Communication from the ASGE Standards of Practice Committee

GUIDELINE

Adverse events associated with ERCP

Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

Vinay Chandrasekhara, MD, Mouen A. Khashab, MD, V. Raman Muthusamy, MD, FASGE, Ruben D. Acosta, MD, Deepak Agrawal, MD, MPH, David H. Bruining, MD, Mohamad A. Eloubeidi, MD, MHS, FASGE, Robert D. Fanelli, MD, FACS, FASGE, SAGES Representative, Ashley L. Faulx, MD, FASGE, Suryakanth R. Gurudu, MD, FASGE, Shivangi Kothari, MD, Jenifer R. Lightdale, MD, MPH, FASGE, NASPGHAN Representative, Bashar J. Qumseya, MD, MPH, Aasma Shaukat, MD, MPH, FASGE, Amy Wang, MD, FASGE, Sachin B. Wani, MD, Julie Yang, MD, John M. DeWitt, MD, FASGE, Chair

This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this guideline, we performed a search of the medical literature by using Pubmed. Additional references were obtained from a search of Web of Science, SCOPUS, the bibliographies of the identified articles, and from recommendations of expert consultants. Guidelines for appropriate use of endoscopy were based on a critical review of the available data and expert consensus at the time the guidelines were drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence by using the GRADE criteria[1] (Table 1). The strength of individual recommendations is based on the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as "we suggest…," whereas stronger recommendations are typically stated as "we recommend…"

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.

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Since its introduction in 1968, ERCP has become an invaluable procedure in the diagnosis and management of a variety of pancreaticobiliary disorders. The role of ERCP has evolved from a diagnostic to a mainly therapeutic intervention because of improvements in other imaging modalities including magnetic resonance imaging and/or MRCP and EUS. For endoscopists to accurately consider the clinical appropriateness of ERCP, it is important for them to have a thorough understanding of available alternatives and of the potential adverse events associated with the procedure. In addition, they must understand and attempt to follow maneuvers that reduce the risk of adverse events. Early recognition and appropriate management of potential adverse events are critical to reducing morbidity and mortality associated with the procedure. The diagnosis and management of all adverse events of ERCP are beyond the scope of this document; however, general principles are discussed.

PANCREATITIS

Introduction

Post-ERCP pancreatitis (PEP) is the most common serious adverse event attributed to the procedure, resulting in annual estimated costs exceeding 150 million dollars in the United States.[2,3] Controversy exists on how PEP should be defined. Elevated serum pancreatic enzyme levels alone do not constitute PEP, because transient increases in serum pancreatic enzyme levels may occur in up to 75% of individuals after the procedure, regardless of symptoms.[4] Conversely, individuals with low serum amylase levels less than 1.5 times the upper limit of

TABLE 1. GRADE system for rating the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕◯
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕◯◯
Very low quality	Any estimate of effect is very uncertain.	⊕◯◯◯

Adapted from Guyatt et al.[1]

normal, obtained 2 to 4 hours after ERCP, are unlikely to have or develop PEP.[5]

Most studies investigating PEP use the consensus definition and classification proposed by Cotton et al[6] in 1991 (Table 2). Some have proposed modifying the definition to "new or worsened abdominal pain" rather than "clinical pancreatitis" to account for patients with pre-existing pain from acute or chronic pancreatitis.[7] Based on this definition, the overall incidence of PEP is estimated to be 3% to 10% in systematic reviews.[2,3,8] A recent meta-analysis of 108 randomized, controlled trials involving 13,296 patients, reported a 9.7% overall incidence of PEP (95% confidence interval [CI], 8.6%-10.7%), with an increased incidence of 14.7% (95% CI, 11.8%-17.7%) in high-risk patients.[3] The majority of PEP cases were mild, with a mortality rate of 0.7% (95% CI, 0%-0.4%). Although not specific for PEP, the revised Atlanta Classification of acute pancreatitis[9] consensus definitions stratify pancreatitis severity based on the presence and duration of organ failure rather than duration of hospitalization and may provide an alternative for assessing PEP severity (Table 2).

RISK FACTORS

Patient-related factors

Large studies have identified numerous patient-related, procedure-related, and operator-related factors that have been associated with PEP (Table 3). Patients with suspected sphincter of Oddi dysfunction (SOD) have an increased risk of PEP.[7] Performance of SOD manometry does not increase the incidence of PEP, particularly when continuous aspiration or solid-state catheters are used.[7,10-12] Other patient-related risk factors include prior PEP, female sex, younger patient age, normal serum bilirubin levels, and history of acute recurrent pancreatitis.[7,8,10,13-15] A recent, retrospective, matched-cohort study from the National Inpatient Sample suggested that pregnancy is an independent risk factor for PEP[16] (12% vs 5%; $P < .001$), with an adjusted odds ratio (OR) of 2.8 (95% CI, 2.1-3.8), although this has not been noted in other studies. Chronic pancreatitis has been demonstrated to be protective against PEP, possibly because of decreased enzymatic exocrine function and pancreatic atrophy.[13] The presence of pancreas divisum is not an independent risk factor for PEP, but dorsal duct manipulation and minor papilla sphincterotomy increases the rate of PEP.[14] Risk factors for PEP are synergistic; therefore, the risk of PEP is additive for each risk factor that an individual has.[10] The rate of PEP has been reported to be as high as 40% in patients with multiple risk factors.[4]

Procedure-related factors

Difficult cannulation, defined as repetitive attempts or prolonged duration before cannulation (>5-10 minutes) increases the risk of PEP.[4,17] Easy cannulation (<5 attempts) has a lower rate of PEP (3%) compared with moderately difficult cannulation (>6 attempts; PEP rate of 7%-9%) and difficult cannulation (>15-20 attempts; PEP rate of 13%-15%).[7,15] In these studies, difficult cannulation was an independent risk factor for PEP (OR 2.4-2.8; 95% CI, 1.07-5.36). A systematic review of 15 randomized clinical trials involving 1768 patients demonstrated significantly higher rates of PEP with endoscopic papillary large-balloon dilation (EPLBD) of an intact biliary sphincter for extraction of large choledocholithiasis compared with biliary sphincterotomy (RR 1.96; 95% CI, 1.34-2.89).[18] A prospective randomized trial demonstrated that a short duration with EPLBD of an intact biliary sphincter of 1 minute is associated with higher rates of PEP as compared with 5-minute dilation (15.1% vs 4.8%; $P = .038$).[19] A subsequent meta-analysis similarly identified higher rates of pancreatitis with short duration EPLBD ≤1 minute compared with EPLBD longer than 1 minute.[20] Conversely, adjunct balloon sphincteroplasty (ie, balloon dilation after biliary sphincterotomy), does not increase the risk of PEP.[21,22] Other procedure-related factors that have been attributed with higher rates of PEP include pancreatic duct cannulation and/or injection and pancreatic sphincterotomy (including minor papillotomy) (Table 3). Endoscopic papillectomy has been demonstrated to increase the risk of pancreatitis, but pancreatic duct stenting appears to reduce this risk.[23]

Historically, precut (access) sphincterotomy has been attributed to be a risk factor for PEP. In these studies, precut sphincterotomy was primarily used after difficult cannulation. In 1 study, 64% of patients underwent a precut sphincterotomy only after prolonged attempts at cannulation (>15 attempts).[7] It is likely that this increased

TABLE 2. Classification of post-ERCP pancreatitis

	Mild	Moderate	Severe
Cotton et al[6]	a) Clinical pancreatitis* AND b) Amylase at least three times normal at more than 24 hours after the procedure AND c) Requiring admission or prolongation of planned admission to 2-3 days	Pancreatitis requiring hospitalization of 4-10 days	a) Hospitalization for more than 10 days OR b) Development of hemorrhagic pancreatitis, phlegmon, pseudocyst, or infection OR c) Need for percutaneous drainage or surgery
Revised Atlanta classification[9,†]	Two of the following: a) Pain consistent with acute pancreatitis b) Amylase or lipase > 3 times normal limit c) Characteristic imaging findings AND No organ dysfunction or other adverse events	a) Transient organ failure <48 hours OR b) Local or systemic adverse events without persistent organ failure	a) Persistent single or multi-organ failure >48 hours OR b) Present or persistent systemic inflammatory response syndrome (SIRS)

*Proposed clarification of definition to include "new or worsened abdominal pain."
†Classification designed for categorizing acute pancreatitis, not specific for post-ERCP pancreatitis.

TABLE 3. Independent risk factors for post-ERCP pancreatitis identified with multivariable analysis.[168]

	Odds ratio (95% confidence interval)
Patient-related risk factors	
Prior post-ERCP pancreatitis	8.7 (3.2-23.86)
Female sex	3.5 (1.1-10.6)
Previous recurrent pancreatitis	2.46 (1.93-3.12)
Suspected sphincter of Oddi dysfunction	1.91 (1.37-2.65)
Younger patient age (<40 years old)[14] 30 vs 70 years old[7]	1.8 (1.27-2.59) 2.14 (1.413.25)
Absence of chronic pancreatitis	1.87 (1.003.48)
Normal serum bilirubin	1.89 (1.222.93)
Procedure-related risk factors	
Difficult cannulation (>10 minutes)	1.76 (1.13-2.74)
Repetitive pancreatic guidewire cannulation	2.77 (1.79-4.30)
Pancreatic injection	2.2 (1.60-3.01)
Pancreatic sphincterotomy	3.07 (1.64-5.75)
Endoscopic papillary large-balloon dilation of an intact sphincter	4.51 (1.51-13.46)

rate of PEP attributed to precut sphincterotomy is actually related to ampullary trauma from prior attempts with a difficult cannulation rather than the precut sphincterotomy itself. Using a strategy of early precut sphincterotomy for cases with difficult biliary access is associated with similar if not improved rates of cannulation compared with standard techniques and appears to reduce the risk of pancreatitis.[24,25] A recent meta-analysis identified a significant reduction in risk of PEP in patients receiving early precut sphincterotomy versus standard techniques (RR 0.29; 95% CI, 0.10-0.86).[25] These studies used a heterogeneous definition for difficult biliary cannulation, specifying a duration of attempted cannulation of >5 to 12 minutes or >2 to 4 inadvertent pancreatic duct cannulations before randomizing to precut sphincterotomy versus persistence with standard cannulation techniques.

Operator-related factors

Operator-related risk factors, including prior experience, case volume, and trainee participation, have been hypothesized to influence the risk of PEP but have been difficult to evaluate because of confounding variables including the complexity of ERCP at high-volume centers versus low-volume centers.[26] One study demonstrated an independent increase in the risk of PEP with trainee involvement (OR 1.5; 95% CI, 1.0-2.1), but other studies have not demonstrated increased rates of PEP with trainee participation.[13,15,27]

METHODS OF REDUCING POST-ERCP PANCREATITIS

Patient selection

Appropriate patient selection is instrumental in reducing the incidence of PEP. EUS and MRCP are equivalent to ERCP for the detection of some pancreaticobiliary disorders such as choledocholithiasis but lack the risk of pancreatitis associated with ERCP.[28,29] Therefore, ERCP is now largely reserved for indications in which the likelihood of therapeutic intervention is high.[30,31] One high-risk group that should no longer be offered ERCP routinely is individuals with right upper quadrant abdominal pain after cholecystectomy without evidence of bile duct dilation or elevated liver-associated enzyme levels, the so-called type 3 SOD.[32] A randomized, controlled trial of patients with suspected type 3 SOD failed to demonstrate diagnostic or

predictive benefit of ERCP with manometry or a therapeutic benefit with endoscopic sphincterotomy.[33] In this study, 37% in the sham treatment group versus 23% in the sphincterotomy group achieved treatment success with an adjusted risk difference of -15.7 (95% CI, -28 to -3.3).

MODIFICATIONS IN TECHNIQUE TO PREVENT PANCREATITIS

Guidewire cannulation

Cannulation techniques that minimize ampullary trauma reduce the risk of PEP. Data on the risk of PEP with wire-guided versus contrast material–assisted techniques from primary studies have been mixed.[34,35] A recent meta-analysis of 12 randomized controlled trials involving 3450 patients found that the guidewire cannulation technique significantly reduced PEP compared with the contrast-material–assisted technique (RR 0.51; 95% CI, 0.32-0.82) with higher rates of primary cannulation of the desired duct (RR 1.07; 95% CI, 1.00-1.15) and reduced need for precut sphincterotomy (RR 0.75; 95% CI, 0.60-0.95).[36] Wire-guided cannulation also reduces the risk of PEP in cases of inadvertent pancreatic duct (PD) manipulation. However, the differences in rates of PEP were only observed in studies that did not allow crossover to another technique. When additional techniques or rescue approaches were used, including precut sphincterotomy or PD stent placement, there were no differences in PEP rates between the 2 initial cannulation techniques.[36] Although a primary guidewire technique appears to improve cannulation rates and reduce the risk of PEP, in the hands of skilled individuals comfortable with alternative and rescue techniques these rates are likely unchanged.

Pancreatic duct stents

Several randomized, controlled trials and meta-analyses have proven a significant reduction in incidence and severity of PEP with prophylactic pancreatic duct stenting.[37,38] A recent meta-analysis of 14 studies including 1541 patients demonstrated a significant reduction of PEP with pancreatic duct stent placement (RR 0.39; 95% CI, 0.29-0.53).[38] One study found the absolute risk difference with pancreatic duct stenting was 13.3% (95% CI, 8.8%-17.8%), with the number needed to treat of 8 to avoid 1 episode of PEP.[37] Therefore, pancreatic duct stenting is recommended in patients considered at high risk for PEP (eg, after repeated inadvertent PD cannulation), particularly in cases with difficult biliary cannulation. A recent network meta-analysis has shown that 5F stents are superior to 3F stents for the prevention of PEP.[39] Current data suggest that stents should not be removed at the conclusion of the procedure. In a single-center, randomized, prospective study, PEP occurred in 21.3% of individuals who had the PD stent immediately removed versus 4.3% when the stent was left in place for 7 to 10 days ($P = .027$).[40] In a secondary analysis of randomized, controlled trial data, failed pancreatic stent placement was shown to be an independent risk factor for PEP with pancreatitis rates of 34.7% after failed PD stent placement compared with 12.1% without stent attempt ($P = .02$).[41]

Pharmacologic prophylaxis

Many agents have been studied for pharmacologic prophylaxis of PEP, each directed toward interruption or amelioration of an aspect of the inflammatory cascade that accompanies and potentiates acute pancreatitis. Rectal administration of nonsteroidal anti-inflammatory drugs (NSAIDs) has the most robust data for significantly reducing the incidence and severity of PEP.[42-46] The pivotal study by Elmunzer et al[42] randomized 602 patients considered high-risk for PEP to receive a single dose of 100 mg rectal indomethacin or placebo immediately after ERCP. In this study, pancreatic duct stenting was performed at the discretion of the endoscopist. PEP occurred in 9.2% of the indomethacin group versus 16.9% of the placebo group ($P = .005$). Furthermore, those receiving indomethacin were less likely to develop moderate-to-severe pancreatitis compared with those receiving placebo (4.4% vs 8.8%; $P = .03$). Rectal administration of diclofenac appears to have a similar beneficial effect in reducing PEP.[47,48] Several recent meta-analyses of rectal NSAID use have shown that these agents reduce the risk of moderate or severe PEP, with a number needed to treat to prevent 1 case of PEP ranging from 11 to 17.[43,47,48] Rectal NSAID use appears to be equally effective in reducing PEP when given before or immediately after the procedure[47,49] as well as in cases of attempted but failed prophylactic pancreatic stent placement.[41] Furthermore, indirect evidence from recent studies has suggested that rectal administration of NSAIDs may be superior to pancreatic duct stenting as well as the combination of rectal NSAIDs and pancreatic duct stenting for reducing PEP in high-risk patients.[50,51] Ongoing, randomized, controlled trials are being conducted to investigate these observations. Although the majority of the data show favorable results for preventing PEP with rectal NSAIDs, a recent, prospective, double-blind, placebo-controlled trial in 449 consecutive patients, of whom 70% were average risk for PEP, demonstrated no benefit with rectal indomethacin.[52] The authors concluded that rectal indomethacin should be reserved for patients at high risk for PEP and should not be routinely offered for average-risk patients. However, a multicenter, single-blinded, randomized, controlled trial of 2600 patients undergoing ERCP in China that included low-risk individuals demonstrated a significant reduction in PEP in those who universally received rectal indomethacin (4%) before the procedure, compared with a group that received the medication after the procedure based on risk stratification (8%, *RR* 0.47; 95% CI, 0.34-0.66; $P < .0001$).[53] A retrospective cohort study of 4017 patients undergoing ERCP that included individuals at low risk for PEP at a single

institution found a 65% reduction in the rate of PEP (65%, OR 0.35; 95% CI, 0.24-0.51; $P < .001$) with the administration of postprocedural rectal indomethacin.[54] Furthermore, administration of rectal indomethacin was found to reduce the odds of moderate to severe PEP by 83% (OR 0.17; 95% CI, 0.09-0.32; $P < .001$). Rectal indomethacin has not been associated with higher rates of GI bleeding or other adverse events. With current evidence demonstrating a possible reduction of PEP and favorable safety profile of rectal NSAID use, it is reasonable to administer rectal indomethacin for the prevention of PEP in average-risk individuals. A recent systematic review and network meta-analysis have suggested additional agents that merit investigation for the prevention of PEP include topical epinephrine (adrenaline), nafamostat, sublingual nitroglycerin, somatostatin, and antibiotics.[55,56]

IV hydration

IV hydration is a fundamental therapy for treatment of acute pancreatitis. IV hydration is thought to prevent further injury to the pancreas from microvascular hypoperfusion. A pilot study of 62 patients that randomized patients to aggressive IV hydration with lactated Ringer's (LR) solution versus standard hydration demonstrated significant reduction in PEP (0% vs 17%; $P = .016$).[57] Patients in the aggressive hydration group received 3 mL/kg/hour during the procedure, a 20 mL/kg bolus immediately after the procedure, and 3 mL/kg/hour for 8 hours after the procedure. It is important to note that patients with cholangitis, sepsis, acute or chronic pancreatitis, and patients at risk of fluid overload were excluded. The use of LR solution rather than normal saline solution may prevent further acidosis, which may activate pancreatic enzymes. Using the same protocol, similar results were noted in a randomized, double-blind, controlled study of 150 patients in which PEP was noted in 5.3% of patients receiving aggressive hydration compared with 22.7% receiving standard hydration ($P = .002$).[58] The use of LR solution for the prevention of PEP appears promising and warrants additional investigation.

BLEEDING

Bleeding is a serious adverse event with ERCP and is most commonly the result of endoscopic biliary and/or pancreatic sphincterotomy. The rate of postsphincterotomy bleeding after ERCP is estimated to be 0.3% to 2%[7,10,49] but varies according to the definition of bleeding. Other etiologies of post-ERCP bleeding include splenic injury, hepatic injury, and vascular injury and/or pseudoaneurysm.[59-62] In addition, hemobilia may occur after ERCP, especially after stricture dilation, biopsy of the biliary tree, and ablative biliary therapies.[63] This section will detail grading of post-ERCP bleeding, risk factors associated with bleeding, and its management and prevention.

Classification and grading

Bleeding after ERCP is classified as either immediate or delayed, with the former generally referring to bleeding that occurs during the procedure or immediately afterward. Delayed bleeding occurs from hours up to several weeks after endoscopic sphincterotomy. Furthermore, bleeding can be classified as clinically significant or insignificant, based on the presence or absence of overt GI bleeding and change in hemoglobin level.[64]

Cotton et al[6] graded the severity of clinically significant bleeding as mild, moderate, or severe in a consensus document based on the number of transfused units and requirement for angiographic or surgical intervention (Table 4). More recently, an ASGE lexicon for grading of severity of procedural adverse events was proposed.[65] Based on this lexicon, requirement of blood transfusion or angiographic therapy is classified as moderate in severity. Bleeding is rated as severe if it results in prolonged hospital stay (>10 days), prolonged intensive care unit stay (>1 day), or required surgical intervention.

Risk factors

Freeman et al[7] studied adverse events of endoscopic biliary sphincterotomy in a landmark prospective study of 2347 patients undergoing ERCP (85% for the removal of stones). Clinically significant bleeding occurred in 2% of patients (n =48) and was mild in 0.6%, moderate in 0.9%, and severe in 0.5%. Death related to delayed bleeding occurred in 2 patients with Child-Pugh class C cirrhosis despite appropriate endoscopic and radiologic interventions.

Multivariable analysis identified 5 independent risk factors for post-ERCP bleeding, including 3 patient-related factors: the presence of coagulopathy (OR 3.32; $P < .001$), active cholangitis (OR 2.59; $P < .001$), or anticoagulant therapy within 3 days after ERCP (OR 5.11; $P < .001$). Endoscopist case volume $\leq$1 per week was the only operator-related factor (OR 2.17; $P = .002$). The fifth risk factor was the occurrence of any observed bleeding during the procedure (OR 1.74; $P = .004$). Cirrhosis was not a risk factor in the multivariable analysis ($P = .06$). Important factors that were not associated with bleeding included length of sphincterotomy incision, the presence of a periampullary diverticulum, and the use of aspirin or other NSAIDs within 3 days of the procedure.

Masci et al[66] studied adverse events of ERCP in a multicenter, prospective study that included 2013 patients and 2444 procedures. Clinically significant bleeding occurred in 1.2% of cases, and no deaths occurred. Only precut sphincterotomy and stenosis of the orifice of the papilla were significantly associated with bleeding on multivariable analysis. Precut sphincterotomy also has been associated with increased incidence of bleeding in other studies.[67]

The type of current used during endoscopic sphincterotomy seems to affect the risk of bleeding, with 1 meta-analysis showing that pure-cut current significantly

TABLE 4. The severity of clinically significant bleeding as mild, moderate, or severe from a consensus document based on the number of transfused units and requirement for angiographic or surgical intervention

	Mild	Moderate	Severe
Bleeding	Clinical (ie, not just endoscopic) evidence of bleeding Hemoglobin drop <3 g/dL and no need for transfusion	Transfusion (≤4 units), no angiographic intervention or surgery	Transfusion ≥5 units or intervention (angiographic or surgical)

Cotton et al.[6]

increased bleeding risk compared with mixed current.[68] The use of microprocessor generators was associated with decreased risk of minor, but not clinically significant, bleeding in multiple trials.[68-70]

Patients having any form of coagulopathy and those started on anticoagulation within 3 days of ERCP have an increased risk of postprocedure bleeding.[7,71,72] Use of aspirin or NSAIDs in the periprocedural period is safe and does not increase the risk of bleeding after ERCP.[7,73,74] Current guidelines suggest that low doses of aspirin or NSAIDs may be continued safely in the periendoscopic period.[75] Although the risk of bleeding associated with the use of a thienopyridine (ticlopidine, clopidogrel, and prasugrel) has not been well studied, it is recommended that these medications be discontinued at least 5 to 7 days before high-risk endoscopic procedures (eg, ERCP with sphincterotomy) with patients continued on or switched to aspirin monotherapy until the thienopyridine can be safely resumed.[75]

Prevention and management

The risk of post-ERCP bleeding is minimized by avoiding unnecessary sphincterotomy, especially in patients with 1 or more risk factors for bleeding. However, if sphincterotomy is required, a number of factors may be used to prevent postprocedure bleeding. First, EPLBD has been studied as an alternative to endoscopic sphincterotomy in patients with coagulopathy at high risk for bleeding after sphincterotomy.[76] A recent meta-analysis of randomized trials found that the EPLBD was associated with decreased risk of bleeding compared with endoscopic sphincterotomy (OR 0.15; 95% CI, 0.04-0.50; $P = .002$).[22] However, risk of post-ERCP pancreatitis is increased in patients who undergo EPLBD without initial sphincterotomy.[77] Therefore, EPLBD without endoscopic sphincterotomy is best reserved for patients with coagulopathy who are at significantly increased risk for postsphincterotomy bleeding. Second, the use of blended rather than pure-cutting current and use of a microprocessor-controlled generator may decrease the risk of postsphincterotomy bleeding.[78] Third, a randomized trial of 120 patients found that prophylactic injection of hypertonic saline-epinephrine proximal to the papilla significantly reduced the risk of postsphincterotomy bleeding.[79] Additional studies are needed to investigate the benefits of this practice in patients at high risk for postsphincterotomy bleeding.

Initial management of postsphincterotomy bleeding includes adequate fluid resuscitation, reversal of coagulopathy, and blood transfusion, as needed. Endoscopic management is indicated for significant procedural bleeding or clinically significant delayed bleeding. The most commonly used treatment is injection of dilute epinephrine into and around the sphincterotomy site, which is effective in most cases.[71,80] The volume of injectate varies between studies but typically is 0.5 mL to 4 mL.[71] Thermal therapies such as multipolar electrocautery and argon plasma coagulation also may be used alone or in combination with epinephrine injection.[64] However, there are no randomized trials to support superiority of dual-modality therapy over epinephrine injection alone. Balloon tamponade of the sphincterotomy site also may be used to treat intraprocedural bleeding.[49] Placement of through-the-scope clips onto the bleeding site (typically at the apex) by using a duodenoscope is challenging but may be facilitated by use of a forward-viewing endoscope with a cap.[55] Care must be taken to avoid the pancreatic orifice during thermal and mechanical applications. Several recent studies of refractory postsphincterotomy bleeding have reported excellent outcomes with the use of fully covered self-expandable metal stents (FCSEMSs) for refractory postsphincterotomy bleeding with excellent outcomes in the vast majority (100% in most series).[81,82] FCSEMSs also can be used to tamponade bleeding originating from deep within the ampulla or mid/distal common bile duct.[81] Because of the cost of self-expandable metal stents (SEMSs) and the need for a repeat procedure for stent removal, this practice is best reserved for patients with postsphincterotomy bleeding refractory to standard endoscopic therapies.

Angiographic embolization and surgery are equally effective therapies for refractory bleeding.[83-85] Angiographic interventions successfully control bleeding in 83% to 100% of patients in reported series and should be considered before surgery.[83-85] Angiographic embolization also should be used for hemobilia originating from above the hilum and for distal bleeding that is refractory to SEMS placement.

INFECTIOUS ADVERSE EVENTS

Infectious adverse events associated with ERCP and their prevention by using antibiotic prophylaxis are

discussed in a separate guideline.[86] Cholangitis is the most common infectious adverse event associated with performance of ERCP. Other potential infectious events include cholecystitis, duodenoscope-related transmission of infection, and infective endocarditis. Infective endocarditis has been discussed previously in the document mentioned earlier[86] and is not addressed further here.

Cholangitis

ERCP is the endoscopic modality of choice for the treatment of acute cholangitis.[87] Cholangitis and sepsis also are known adverse events associated with ERCP, occurring in up to 0.5% to 3% of cases.[2,66,88-91] Patients typically present with fever, jaundice, and abdominal pain, but hypotension and altered mental status can ensue in severe cases. Freeman et al[7] identified cholangitis in 1% of patients undergoing biliary sphincterotomy. Significant risk factors in the univariate analysis were combined percutaneous–endoscopic procedures ($P < .001$), stenting of malignant strictures ($P < .001$), and failed biliary access or drainage ($P < .001$).

The risk of post-ERCP cholangitis is highest in patients with incomplete biliary drainage (ie, hilar cholangiocarcinoma and primary sclerosing cholangitis) and prior history of liver transplantation. Therefore, periprocedural antibiotics and meticulous biliary drainage techniques are essential in these patients.[92-94] Current guidelines recommend antibiotic prophylaxis before ERCP in patients who have had liver transplantation or when patients with known or suspected biliary obstruction may be incompletely drained, and these guidelines discourage the routine use of antibiotic prophylaxis before ERCP when complete biliary drainage is anticipated or for cases in which biliary obstruction is not suspected. Antibiotics that cover biliary flora such as enteric gram-negative organisms and enterococci should be used and continued after the procedure if biliary drainage is incomplete.[86]

Proper ERCP techniques should be used to minimize risk of post-ERCP cholangitis. In cases of hilar obstruction, cholangitis can occur if only unilateral drainage is accomplished after bilateral contrast-material opacification.[92] Therefore, it is recommended to use noninvasive imaging (MRCP) to format a "roadmap" before ERCP.[95] Only biliary segments in a liver lobe that is not atrophied, which are accessed by wire cannulation, should be injected and subsequently stented.

Incomplete biliary drainage leading to cholangitis also may occur in patients with choledocholithiasis and incomplete stone clearance.[7] Retained stone fragments may occur following mechanical lithotripsy, and the risk of cholangitis in these patients has been reported to be as high as 10%.[96] A biliary stent should be placed when complete stone extraction has not been accomplished. An alternative technique to avoid retained stone fragments is to perform EPLBD, which facilitates large stone removal and obviates the need for lithotripsy. A prospective, randomized trial comparing endoscopic sphincterotomy with EPLBD to endoscopic sphincterotomy with mechanical lithotripsy in 90 patients with choledocholithiasis (12-20 mm in size)[97] found that both techniques were highly and equally effective in achieving stone clearance (98% vs 91%; $P = .36$). However, there was a statistically higher rate of cholangitis in the lithotripsy group (13.3%) compared with the EPLBD group (0%; $P = .03$). This higher rate of cholangitis was not reproduced in another randomized trial.[22]

Cholangitis can also be a delayed adverse event with ERCP when a plastic or metallic stent has been placed previously, although the risk is small after placement of metal stents.[98] Stents may become obstructed because of stone fragments, bacterial biofilm, and/or sludge, and tumor and/or tissue ingrowth and/or overgrowth occluding the stent lumen. In addition, cholangitis can occur because of stent migration in the setting of an obstructed bile duct. Appropriate choice of stent (plastic vs metal) may help minimize these adverse events. Factors that should be taken into consideration include stricture etiology, stricture location, response to prior therapy, local expertise, stent availability, cost of stents, and expected patient survival.[99] Plastic stents are typically exchanged at scheduled intervals (eg, every 3 months) or at the first sign, symptom, or laboratory anomaly suggesting stent occlusion. Placement of multiple plastic stents may aid in avoiding early stent occlusion and cholangitis.[100]

Othman et al[101] prospectively studied the risk of bacteremia and subsequent infectious adverse events after ERCP with cholangioscopy in 57 patients. Postprocedure bacteremia was seen in 5 of 57 procedures (8.8%), whereas 4 patients (7%) developed clinical cholangitis. Bacteremia was more common in patients who had cholangioscopy with biopsy sampling compared with patients who had cholangioscopy without biopsy sampling ($P = .01$). Cholangitis was significantly more common in patients with bacteremia than in those patients with a negative blood culture ($P = .03$).

Cholecystitis

Post-ERCP cholecystitis is an uncommon adverse event but should be recognized early and not be mistaken for acute cholangitis. Patients may present with fever, abdominal pain, leukocytosis, and a positive Murphy's sign. Diagnosis should be confirmed by imaging findings. Pathogenesis is believed to be related to gallbladder contamination by nonsterile contrast material in the context of gallbladder dyskinesia or outflow (cystic duct) obstruction. In the study by Freeman et al,[7] newly diagnosed cholecystitis requiring emergency cholecystectomy occurred in 11 patients (0.5%), up to 16 days after ERCP. Gallbladder stones were present in 10 of 11 patients. Otherwise, no predictors of cholecystitis were identified. Therefore, it is believed that the presence of cholelithiasis increases the risk of post-ERCP cholecystitis.

Acute cholecystitis following biliary FCSEMS placement occurs in 1.9% to 12% of cases and is believed to result from cystic duct obstruction.[102] Tumor involvement of the cystic duct orifice appears to be a major risk factor for acute cholecystitis in this setting. Theoretically, the open interstices of uncovered stents should eliminate the possibility of cystic duct obstruction and resultant cholecystitis. However, 2 meta-analyses reported a similar incidence of cholecystitis between covered and uncovered SEMSs.[103,104]

The role of prophylactic periprocedural intravenous antibiotics to prevent cholecystitis has not been studied. Treatment of post-ERCP cholecystitis traditionally includes surgery or percutaneous cholecystostomy. However, transpapillary and EUS-guided gallbladder drainage may be considered, especially in patients who are not surgical candidates (eg, inoperable periampullary carcinoma).[105,106] Successful management of acute cholecystitis after covered SEMS placement with stent removal and replacement with either uncovered stents or plastic stents has been reported.[102]

Duodenoscope-related transmission of infection

Duodenoscope-transmitted infection was first described nearly 30 years ago.[107] The elevator mechanism intrinsic to these devices is difficult to clean manually and makes duodenoscope reprocessing challenging.[108] Transmission of multidrug-resistant organisms, including carbapenem-resistant Enterobacteriaceae, has been reported recently, which is not attributable to recognized breaches of standard reprocessing protocol.[109-111] There is some evidence that bacterial contamination may occur in difficult to clean or even sealed portions of the duodenoscope.[111] At present, patient-specific and procedure-specific risk factors associated with carbapenem-resistant Enterobacteriaceae transmission remain unclear.

With the recognition of this rare but serious adverse event, renewed emphasis has been placed on diligent mechanical cleaning of the duodenoscope (including the introduction of a new cleaning brush) as well as strict adherence to the manufacturer's standard protocol for high-level disinfection (HLD).[108] In addition, 4 methods of enhanced reprocessing of duodenoscopes have been proposed: microbiological culturing, repeated HLD, gas sterilization by using ethylene oxide, or the use of a liquid chemical sterilant processing system such as peracetic acid.[108]

Each of the aforementioned strategies is associated with drawbacks and limitations, and the optimal technique for duodenoscope reprocessing remains to be determined. One study performed at the site of a duodenoscope-associated carbapenem-resistant Enterobacteriaceae outbreak identified a nearly 2% occurrence of bacterial contamination when routine culturing of devices was performed after standard processing with an HLD protocol.[112] Using a culture and quarantine protocol, by which reprocessed duodenoscopes were not used for approximately 48 hours until culture results returned negative, no further infections occurred in 1625 subsequent ERCP procedures. However, several carbapenem-resistant Enterobacteriaceae outbreak sites have reported negative cultures from implicated duodenoscopes, raising concerns that culturing methods still may fail to identify contaminated instruments. The use of sterilization with ethylene oxide has been hindered by its flammability, toxicity, limited availability, and potential for instrument damage. Pending long-term solutions to this problem that may include duodenoscope redesign and new methods for duodenoscope sterilization, further research to improve current HLD reprocessing is needed to minimize the risk of instrument contamination.

PERFORATION

Perforation during ERCP transpires by several mechanisms: (1) luminal perforation by the endoscope, typically resulting in intraperitoneal perforation; (2) extension of a sphincterotomy incision beyond the intramural segment of the bile duct or pancreatic duct with retroperitoneal leakage; and (3) extramural passage of guidewires or migration of stents. The incidence of duodenal perforations during ERCP is approximately 0.08% to 0.6%.[10,66,113] Perforations must be promptly diagnosed and treated, because delayed therapy may result in sepsis and multiple organ failure, which are associated with an 8% to 23% mortality rate.[114] This section will focus on duodenal and pancreaticobiliary perforations as a result of ERCP. Perforations of the esophagus, stomach, and afferent limb in the setting of surgical upper GI anatomy have been reported with ERCP but are not covered here.[66,115]

Risk factors for perforation

Patient-related and procedure-related risk factors for perforation during ERCP have been described. Patient-related factors include suspected SOD, female sex, older patient age, and surgical or altered anatomy (ie, situs inversus or Billroth II gastrectomy).[116-123] Procedure-related factors include difficult cannulation, intramural injection of contrast material, longer duration of procedure, sphincterotomy and precut papillotomy, biliary stricture dilation, procedure performed by lesser experienced operators, and EPLBD.[67,115-123]

Although endoscopic sphincterotomy with EPLBD and complete endoscopic sphincterotomy alone are risk factors for ERCP-related perforation, there is a lower rate of perforation with the former approach.[22,124,125]

Classification of ERCP-related perforations

ERCP-related duodenal perforations are commonly classified according to the location or mechanism of injury

for the purposes of dictating management. Stapfer et al[116] classified perforations into 4 types in decreasing order of severity with the goal of correlating the mechanism of injury and the anatomic location of perforation as predictors of outcomes and the need for surgery. Type I perforations are perforations of the duodenal wall caused by the duodenoscope. Type II perforations are periampullary perforations of the medial wall of the duodenum that typically result from biliary or pancreatic sphincterotomy or precut papillotomy and are variable in their severity. Type III perforations are bile duct or pancreatic duct injuries caused by instrumentation (guidewires), stone extraction and/or stenting. Type IV perforations are diminutive retroperitoneal perforations of no clinical significance that result from excessive insufflation during endoscopy together with sphincter manipulation.

Clinical and imaging features

Symptoms and signs suggestive of duodenal perforation are severe epigastric and back pain, epigastric tenderness progressing to generalized abdominal wall rigidity, subcutaneous emphysema, fever and tachycardia.[120,121,126] Signs of peritonitis often develop after 4 to 6 hours when duodenal contents extravasate into the peritoneal cavity.[122,127,128] The presence of a systemic inflammatory response is often present 12 hours or more following endoscopy.

If a perforation is suspected during or following sphincterotomy, careful injection of a small amount of contrast material under fluoroscopy while the catheter is pulled through the papilla over a guidewire can diagnose or exclude extravasation and allow proactive therapy.

In the absence of contrast material extravasation on fluoroscopy, differentiating ERCP perforation from post-ERCP pancreatitis can be challenging and can cause a delay in diagnosis that has implications on patient outcome. Therefore, there should be a low threshold to perform an abdominal CT scan with oral contrast material because this is the most sensitive and specific modality to assess for the presence of a perforation.[120,121,129] Intraperitoneal gas likely represents an uncontained leak, whereas isolated retroperitoneal gas is suggestive of a periampullary site perforation.[120,130] It is important to note that the amount of gas on imaging correlates with the degree of insufflation during the procedure as opposed to the size of the perforation and is not related to patient outcome.[119-121]

OVERVIEW OF MANAGEMENT CONCEPTS

If duodenal perforation is suspected, fasting, intravenous fluids, and intravenous antibiotics should be commenced while the diagnosis is being confirmed. After initial resuscitation and establishment of diagnosis, the first step in management is to determine whether the patient should be managed medically or surgically. This is determined by the patient's condition (presence of peritoneal signs, systemic inflammatory response), the mechanism of injury, anatomical location, and degree of leakage.[116,118,121,131] Despite high-quality imaging, it may be impossible to precisely define the location of perforation.[122,126]

Medical treatment involves hospitalization, frequent physical examinations, laboratory tests, and possibly serial imaging. If the patient's clinical status improves, an oral contrast study to document the absence of ongoing leakage before commencement of diet is advisable.[129] The principles of surgical management for ERCP-related perforations are 2-fold: control of sepsis by drainage of retroperitoneal and intraperitoneal collections and repair of the defect with or without diversion.[132]

An algorithm for management has been proposed.[129] In summary, if peritoneal signs are present or there is an ongoing leak on imaging, a surgical approach usually is required. If the perforation is identified at the time of the ERCP, initial endoscopic management may be appropriate. Use of CO_2 insufflation during endoscopic management minimizes the risk of tension pneumothorax and pneumoperitoneum.[133] In the absence of peritoneal signs, systemic inflammatory response and active leakage by CT, nonsurgical therapy successfully seals the perforation in 50% to 90% of cases.[120-122,126,134] Medical management may be suitable in patients with delayed detection of perforation (>6 hours post ERCP) if peritoneal signs and systemic inflammatory response are absent.[129,131] Surgical management generally should be undertaken if these criteria are present; however, patient comorbidities can impact the appropriateness of surgical intervention.

Management based on type of perforation

Duodenal wall perforation. Duodenal wall perforations traditionally have been managed with immediate surgical repair. Because iatrogenic perforation has a lower risk of bacterial contamination with patients in the fasting state, patients potentially can be treated endoscopically.[129] Successful intraprocedural closure of duodenal perforations has been reported with the use of endoclips, the over-the-scope clip, and endoscopic suturing devices.[131,135,136] Closure of large, luminal defects may be difficult with the earlier-mentioned techniques, but the combination of endoclips and a detachable plastic snare (PolyLoop; Olympus Inc, Center Valley, Pa) has been successful in some cases.[137]

Periampullary perforations. Sphincterotomy accounts for the majority of recognized ERCP-related perforations.[114] The incidence can be minimized by limiting the length of cutting wire in contact with the tissue and performing stepwise cutting. The optimal management of perforations related to sphincterotomy, precut papillotomy, or EPLBD is debated. However, if a periampullary perforation is recognized during the procedure, immediate

endoscopic therapy should be attempted if feasible.[129] The deployment of an FCSEMS to seal the perforation and divert biliary contents is a simple and effective first-line treatment.[138,139] The optimal duration of stent dwell is unknown, but the stent can likely be removed safely after 2 weeks. For large perforations, a nasoduodenal decompression tube may be placed. Alternatively, a nasobiliary tube may be placed to decompress and divert bile directly from the biliary tree.[6] Additionally, endoclips have been successfully used to close these perforations.[131]

Instrument-related perforations. To reduce the risk of guidewire perforations, it is important to monitor the wire frequently and advance the wire only under fluoroscopic guidance. These perforations tend to be small, contained, and likely to heal spontaneously, and hence are almost always managed without surgery. Additionally, it is often challenging to identify the site of perforation during surgical exploration.[122,126] Placement of biliary or pancreatic stents allows appropriate diversion of fluid away from the area of perforation. Asymptomatic patients with retroperitoneal free gas alone detected intraprocedural or afterward should be managed with observation alone.

Stent-induced perforation

Luminal perforation has been reported following migration of plastic and metal stents,[140] and no particular stent is considered higher risk than another. The treatment for stent-induced perforation is endoscopic removal and endoscopic closure of the perforation if the patient does not have clinical features of peritonitis. Surgical management is appropriate for patients with peritonitis or a retroperitoneal fluid collection.[140]

CARDIOPULMONARY ADVERSE EVENTS

Depending on the definitions used, cardiopulmonary adverse events account for 4% to 16% of ERCP-related adverse events and often are related to procedural sedation.[141] These adverse events include hypoxia, hypotension, cardiac dysrhythmia, and aspiration. Although there have been efforts to standardize reporting of cardiopulmonary adverse events with endoscopy, few studies use these definitions.[65] Transient episodes of hypoxia or hypotension may not be reported because they are not considered clinically significant. When transient episodes of hypoxia and hypotension are excluded, the rates of clinically significant cardiopulmonary adverse events with ERCP range from 0.07% to 2.4%.[117,142-144] Large, retrospective studies report cardiopulmonary adverse events in 2.1% to 5.3% of patients undergoing ERCP, which is higher than those reported with colonoscopy (1.1%) and upper endoscopy (0.6%).[145,146] The majority of cardiopulmonary adverse events are mild or moderate, with hypotension and hypoxia being the most common.[145] A systematic survey reported a 0.07% mortality rate due to cardiopulmonary adverse events.[2]

A Cochrane review of 4 randomized trials identified no differences in mortality or serious cardiopulmonary adverse events between those who were sedated for ERCP with propofol versus traditional medications for moderate sedation.[147] A meta-analysis of propofol versus moderate sedation for all advanced endoscopic procedures found that propofol was associated with shorter recovery times, better sedation, and higher rates of amnesia without higher rates of cardiopulmonary adverse events.[47] Additionally, ERCP can be performed safely without requiring universal intubation in patients receiving propofol-based anesthesia.[148,149] In a single-institution randomized study, ERCP with capnography monitoring was associated with fewer episodes of hypoxemia and apnea compared with standard monitoring.[150] The role of sedation and anesthesia in endoscopy is reviewed in another ASGE document.[151]

Unlike other upper GI endoscopic procedures, ERCP is traditionally performed in the prone or semiprone position. This position is thought to be associated with a lower risk of aspiration. One small study suggested that patients in the prone position had a lower risk of cardiopulmonary adverse events compared with those who were supine (41% vs 6%; $P = .039$).[152] Two subsequent larger studies demonstrated no differences in rates of hypoxia, hypotension, or dysrhythmia, based on patient position.[153,154]

Air embolism

Air embolism is a rare but potentially devastating adverse event that occurs as a result of direct communication with the vasculature and an external pressure gradient (ie, from the GI tract or the bile duct) allowing the passage of air into the circulation. Mechanisms associated with air embolism include trauma or inflammation of the bile ducts from contrast administration, insufflation, or from the endoscope or ERCP accessories. Air embolism has been associated with direct cholangioscopy.[155,156] Venous air embolism is readily diagnosed with air in the portal vein and can be managed conservatively with IV antibiotics and decompression via nasogastric tube. The presence of portal vein gas also can be noted with perforation and intestinal ischemia and should therefore be evaluated for such in the correct clinical context. Systemic air embolism, including intracardiac and intracerebral air embolism, is highly lethal. Systemic air embolism should be considered if a patient suddenly develops hypotension or hypoxia when being moved from the prone to supine position or if the patient develops new neurologic symptoms after the procedure. If intracardiac or intracerebral air embolism is suspected, the patient should be endotracheally intubated, ventilated with 100% oxygen, and positioned in the Trendelenburg and left lateral decubitus position to minimize the amount of air traveling to the brain and encourage egress of air from the right ventricular outflow

tract.[157] CT of the chest and head, and a transthoracic echocardiogram should be performed to assess for air embolism. The routine use of CO_2 insufflation during ERCP or the use of water instillation to distend the biliary tree during cholangioscopy may reduce the risk of this life-threatening adverse event.

MISCELLANEOUS ADVERSE EVENTS

A wide variety of additional adverse events have been reported with ERCP. These include ileus, pneumothorax and/or pneumoperitoneum, hepatic abscess formation, pseudocyst infection, and biliary or pancreatic duct fistulae. Passage of the duodenoscope through the greater curvature of the stomach can rarely result in splenic injury due to traction forces, which may require surgical management.[141,158]

ERCP accessory–related adverse events

Subcapsular hepatic hematoma may result from guidewire perforation and laceration of small hepatic vessels and often is managed conservatively with intravenous fluids and antibiotics, because these individuals are at risk for infection from an instrumented biliary tree.[159]

One of the most discouraging technical adverse events during ERCP is impacting a retrieval basket around a large bile duct stone. Fortunately, endoscopic balloon sphincteroplasty as an adjunct to sphincterotomy facilitates extraction of large choledocholithiasis and likely reduces the risk of basket impaction.[21,22] If a basket is impacted around a large biliary stone, the basket catheter has to be cut and the duodenoscope removed. A salvage lithotripter may be attached to the internal wires of the device to fragment the stone for device extraction. New baskets have safety mechanisms that allow the basket to break at their tips in order to facilitate device removal from the bile duct if a stone cannot be crushed. A variety of novel endoscopic salvage techniques have been described, including the use of balloon catheters, rat-tooth forceps, cholangioscopy with electrohydraulic or laser lithotripsy, and use of additional baskets.[141] Extracorporeal shock wave lithotripsy has been described to fragment stones with impacted baskets.[160]

Numerous stent-related adverse events have been described, including stent occlusion, bowel wall perforation, and injury to the biliary or pancreatic duct. Unintended migration of plastic biliary or pancreatic stents has been reported in 5% to 6% of patients.[161] Pancreatic duct stenting has been associated with the development of ductal irregularity, side branch dilation, and stricture formation, the appearance of which can mimic changes seen with chronic pancreatitis.[7] Modifications in stent design without an internal flange may reduce the risk of these ductal changes. Internally migrated biliary or pancreatic stents should be removed, because these can result in jaundice, cholangitis, pancreatitis, or perforation. Various techniques for removal of a proximally migrated stent have been described, including the use of stent retrieval devices, forceps, snares, or retrieval balloons.[162,163] Rarely, patients may require surgery to remove these migrated stents.

Adverse reaction to contrast material

Although systemic absorption of contrast material has been well-documented, adverse reactions to contrast material have rarely been described with ERCP.[164,165] Reaction to contrast material is idiosyncratic and can range from a rash to anaphylaxis. A prospective study of 601 patients undergoing ERCP, including a subset of patients with a history of intravenous contrast material or shellfish allergy, identified no adverse events with the use of full-strength high osmolality contrast material.[166] For individuals with a documented IV contrast allergy, some centers use non-iodinated contrast materials, whereas others premedicate with oral prednisone and diphenhydramine before the procedure, although there is lack of evidence for any benefit with premedication.[141,167]

RECOMMENDATIONS

1. We recommend that physicians who perform ERCP be facile with procedural techniques that reduce the risk of pancreatitis (ie, wire-guided cannulation, prophylactic pancreatic duct stenting). ⊕⊕⊕⊕
2. We recommend early precut sphincterotomy for difficult biliary cannulation when expertise is available. ⊕⊕⊕◯
3. We recommend pancreatic duct stenting to reduce the incidence and severity of post-ERCP pancreatitis (PEP) in high-risk individuals. ⊕⊕⊕⊕
4. We recommend administration of rectal nonsteroidal anti-inflammatory drugs (NSAIDS) to reduce the incidence and severity of PEP in high-risk individuals without contraindication. ⊕⊕⊕◯
5. We suggest that rectal indomethacin may reduce the risk and severity of post-ERCP pancreatitis in average-risk individuals. ⊕⊕◯◯
6. We suggest that there is insufficient evidence that a combination of rectal NSAIDs and pancreatic duct stenting is superior to either technique alone for prevention of post-ERCP pancreatitis in high-risk individuals. ⊕⊕◯◯
7. We suggest periprocedural intravenous hydration with lactated ringers when feasible to decrease the risk of post-ERCP pancreatitis. ⊕◯◯◯
8. We recommend against the routine use of endoscopic papillary large balloon dilation (EPLBD) of an intact sphincter rather than endoscopic sphincterotomy with or without adjunct balloon sphincteroplasty to facilitate biliary stone extraction in

patients without coagulopathy because of the increased risk of pancreatitis. If EPLBD alone is used, dilation more than 1 minute is recommended. ⊕⊕⊕○

9. We recommend that sphincterotomy should be selectively performed in patients considered high-risk for bleeding. Routine sphincterotomy should not be offered in high-risk individuals for bleeding when not absolutely indicated. ⊕⊕⊕○
10. We recommend the use of a microprocessor-controlled generator with mixed current when sphincterotomy is being performed to reduce the risk of post-sphincterotomy bleeding. ⊕⊕⊕○
11. We recommend that antibiotic prophylaxis be administered before ERCP in patients who have had liver transplantation or when there is a possibility of incomplete biliary drainage. Antibiotics that cover biliary flora such as enteric gram-negative organisms and enterococci should be used and continued after the procedure if biliary drainage is incomplete. ⊕⊕⊕○
12. We recommend that facilities ensure strict compliance with current manufacturer protocols and U.S. Food and Drug Administration recommendations for duodenoscope reprocessing to limit duodenoscope-related transmission of infections. ⊕⊕⊕⊕
13. We suggest that patients with suspected periampullary or instrument-related perforations from ERCP without evidence of peritonitis or systemic inflammatory response syndrome (SIRS) may be managed non-operatively. ⊕⊕○○
14. We suggest that premedication is not necessary to prevent contrast media allergy during ERCP in patients with a prior history of food or intravenous contrast allergies. ⊕⊕○○

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; EPLBD, endoscopic papillary large-balloon dilation; FCSEMS, fully covered self-expandable metal stent; HLD, high-level disinfection; IV, intravenous; LR, lactated Ringer's; NSAID, nonsteroidal anti-inflammatory drug; PEP, Post-ERCP pancreatitis; SEM, self-expandable metal; SOD, sphincter of Oddi dysfunction.

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