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Complications of Endoscopic and Radiologic Investigation of Biliary Tract Disorders

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Abstract The investigation and treatment of disorders of the human biliary tree depend considerably on invasive endoscopic and radiologic procedures. These are associated with a significant risk of complications, some of which can be fatal. This review looks at these complications through the lens of 40 years of publications in the medical literature, and identifies the strengths and weaknesses of their current classification, diagnosis, and treatment.

Keywords Complications · Adverse events · Endoscopy · Endoscopic retrograde cholangiopancreatography · Percutaneous transhepatic cholangiography · Percutaneous transhepatic biliary drain · Cholangiography · Perforation · Sphincterotomy · Precut · Bleeding · Hemostasis · Pancreatitis · Cholangitis · Cholecystitis · Primary sclerosing cholangitis · Sedation · Contrast allergy · Anaphylaxis · Hemobilia · Bile leak · Sepsis

Introduction

Complications are undesired and adverse outcomes of medical interventions. All procedures carry some risk, and complications are an unavoidable part of modern medical practice. However, these risks can be minimized by a better understanding of their causation and implementing strategies to avoid them, from improved training of physicians in complex techniques to modifications of techniques, equipment, or both [1•].

Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) and percutaneous transhepatic biliary drain (PTBD) placement are complex interventions used to achieve diagnostic and therapeutic access to the biliary tree. Both endoscopic and percutaneous approaches carry risk of significant complications. Unfortunately, study of this important problem is hampered by lack of uniform definitions and terminology [2, 3•]. Several quite basic systems are used for classification of ERCP complications, but none exist for radiologic procedures [4••]. Added to this difficulty are the limitations of published reports of complications, which are often anecdotal or retrospective small case series. This review looks at the common—and some uncommon—complications of ERCP and PTC/PTBD, and offers a perspective on the current body of literature regarding them.

Complications of ERCP

ERCP has become the preferred method for accessing the biliary tree to diagnose and treat a variety of biliary diseases. It is one of the most invasive procedures performed by endoscopists, and as such carries the potential for significant complications. Given the risk of serious complications, including death in 0.4% of patients, the first important clinical decision is whether the indication for ERCP is strong enough to warrant the potential risks. For low suspicion cases, alternative imaging with endoscopic ultrasound (EUS), magnetic resonance cholangiopancreatography (MRCP), or CT scan should be considered. The second consideration is whether the performing physician has adequate case volume

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and expertise to perform the potentially required therapy; low case volume has been found to be an independent predictor of ERCP complications in most multivariate analyses [5].

Several multicenter studies involving large numbers of patients in community and tertiary environments have identified the risk factors associated with ERCP complications (Tables 1 and 2) [6–9, 10•, 11]. Independent risk factors for complications recognized in most studies include operator-related factors (e.g., low ERCP case volume), method-related factors (e.g., difficulty of cannulation, biliary sphincterotomy, use of precut technique), and patient-related factors (e.g., sphincter of Oddi dysfunction [SOD], periampullary diverticulum, liver cirrhosis).

Several additional risk factors have been suggested in other reports, including older age, comorbid diseases, small bile duct diameter, and Billroth II gastrectomy. Although these conditions have not been proven to increase the *overall* risk of complications of ERCP in multivariate analyses, some can increase the risk of *selective* complications in some subgroups, such as intestinal perforation in patients with a Billroth II gastrectomy or cardiopulmonary complications in elderly patients with serious comorbidities. Severe systemic disease was an independent predictor of severe complications of ERCP in a large retrospective study [12]. On the other hand, some factors may be protective: for example, the incidence of post-ERCP pancreatitis is lower in the elderly [6, 13]. Hospital volume also appears to correlate with ERCP outcomes. A database study involving 2,629 hospitals (and 199,625 ERCPs performed on inpatients) found a significantly lower procedural failure rate, and shorter length of stay, in hospitals where more than 200 ERCPs are performed per year [14].

The most frequent specific complications of ERCP are pancreatitis, bleeding, perforation, and acute cholangitis. Contrast-related reactions, which may occur with both ERCP and PTC/PTBD, are discussed at the end of this article.

Post-ERCP Pancreatitis

Acute pancreatitis is the most common complication of ERCP, occurring in 5–7% of all cases. However, the risk can be as

Table 1 Overall complications of ERCP: risk factors identified by multivariate analysis in large (>1,000 patients) prospective studies

Author	Number	Overall complication rate	Independent risk factors
Freeman et al. [6], 1996	2,347 patients	9.8%	-Difficulty of cannulation -Precut sphincterotomy -Percutaneous procedure -Sphincter of Oddi dysfunction -Cirrhosis
Loperfido et al. [7], 1998	2,769 patients	4.0%	-Small center -Precut sphincterotomy
Masci et al. [8], 2001	2,444 patients	4.9%	-Age <60 years -Precut sphincterotomy -Failed clearance of biliary stones
Christensen et al. [9], 2004	1,177 patients	15.9%	-Dilated bile duct -Placement of stent ->40 mg of hyoscine-*N*-butyl bromide given
Williams et al. [10•], 2007	4,561 patients	5%	-Difficult cannulation -Precut sphincterotomy -Sphincter of Oddi dysfunction
Wang et al. [11], 2009	2,691 patients	7.9%	-Female gender -Periampullary diverticulum -Difficult cannulation -Pancreatic cannulation -Precut sphincterotomy

ERCP endoscopic retrograde cholangiopancreatography

Table 2 ERCP-induced pancreatitis: risk factors identified by multivariate analysis in selected large prospective studies

Study	Number	Independent risk factor	Odds ratio
Loperfido et al. [7], 1998	2,769 patients	-Small bile duct (≤10 mm)	3.79
		-Younger age (≤70 years)	2.87
		-Pancreatic duct opacification	3.21
Freeman et al. [16], 2001	1,963 patients	-History of post-ERCP pancreatitis	5.35
		-Biliary sphincter balloon dilation	4.51
		-Moderate-to-difficult cannulation	3.41
		-Pancreatic sphincterotomy	3.07
		-≥1 pancreatic contrast injection	2.72
		-Suspected SOD	2.60
		-Female gender	2.51
		- Normal serum bilirubin	1.89
		-Absence of chronic pancreatitis	1.87
Masci et al. [8], 2001	2,444 patients	-Younger age (≤60 years)	2.11
		-Use of precut sphincterotomy	2.80
		-Failure to clear biliary stones	3.35

ERCP endoscopic retrograde cholangiopancreatography; *SOD* sphincter of Oddi dysfunction

high as 25–40% in certain subgroups of patients, such as young women with suspected SOD. Fortunately, most cases of post-ERCP pancreatitis (about 80%) are "mild" (requiring <4 days' hospitalization); however, "moderately severe" (requiring 4–10 days' hospitalization) and "severe" acute pancreatitis (requiring >10 days' hospitalization), which together account for about 20% of cases, do occur [15].

The important risk factors for post-procedure pancreatitis can be categorized as patient-specific or technique-related. In a commonly quoted multivariate analysis [16], patient-related risks included a prior history of ERCP-induced pancreatitis, the procedural indication of suspected SOD, female gender, a normal serum bilirubin, and the absence of chronic pancreatitis. Procedural risks include difficult cannulation (presumably related to ampullary trauma from multiple cannulation attempts), increased number of injections into the pancreas, biliary sphincter balloon dilation, and pancreatic sphincterotomy. Multiple other risk factors are significant in univariate analysis, but may simply reflect confounding cofactors [17]. The use of pre-cut techniques and small bile duct diameter are two examples of such risk factors noted in several studies. When sphincterotomy is performed, study results are controversial with regard to whether using a pure cutting current lowers the risk of pancreatitis [18]. Use of a soft-tipped wire for cannulation may also lower the risk. The osmolality of the contrast material used appears to have no effect.

From the discussion above, it follows that the best way to prevent post-ERCP pancreatitis is to avoid unnecessary ERCPs, especially in high-risk patients. ERCP endoscopists should be highly skilled; less experienced providers should consider referring complex cases to high-volume centers. Most studies show no benefit from using low- rather than high-osmolality radiologic contrast media during ERCP as a way to reduce the incidence of post-ERCP pancreatitis [19]. Multiple pharmacologic agents have been studied in an attempt to reduce this complication. The severity of acute pancreatitis appears to be determined very early in the course of the illness. Therefore, medical pretreatment aimed at prevention or modification of severity is very attractive. Unfortunately, most of the drugs studied in clinical trials have failed to prevent pancreatitis, or the results have been contradictory. Allopurinol, corticosteroids, heparin derivatives, interleukin-10, gabexate mesylate, nitrates, and octreotide are examples of the medications studied [17].

Temporary pancreatic duct stenting was initially shown in a randomized study to reduce post-procedure pancreatitis from 26% to 7% in patients with SOD [20]. This rather dramatic result has led to the generalization of this technique to other high-risk patients. A meta-analysis showed that high-risk patients without pancreatic stent placement had threefold higher odds of developing pancreatitis when compared with those with pancreatic stents (15.5% vs 5.8%) [21]. Many experts now encourage prophylactic pancreatic stenting in the following settings and groups of patients: difficult cannulation, pancreatic or precut sphincterotomy, pancreatic endotherapy, suspected SOD, balloon dilation of an intact sphincter, and endoscopic ampullectomy. Problems with temporary stenting are technical difficulty (including pancreatic trauma) related to placing the stent, the need to remove some of these stents endoscopically, and the risk that the stent itself can induce pancreatic duct damage. The use of a single pigtail, 3 French (Fr) gauge plastic stent without internal flanges appears to minimize these problems. However, if flanges are not used, the stent

has to be long enough (at least 6 cm) not to immediately migrate from the pancreatic duct. Rather than using a relatively stiff 0.018-inch guide wire, these 3Fr stents can often be placed over a softer, 0.021-inch hydrophilic wire.

Bleeding

Bleeding during or after ERCP is usually related to sphincterotomy. The incidence of post-sphincterotomy hemorrhage depends upon its definition. Most experts exclude endoscopic evidence of minor bleeding, because most of these episodes are temporary and stop spontaneously. When using clinical criteria such as hematemesis, melena, a greater than 2 g/dL drop in hemoglobin level, or transfusion requirement, the overall incidence of bleeding is around 1% to 2%, with larger studies showing mortality rates of 0.1–0.3% [6, 7, 9, 10•, 11]. The severity of post-sphincterotomy bleeding has been classified into four categories: (1) mild (clinical evidence for bleeding but drop in hemoglobin is <3 g/dL; no blood transfusions), (2) moderate (endoscopic treatment required; transfusion requirement ≤4 units), (3) severe (transfusion of ≥5 units and/or surgery or angiographic treatment), and (4) fatal [4, 15]. In 50–60% of patients, bleeding occurs during or immediately after sphincterotomy [6, 22, 23]. Other patients present with melena after a delay that may range from 24 h to several days. Patients with suspected post-sphincterotomy bleeding should undergo endoscopy using a side-viewing endoscope to assess and treat the bleeding site at the papilla.

Several risks for post-sphincterotomy hemorrhage have been identified, but the significance of some of them remains controversial. Because bleeding tends to appear at the top end of a cut, the length of the incision has been suggested as a risk factor. However, this was not confirmed in the large prospective study by Freeman et al. [6]. The vascular anatomy of the ampulla may also constitute a risk; autopsy data suggest that 4% of the population have an aberrant branch of the gastroduodenal artery in the papillary area. Some authors have reported an increased bleeding risk with needle-knife sphincterotomy [8], although this has been disputed by others [24]. Ampullary stone impaction and periampullary diverticula have also been reported as risk factors. In the study by Freeman et al. [6], five risk factors were significant in a multivariant analysis: coagulopathy prior to sphincterotomy, cholangitis, anticoagulant therapy within 3 days following sphincterotomy, the endoscopist's low case volume, and endoscopic evidence of bleeding during the procedure. Because of the importance of coagulopathy, most endoscopists performing endoscopic sphincterotomy require a platelet count greater than 50,000/mm^3 and an international normalized ratio (INR) of less than 1.5–2 for prothrombin time. The optimal timing of re-anticoagulation after an uneventful sphincterotomy has not been determined in controlled trials.

Many types of endoscopic treatment may be used for post-sphincterotomy bleeding. Some endoscopists who use dilute epinephrine irrigation of the bleeding papilla report cessation of bleeding in up to 50% of patients, although this may simply reflect spontaneous resolution. Injection therapy using a 1:10,000 solution of epinephrine [22] is also popular. Needles with a metal shaft may be easier to use through a side-viewing scope, because kinking over the elevator is minimized. Both saline and contrast media have also been used successfully to create local tamponade. The application of electrocautery is most effective if a specific bleeding point can be identified. Whether combination therapy (epinephrine plus cautery) for post-sphincterotomy is more effective than injection therapy alone, as is the case in peptic ulcer bleeding, has not been studied in large-scale trials.

When large volumes of fluid are being injected or thermal therapy is used, it is advisable to avoid the vicinity of the pancreatic duct orifice or place a pancreatic stent if feasible. Endoscopic clip placement can be considered as another alternative, but the currently available metal clips are often difficult to deploy through a side-viewing endoscope, because of the angulation of the elevator. Additionally, inadvertent clipping of the pancreatic orifice can cause severe pancreatitis and must be avoided. Local balloon tamponade of the bleeding site can often be obtained by using a standard extraction balloon. Angiographic remobilization and surgery for persistent post-sphincterotomy bleeding are rarely required, and should be reserved for patients with refractory or recurrent hemorrhage that has failed endoscopic intervention(s).

Perforation

Perforation represents an uncommon complication of ERCP, occurring in 0.3–0.6% of cases [10•, 11, 25, 26]. Three types of perforations can be distinguished: (1) retroperitoneal duodenal perforations, (2) perforation of the bile (or pancreatic) duct, and (3) free bowel-wall perforations. Retroperitoneal perforations are the most common, and usually occur as the result of a sphincterotomy that extends beyond the intramural portion of the bile duct. They are not usually apparent endoscopically, but are recognized by extravasations of contrast material or air on fluoroscopy or plain radiography films. Precut access techniques are highly operator-dependent and may also increase the risk of perforation. It appears that small retroperitoneal perforations often remain asymptomatic, because retroperitoneal air can be found incidentally on routine post-procedure CT scans. One prospective series of patients undergoing sphincterotomy observed retroperitoneal air in 6 of 21 individuals (29%), all of whom remained asymptomatic and had an uneventful post-procedural course [27].

Wire-related perforations of the bile duct have become less common with the use of floppy-tip, hydrophilic wires. Dilation of biliary strictures, and the use of a large extraction balloon in a small-caliber bile duct, are other causes of intraductal perforation. Ductal perforations are often noticed on fluoroscopy during the procedure. If detected, small retroperitoneal and contained ductal perforations can often be treated conservatively with antibiotics and close observation. Free peritoneal perforations, and large and/or symptomatic retroperitoneal perforations, should be jointly managed with an experienced abdominal surgeon. Ten percent to 20% of patients with ERCP-related perforations will require surgery. Anecdotal evidence supports the use of endoscopic clips to close small, sphincterotomy-related perforations [28], but whether this improves the clinical outcome of the patient remains to be demonstrated in systematic studies.

Free bowel wall perforation is thankfully rare, but almost always requires surgical repair [25]. Because of the large mechanical forces that can be generated using it, the duodenoscope used to perform ERCP requires careful handling during insertion. Intubation of the esophagus is essentially "blind," so the potential presence of a Zenker's diverticulum, esophageal stricture, paraesophageal diverticulum, or other anatomic obstacle must be considered, and the endoscope manipulated with care at all times. Gastrointestinal tract–altering surgeries, such as a Billroth II partial gastrectomy, usually do not pose a significant challenge for the experienced endoscopist, but on occasion can lead to "fixed" and acutely angulated bowel loops from adhesions, which increase the risk of perforation if the endoscope is not advanced with great caution [29]. Gastric outlet obstruction, which occurs in many patients with advanced pancreatic cancer, increases the difficulty and risk of duodenal intubation. If in doubt, the endoscopist should consider using a forward-viewing endoscope to better define the local anatomy before attempting to manipulate the side-viewing instrument through difficult areas.

Infection

The reported rate of acute cholangitis and cholecystitis after ERCP varies, but was less than 2% in larger case series [10•, 11, 26]. Risk factors for ERCP-related biliary infections include jaundice, stent placement for malignant strictures, low endoscopist case volume, and the performance of a combined percutaneous/endoscopic procedure (i.e., "rendezvous technique"). The most important risk factor for acute cholangitis after ERCP is inadequate biliary drainage, which was illustrated in a prospective study of 242 patients undergoing sphincterotomy for bile duct stones [30]: cholangitis developed in 75% of patients with retained stones and failed drainage, as compared to only 3% of those with successful drainage. Primary sclerosing cholangitis (PSC) is also a risk factor for acute cholangitis; this is thought to be secondary to poor drainage of injected contrast from a strictured biliary tree. A history of prior episodes of acute cholangitis, and the performance of therapeutic manipulations (e.g., biliary stent placement), further increases the infection risk in PSC patients. Cholecystitis is being reported after less than 0.5% of ERCPs, and should be suspected in patients who develop right upper quadrant tenderness, fever, leukocytosis, gallbladder wall thickening, and/or pericholecystic fluid following an ERCP.

The guidelines for antibiotic prophylaxis related to ERCP have changed recently [31••]. In patients with bile duct obstruction without cholangitis, the American Society for Gastrointestinal Endoscopy (ASGE) guidelines now recommend antibiotic prophylaxis only in cases with incomplete biliary drainage, for example, in patients with failed stone extraction, primary sclerosing cholangitis (PSC) or bifurcation strictures. Conversely, antibiotics are not generally recommended if complete biliary drainage has been achieved. The same ASGE guidelines provide modified recommendations for the prevention of infective endocarditis. Antibiotic prophylaxis is no longer recommended for the sole purpose of preventing infective endocarditis, even if the patient has a preexisting high-risk cardiac lesion (e.g., prosthetic cardiac valve, history of infective endocarditis, valvular abnormalities in cardiac transplant recipients, or certain types of congenital heart disease) unless the patient undergoes emergent ERCP as treatment for acute cholangitis.

A few principles help minimize the risk of post-ERCP infectious complications: (1) the volume of contrast injected into the biliary tree should be the minimum necessary to obtain adequate radiographs; (2) infected bile should be aspirated from an obstructed system prior to contrast injection to avoid a significant rise in intraductal pressure, which encouraged translocation of biliary bacteria into the bloodstream; (3) every effort should be made to achieve prompt endoscopic decompression of an obstructed biliary system, and if bile flow cannot be restored endoscopically, a percutaneous or surgical procedure should be undertaken without delay.

Cardiopulmonary Events

Compared to general endoscopy, ERCP requires higher doses of sedatives over a longer period of time. Patients undergoing ERCP are often elderly, may have multiple comorbidities, and are usually examined in a prone position. The combination of these factors may be responsible for a higher rate of cardiopulmonary complications. Overall, cardiopulmonary complications occur in 1–3% of patients undergoing ERCP, and are the leading cause of death. As a result, close monitoring of cardiac function

and oxygen saturation, regular suctioning of secretions, and an ERCP team well trained in resuscitation, should all be part of the routine for ERCP procedures. "Oversedation" in the setting of acute illness and pre-existing comorbidities contributes to most cardiopulmonary complications from ERCP, many of which respond rapidly to intravenous reversal agents (flumazenil and/or naloxone) and supportive care. Increasingly, ERCP is being performed with the help of anesthesia providers, employing either monitored anesthesia care, typically with propofol (Diprivan; AstraZeneca, Wilmington, DE, USA), or general anesthesia. This results in better-sedated patients and, if general anesthesia is used, airway protection from endotracheal intubation. However, the disadvantage of anesthesia for ERCP is the considerable prolongation of every procedure because of pre- and post-anesthesia issues. Anesthesia for endoscopic sedation is the subject of heated debate in the United States at present, mainly regarding the use of anesthetic agents by nonspecialist providers. Unfortunately, discussion of this issue is beyond the scope of the present review.

Miscellaneous Complications

A large number of uncommon complications have been described in conjunction with ERCP. These include opacification of portal venous, arterial, and lymphatic vessels; air and bile embolism; hepatic and splenic trauma; biloma; intestinal pneumatosis; pneumothorax and pneumomediastinum; intramural hematoma along the upper gastrointestinal tract; Mallory-Weiss tear; parotitis; and several others. Any new or unusual problem occurring around the time of ERCP should prompt a thorough investigation to identify any potential causal link.

Complications of PTC and PTBD

Percutaneous transhepatic cholangiography (PTC) is a diagnostic procedure that involves the use of a sterile, small-gauge needle to puncture peripheral bile ducts under fluoroscopic guidance. Successful biliary access is followed by contrast injection to outline the biliary anatomy and potential pathologic processes. The first PTC is reported to have been performed in Hanoi (now Vietnam) in the 1930s. The success of injecting a bile duct is highly operator-dependent, and increases as the bile ducts dilate, reaching nearly 100% when the dilation is significant. When the intrahepatic bile ducts are not dilated, the success rate drops, often well below 90% [32, 33]. The therapeutic counterpart of PTC, percutaneous transhepatic biliary drainage (PTBD) is a procedure that uses guide wire and catheter manipulations after percutaneous access to a peripheral bile duct to facilitate placement of tubes or stents to accomplish external and/or internal drainage.

PTC has a high sensitivity and specificity for identifying the cause and site of biliary tract obstruction. PTBD then permits a number of therapeutic interventions, including drainage of infected bile in the setting of cholangitis, extraction of biliary tract stones, dilation of benign biliary strictures and placement of a stent (or stents) across a malignant stricture. With ERCP having become the preferred method for direct biliary access, percutaneous approaches are now most commonly used as "rescue techniques," for example, when surgically altered biliary anatomy precludes endoscopic access, if bile duct cannulation fails, or if therapeutic goals cannot be accomplished endoscopically despite access to the bile duct. The patient population undergoing PTC/PTBD is therefore different from the group of patients undergoing ERCP, making it difficult to draw direct comparisons regarding outcomes and complication rates between these two quite different techniques.

Published reports on PTC/PTBD complications are subject to the same limitations outlined for ERCP: there is no standardized definition of what constitutes a PTC/PTBD complication, and no generally accepted classification system. Few high-quality studies have systematically evaluated the complication rate of PTC/PTBD; most of the available reports are outdated because of changes in the equipment used, or the types of patients now undergoing the procedure. The Health and Inventory Information for Quality (HI-IQ) data set [34] was developed by the US Society of Interventional Radiology to provide templates for reporting adverse events, but it does not define all of them. The system has not been used widely, and there is no central organization to provide comparative data (benchmarking) [4]. Recently, the Standards of Practice Committee of the US Society of Interventional Radiology developed quality improvement guidelines for PTC/PTBD. As part of this process, the committee reviewed classification systems, indications, outcomes, and complication rates for these procedures [35••]. Complications of PTC/PTBD are typically classified into "major" and "minor" on the basis of outcome. Major complications result in admission to a hospital, an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death. Minor complications are those that result in no significant adverse sequelae; instead, they may require "nominal therapy" or a short hospital stay for observation.

Complications of PTC/PTBD include sepsis, acute cholangitis, bile leak, hemorrhage, and pneumothorax. Published rates for each of these complications are highly dependent on patient selection; those in the literature are based on cases series comprising several hundred patients, a larger volume than most individual practitioners are likely

to treat in the course of a year or two. An overall PTC complication rate of 2% is commonly quoted [35••]. The reported incidence of major complications associated with PTBD is 4.6–25%; the incidence of procedure-related deaths is cited as 0–5.6% [36, 37]. Several authors have suggested that complications related to internal/external tubes as a result of inadequate bile flow and tube dislodgement (sepsis and hemorrhage) can be minimized by placing a self-retaining tube of at least 10Fr gauge through the ampulla or anastomosis [32, 38, 39].

Patients with coagulopathies, acute cholangitis, biliary stones, malignant obstruction, or benign proximal bile duct obstruction can be expected to have the highest complication rates. In a review of the literature combining the results of six groups of investigators and including a total of 702 patients, Yee and Ho [40] found that the major morbidity and mortality associated with biliary drainage were 8% and 2%, respectively; in 87% of these patients, biliary obstruction was due to malignancy. The authors conclude that a patient's general physical condition is a most important determinant of whether or not complications will occur.

Hemobilia

Hemobilia represents the most common major complication of PTC/PTBD, occurring in 2.6–9.6% of cases [32, 33, 37, 38]. It results from interaction of the needle or catheter with a major vascular structure. In patients who are observed to develop hemobilia during percutaneous procedures, a cholangiogram is performed first to make certain that the side-holes of the biliary drainage catheter are not peripheral to the bile ducts. If bleeding is mild and thought to be venous (i.e., nonpulsatile and darker in color than arterial blood), and the side-holes are found to be outside the bile ducts, repositioning of the biliary drainage catheter so that side-holes are again located within the biliary system may be all that is necessary to control bleeding. Although hemorrhage is the most common cause of serious procedure-related morbidity after PTC/PTBD placement, it is rarely fatal. In one series of 333 procedures, severe hemobilia occurred in 4% of cases [41]. Hepatic arteriography was used to identify the source of bleeding, which included hepatic artery pseudoaneurysm in nine patients, hepatic artery-bile duct fistulae in four, and a hepatic artery-portal vein fistula in one patient. Transcatheter embolization with microcoils, cyanoacrylate, detachable balloons, or gelatin sponge pledgets effectively stopped the bleeding.

Cholangitis

Transient bacteremia is frequently detected with PTC/PTBD, and cholangitis with possible sepsis represents a major complication, occurring in 1–3% of cases [42]. It is recommended that all patients undergoing PTC/PTBD receive antibiotic prophylaxis to minimize septic complications [43, 44]. The duration of antibiotic therapy after the procedures will be determined by the clinical course of individual patients.

Contrast Allergy

Contrast-related reactions may occur with both endoscopic and percutaneous cholangiography, and they can be potentially life-threatening. Mild symptoms include sensation of warmth, metallic taste in mouth, pruritus, nausea, diaphoresis, rhinorrhea, and dizziness. Moderate symptoms include diffuse urticaria or rash, vomiting, headache, facial or laryngeal edema, dyspnea, vasovagal reaction, palpitations, and abdominal cramping. Severe reactions include life-threatening arrhythmias, hypotension, shock, severe bronchospasm, laryngeal edema, pulmonary edema, seizures, syncope, and death.

As part of the pre-procedural assessment before cholangiography, all patients should be asked whether they are allergic to intravenous contrast media used in CT studies, or are allergic to iodine or shellfish. Such patients are at increased risk for adverse reactions from the contrast used in ERCP and PTC/PTBD; most experts recommend that these patients receive nonionic contrast agents as well as appropriate premedication (see below). Recommendations for prophylaxis from the American College of Radiology are for intravenous contrast-related reactions; endoscopists extrapolate them for use in ERCP [19]. However, the actual risk of systemic contrast-related reactions from endoscopic or percutaneous cholangiography is probably much less than with intravenous contrast administration because of limited systemic absorption. A study of 601 patients who did not receive prophylaxis (including 80 patients with a documented history of reactions to intravascular contrast media) failed to show any adverse reactions associated with the administration of contrast media [45]. Nonetheless, severe idiosyncratic anaphylactic reactions to contrast used for ERCP have been described [46, 47]. Most experts recommend premedication with oral steroids starting the day before ERCP or PTC/PTBD, or intravenous steroids if allergy is discovered just before the procedure. Some providers also administer an intravenous antihistamine in combination with the steroids.

Conclusions

Endoscopic and percutaneous cholangiography are valuable and potentially lifesaving procedures for the management of patients with a variety of biliary diseases. However, these interventions also carry a significant potential for compli-

cations. For each patient, the risks and benefits of ERCP and PTC/PTBD should be carefully considered by the provider. In some circumstances, less invasive imaging modalities may be preferred. Physicians practicing ERCP or percutaneous cholangiography should be skilled at performing both diagnostic and therapeutic interventions, and be adept at recognizing and effectively treating complications when they occur. In the era of quality measurement, benchmarking, and performance "dashboards," improved definitions of complications and a standardized reporting system are needed. These will lay the foundation for more meaningful research on this important topic, and more reliable comparisons between different procedures and providers, than are currently available.

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- • Of importance
- •• Of major importance

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