

# Complications Related To Endoscopic Retrograde Cholangiopancreatography: A Comprehensive Clinical Review

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## Abstract

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most commonly performed endoscopic procedures. It provides the treating physician with both diagnostic and therapeutic options. The recent shift towards interventional uses of ERCP is largely due to the emergence of advanced imaging techniques, including magnetic resonance cholangiopancreatography and ultrasonography. With over 500,000 ERCP procedures performed yearly in the United States alone, it is important that all medical and surgical practitioners be well versed in indications, contraindications, potential complications, benefits, and alternatives to ERCP. The authors present an in-depth review of ERCP-related complications (pancreatitis, bleeding, perforation, etc) as well as special topics related to ERCP (perioperative antibiotic use, performance of intraoperative ERCP, performance of ERCP during pregnancy, etc).

## Keywords

Endoscopic retrograde cholangiopancreatography – complications – diagnosis and management – pancreatitis – sphincterotomy – stenting – cholangitis.

## Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is an important endoscopic procedure, with over 500,000 performed yearly in the United States [1-2]. More recently, the focus of ERCP has become more interventional, largely due to greater reliance on advanced imaging (magnetic resonance cholangiopancreatography – MRCP, multi-detector computed tomography – MDCT, endoscopic

ultrasonography – EUS) [1,3-5]. ERCP entails certain risks, which increase with the complexity of the procedure and the severity of patient disease [3,6]. This is a comprehensive review of ERCP-related complications and related topics.

### ERCP: indications and contraindications

#### Indications

ERCP is indicated for the diagnosis and treatment of three main disease categories: (a) biliary tract disorders; (b) pancreatic disorders; and (c) ampullary disorders (Table I) [7-10]. In biliary tract disease, ERCP is helpful in diagnosing and treating choledocholithiasis, benign and malignant biliary strictures, operative and traumatic ductal injuries, and sphincter of Oddi dysfunction [5,7-9]. In pancreatic disease, ERCP is used to treat complications of both acute and chronic pancreatitis (pancreatic duct strictures, pseudocysts, pancreatic duct leaks) [7-8]. In ampullary disease, ERCP can be utilized to treat sphincter of Oddi dysfunction and to remove ampullary adenomas [7-8]. ERCP also allows the endoscopist to obtain tissue and cytology specimens of the biliary tract, the pancreas, and the ampulla [10].

#### Contraindications

Absolute contraindications to ERCP include pharyngeal or esophageal obstruction, active coagulopathy, and anaphylactic reaction to contrast dye [6,11]. Relative contraindications include portal hypertension with esophageal and/or gastric varices, acute pancreatitis (except gallstone pancreatitis), recent myocardial infarction, and severe cardiopulmonary disease [2]. Patients with previous Roux-en-Y anastomosis are unable to undergo traditional ERCP secondary to altered anatomy [12]. Patients with Billroth II surgical reconstruction or pancreaticoduodenectomy are considered a high risk for ERCP due to associated technical procedural challenges [7,13].

#### Alternatives to ERCP

There are several diagnostic/therapeutic alternatives to ERCP, which include MDCT, MRCP, and EUS [4-5,10,14-16]. Biliary anatomy can be accurately visualized using 64-channel MDCT [14]. EUS is a low-risk alternative for visualizing biliary tree in populations with low prevalence of biliary disease [4]. MRCP may help improve resource

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**Table I.** Generally accepted indications for ERCP [7-10, 25].

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<ul style="list-style-type: none"> <li>• Clinical, biochemical, or imaging data suggestive of pancreatic or biliary tract disease</li> <li>• Biliary diagnostics - Jaundice due to suspected benign or malignant biliary obstruction, primary sclerosing cholangitis, recurrent infectious cholangitis, suspected operative or traumatic bile duct injury</li> <li>• Biliary therapeutics - Endoscopic sphincterotomy for choledocholithiasis, intraductal gallstone removal, balloon dilatation of ductal strictures, placement of nasobiliary drains, treatment of sump syndrome, and stent placement across benign or malignant biliary strictures, fistulae, postoperative/traumatic bile leaks, or large common bile duct (CBD) stones</li> <li>• Pancreatic diagnostics - Idiopathic pancreatitis, pancreatic trauma, preoperative evaluation of chronic pancreatitis or pancreatic pseudocyst, clinical situations when signs or symptoms suggest pancreatic malignancy with equivocal or normal findings on noninvasive imaging</li> <li>• Pancreatic therapeutics - Access to pancreatic duct, ductal stenting, and pseudocyst drainage (in appropriately selected cases)</li> <li>• Other diagnostic and therapeutic indications - Suspected sphincter of Oddi dysfunction, papillary stenosis or severe sphincter of Oddi dysfunction, suspected choledochocoele</li> <li>• Advanced applications – Fiberoptic choledochoscopy and endoluminal therapy, tissue sampling from pancreatic or bile ducts, treatment of ampullary carcinoma in poor surgical candidates, and palliative or preoperative stenting of malignant biliary-pancreatic strictures</li> </ul>
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use and identify patients who require therapeutic ERCP [4]. The reported high sensitivity (81-100%), specificity (94%-98%), and diagnostic accuracy (94-97%) of MRCP make this diagnostic option very attractive [15,17].

Percutaneous transhepatic cholangiography (PTC) constitutes the most invasive nonoperative alternative to ERCP [15]. Indications for PTC include failure or contraindication to ERCP in patients who: (a) are not candidates for alternative advanced imaging study; (b) failed advanced diagnostic imaging; and/or (c) require invasive intervention [18]. PTC can be associated with significant complications and provides only limited visualization of the pancreatic duct [15]. From interventional standpoint, PTC offers many of the advantages of ERCP (i.e., ability to place biliary stents, treatment of biliary strictures, and long-term biliary decompression/drainage) [19].

#### **ERCP: the equipment**

ERCP facilitates the acquisition of radiographic images of the biliary-pancreatic tree while providing direct visualization of the duodenal lumen. Typical ERCP system consists of a side-viewing endoscope, light source, and image-processing unit. The ERCP endoscope itself consists of an umbilical cord, control head (manual controls for up/down and left/right, an elevating lever, air/water button, and suction button), a flexible 100-centimeter insertion tube with 8-11 millimeter external diameter, and an adjustable segment at the tip which contains the camera and allows up to 180° maneuverability of the endoscope. The endoscope also has ports for air insufflation, fluid irrigation, and a 2-4 millimeter diameter working channel [20]. The working channel of the endoscope can accommodate biopsy forceps, snares, sclerotherapy needles, heater probes, electrocautery probes, balloon dilation devices, different types of nets, baskets, and stents. Specialized add-on devices allow for endoscopic mucosal resections and choledochoscopy [21]. Static and moving images can be recorded/printed. While ERCP is ideally performed in a dedicated procedure room, portable equipment can be deployed to other settings, including the operating room [12,20].

#### **ERCP: basic procedural considerations**

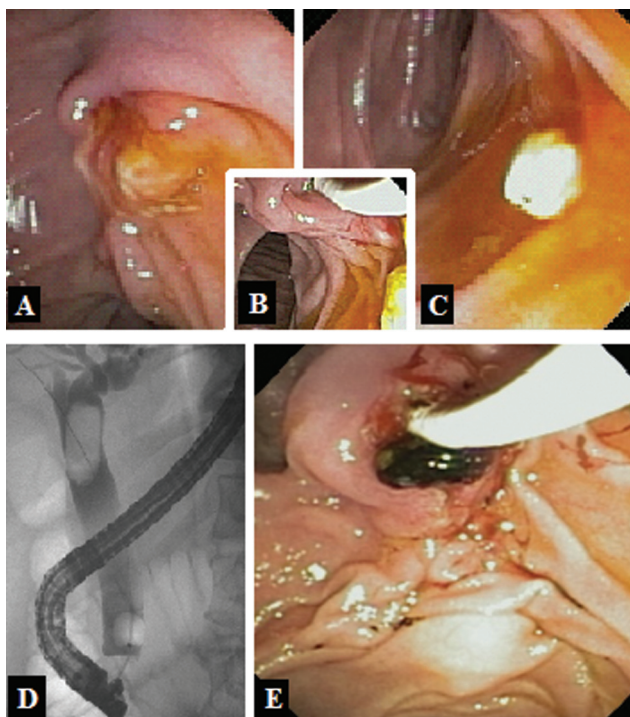
The patient is required to fast for approximately 6-8 hours before the procedure. He is initially placed in left lateral

decubitus position, followed by prone positioning for the procedure. Parenteral conscious sedation (opioid-sedative combination) is administered, in conjunction with a topical anesthetic applied to posterior oropharynx [22]. Arterial oxygen saturation, heart rate, and blood pressure are closely monitored [22].

After achieving adequate sedation, the ERCP endoscope is advanced through a bite-block into the posterior oropharynx. The scope may be introduced either blindly, with manual guidance, or under direct endoscopic vision [22-23]. Worth noting is that blind advancement may result in perforation if the tip of the scope enters a Zenker's diverticulum or pyriform sinus [6]. After entering the upper esophageal lumen, the endoscope is gently advanced while maintaining visualization of the lumen during the descent. The endoscope is then passed through the lower esophageal sphincter, the stomach, and into the duodenal bulb [22-23].

The scope is subsequently passed toward the second portion of the duodenum, which is retroperitoneal and turns sharply in posterior and caudal direction. The endoscope is pulled back so that the gastric loop is straightened and the tip of the scope lies next to the ampulla (i.e., short scope position). A small plastic cannula is passed through the channel of the endoscope and introduced into the ampullary orifice. Glucagon can be intravenously administered to decrease duodenal motility and to help relax the sphincter of Oddi [24]. Contrast material is injected under fluoroscopic guidance to provide visualization of the common bile duct (CBD) and pancreatic duct (PD). Low-pressure injection prevents excessive filling of pancreatic duct branches. The orifice of the CBD is typically found at the 11 o'clock position in the ampulla and continues in cephalad direction. Normal diameter of the CBD is 4-9 mm, providing the patient has not had a prior cholecystectomy or other anatomy-modifying surgical procedure. The PD is located at the 5 o'clock position and continues in horizontal direction, perpendicular to the CBD.

Endoscopic appearance of the papilla is often suggestive of the underlying pathology: (a) "bulging" of the papilla in stone impaction (Fig. 1); (b) exophytic mass in cases of malignancy; (c) purulent drainage in suppurative cholangitis; (d) hemorrhage in hemobilia; and (e) edema, erythema, and



**Fig 1.** Therapeutic applications of ERCP. (A) Impacted gallstone bulging from the papilla; (B) Ductal cannulation and sphincterotomy; (C) Retrieved gallstone in the duodenal lumen. (D) Large gallstone noted in the proximal common bile duct; (E) Following endoscopic sphincterotomy, the stone was retrieved using a balloon device.

patency in the setting of recent biliary stone passage. In addition, new diagnostic techniques, including intraductal ultrasound can aid in the evaluation of intraductal pathology [22]. A more recent development is the SpyGlass™ technology (Boston Scientific, Natick, MA, USA) – a fiberoptic choledochoscopy system that can visualize the biliary tree, accommodate a laser device to ablate large stones, and facilitate biopsy/tissue sampling [25].

Various catheters and guidewires are available for accessing the ampulla. Wire-guided hydrostatic balloons and dilating catheters are used for serial dilation of strictures. Plastic stents are used for most benign strictures or acute ductal disruptions in the setting of a leak and can be removed. Self-expanding metal stents are used more frequently for malignant strictures due to better long-term patency. Tissue sampling techniques include brush cytology, fluoroscopic-guided biopsy, and aspiration. Common stone extraction techniques include mechanical lithotripsy, balloons, and wire baskets. Prior to stone retrieval, a sphincterotome is used to divide the papilla using either electrocautery or cold-knife technique [10,23].

In addition to the traditional medical record, the procedure/findings can be documented using endoscopic photographs and/or a video recording [22-23]. After completion of the procedure, the patient is transferred to recovery room for close monitoring during emergence from conscious sedation. Once fully recovered (after approximately one hour), the patient is allowed to leave the recovery room, is given appropriate dietary and activity instructions, and is advised

to observe for signs and symptoms of post-procedural complications.

#### **Peri-procedural antibiotic use**

Antibiotics should be considered for patients who are at high-risk for developing infective endocarditis (i.e., those with prosthetic cardiac valves, previous bacterial endocarditis, surgically constructed systemic pulmonary shunts, complex cyanotic congenital heart disease) and for patients at risk for artificial prosthetic implant infections (i.e., synthetic vascular or joint prostheses placed within one year prior to ERCP) [26-27]. In addition, patients with primary sclerosing cholangitis, predicted incomplete ductal drainage, biliary obstruction (i.e., hilar tumors) and pancreatic pseudocysts are at higher risk for infection and should receive prophylactic antibiotics before the ERCP [26-27]. In cases where incomplete drainage is not predicted but does occur, antibiotics can be given right after the ERCP [27]. Antibiotics should be continued for 48-72 hours in these high-risk patients. There is controversy with regards to the choice of antimicrobial prophylactic agent, with various regimens utilizing fluoroquinolones, piperacillin, ticarcillin-clavulanic acid, and amoxicillin-clavulanic acid [26-27].

#### **ERCP: overview of complications**

Avoidance of unnecessary ERCP is the best way to reduce ERCP-related complications [11]. Cardiopulmonary depression is the most common complication associated with endoscopy (up to 50% of overall complications; 1% of events considered to be severe) and is usually associated with the use of sedation [1,6]. Hypoxia (incidence of 7-40%) and aspiration (incidence of 0.3-1.0%) are associated with increasing age, chronic illness, depressed mental status, supine positioning, and sedation [28-29].

The risk of perforation during endoscopy/ERCP is minimal (<0.05%) [28]. Over 50% of perforations are associated with underlying anatomic abnormalities (Zenker's or epiphrenic diverticula, benign/malignant esophageal strictures, other mass lesions). Perforations most likely occur in the three zones of esophageal narrowing (cricopharyngeus muscle, aortic knob, and diaphragmatic hiatus). Early recognition and treatment result in much lower mortality [6]. Management includes fluid resuscitation, broad-spectrum antibiotics, and drainage as indicated. Select patients with minimal, contained perforations may be treated conservatively, while others with free contrast extravasation and/or evidence of sepsis need surgical therapy.

Complications of ERCP can be broadly divided into short-term (within 3 days of the procedure) and long-term (> 3 days after the procedure) complications. Short-term complications are generally sedation- and/or endoscopy-related, and include bleeding, infection, perforation, and cardiopulmonary events. Long-term complications include mainly infections associated with indwelling stents and inflammatory changes secondary to ductal manipulation. The reported incidence of ERCP-specific complications ranges from 5% to 40%, depending on the complexity of the procedure, the underlying diagnosis, and patient comorbidities [6,9,30-31]. Post-ERCP pancreatitis is seen most

commonly, followed by cholangitis, duodenal hemorrhage, stent migration, and duodenal perforation [30-31].

In terms of severity of complications as measured by the number of hospital days attributed to each particular event, the incidence of mild complications (requiring 1 to 4 hospital days) was 4.3% and the incidence of moderate complications was 5.2% in one study [32]. Lal et al reported that 19/20 ERCP-related complications were associated with therapeutic ERCP versus only 1/20 being associated with diagnostic ERCP [32]. In addition, practitioners who perform more ERCP procedures have been shown to have fewer adverse events than less experienced endoscopists, with more complications seen among endoscopists who perform < 200 ERCPs per year [33].

Mortality associated with ERCP ranges from 0% to 0.5%. Mortality following therapeutic ERCP (0.5%) is approximately two times higher than mortality following diagnostic ERCP (0.2%) [1,6,32].

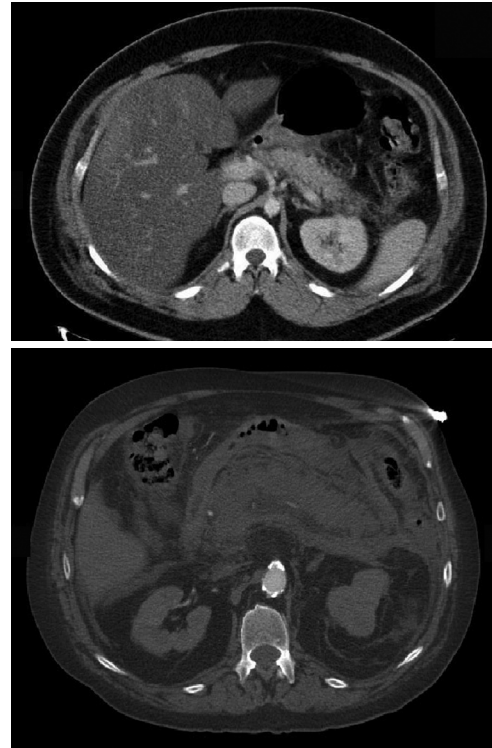
#### **Methemoglobinemia**

Methemoglobinemia is a serious complication associated with the use of benzocaine- and lidocaine-containing sprays [34]. Recommended dosages of topical local anesthetic should not be exceeded (20% benzocaine given as 0.5-1.0 second spray burst delivers 30-60 mg) [35]. Diagnosis is suggested by the appearance of chocolate-colored cyanosis and an oxygen-unresponsive drop in oxygen saturation on pulse oximetry. Intravenous methylene blue (1-2 mg/kg given over 10 minutes) is the treatment of choice [34].

#### **ERCP-related pancreatitis**

The definition of post-ERCP pancreatitis includes: (a) new-onset or worsening abdominal pain; (b) elevation of serum amylase three times above normal at 24 hours post procedure; and (c) requirement for >2 days of pancreatitis-related hospitalization [36]. While the overall incidence of post-ERCP pancreatitis ranges from 1% to 6%, the incidence of pancreatitis may exceed 30% in patients considered to be high-risk (Fig. 2) [3,9,25,33,37-39].

Pathophysiology of post-ERCP pancreatitis is multifactorial (mechanical, chemical, hydrostatic, enzymatic, microbiologic, and thermal) and is mediated via premature intracellular activation of proteolytic enzymes within acinar cells resulting in cellular injury and pancreatic tissue autodigestion. Patient history of previous post-ERCP pancreatitis, suspected sphincter of Oddi dysfunction, female gender, normal serum bilirubin, absence of chronic pancreatitis, balloon dilatation of the biliary sphincter, difficult cannulation, pancreatic sphincterotomy, and >1 injections of contrast into the pancreatic duct are associated with post-ERCP pancreatitis [39]. Masci et al found that age <60 years, the use of precut sphincterotomy, and failure to clear biliary stones are also associated with post-ERCP pancreatitis [3]. Loperfido et al identified age <70 years, pancreatic ductal opacification, and nondilated common bile duct as risks [33]. Manipulation of the papilla during cannulation, direct thermal injury to the papilla, and intraductal contrast injection (independent of contrast osmolality) may also contribute to pancreatitis [3,33,37,39-



**Fig 2.** Post-ERCP pancreatitis. In the first case (top image) three risk factors for post-ERCP pancreatitis were present: age <60 years, non-therapeutic ERCP, and >1 injection of contrast. Pancreatitis resolved following five days of hospitalization. In the second case (bottom image) the patient had a normal CBD (<5 mm) without choledocholithiasis during diagnostic ERCP. The patient developed multi-organ failure and eventually succumbed to pancreatitis.

40]. Prospective studies show that selective guidewire cannulation of the bile duct may prevent inadvertent contrast injection into the pancreatic duct and reduce chemical and/or pressure injury to the duct [40-42].

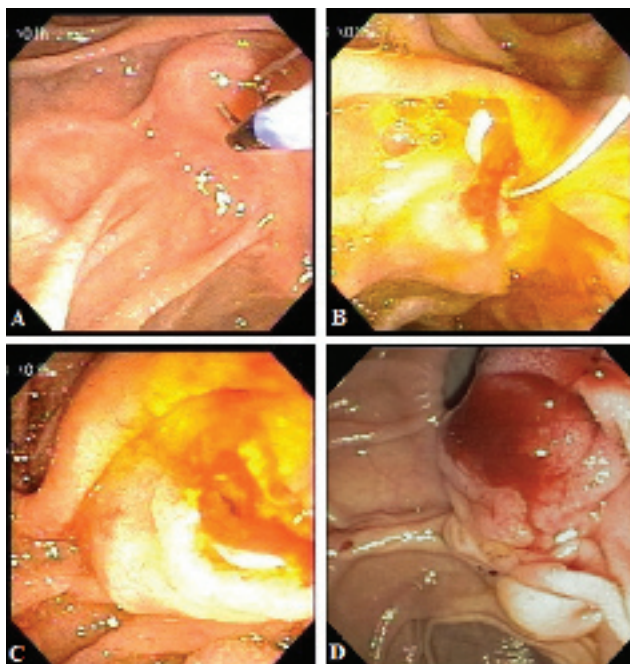
Unexpectedly high rates of ERCP-associated pancreatitis (27%) have been noted in younger patients (age <59 years) who underwent sphincterotomy for suspected choledocholithiasis without a stone in the CBD [43]. Patients with suspected sphincter of Oddi dysfunction (SOD) also carry a substantial risk (24%) of pancreatitis after diagnostic, manometric, or therapeutic ERCP [44]. In one study, stent placement enhanced ductal drainage past the hypertensive sphincter and reduced the incidence of pancreatitis from 26% to 7% [45]. Of note, pancreatic stents placed after balloon dilatation of the major papilla for gallstone removal do not provide similar benefits [46]. Thermal injury to the papilla can contribute to secondary pancreatitis [47]. Coagulation current causes more tissue injury and edema than cutting current, and the use of pure cut current has been shown to cause less pancreatitis than blended current sphincterotomy [47-48].

Numerous clinical trials evaluated potential pharmacologic interventions to reduce the incidence of post-ERCP pancreatitis. Neither somatostatin, nor its analogue,

octreotide, appeared to reduce the rate of post-ERCP pancreatitis [49-51]. Nifedipine and nitroglycerin reduce contraction of the sphincter of Oddi. While nifedipine was ineffective in one trial, nitroglycerin significantly reduced post-ERCP pancreatitis in two studies [52-54]. Other studies examined the effects of anti-inflammatory agents on post-ERCP pancreatitis. Corticosteroids were ineffective in three prospective trials after a retrospective study suggested potential benefit [55-58]. Allopurinol failed to reduce the rate of post-ERCP pancreatitis in one randomized study [55]. Modulation of cytokine release with IL-10 showed benefit in one study but was subsequently found to be ineffective [59-60]. The protease inhibitor gabexate mesilate decreased post-procedural serum amylase levels, abdominal pain, and pancreatitis in one study [61]. However, a larger, more recent study comparing gabexate, somatostatin, and placebo demonstrated no benefit [50].

#### **Hemorrhagic complications**

Bleeding occurs in 1-2% of patients during or after ERCP, is associated with approximately 0.3% mortality, and is related to the performance of sphincterotomy (Fig. 3) [3,33,36,62]. In approximately 50% of cases, post-ERCP bleeding is delayed, and may occur as much as 1-2 weeks following the procedure [1,63]. Although the assessment of bleeding after ERCP is most often based on its clinical manifestations, an objective classification has been defined as follows: (a) mild bleeding - hemoglobin drop  $<3$  gm/dL; (b) moderate bleeding - transfusion requirements  $<4$  units of packed red blood cells (PRBCs) with no intervention; and (c) severe hemorrhage - transfusion requirements  $>4$  units of PRBCs or intervention [64].



**Fig 3.** ERCP-associated bleeding. (A) Positioning of the ERCP equipment for a sphincterotomy; (B) Post-sphincterotomy oozing that evolved into (C) continued bleeding requiring epinephrine injection for control. (D) Self-limited post-sphincterotomy bleeding.

The risk of bleeding increases with coagulopathy (prothrombin time  $>1.5$  to  $2.0$  times normal), recent (within 72 hours) use of anticoagulants, hemodialysis, acute cholangitis, the presence of intra-procedural bleeding, endoscopist with low sphincterotomy volume (average  $<1$  per week), and the performance of extended sphincterotomy [3,33,37,62,65]. Periprocedural bleeding may be reduced by using a “smart” electrocautery generator or by avoiding sphincterotomy in high-risk cases altogether and relying on balloon dilatation instead [39,62,66]. First-line treatment of post-sphincterotomy bleeding is flushing the site with 1:100,000 epinephrine solution, followed by a direct injection of 1:10,000 epinephrine if bleeding continues. The risk of clinically significant hemorrhage requiring transfusion of  $>2$  units of blood, surgical or angiographic intervention, is low (0.1%-0.5%) [62,66].

#### **Perforations**

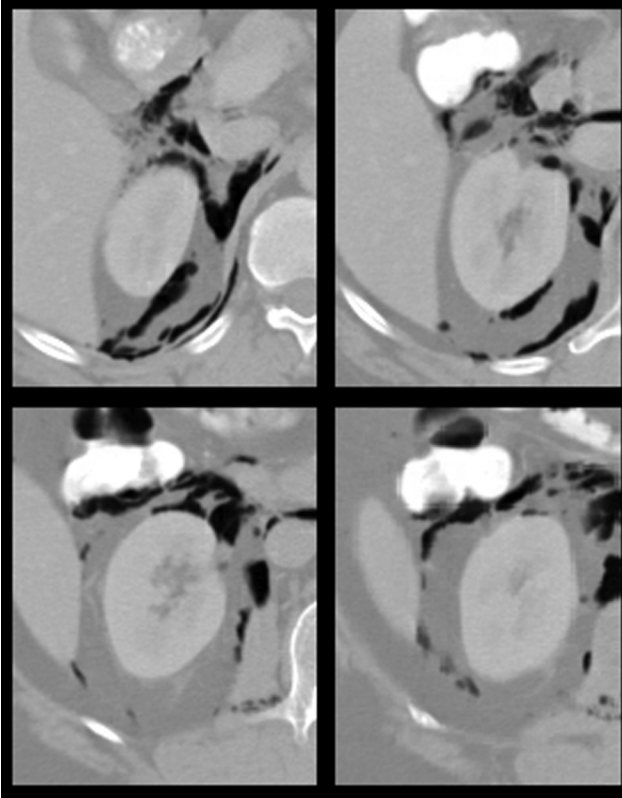
Perforations occur in 0.3% to 0.6% of ERCP cases [1,67]. Mallery et al described three distinct types of ERCP-related perforations: (a) guidewire-related perforations; (b) peri-ampullary perforations during sphincterotomy; and (c) perforations that are remote from the papilla [1]. Risk factors for ERCP-related perforation include the performance of sphincterotomy, the presence of Billroth II anatomy, intramural injection of contrast, performance of biliary stricture dilatation, presence of sphincter of Oddi dysfunction, long duration of the procedure [33,68].

Retroperitoneal perforations related to guidewire use or the performance of sphincterotomy may be initially treated with broad-spectrum antibiotics, biliary and duodenal decompression (i.e., via nasobiliary and nasogastric tubes) [1,3,69-70]. This approach is successful in over 85% of cases (Fig. 4) [1]. Additional procedural/surgical interventions may be required if continuing biliary-pancreatic pathology requires further treatment (i.e., retained bile duct stones, persistent bile leak) or if the patient worsens clinically (i.e., onset of peritonitis).

Perforations remote from the papilla (esophageal, gastric, and duodenal) tend to be more extensive, are often associated with anatomic factors such as the presence of luminal obstruction or surgically altered anatomy, and are frequently recognized late. In contrast to the success of nonoperative management in the setting of localized perforations related to sphincterotomy or guidewire use, perforations remote from the papilla are more likely to require surgery [67-68].

#### **Cholangitis**

The reported incidence of post-ERCP cholangitis is 1-3% [27,32-33,66]. Risk of cholangitis increases with stenting across malignant strictures, combined percutaneous-endoscopic procedures, the presence of jaundice, incomplete or failed biliary drainage, and low ERCP case volume [33,66]. One study reported no episodes of cholangitis for diagnostic ERCP versus a 2.8% rate of cholangitis for therapeutic ERCP [32]. Adequate biliary drainage is essential to avoid delayed cholangitis in an obstructed system, with stents and nasobiliary tubes being equally effective. Placement of plastic stents may be helpful in preventing cholangitis in



**Fig 4.** Retroperitoneal duodenal perforation following ERCP and sphincterotomy. The patient underwent successful nonoperative therapy: bowel rest, nasogastric suctioning, and broad-spectrum antibiotics.

cases of incomplete or unsuccessful gallstone extraction [1]. For hilar obstructions, some experts emphasize the avoidance of filling all intrahepatic segments and the importance of drainage of all intrahepatic segments that have been filled with contrast [71]. Placement of unilateral stents results in similar relief of jaundice but a lower rate of cholangitis when compared to bilateral stents [72]. Stent obstruction is also associated with the risk of cholangitis [73].

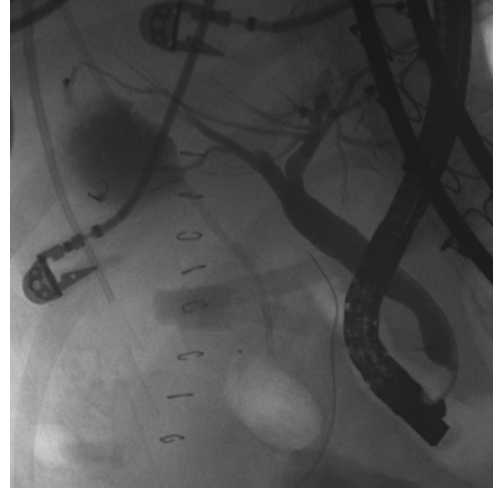
#### ***Cholecystitis***

The incidence of post-ERCP cholecystitis is approximately 0.5% [3,66]. This entity may be associated with intraprocedural filling of the gallbladder with contrast in the presence of gallbladder stones [1,66]. Treatment consists of cholecystectomy, and there is no effective method of preventing this complication other than a previous cholecystectomy.

#### ***Complications related to stent placement/manipulation***

Plastic (polyethylene) stents are commonly utilized in the setting of benign biliary strictures, postoperative bile leaks, or pancreatic disease (Fig. 5). With extended patency rates, self-expanding metal stents are used more frequently in the setting of malignancy. Of interest, up to one fifth of all ERCP procedures are related to either stent occlusion or change [32].

Acute stent-related complications are rare. Perforation occurs in <1% of cases and is most often associated with



**Fig 5.** ERCP study in a patient with a postoperative bile leak. The patient underwent endoscopic sphincterotomy and stent placement, followed by resolution of the bile leak one week later.

concurrent sphincterotomy [37,66]. Other stent-related complications include stent obstruction (often leading to infection/cholangitis), stent migration, recurrent ductal stenosis post-stent removal, pancreatitis, and bleeding [1,73-75].

In patients who have biliary obstruction due to unresectable malignancy, endoscopic stenting can provide effective palliation (self-expanding metal stents are preferred in the setting of malignancy due better patency rates) [74]. Maire et al demonstrated mean stent patency of 7 months with metal stents versus 2.5 months with plastic stents in patients with unresectable pancreatic cancer and biliary obstruction [75].

Stent migration rates vary depending on stent type. Plastic stents migrate more often (5%-10%) than metal stents (<1%) [76]. Proximal stent migration may lead to biliary obstruction while distal stent migration is associated with perforation and/or obstruction [77]. Stent penetration through the bowel wall into another organ generally does not cause overt peritonitis, but may lead to fistula development.

Perforation caused directly by stent placement usually occurs secondary to extramural passage of the guidewire or stent [1]. Clinical management depends on the location and the extent of perforation.

Postoperative biliary strictures are commonly treated with stent placement. In this population, up to 20% of patients develop recurrent stenosis within 2 years of stent removal [77]. Postoperative bile leaks are also frequently treated with stent placement. There is a 3-13% risk of pancreatitis after biliary stenting, and some authors advocate that concomitant sphincterotomy may reduce the incidence of this complication [27-28]. Bleeding rarely complicates endoscopic stenting, and is usually associated with other therapeutic maneuvers (i.e., sphincterotomy, transmural pseudocyst drainage).

#### ***Complications of sphincterotomy***

The reported complication rate of endoscopic

sphincterotomy (ES) is 6.9-9.8% [66,78]. Complications most commonly associated with ES include pancreatitis (5.2-5.4%) and hemorrhage (2.0%) [67]. Mortality directly or indirectly related to ES is between 0.2% and 0.4% [67, 80-81]. Patient-related risk factors for ES-associated complications include suspected sphincter of Oddi dysfunction, small CBD size (<5 mm) and cirrhosis [66,78-79]. Technique-related factors for ES-associated complications include difficulty in cannulating the bile duct, bile duct access obtained by "precut" ES, and the use of a combined percutaneous-endoscopic procedure [66]. The risk of ES-related complications does not appear to be related to the patient's age or co-morbidities [66]. The incidence of ES-related complications is highest for patients with suspected sphincter of Oddi dysfunction (10.8-21.7%) and lowest in the setting of choledocholithiasis following laparoscopic cholecystectomy (4.9%) [66,78]. Endoscopists who perform >1 ES per week had significantly lower rates of total complications (8.4% vs 11.1%) and severe complications (0.9% vs 2.3%) in one study [66].

Hemorrhage associated with ES can usually be treated endoscopically, using injection of epinephrine solution (1:10,000), electrocoagulation (gold probe catheter), or balloon tamponade (see section above).

Iatrogenic ampullary stenosis is a long-term complication of ES [80]. Two types of iatrogenic ampullary stenosis have been described: (a) type I – limited to intraduodenal portion of the sphincter complex; and (b) type II – includes all other types up to the extension of the stenosis into the common bile duct [80]. In one study, procedural treatment of type I stenoses consisted of ES while type II stenoses were treated with stent and/or balloon dilation [80]. Procedural complication rate was 16%, with long-term success rate of 83% for type I and 65% for type II stenoses [80].

#### **Guidewire entrapment and fracture**

Wire entrapment during ERCP is extremely rare, and may be associated with subsequent wire fracture due to excessive traction [81]. Fluoroscopic guidance may help avoid this complication [82-83]. Hydrophilic wires require continuous moistening of exposed portions to avoid desiccation and fracture [82-83]. Some authors question the use of guidewires to achieve ductal cannulation [84]. Guidewire fracture can also be related to retrieval basket impaction, which most commonly occurs around the ampulla [85]. Irregular, hard, or multiple stones are associated with increased risk of basket impaction. Surgery may be needed to remove fractured ERCP devices.

#### **ERCP: special topics**

##### **Unsuccessful ERCP attempt**

Lal et al reported failed ERCP rate of approximately 7% [32]. Most unsuccessful ERCP attempts are associated with the inability to reach papilla secondary to either gastric outlet obstruction or the presence of Billroth II anatomy [32]. Following unsuccessful but otherwise uncomplicated ERCP, one must consider risks and benefits of re-attempting ERCP, using less invasive (EUS) or non-invasive (MDCT or MRCP) diagnostic techniques, or resorting to other invasive

procedural options (PTC versus surgery).

##### **ERCP: miscellaneous complications and considerations**

Inadequate endoscope decontamination procedures may be associated with rare but very severe bacterial infections (mainly Salmonella and Pseudomonas spp) [27,86]. Fatalities have been reported following such infections [27,86]. Pseudocyst infections may occur following ERCP, and it is important to avoid the filling of the pseudocyst in the absence of subsequent drainage procedure [1].

Drug reactions during ERCP are rare (incidence 0.5%) [32]. Other complications include duodenal hematoma, malfunction of therapeutic devices (i.e., stone retrieval baskets), post-procedural ileus, post-procedural diarrhea (usually antibiotic-related), hepatic abscess formation, portal venous gas, failed fluoroscopic imaging attempts, and distal (i.e., small bowel or colonic diverticular) perforations [1,6,32,87].

##### **ERCP and risk of subsequent biliary malignancy**

Endoscopic sphincterotomy leads to reflux of intestinal contents into the biliary-pancreatic system. This, in turn, contributes to alterations in intraductal bacterial flora and bile composition, leading to significantly higher concentrations of cytotoxic dihydroxy bile salts [88]. Resulting histologic changes within biliary-pancreatic ducts include fibrosis, inflammation, mucosal hyperplasia, pseudopyloric gland metaplasia, and intestinal metaplasia [89-90]. Although controversy continues as to whether ERCP and/or ES increase the risk of subsequent biliary malignancy, no definitive evidence exists with regards to such association at present [91-92].

##### **Intraoperative ERCP**

Trans-oral intraoperative ERCP has been used in patients who require both cholecystectomy and removal of ductal stones [93-94]. Suspected pancreatic duct injury has been described as an indication for intraoperative ERCP during trauma celiotomy [95-96]. Transjejunal and transgastric approaches to ERCP were utilized in the setting of suspected papillary stenosis when other approaches failed or were contraindicated and in the setting of choledocholithiasis following previous Roux-en-Y gastric bypass [12,97].

##### **ERCP in pregnancy**

Although symptomatic gallstone disease is common in pregnant women (incidence >10%), choledocholithiasis requiring intervention during pregnancy is rare (incidence <1%) [98-100]. If possible, it is acceptable to delay intervention until postpartum period or until second trimester, when surgical intervention is relatively safer.

ERCP is relatively safe during pregnancy. Important considerations include: (a) strong procedural indication; (b) avoidance of maternal-fetal hypoxia/hypotension during conscious sedation; and (c) minimizing radiation exposure [99]. A multidisciplinary approach that involves anesthesiologists, obstetricians, surgeons, and gastroenterologists should incorporate: (a) fetal monitoring; (b) experienced endoscopist; and (c) minimizing procedural time [99-100]. Patients may have difficulty maintaining

prone position in the second/third trimester of pregnancy, necessitating left lateral position. The gravid uterus can compress the vena cava and cause maternal hypotension/placental hypoperfusion [99]. Because amniotic fluid can conduct electrical current to the fetus, the grounding pad should be placed above the level of uterus [101].

Limiting radiation exposure to <100 millirems during the first trimester is recommended (accepted teratogenic dose is 500 millirems) [98-99,101]. Iodine-containing contrast agents may cause hypothyroidism in the fetus. Therefore, using low concentrations of contrast, limiting the number of intraductal injections, and avoiding unnecessary pancreatography is advised [99]. While approaches that eliminate radiation exposure have been described, they do not provide real-time information regarding ductal anatomy/stone clearance [102]. Some advocate using choledochoscopy to confirm ductal clearance [99].

## Conclusions

Both medical and surgical practitioners should be well versed in indications, contraindications, potential complications, benefits, and alternatives to ERCP. Knowledge of ERCP-related complications and associated risk factors may allow the endoscopist to promptly recognize these risks and institute appropriate preventive measures. Operator experience, avoidance of unnecessary procedures, adequate pre-procedural preparation, and meticulous attention to detail during the procedure, all contribute to minimizing the risk of ERCP-related complications.

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## Conflict of interest statement

The authors declare no conflicts of interest with regards to the preparation and/or publication of this written work.

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