the duct leak, while large pseudocysts are typically treated with transmural drainage or percutaneous drainage. In contrast, walled off necrosis often requires direct debridement as well as transpapillary or transmural drainage [144].

The role of ERCP in pancreatic ductal leaks is to place a transpapillary stent into the pancreatic duct, at least across the sphincter and preferably to bridge the area of the leak, with resolution reported in three-quarters of patients, depending on a number of factors including whether or not the site of leak could be bridged [190,200–204].

Endoscopic retrograde cholangiopancreatography in surgically altered upper gastrointestinal anatomy

Surgical procedures that result in alterations of the gastric, duodenal, and/or biliary anatomy may result in anatomic changes that make ERCP access to the major papilla/biliary tree technically difficult or impossible (Box 135.5). In patients with Billroth II gastrectomy and those with a short Roux limb, the major papilla can be reached with a duodenoscope or forward-viewing endoscope and ERCP completed in 67%–84% of patients [205,206]. In contrast, in patients with Roux-en-Y gastric bypass (RYGB) as currently performed, access to the major papilla with a duodenoscope is usually not possible (Figure 135.39).

Box 135.5 Altered upper gastrointestinal anatomy in which conventional endoscopic retrograde cholangiopancreatography is challenging.

Partial gastrectomy with Billroth II gastrojejunostomy
 Gastrojejunostomy or “bypass” performed for gastric outlet obstruction
 Pancreaticoduodenectomy (Whipple procedure)
 Roux-en-Y gastric bypass for obesity
 Roux-en-Y choledochojejunostomy or hepaticojejunostomy
 Roux-en-Y biliary diversion “duodenal switch”
 Total gastrectomy with Roux-en-Y esophagojejunostomy

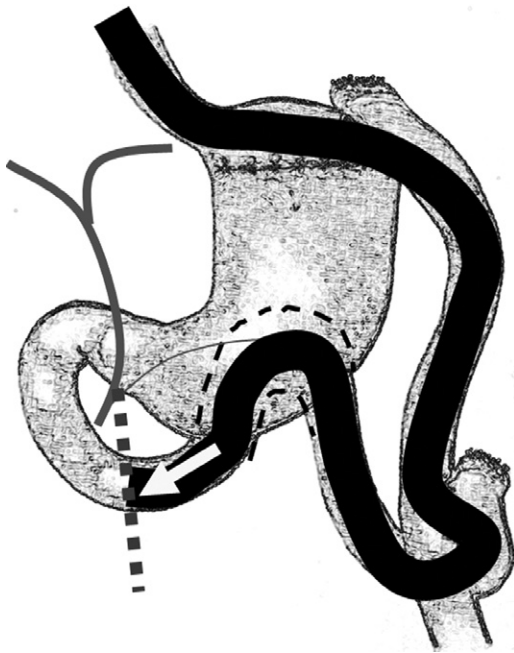


Figure 135.39 Schematic showing the challenges of endoscopic retrograde cholangiopancreatography in patient after Roux-en-Y gastric bypass, with difficulty advancing the endoscope to end of limb.

The choice of endoscope and the associated success rate for biliary access and treatment depends primarily on the underlying surgical anatomy. A standard duodenoscope or pediatric colonoscope may be used to reach the ampullary orifice in patients with a Billroth II anastomosis or short Roux limb RYGB. For pancreatic duct access, particularly after pancreatoduodenectomy (Whipple resection), EUS-guided rendezvous may be required to advance a wire through the stenotic anastomosis and allow retrograde access [207].

The difficulty in long Roux limb RYGB patients is that the scope may need to be inserted as much as 200 cm or more to traverse the Roux limb and jejunojunction anastomosis to reach the major papilla or anastomosis. There are two choices in the approach to ERCP for patients with a RYGB: (1) deep enteroscopy-guided access followed by enteroscope-assisted ERCP or (2) gastric remnant access (laparoscopy-assisted or percutaneous) with conventional ERCP through the gastric remnant for ERCP. The field of deep enteroscopic ERCP is rapidly evolving. The introduction of the double-balloon enteroscope (Fujinon Corp., Saitama, Japan) in 2003, followed by the single-balloon enteroscope (Olympus, Tokyo, Japan) and the spiral enteroscopy overtube (Endo-Ease, Spirus Medical, Stoughton, MA), have provided several endoscopic options [208,209]. The long Roux limb is traversed to reach the biliary orifice, and ERCP is performed through the forward-viewing enteroscope. The double-balloon enteroscope systems require a dedicated processor and endoscope system, whereas the spiral enteroscopy overtube is compatible with both single-balloon and double-balloon enteroscopes. Balloon-assisted enteroscopy uses a balloon attached to an overtube to anchor the enteroscope and overtube as the enteroscope is advanced through the small bowel. Spiral enteroscopy makes use of a spiral overtube that is placed over the enteroscope. As the spiral overtube is rotated, the small bowel is pulled onto the overtube, and this advances the enteroscope through the small bowel, but is no longer available. Limitations of the enteroscopic approach are that the major papilla or surgical anastomosis may not be reached (because of an unfavorable surgical anatomy or adhesions), there is limited selection of accessories and devices that can be used with the enteroscope, lack of an elevator, and thus limited maneuverability of the scope in the region of papilla resulting in potentially difficult cannulation. The success rate of enteroscopy insertion to the major papilla or biliary anastomosis is 55%–100%, with successful cannulation in 63%–100% and successful therapy in 72%–100% of patients overall, though rates for RYGB patients are lower than those for Roux-en-Y hepaticojejunostomy [209].

A more invasive but direct approach to the major papilla in patients with a Roux-en-Y gastric bypass is creation of a gastrotomy, via a surgical approach (laparoscopic or open) [210–212]. According to published series, with this approach successful cannulation and therapy can be achieved in nearly 100% of cases [206,209,210]. The main advantage of a surgical approach for ERCP in patients with altered anatomy is the

ability to perform ERCP in a single-step procedure using a duodenoscope. In contrast to an enteroscopic approach, this allows a conventional approach to the papilla making biliary access easier and enables usage of all available ERCP accessories. In addition, it allows correction of any surgical problems such as internal hernias, which may not otherwise be diagnosed. In a study of patients with a Roux-en-Y gastric bypass, biliary intervention was achieved in all patients using a surgical approach compared to only 58% of patients in whom deep enteroscopy was performed, with lower success in patients with a Roux limb greater than 150 cm [211]. A novel approach for access to the gastric remnant involves EUS-assisted technique for direct percutaneous gastrostomy followed by fixation and dilation of the tract, with ERCP performed via the gastrostomy [193].

References are available at www.yamadagastro.com/textbook

Further reading

- Arain M.A., Attam R., Freeman M.L. Advances in endoscopic management of biliary tract complications after liver transplantation. *Liver Transpl* 2013;19:482.
- Cavell L.K., Allen P.J., Vinoya C., et al. Biliary self-expandable metal stents do not adversely affect pancreaticoduodenectomy. *Am J Gastroenterol* 2013;108:1168.
- Costamagna G., Tringali A., Mutignani M., et al. Endotherapy of post-operative biliary strictures with multiple stents: results after more than 10 years of follow-up. *Gastrointest Endosc* 2010;72:551.
- Elmunzer B.J., Scheiman J.M., Lehman G.A., et al. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N Engl J Med* 2012;366:1414.
- Freeman M.L., Nelson D.B., Sherman S., et al. Complications of endoscopic biliary sphincterotomy. *N Engl J Med* 1996;335:909.
- Mazaki T., Mado K., Masuda H., et al. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: an updated meta-analysis. *J Gastroenterol* 2014;49:343.
- Schreiner M.A., Chang L., Gluck M., et al. Laparoscopy-assisted versus balloon enteroscopy-assisted ERCP in bariatric post-Roux-en-Y gastric bypass patients. *Gastrointest Endosc* 2012;75:748.
- Tandan M., Reddy D.N., Talukdar R., et al. Long-term clinical outcomes of extracorporeal shockwave lithotripsy in painful chronic calcific pancreatitis. *Gastrointest Endosc* 2013;78:726.
- 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.
- Yoon W.J., Brugge W.R. Endoscopic evaluation of bile duct strictures. *Gastrointest Endosc Clin N Am* 2013;23:277.