Prevention and Management of Post-Endoscopic Retrograde Cholangiopancreatography Complications

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Endoscopic retrograde cholangiopancreatography (ERCP) is associated with a spectrum of complications such as pancreatitis, hemorrhage, perforation, and cardiopulmonary events. These complications can range from mild to severe resulting in extended hospitalization, requiring surgical intervention, and leading to permanent disability or even death. Complications of ERCP have been better understood in the past decade, with adoption of standardized consensus-based definitions of complications and introduction of new recommendations to minimize risks of ERCP. Adequate selection of patients undergoing ERCP, skilled operators using novel techniques and prompt identification and treatment are key to successful prevention and management.

Key Words: Endoscopic retrograde cholangiopancreatography; Pancreatitis; Prevention

INTRODUCTION

Standardized definitions for complications of sphincterotomy were introduced first in 1991.[1] Severity is assessed primarily by length of hospital stay, and intervention required to treat the complications. The spectrum of outcomes encompasses failures, long-term sequelae, costs, extended hospitalization, and patient satisfaction.

Complication rates of endoscopic retrograde cholangiopancreatography (ERCP) vary widely, even between apparently similar prospective studies. Variation is substantial. For example, in one large prospective study, post-ERCP pancreatitis rates were reported at 0.74% for diagnostic ERCP, and 1.4% for therapeutic ERCP respectively;[2] in another similar study, post procedure pancreatitis rates were 5.1% (7 fold higher) for diagnostic ERCP and 6.9% (5 fold higher) for therapeutic ERCP.[3] Possible reasons for such wide variation in reported complication rates include variation in 1) definitions; 2) thorough-

ness of protocol for detection of complications; 3) patient population with attendant risk factors; and 4) differences in spectrum of technical approach such as use of pancreatic stents, or different endpoints of therapy.

Complications of diagnostic and therapeutic ERCP

Prospective series of ERCP generally report an overall short-term complication rate of approximately 5% to 10%.[2-9] There is a particularly high rate of complications (up to 20% or more, primarily pancreatitis, with up to 5% severe complications) for ERCP and sphincterotomy for suspected sphincter of Oddi dysfunction. In contrast, there is a consistently low complication rate for routine bile duct stone extraction (under 5% in most series).[4] Hemorrhage occurs primarily after sphincterotomy, and primarily in patients with bile duct stones, coagulopathy, and acute cholangitis. Cholangitis occurs mostly after ERCP in patients with malignant biliary obstruction and/or failed drainage, or after stent malfunction or occlusion. Perforation occurs primarily after sphincterotomy, or endoscope-related, but risk factors are more difficult to determine.

Although relevant studies are heterogeneous and sometimes omit potentially key risk factors, several patterns are apparent. Indication of suspected sphincter of Oddi dysfunction is a significant risk factor; technical factors, likely related to specific expertise or approach of the endoscopist and center, are also significant risk factors for overall complications. These tech-

nical factors include difficult cannulation, use of precut or "access" papillotomy to gain bile duct entry, failure to achieve biliary drainage, and use of simultaneous or subsequent percutaneous biliary drainage for otherwise failed endoscopic cannulation. In turn, the ERCP case volume of the endoscopists or medical centers, when examined, has almost always been a significant factor in complications by both univariate or multivariable analysis.[2-9] Death from ERCP is rare (less than 0.5%), but is most often caused by cardiopulmonary complications. It is unclear whether the increasing use of anesthesia services for monitored anesthesia care or general anesthesia during ERCP has affected the cardiopulmonary complication rate.

Contrary to intuition and commonly held beliefs, risk factors found not to be significant for overall complications include older age or increased number of coexisting medical conditions - on the contrary, younger age generally increases the risk both by univariate and multivariate analysis; smaller bile duct diameter; and anatomic variants such as periampullary diverticulum or Billroth II gastrectomy, although they do increase technical difficulty for the endoscopist.[2-9]

Post-ERCP pancreatitis

Pancreatitis is the most common complication of ERCP, with reported rates varying from 1% to 40%, with a rate of about 5% being most typical.[2-9] In the Cotton consensus classification, post-ERCP pancreatitis is defined as clinical syndrome consistent with pancreatitis (i.e., new or worsened abdominal pain) with an amylase at least three times normal at more than 24 hours after the procedure, and requiring more than one night of hospitalization.[1]

Risk factors for post-ERCP pancreatitis related to the patient

Mechanical, chemical, hydrostatic, enzymatic, microbiologic, and thermal injury have all been postulated as potential mechanisms of injury to the pancreas during ERCP and endoscopic sphincterotomy. The risk of post-ERCP pancreatitis is determined at least as much by the characteristics of the patient as by endoscopic techniques or maneuvers. Factors found to be significant in one or more major studies include younger age, indication of suspected sphincter of Oddi dysfunction, history of previous post-ERCP pancreatitis, and normal serum bilirubin.[2-9] Women may be at increased risk, but it is difficult to determine the confounding effect of sphincter of Oddi dysfunction, a condition that occurs almost exclusively in women. In one meta-analysis, female gender was clearly a risk,[10] and women account for a majority of cases of severe or fatal post-ERCP pancreatitis.[4,11]

Sphincter of Oddi dysfunction, a controversial syndrome

that is primarily suspected in women with post-cholecystectomy abdominal pain, poses a tremendous risk for pancreatitis after any kind of ERCP whether diagnostic, manometric or therapeutic. The risk of post ERCP pancreatitits triples to 10% to 30% in patients with suspected sphincter of Oddi dysfunction.[3-6] Two studies specifically compared risk of post-ERCP pancreatitis in patients having ERCP for suspected sphincter of Oddi dysfunction with and without sphincter of Oddi manometry and found no detectable independent effect of manometry on risk.[4,12] Patients with suspected choledocholithiasis who are found not to have stone disease are at similarly high risk for post-ERCP pancreatitis. Increased use of endoscopic ultrasound and magnetic resonance cholangiopancreatography (MRCP) allow determination in advance that such patients do not harbor bile duct stones, and either eliminate the need for conventional ERCP, or allow triage of the patients to ERCP performed with maximal therapeutic benefit (dual sphincter manometry and therapy) and protective measures (pancreatic stents).

A history of previous post-ERCP pancreatitis increases risk substantially (up to 4 fold),[3,5] Advanced chronic pancreatitis, on the other hand, confers some immunity against ERCP-pancreatitis, perhaps because of atrophy and decreased enzymatic activity.[3] Pancreas divisum is only a risk factor if minor papilla cannulation is attempted. Despite many early studies suggesting small bile duct diameter to be a risk factor for pancreatitis, most recent studies have shown no independent influence of duct size on risk; small duct diameter may have been a surrogate marker for sphincter of Oddi dysfunction or patients without true obstructive biliary disease in older studies suggesting higher risk. ERCP for removal of bile duct stones has been found to be relatively safe with respect to pancreatitis rates (usually under 3% to 4%) in multicenter studies regardless of bile duct diameter.[4] Periampullary diverticula nor Billroth II gastrectomy do not appear to influence risk of post-ERCP pancreatitis.[4]

Risk factors for post-ERCP pancreatitis related to technique

Technique-related issues have long been recognized to be important in causing post-ERCP pancreatitis. Papillary trauma induced by difficult cannulation has a negative effect that is independent of the number of pancreatic duct contrast injections.[2-10] Importance of contrast injection alone in causing post-ERCP pancreatitis has probably been overemphasized. Pancreatitis occurred after 2.5% of ERCP in one study involving no pancreatic duct contrast injection at all.[3] Acinarization of the pancreas, although undesirable, is probably less important than generally thought and has not been found to be significant in two recent studies.[3,5] Risk of pancreatitis is gen-

erally similar after diagnostic and therapeutic ERCP.[2-10] Performance of biliary sphincterotomy does not appear to add significant independent risk of pancreatitis to ERCP.[3,5] This observation does not reflect the safety of sphincterotomy, but rather the risk of diagnostic ERCP. Pancreatic sphincterotomy of any kind,[3] including minor papilla sphincterotomy[3,5] has been found to be a significant risk factor for pancreatitis, although the risk of severe pancreatitis has been very low (less than 1%), perhaps because nearly all of these patients had pancreatic drainage via a pancreatic stent.

Risk related to use of precut or access papillotomy is controversial and difficult to sort out from other variables, including difficult cannulation. Use of precut to access bile duct varies widely among endoscopists, from under 5% to as many as 30% of cases.[13] There are many variations on precut technique: standard needle-knife inserted at the papillary orifice and cutting upwards; needle-knife "fistulotomy" starting the incision above the papillary orifice and then cutting either up or down; use of a pull-type sphincterotome wedged either in the papillary orifice or transpancreatic precut performed by cutting the pancreatic sphincter intentionally. Any of the access techniques has the potential to lacerate and injure the pancreatic sphincter. Precut techniques have been uniformly associated with a higher risk of pancreatitis by univariate and multivariate analysis in multicenter studies involving endoscopists with varied experience.[2,4] In contrast, many series from tertiary referral centers have found complication rates no different than for standard sphincterotomy, suggesting that risk of precut sphincterotomy is highly operator-dependent.[14] In one study, endoscopists performing more than one sphincterotomy a week averaged 90% immediate bile duct access after precutting, versus only 50% for lower volume endoscopists, a success rate which hardly justifies the risk of complications.[4] Comparative studies of precut with standard sphincterotomy are hard to interpret because indications and settings may be very different, with precut preferentially performed in lower risk situations such as obstructive jaundice, and prominent papillae. In addition, increasing use of pancreatic stents in series from tertiary centers may have neutralized the otherwise higher risk of precut sphincterotomy.[2] Complications of precut sphincterotomy vary with the indication for the procedure, occurring in as many as 30% of patients with sphincter of Oddi dysfunction in older studies without use of pancreatic stents.[4] Paradoxically, in patients with sphincter of Oddi dysfunction, needle-knife sphincterotomy over a pancreatic stent placed early in the procedure has been shown to be substantially safer than conventional pull-type sphincterotomy without a pancreatic stent.[15]

A meta-analysis of six randomized trials comparing precut papillotomy with persistent cannulation provides some insight. These trials included 966 patients assigned to early precut implementation or persistent attempts at standard cannulation.[16] Post-ERCP pancreatitis was significantly less common in patients undergoing precut group compared with the persistent attempts at cannulation group (3% vs. 5%). However, the overall rate of complications including pancreatitis, bleeding, cholangitis, and perforation did not significantly differ between the two groups (5% vs. 6%). Limiting the relevance of these studies is the fact that few of these studies included patients with high risk indications such as sphincter of Oddi dysfunction, or involved use of pancreatic stents, which is now considered fairly standard.

Presence of multiple risk factors for post-ERCP pancreatitis substantially escalates the probability that a patient will develop this complication.[3] The interactive effect of multiple risk factors is reflected in the profile of patients developing severe post-ERCP pancreatitis. In one study predating widespread use of pancreatic stents, females with a normal serum bilirubin had a 5% risk of pancreatitis; with addition of difficult cannulation risk rose to 16%; with further addition of suspected sphincter of Oddi dysfunction (i.e., no stone found), the risk rose to 42%.[3] In two different studies, nearly all of the patients who developed severe pancreatitis were young to middle-aged women with recurrent abdominal pain, a normal serum bilirubin, and with no biliary obstructive pathology.[3,11] These observations emphasize the importance of tailoring the approach of ERCP to the individual patient.

The effect of endoscopist case volumes and experience on post-ERCP pancreatitis seems to be intuitively obvious, but has been hard to demonstrate. A recent study showed that trainee participation adds independent risk of pancreatitis.[5] In contrast, most multicenter studies have failed to show a significant correlation between endoscopists' ERCP case volumes and pancreatitis rates.[2-4] It is possible that none of the participating endoscopists in those studies reached the threshold volume of ERCP above which pancreatitis rates would diminish (perhaps greater than 250 to 500 cases per year). However, most American endoscopists average less than two ERCP's per week,[3] and the reported rates of pancreatitis from the highest volume tertiary referral centers in the US are often relatively higher than those in private practices. All of these observations suggest that case mix is at least as important as expertise in determining risk of post-ERCP pancreatitis.

Specific techniques to reduce risk of post-ERCP pancreatitis

In general, the most atraumatic and efficient method of cannulation will be associated with the fewest complications, but the importance of cannulation difficulty in causing pancreatitis has probably been exaggerated. Use of a papillotome or

steerable catheter for biliary cannulation has been prospectively compared to a standard catheter in randomized trials.[14] All of these studies showed significantly higher success rates with the sphincterotome or steerable cannula - however there was no difference in rates of pancreatitis or other complications. Another randomized trial did show significant reduction of pancreatitis risk when a guidewire was used in conjunction with a papillotome, as opposed to a papillotome and conventional contrast injection alone; the relevance of this study is questionable since few use just a cannula and contrast to access ducts any more.[14]

Using the guidewire as a primary cannulation device is an increasingly used technique, either by leading with the guidewire, or by impacting the cannula or papillotome into the papillary orifice then advancing guidewire without contrast injection. Guidewire cannulation has been shown to lower post-ERCP pancreatitis rates in a number of prospective randomized trials, with rates of 0% to 3% using wire cannulation compared with rates of 4% to 12% using contrast injection.[17] In practice, many advanced endoscopists now use a hybrid of the two techniques, using minimal contrast to outline the course of the distal ducts in combination with wire probes. Such a hybrid technique may avoid dissections or passage of the guidewire out a side branch of the pancreatic duct, but has not been formally evaluated.

Thermal injury is thought to play some role in causing pancreatitis after biliary and pancreatic sphincterotomy. A number of randomized trials have compared the impact of pure cutting versus blended current, with mixed results but generally lower rates of pancreatitis using the pure cut current.[14] Automated current delivery systems programmed to deliver a specific tissue effect are now widely used. None of the available studies suggest a significant difference in rates of pancreatitis between these units compared with blended current, so that it is not yet clear whether automated current delivery systems provide the same benefit for prevention of pancreatitis as do those using pure cutting current.

Pancreatic stents for prevention of post-ERCP pancreatitis

Pancreatic stent placement is increasingly used as a method to reduce risk of post-ERCP pancreatitis. Such use of pancreatic stents now extends into routine practice, and is increasingly becoming considered standard of care in high risk circumstances.[18] Specific situations where placement of a pancreatic stent has been shown to reduce risk include biliary sphincterotomy for sphincter of Oddi dysfunction, suspected sphincter of Oddi dysfunction with normal manometry, pancreatic sphincterotomy, precut sphincterotomy, balloon-dilation of the biliary sphincter, and endoscopic ampullectomy, after pancreatic wire-assisted biliary cannulation, probably after

difficult cannulation in general, and even after unselected ERCP in patients with "virgin papilla," excluding those with pancreas divisum or cancer.[18-27]

Several meta-analyses have shown that use of pancreatic stents in high-risk patients reduced rates of pancreatitis by about two thirds, with virtual elimination of severe post-ERCP pancreatitis.[19,26,27] While effective in high-risk cases, placement of pancreatic stents is usually unnecessary regardless of cannulation difficulty in older, jaundiced patients if they have a pancreatic duct obstructed by cancer. Pancreatic stenting has some limitations as a strategy to reduce risk.[18] Many endoscopists and their assistants are unfamiliar with their placement and may have a substantial failure rate, leaving the patient worse off than if no attempt was made.[23] Small caliber wires (0.018 inch or 0.025 inch) are often optimal for deep insertion into small or tortuous ducts, and ansa pancreaticus (360° alpha loop), all posing a challenge even for the most experienced endoscopist. A technique has been described which allows universal success at placing stents in difficult anatomy; a small caliber nitinol tipped wire can be knuckled inside the main pancreatic duct just beyond the sphincter and allow delivery of a small caliber short inner flanged stent.[23]

Ductal and parenchymal pancreatic injury has been reported to occur in up to 80% of patients with previously normal ducts using conventional 5 Fr or greater polyethylene stents.[28-31] Although it has been assumed that such injury resolves spontaneously, there have been reports and every advanced center has seen cases of permanent ductal stenosis and relapsing acute and chronic pancreatitis.[31] Strategies to avoid this complication included use of smaller caliber stents (3 or 4 Fr), which have been shown to be associated with lower rates of duct injury than conventional polyethylene 5 Fr stents,[30] and use of stents made of softer materials, which are now widely available. Pancreatic stents placed for prevention of post-ERCP pancreatitis should be documented to pass by X-ray or removed within a few weeks.

Balloon-dilation of the biliary sphincter has been introduced as an alternative to sphincterotomy for the extraction of bile duct stones, or as an adjunct to biliary sphincterotomy for extraction of large or difficult bile duct stones. Balloon dilation of intact biliary sphincter has been associated with a markedly increased risk of pancreatitis, resulting in two deaths in one American study,[32] and with a higher risk of pancreatitis by meta-analysis of pooled studies.[33] In general, balloon dilation of the intact biliary sphincter for extraction of bile duct stones is not recommended unless there is a relative contraindication to sphincterotomy such as coagulopathy or need for early anticoagulation, and if it is done, should generally be accompanied by placement of a prophylactic pancreatic stent. In contrast, balloon dilation performed after biliary

sphincterotomy to facilitate large stone extraction may be relatively safe and may reduce need for excessively large sphincterotomy and its associated risk of perforation or bleeding, such that pancreatic stent placement is optional.[34,35]

Pharmacological agents to prevent post-ERCP pancreatitis

Pharmacological agents have been investigated as potential agents to reduce post-ERCP pancreatitis with generally mixed or negative results. Meta-analyses of randomized controlled trials have shown that gabexate (a protease inhibitor) and somatostatin are marginally effective in preventing post-ERCP pancreatitis, but only if given over an extended infusion of up to 12 hours after ERCP, while shorter infusions of less than 4 hours are generally ineffective.[14] The lack of cost-effectiveness of prolonged infusions and lack of availability in the USA limits the practicality of these agents. Agents shown not to be effective include interleukin 10, octreotide, corticosteroids, allopurinol, platelet-activating factor inhibitors, heparin, and use of non-ionic contrast.[14] More promising agents in pilot studies and a meta-analysis have included non-steroidal anti-inflammatory drugs (NSAIDs),[35] as confirmed by a recent trial.[36,37]

Overall strategies to prevent post-ERCP pancreatitis

Avoidance of ERCP for marginal indications, especially in patients at higher risk of complications, is the single most effective way to prevent post-ERCP pancreatitis. ERCP should generally be avoided outside specialized referral centers when the probability of finding stones or other obstructive pathology is low and other methods are available, or situations in which the risk/benefit ratio of conventional diagnostic or biliary therapeutic ERCP is high (such as suspected sphincter of Oddi dysfunction). Alternative imaging techniques such as intraoperative laparoscopic cholangiography, MRCP and endoscopic ultrasound are safer alternatives for excluding obstructive biliary pathology.

Specific ERCP cannulation and sphincterotomy techniques in any given patient are ideally tailored to the risk profile of that individual. In low risk cases such as elderly patients with obstructive jaundice, manipulation is generally well tolerated, and whatever techniques are effective at gaining bile duct access and drainage are reasonable. In high-risk cases, manipulation should be minimized, and placement of a pancreatic stent considered early in the procedure. Placement of pancreatic stents is recommended in most patients with suspected sphincter dysfunction, history of post-ERCP pancreatitis, difficult cannulation, or prior to precut sphincterotomy with unclear papillary anatomy or in those with other risk factors.

Treatment of post-ERCP pancreatitis is like that for any other cause of acute pancreatitis. Early recognition of impending post-ERCP pancreatitis can be facilitated by checking serum amylase or other enzymes within a few hours after the procedure in patients who are at high risk or who have abdominal pain. If serum amylase or lipase is normal, probability of developing pancreatitis is very low and the patient can be considered for same-day discharge if otherwise reasonable. On the other hand, if the pancreatic enzymes are significantly elevated, and there is clinical suspicion of evolving pancreatitis, premature same-day discharge may be avoided, and pre-emptive hospitalization for observation, fasting, and vigorous intravenous hydration initiated. If post-ERCP pancreatitis is recognized very early in patients without a pancreatic stent, or if there is early dislodgement of a prophylactic stent, there may be role for immediate repeat ERCP with placement of a "salvage" stent. Data regarding such an approach are preliminary but encouraging.[38]

Post sphincterotomy hemorrhage

Bleeding observed during sphincterotomy is common but of itself does not represent an adverse outcome to the patient unless there is clinically significant blood loss or change in management. Some degree of bleeding, ranging from oozing to severe bleeding, is seen at the time of sphincterotomy in up to 10% to 30% of cases. Clinically significant hemorrhage is defined in the consensus criteria as clinical evidence of bleeding such as melena or hematemesis, with or without an associated fall in hemoglobin, or requirement for secondary intervention such as endoscopy or blood transfusion, and occurs in 0.1% to 2% of sphincterotomies.[4] As for post-polypectomy bleeding, clinical presentation of hemorrhage after sphincterotomy can be delayed up to 10 days after the procedure.[4]

Risk factors for hemorrhage after sphincterotomy

Risk factors for hemorrhage after sphincterotomy have been defined in a large multicenter cohort study, and include any degree of bleeding during the procedure, presence of any coagulopathy or thrombocytopenia (including hemodialysis-associated coagulation disorders), initiation of anticoagulant therapy within 3 days after the procedure, presence of active cholangitis, and relatively low case-volume on the part of the endoscopist (defined as performance of not more than one sphincterotomy per week).[4] Factors that do not appear to raise risk of bleeding include use of aspirin or NSAIDs, making a longer incision, or extending a previous sphincterotomy.[4] The effect of newer antiplatelet agents is unknown.

Methods to prevent and treat hemorrhage after sphincterotomy

In patients with risk factors such as coagulopathy, post-sphincterotomy hemorrhage can be avoided by finding sub-

stitute procedures such as balloon dilation of the biliary sphincter. Once sphincterotomy is undertaken, risk can be minimized by correction of any coagulopathies, withholding anticoagulant medications for as many as 3 days afterwards, and by use of meticulous endoscopic technique. Prophylactic injection of the sphincterotomy site with epinephrine in patients with coagulopathy has been suggested to possibly reduce risk of delayed bleeding but is of uncertain efficacy. Automated current delivery cautery systems have been shown to reduce risk of immediate bleeding but have not as yet been shown to decrease the incidence of clinically significant hemorrhage, although such complications are increasingly rare.

If significant hemorrhage occurs, either immediately during sphincterotomy, or delayed, it can generally be controlled with endoscopic therapy. First line treatment includes injection of dilute epinephrine which can be done by using a duodenoscope-compatible sclerotherapy needle, but injection can also be performed by impacting an ultratapered cannula or sphincterotome into the cut edges of the sphincterotomy, thereby delivering a submucosal injection. Balloon-tamponade using standard dilating balloons may allow temporary control of bleeding and improve visualization of the bleeding site. Thermal therapy such as bipolar coagulation or placement of clips can follow. Caution should be taken to avoid thermal injury or clip placement over the pancreatic sphincter, especially if the bleeding site is on the right-hand wall of the sphincterotomy incision. Very rarely, angiography or surgery is required for refractory bleeding.

Perforation

Perforation during ERCP may occur in several forms. First, the bowel wall can be perforated by the endoscope, usually resulting in intraperitoneal perforation; second, extension of a sphincterotomy incision beyond the intramural portion of the bile or pancreatic duct with retroperitoneal leakage, or third, at any location due to extramural passage or migration of guidewires or stents. Perforation is now reported in less than 1% of ERCP and sphincterotomies.[2-9] Risk factors for sphincterotomy perforation have been difficult to quantify due to the rarity of perforation. It is probable that bowel perforation is more common in patients with Billroth II or roux-en-Y anatomy, and sphincterotomy perforation more common after needle-knife precut techniques, and in patients with suspected sphincter of Oddi dysfunction, all situations where control and extent of the required incision is uncertain.

Treatment of post-ERCP perforation varies with the type and severity of the leak and clinical manifestations. Bowel wall perforations are generally treated surgically, although there are increasing applications of endoscopic clipping and use of dedicated endoscopic closure devices to treat larger per-

forations. Guidewire or stent-related perforations can usually be treated endoscopically by providing adequate ductal drainage beyond the leak site.[39-41] Sphincterotomy related perforation remains the most common and challenging to avoid and treat. Keys to avoiding perforation during sphincterotomy are to limit the length of cutting wire in contact with the tissue and to use stepwise incisions. If perforation is suspected during a sphincterotomy, careful fluoroscopy and injection of a small amount of contrast while pulling the catheter or papillotome through the incision over a guidewire will confirm or exclude extravasation and allow proactive treatment. Endoscopic clipping may be attempted in order to close a definite leak.[41] In most cases, a nasobiliary and/or nasopancreatic drain should be placed (depending on the sphincter cut). Another approach to biliary sphincterotomy is to place a fully covered removable self-expanding metallic stent to drain the bile duct and occlude the leak. Regardless of endoscopic therapy, the patient is generally treated with nasogastric suction, intravenous antibiotics, strict fasting, surgical consultation, and in-hospital observation. Once a perforation of any kind is suspected, a computed tomography scan of the abdomen should be obtained to assess for contrast leakage and any retroperitoneal or intraperitoneal air. If the leak is sizeable and continuing as suggested by ongoing contrast extravasation, or the patient's clinical condition deteriorates, prompt drainage via surgery or the percutaneous route is advisable. The importance of early recognition and endoscopic drainage of suspected perforations is supported by the observation that nearly all patients with immediate recognition and endoscopic drainage did well with conservative management, in comparison with poor outcomes including need for surgery and some mortality in patients with delayed recognition.[40]

Cholangitis and cholecystitis

Cholangitis (ascending bile duct infection) and cholecystitis (gallbladder infection) are potential complications or sequelae of ERCP and/or sphincterotomy, and of biliary stents, whether plastic or metallic. Risk factors for cholangitis after ERCP and sphincterotomy consist primarily of failed or incomplete biliary drainage[2-9] and use of combined percutaneous-endoscopic procedures.[4] Other risk factors may include jaundice especially if due to malignancy, and operator inexperience.[4] Several studies have shown that prophylactic antibiotics can reduce the rate of bacteremia, but few studies have shown a reduction in clinical sepsis following ERCP, and a meta-analysis concluded that there was no clinical benefit to routine administration of antibiotics.[42] Thus the principal recommendation regarding prevention and treatment of cholangitis is obtaining successful and complete biliary drainage. Once recognized, cholecystitis can be managed conservative-

ly, by surgery, by percutaneous drainage, and increasingly by transpapillary gallbladder drainage at ERCP.

CONCLUSIONS

Complications of ERCP are now well documented and recognized. Adequate selection of patients undergoing ERCP, skilled operators using novel techniques and prompt identification and treatment are key to successful prevention and management.

Conflicts of Interest

The authors have no financial conflicts of interest.

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