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REVIEW

Advances in endoscopic retrograde cholangiopancreatography cannulation

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Abstract

Endoscopic retrograde cholangiopancreatography is an important tool in the diagnosis and treatment of pancreatobiliary diseases. A critical step in this procedure is deep cannulation of the bile duct as failure of cannulation generally results in an aborted procedure and failed intervention. Expert endoscopists usually achieve a high rate of successful cannulation while those less experienced typically have a much lower rate and a greater incidence of complications. Prolonged attempts at cannulation can result in significant morbidity to patients, anxiety for endoscopists, unnecessary radiation exposure and inefficient patient care. Here we review the most common endoscopic techniques used to achieve selective biliary cannulation. Pharmacologic aids to cannulation are also discussed briefly in this review.

Key words: Endoscopic retrograde cholangiopancreatography; Cannulation techniques; Fatty meal; EUS guided cholangiography; Double-balloon endoscopy

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is an important tool in the diagnosis and treatment of pancreatobiliary diseases. It has been used in clinical practice for more than three decades[1]. A critical step in this procedure is cannulation of the common bile duct (CBD) and/or the pancreatic duct as failure of cannulation generally results in an aborted procedure and failed intervention. Cannulation and wire access is required for diagnostic and therapeutic interventions such as sphincterotomy, stone extraction and stent placement. Expert endoscopists usually achieve a high rate of successful cannulation while those less experienced typically have a much lower rate and a greater incidence of complications. With typical anatomy, the pancreatic duct enters the ampulla in a straight fashion, predisposing to pancreatic duct cannulation[2]. The pancreatic duct is more frequently cannulated first by trainees. A periampullary diverticulum, surgically altered anatomy, edema or strictures in the small bowel and blood or excessive fluid in the lumen all increase the procedural difficulty. Prolonged cannulation can result in significant morbidity to patients, anxiety for endoscopists, unnecessary radiation exposure and inefficient patient care[3].

Table 1 ERCP cannulation techniques in patients with normal anatomy

Technical methods
Standard techniques
Catheters
Papillotomes
Guide wires in conjunction with catheters and papillotomes
Placement of pancreatic stent or guide wire to facilitate cannulation
Precut techniques
Precut papillotomy (needle knife papillotomy)
Transpapillary pancreatic sphincterotomy (precut pancreatic sphincterotomy)
Suprapapillary puncture of the common bile duct (needle knife fistuolotomy)
Endoscopic ultrasound-guided cholangiography
Pharmacologic methods
Minor papilla
Intravenous injection of Secretin
Topical Methylene blue
Intraduodenal acid infusion
Major papilla
Intravenous injection of CCK
Topical nitroglycerin
Fatty meal before ERCP

ERCP: Endoscopic retrograde cholangiopancreatography; CCK: Cholecystokinin.

Various methods have been described to facilitate cannulation during ERCP for patients with normal anatomy. These can be divided into technical or pharmacological (Table 1). The cannulation techniques for patients with surgically altered anatomy are reviewed here briefly.

TECHNICAL METHODS TO FACILITATE CANNULATION

Commonly used techniques

The current most commonly used technique of cannulation is the wire-guided cannulation (Figure 1). In this technique, a dual lumen catheter is preloaded with a hydrophilic tipped guide wire and the catheter tip is inserted into the papilla in the direction of the bile duct. The guide wire is then manipulated while attempting to advance it into the bile duct. Fluoroscopy is used to verify its location once it has advanced several centimeters[4]. If the pancreatic duct has been cannulated, the wire is withdrawn. The sphincterotome is repositioned and the wire is advanced again under fluoroscopic guidance. If the guide wire cannulation fails, contrast can be injected to define the anatomy[4]. Another approach to selective biliary cannulation is to use a catheter with contrast injection without a guide wire. A cannula or papillotome is inserted into the papilla and contrast is injected into the bile duct to outline the biliary anatomy. If the common bile duct is injected, the sphincterotome is advanced deeper into the common bile duct. Alternatively, the catheter can be advanced into the bile ducts and fluoroscopy used to assess its direction.

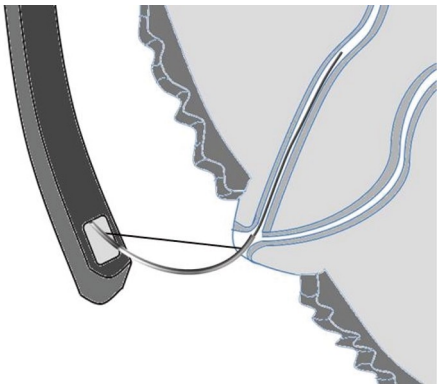

Figure 1 Papillotome and guide wire cannulation.

Contrast can then be injected to confirm that the CBD is cannulated. Cannulation using the cannula with contrast injection has a reported success rate of 60%-70%[5-6] while using a papillotome for contrast injection increases cannulation success rate up to 97%[5-7]. Repeated contrast injections into the pancreatic duct should be avoided because of increased risk of acute pancreatitis[8,9]. The guide wire technique for bile duct cannulation may lower the likelihood of post-ERCP pancreatitis (PEP) compared to the contrast injection methods by avoiding unintentional pancreatic duct injection and reducing the need for precut sphincterotomy[4,10,11]. However, a conflicting study found no difference in the incidence of PEP and suggested that successful cannulation with fewer attempts at the papilla is a more important factor than whether guide wire or contrast is routinely used first to achieve biliary cannulation[12]. It was also reported that using a hydrophilic guide wire achieves a higher rate of selective CBD cannulation compared to a standard ERCP catheter but the complication rates including PEP were similar in both groups[13]. A meta-analysis of the above randomized controlled trials[4,10-13] showed that the wire-guided technique increases the primary cannulation rate and reduces the risk of PEP compared with the standard contrast-injection method[14]. However this meta-analysis excluded the studies by Bailey *et al*[12] and Katsinelos *et al*[13] in calculating PEP outcomes because of their crossover design. This finding was confirmed by another meta-analysis study[15]. A third meta-analysis included the study by Bailey and used PEP outcomes before crossover[16]. This meta-analysis showed only a non-significant reduction in the rate of PEP with the use of wire guided cannulation. In summary, we recommend the use of the wire guided cannulation technique because of its proven superior cannulation rate and potential decrease in PEP rate.

The size of the ERCP cannulas varies but it is typically 5F to 7F with a tapered tip that accepts a 0.035-inch guide wire[17]. Some endoscopists may use ultra tapered (5F-4F-3F) tip catheters for cannulation of the biliary and pancreatic ducts which require smaller caliber guide wires (down to 0.018 inch). A smaller 3F cannula can be passed through the channel of a standard cannula or papillotome

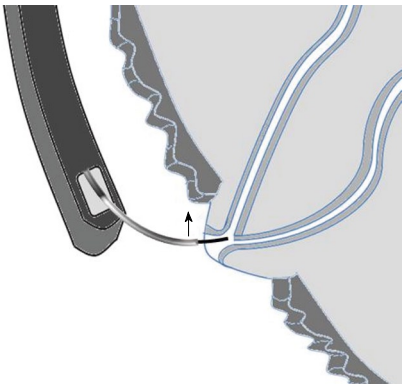

Figure 2 Needle knife precut papillotomy.

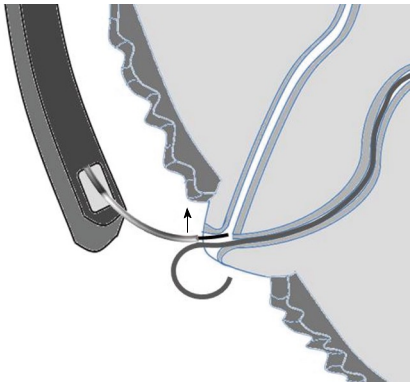

Figure 3 Precut papillotomy using needle knife over pancreatic stent.

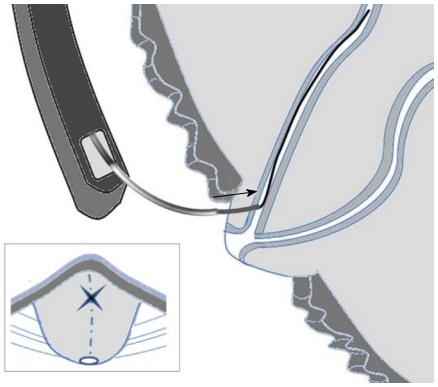

Figure 4 Suprapapillary puncture of the common bile duct (fistulotomy) followed by insertion of guide wire. Inset shows location of the puncture[31] (see text).

to convert to a smaller diameter[17]. In a randomized trial of 107 patients undergoing CBD cannulation, the 4F and 5F sphincterotomes were not significantly different in terms of success rates, number of attempts, time to cannulation or complications[18].

Precut techniques

Precut papillotomy using a needle knife[19] or a "precut" papillotome[20] is a method used to facilitate cannulation when the aforementioned standard methods fail (Figure 2). An electrocautery needle knife can be used to create an incision through the anterior wall of the major papilla. This technique is referred to as needle knife sphincterotomy, needle knife papillotomy or needle knife fistulotomy depending on the extent and location of the incision on the papilla[9,21-23]. The correct technique is important for success and for prevention of complications. Repeated longitudinal strokes with the needle knife should be shallow enough to prevent perforation and dynamic so that the needle does not adhere to the tissue[9]. The incision should be directed along the longitudinal course of the intraduodenal portion of the papilla. The length of the incision on the mucosal surface is usually 5-8 mm[9]. The needle knife assisted technique was shown to markedly improve the success rate of selective biliary cannulation without increasing the rate of complications[9,24]. However, the technique carries a risk of bleeding, perforation of the duodenal wall and acute pancreatitis if the procedure is performed by less experienced hands[25]. Placing a pancreatic stent prior to precut sphincterotomy may aid in defining the anatomy and protecting the pancreatic sphincter from injury (see below, Figure 3). It has been debated whether the complications related to precut papillotomy are due to the precut itself or to the prior prolonged attempts at cannulation. A recent meta-analysis of six randomized controlled trials (total 966 subjects) compared early precut implementation with persistent attempts by the standard cannulation approach[26]. Overall cannulation rates were 90% in both groups. PEP developed in 2.5% of patients randomized to the early precut groups and in 5.3% of patients from the persistent cannulation attempts groups. The overall complication rates including pancreatitis, bleeding, cholangitis and perforation rates were 5.0% in the early precut groups and 6.3% in the persistent cannulation attempts groups. The authors concluded that in experienced hands the early implementation of precut and persistent cannulation attempts have similar overall cannulation rates and early precut implementation reduces PEP risk but not the overall complication rate[26]. In another analysis, the number of attempts at cannulating the papilla was independently associated with PEP and the risk increased with increasing number of attempts[27,28]. Needle knife sphincterotomy was not an independent predictor of PEP[28]. It should be emphasized that precut sphincterotomy, which is generally followed by conventional sphincterotomy, should be performed only by experienced endoscopists as complication rates are high when performed by inexperienced endoscopists performing one sphincterotomy per week or less[29].

Suprapapillary puncture of the CBD (also referred to as needle knife fistulotomy) was described for diagnostic ERCP as early as 1978[30] and recently reported in more detail for therapeutic procedures[31] (Figure 4). This technique uses a specially designed polyethylene catheter (Artifon Catheter) with an 18-gauge needle and a flexible metallic sheath at the distal end which allows puncture of the bile duct and insertion of a guide wire. Suprapapillary puncture of the bile duct is performed by

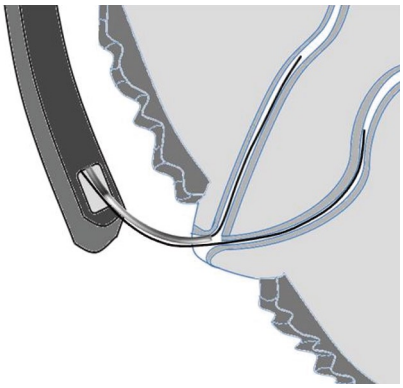

Figure 5 Pancreatic guide wire to aid cannulation.

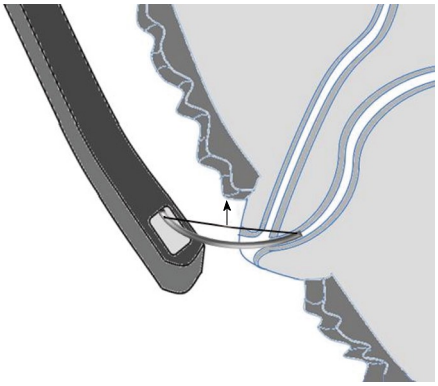

Figure 6 Transpapillary pancreatic sphincterotomy.

using the Artifon Catheter in the direction of the CBD at a point corresponding to the proximal third of the line between the transversal fold and the papillary ostium. This is followed by insertion of a guide wire and slow injection of contrast to obtain a cholangiogram. In the first pilot study, suprapapillary puncture was successful in 25 out of 28 patients. None of the patients developed post-ERCP pancreatitis. However, there was a higher complication rate, including 2 perforations, 2 minor bleeds and 1 submucosal injection[31]. A subsequent study reported the efficacy and safety of needle knife fistulotomy in a retrospective analysis of 352 patients after unsuccessful standard guide wire cannulation[32]. The successful cannulation rate in these patients was 90%. The complication rate was significantly higher for the patients who underwent fistulotomy than for those who did not (4.8% *vs* 2.1%) which was mainly related to higher rate of mild bleeding in the fistulotomy group. There was no significant difference in pancreatitis or perforation rates. This technique appears promising and there is growing evidence for it but more studies are needed before it can be recommended for difficult cannulations.

Pancreatic techniques

Use of pancreatic techniques is a new and useful method to improve biliary cannulation. Pancreatic guide wire placement (P-GW) has been shown to be effective in increasing the rate of selective biliary cannulation[33-36]. It involves inserting a guide wire into the pancreatic duct from a cannula after pancreatic duct cholangiography (Figure 5). This stabilizes the ampulla of Vater and straightens the terminal common bile duct. After withdrawal of the cannula, the guide wire is left in the pancreatic duct and is monitored by fluoroscopy[35]. The cannula is then reinserted next to the guide wire and cannulation of the bile duct is attempted[37]. This method can be followed by placement of a small caliber (3F or 4F) pancreatic stent for prophylaxis of post-ERCP pancreatitis. In one study of 113 patients, selective bile duct cannulation with P-GW was achieved in 73% of patients who were difficult to cannulate. Post-ERCP pancreatitis occurred in 12% of patients. The rate of pancreatitis was lower in patients who underwent prophylactic pancreatic stenting (4.7%) compared to those who did not (22%)[36]. In a later study of 107 patients undergoing ERCP, selective biliary cannulation was difficult in 53 patients (unsuccessful after 10 min) and these patients were randomly assigned to either preinsertion of a guide wire into the pancreatic duct or persistent attempts with a conventional catheter[35]. In the pancreatic duct guide wire group (n = 27), the success rate was significantly higher than in the conventional group (93% *vs* 58%). Pancreatic duct stenting was not used in this study but there were no cases of post ERCP pancreatitis in either group. The pancreatic duct guide wire group had more hyperamylasemia compared to the conventional group but no patients had abdominal pain[35]. A more recent randomized controlled trial compared the pancreatic duct guide wire technique and standard cannulation technique in 188 patients with difficult CBD cannulation[38]. No significant differences were observed in success rates, cannulation times or number of attempts. A higher rate of post-ERCP pancreatitis was seen in the pancreatic duct guide wire group although this was not statistically significant[38]. We recommend the use of the pancreatic guide wire technique in difficult cannulation cases as it is the most efficient and safe method in our experience.

Transpapillary pancreatic sphincterotomy, also called transpancreatic sphincterotomy or pancreatic precut sphincterotomy (PPS), is also used to achieve selective biliary cannulation (Figure 6). This is performed by deep cannulation of the main pancreatic duct and orienting the sphincterotome in the direction of the bile duct at 11 o'clock and performing the pancreatic sphincterotomy with the aim of exposing the bile duct orifice or the bile duct itself[39]. In a prospective study evaluating the use of PPS in patients who failed standard cannulation (n = 116), immediate biliary access was achieved after PPS in 99 cases (85%). Pancreatic stents (7F) were placed in 29 patients (25%) at the discretion of the endoscopist if pancreatic drainage was considered inadequate. Complications occurred in 14 patients (12%): 3 (2.6%) postsphincterotomy bleeding, 9 (8%) pancreatitis (8 mild, 1 moderate) and 2 (1.7%) retroperitoneal perforations managed conservatively[39]. A retrospective analysis comparing PPS with needle knife sphincterotomy showed

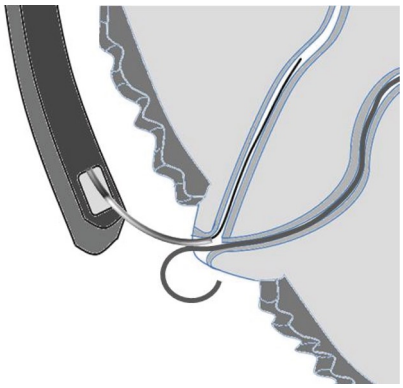

Figure 7 Pancreatic stent and guide wire cannulation.

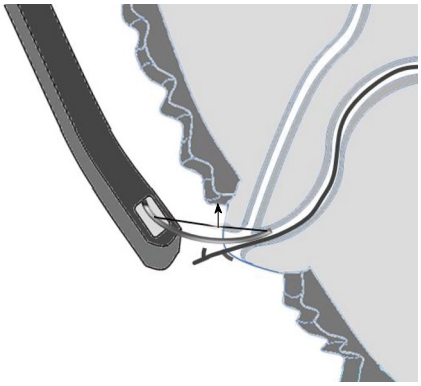

Figure 8 Transpancreatic sphincterotomy over pancreatic stent.

no significant difference in the success rates between the two techniques (90.0% *vs* 90.8% respectively)[40]. The overall complication rate and acute pancreatitis were also similar in both groups.

Another technique involves placing a pancreatic stent to facilitate biliary cannulation as this stent can deflect a guide wire or a catheter into the bile duct (Figure 7). If this fails, the pancreatic stent can serve as a guide and aid in performing a precut sphincterotomy as described above to gain access to the biliary duct. This sphincterotomy can be performed by either a needle-knife to make an incision from the pancreatic duct stent toward the biliary orifice (Figure 3) or a standard sphincterotome is inserted into the pancreatic duct above the pancreatic stent and a transpancreatic sphincterotomy is performed toward the biliary orifice (Figure 8)[40]. In a retrospective study of ERCPs with difficult cannulation, successful biliary access was achieved in 38 out of 39 patients (97.4%) where pancreatic duct stenting was used to aid cannulation: thirty-five patients had successful biliary cannulation at the initial attempt (89.7%) with an additional three patients having successful cannulation on the second attempt at a later time. In order to achieve cannulation, 23 patients (59%) required a precut sphincterotomy over the pancreatic duct stent. In 16 patients (41%), no precut sphincterotomy was required to gain access to the bile duct[41]. Post ERCP pancreatitis occurred in two patients (5%). Pancreatic duct stent placement was also shown to facilitate difficult biliary cannulation caused by periampullary diverticula where ampullary anatomy is distorted and can be straightened by the pancreatic stent[42].

ENDOSCOPIC ULTRASONAGRAPHY GUIDED CHOLANGIOGRAPHY

In recent years, interventional endoscopic ultrasound-guided cholangiography (IEUC) has been reported as an alternative to surgery or percutaneous transhepatic cholangiography (PTC) if ERCP is unsuccessful[43-46]. The technique involves puncturing the bile ducts under real time ultrasound control from the intestinal lumen. This is followed by inserting a wire through the needle and placing a stent through the wall of the stomach/duodenum. Using another "rendezvous" technique, the guide wire is manipulated through the stricture and the papilla and then captured with a standard duodenoscope and a biliary drainage is performed through the papilla in a regular fashion[45]. A recent study describing a single centre experience with IEUC was published: 49 patients underwent IEUC after failed ERCP. 35 had biliary obstruction due to malignancy and 14 had a benign etiology. The overall success rate of IEUC was 84 % with an overall complication rate of 16 %[44]. IEUC has possible advantages over PTC in patient comfort, lower morbidity and offers a possible alternative to patients with obstructive jaundice in whom ERCP has failed. However these advantages have not yet been proven in randomized trials.

PHARMACOLOGIC METHODS TO FACILITATE CANNULATION

In addition to the technical methods to increase the rate of successful cannulation, pharmacologic interventions have been used to facilitate cannulation at ERCP. The strongest data is for secretin in minor papilla cannulation. Secretin is a gastrointestinal polypeptide that is secreted from mucosal cells in the proximal intestine in response to luminal acidification. Circulating secretin acts via specific G-protein-coupled receptors to stimulate the secretion of water and bicarbonate from pancreatic duct cells[47]. Identification of the minor papilla may be facilitated by increasing the production of pancreatic secretions. This is particularly important in pancreas divisum where identification of the minor papilla, cannulation and contrast injection can be used to confirm dominant dorsal pancreatic duct drainage. In a randomized controlled trial in 29 patients with previously failed minor papilla cannulation, secretin improved cannulation rate from 7.7% in the placebo group to 81% in the secretin group; crossover to secretin allowed cannulation in a total of 89% of patients[47].

Methylene blue has also been used to aid in identification of the minor papilla and facilitate cannulation.

Techniques include methylene blue spraying over the duodenal mucosa in the vicinity of the minor papilla or injection of contrast medium containing methylene blue into the ventral pancreatic duct though the major papilla in cases of incomplete pancreas divisum. This was shown to be helpful in identification of an inconspicuous minor papilla[48].

Intraduodenal acid infusion (IDAI) is a physiological method to induce secretin release in the human body[49]. We examined the effect of intraduodenal hydrochloric acid infusion on minor papilla cannulation in a small pilot study[50]. IDAI improved cannulation rate from 14% in the placebo group to 80% in the IDAI group[50]. IDAI can potentially be a cost-effective method of increasing minor papilla cannulation rate.

The Sphincter of Oddi is a muscular valve that connects the bile duct and pancreatic duct within the duodenum. Cholecystokinin (CCK), a hormone that stimulates gallbladder contraction and relaxation of the sphincter of Oddi, may increase cannulation rate. Sincalide (Kinevac), a synthetic carboxyl-terminal octapeptide CCK agonist, was helpful in facilitating cannulation in a prospective nonrandomized, single centre study[51]. In this study sincalide was used in 19 patients with unsuccessful initial cannulation using the standard catheter technique. Successful cannulation was obtained in 12 patients and cannulation rate increased from 80.7% (88/109 patients) to 91.7% (100/109 patients) without the need for needle knife papillotomy or guide wire to aid cannulation. However, another randomized controlled trial showed that intravenous administration of CCK during ERCP had no effect on cannulation[52]. Topical nitroglycerin was also shown to relax the sphincter of Oddi but there was no effect on rates of selective bile duct cannulation[53,54].

A LIQUID FATTY MEAL BEFORE ERCP

Fats are the most potent natural stimulator of bile secretion and the relaxation of the sphincter of Oddi. Therefore, we postulated that ingestion of a fatty meal would improve the cannulation rate during ERCP. A randomized double-blind study in 84 patients examined the effect of a liquid fatty meal on deep CBD cannulation during ERCP[55]. In the study group, each patient had a liquid fatty meal orally about 1 h before the procedure. In the control group, each patient had the same volume of a non-fat meal. There was no difference in the success rates of cannulation between the study and the control group (88% *vs* 85% respectively). However, compared with the non-fat meal group, the orifice of the CBD/pancreatic duct was much more easily identified in the fatty meal group. The cannulation and the fluoroscopy times were significantly shorter in the fatty meal group. Ingestion of a fatty meal may provide a simple and less expensive method of facilitating cannulation and decreasing fluoroscopy times. However further larger studies are needed.

CANNULATION IN PATIENTS WITH SURGICALLY ALTERED ANATOMY

Although the cannulation success rate is greater than 90% in patients with normal anatomy[17], ERCP in patients with surgically altered anatomy, especially with a Roux-en Y anastomosis, can be more challenging: firstly, the endoscopic approach to the blind end, the afferent loop and the choledochojejunostomy site is difficult using a conventional endoscope because of the relatively long distance from the gastrojejunal anastomosis site and the unusual anatomical features after surgery. Secondly, even if the scope reach the papilla of Vater or the site of choledochojejunostomy, selective cannulation of the pancreatic and/or biliary duct is still more difficult than usual. Therefore, patients with surgically altered anatomy have been considered unsuitable for ERCP in the past despite of reported successful ERCP using colonoscopes in such patients[56].

However, the balloon enteroscopy, a recently developed technology, can be useful for performing ERCP in patients with such surgically altered anatomy. In particular, double- or "short" double-balloon endoscopy has been reported several times in this population of patients[57-62] and single-balloon endoscopy has also been reported[63-65]. The successful rates in those reports are above 60% for patients with a Roux-en Y anastomosis and up to 100% for patients with Billroth-Ⅱ anastomosis[57-65].

CONCLUSION

Since ERCP was first introduced in 1968[1], the techniques used to achieve successful deep bile duct cannulation have expanded significantly. Endoscopists should be familiar with the different techniques and equipment used to maximize the rates of successful cannulation and decrease the rate of complications. The addition of steps to decrease the rate of post ERCP pancreatitis such as placing a pancreatic stent should be considered in high risk patients. IEUC is evolving as an alternative to PTC when ERCP fails and is increasingly performed in specialized tertiary care centers. Intravenous injection of secretin can facilitate minor papilla cannulation. Intraduodenal acid infusion is a promising method in increasing minor papilla cannulation. Using single-, double- or "short" double-balloon enteroscopy has achieved a high successful rate of cannulation in patients with surgically altered anatomy.

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