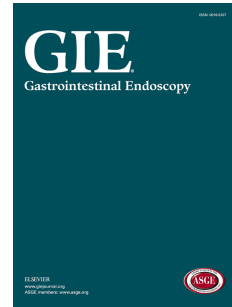


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International Consensus Recommendations for Difficult Biliary Access

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International Consensus Recommendations for Difficult Biliary

Access

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4. Peter V Draganov: critical revision of the manuscript for important intellectual content.

ERCP is the standard procedure for endoscopic biliary therapy. Endoscopic approach to the ampulla followed by selective deep biliary cannulation is the first step before further therapy. Difficult biliary access can occur during endoscope intubation or when attempting selective biliary cannulation in normal or surgically altered anatomy. Difficult cannulation increases the risk of post-ERCP adverse events, particularly post-ERCP pancreatitis (PEP) and perforation. In normal anatomy, about 11% of therapeutic ERCPs may be considered difficult biliary cannulation.¹ Biliary access in patients with surgically altered anatomy, such as Billroth II or Roux-en-Y anastomosis, is considered difficult as special instruments and maneuvers are often needed.

Various methods are used to overcome difficult biliary access, including advanced ERCP-based techniques using precut or double guidewires (DGW), specialized instruments like echoendoscopes or device-assisted enteroscopy, or percutaneous approach. These techniques/procedures are more complex and carry significant risks, requiring specific training. This consensus aims to develop an evidence-based framework for biliary endoscopists to tackle difficult biliary access.

Methods

Based on literature search through MEDLINE, Cochrane Library, and Embase, a planning panel (H.P.W., H.I., R.R., W.C.L., and P.A.) drafted statements on 3 areas: difficult biliary access in normal anatomy, difficult biliary access in surgically altered anatomy, and EUS- or percutaneous-guided biliary access. The first draft was distributed electronically to the panel members who evaluated each statement (Table 1). A face-to-face meeting was conducted in July 2015 in Taipei, Taiwan, to review and discuss the evidence and revise the statements. The members then independently voted on each statement via an electronic system. Consensus was considered to be achieved when 80% or more of voting members indicated “accept completely” or “accept with some reservation.” A statement was rejected when 80% or more of voting members “reject completely” or “reject with some reservation.” Finally, 13 statements achieved consensus. The level of evidence and grade of recommendation were rated with the evidence leveling system² (Table 1).

Consensus statements

1. Difficult biliary access is defined as the inability to achieve selective biliary cannulation by standard ERCP techniques within 10 minutes or up to 5 cannulation attempts, or failure of access to the major papilla.

Evidence level: II-A

Recommendation grade: B

Voting on recommendation: A, 56%; B, 44%; C, 0%; D, 0%; E, 0%

Guidewire-assisted cannulation is considered the standard technique for biliary access.^{3,4} Increased cannulation time, number of cannulation attempts, and number of pancreatic duct injections/cannulations have been associated with increased risk of PEP.⁵⁻⁷ Therefore, an upper limit of cannulation time and number of attempts should be set to limit PEP risk. A cannulation attempt has been defined as an intentional continuous contact with the papilla.⁷ The definition of difficult cannulation varied widely among previous studies; Table 2 summarizes prospective randomized controlled trials (RCTs) that reported the definition of difficult cannulation and the number of eligible patients and those with difficult cannulation.⁸⁻¹⁹ A prospective study showed that 97.4% of successful primary cannulations were achieved within 5 attempts, and the risk of PEP jumped from 6.1% to 11.9% with more attempts.⁷ The risk of PEP also significantly increased when cannulation time exceeded 10 minutes [odds ratio (OR) 1.76; 95% CI, 1.13-2.74].²⁰ Alternatively, situations such as gastric outlet obstruction prevent access to the papilla and subsequent biliary cannulation.

The consensus panel defined difficult cannulation as inability to achieve selective biliary cannulation by standard ERCP technique within 10 minutes or 5 attempts, or failure of access to the major papilla.

The association between difficult cannulation and higher PEP risk supports for tracking cannulation time/attempt and rates of success and adverse events; it also underscores the importance of achieving competence during ERCP training and the issue of low-volume ERCP providers. An 80% success rate for biliary cannulation has been proposed as the goal for ERCP training,²¹ and one study suggested that 350 to 400 supervised procedures are required to achieve an 80% success rate in patients with native papilla²². It is reasonable to project that even more cases are needed to achieve competence in advanced procedures to tackle difficult cannulation (e.g. precut, pancreatic stent placement, EUS-guided biliary access, etc); future research is needed to better define the minimum volume/outcome requirements for these advanced procedures. However, a survey in the United States found that graduating fellows performed only a median of 140 ERCPs during training and 64% of those fellows did not achieve the recommended competency, but 91% planned to perform unsupervised ERCP after graduation.²³ Low endoscopist ERCP volume (<25 per year) has been shown to be associated with a higher failure rate for ERCP and a greater need for

post-ERCP hospitalization.²⁴ Further efforts to tackle inadequate ERCP training and low provider volume are needed to ensure ERCP quality/safety.

2. When endoscopic biliary access is difficult, alternative techniques may be required.

These require specific expertise, and are potentially associated with a higher risk of adverse events.

Evidence level: III

Recommendation grade: C

Voting on recommendation: A, 94%; B, 0%; C, 6%; D, 0%; E, 0%

When encountering difficult cannulation, one should avoid persisting with the same technique to reduce the risk of further injury to the papilla. One option is to repeat ERCP in next 24 to 48 hours, or referral to an expert center.²⁰ If a regular cannula is initially used, an alternative method is to change to a sphincterotome or a bendable-tip catheter.^{25, 26} Other alternative methods including DGW or precut technique, and EUS-guided or percutaneous transhepatic biliary access may be applied if the expertise is available. The use of these alternatives may be associated with a higher risk of adverse events; however, it is difficult to determine whether the higher risk is due to difficult cannulation or to the alternative procedures per se.^{15, 27}

These alternative methods are further discussed in the following respective statements.

3. Prophylactic measures against PEP, such as rectal NSAIDs and/or pancreatic stent placement, are recommended when standard biliary cannulation fails.

Evidence level: I-B

Recommendation grade: A

Voting on recommendation: A, 94%; B, 0%; C, 6%; D, 0%; E, 0%

Difficult cannulation is considered an independent risk factor for PEP.²⁰ A prospective study demonstrated that PEP risk was significantly higher when standard cannulation failed (11.5%), compared with successful cannulation (2.8%).⁷

Techniques such as precut and DGW technique that are used after failed standard cannulation may also increase PEP risk. The OR for precut from a recent meta-analysis was 2.30 (95% CI, 1.85-2.85),²⁸ and DGW technique appeared to increase PEP risk in an RCT.¹⁶

A meta-analysis including 2,133 patients from 7 RCTs showed that rectal diclofenac or indomethacin reduced the rates of overall PEP (RR 0.44; 95% CI,

0.34-0.57) and of moderate-to-severe PEP (RR 0.37; 95% CI, 0.21-0.63).²⁹ Rectal NSAIDs should be administered early when encountering difficult cannulation, preferably before moving to alternative techniques such as precut and DGW technique. Temporary placement of a pancreatic stent (3F or 5F) to facilitate pancreatic drainage for 5 to 10 days has also been shown to reduce PEP risk^{20, 30, 31}, and is recommended in patients at high risk of PEP²⁰. An RCT in patients with difficult cannulation found that pancreatic stenting significantly reduced the rate of PEP from 29.4% in the no-stent group to 12% in the stented group (OR 0.33; 95% CI, 0.12-0.93).¹⁸ Pancreatic stenting also reduced PEP after DGW technique for difficult cannulation in an RCT; the rate of PEP was 23% in the no-stent group versus 2.9% in the stented group (RR 0.13; 95% CI, 0.02-0.95).¹⁹ Leaving the stent for 7 to 10 days after precut papillotomy over a pancreatic stent significantly reduced the risk and severity of PEP, compared with immediate removal of the stent; the rates of PEP in stent-in-place and stent-removed groups were 4.3% versus 21.3% ($p < 0.05$), and those of moderate to severe PEP were 0% versus 12.8% ($p < 0.05$), respectively.³²

Whether rectal NSAIDs can obviate the need for pancreatic stenting in patients at high risk of PEP is not clear and warrants further study.

4. Precut or pancreatic guidewire-assisted techniques are appropriate when biliary cannulation is difficult.

Evidence level: I-B

Recommendation grade: A

Voting on recommendation: A, 94%; B, 6%; C, 0%; D, 0%; E, 0%

When repeated standard cannulation attempts fail to access the bile and pancreatic duct, precut involves deroofing the ampullary mucosa to expose biliary lumen and is the preferred next-line method.¹ A meta-analysis showed that precut had higher success rate but similar PEP rate compared with persistent cannulation attempts.³³ The rates of success and PEP for precut and persistent cannulation were 86.7% versus 66.7% [relative risk (RR) 1.32; 95% CI, 1.04-1.68] and 6.1% versus 9.1% (RR 0.62; 95% CI, 0.28-1.36), respectively.³³ Another meta-analysis showed that the ORs (95% CI) of PEP for immediate precut and precut within 5 or within 10 minutes of standard cannulation were 0.73 (95% CI, 0.23-2.33), 0.85 (95% CI, 0.40-1.80), and 0.55 (95% CI, 0.29-1.03), respectively.³⁴ In terms of PEP, 10 minutes appears to be the optimum time allowed for standard cannulation technique before considering precut. Notably, precut requires expertise and is associated with a higher

risk of adverse events, particularly perforation and bleeding, when performed by low-volume endoscopists.³⁵ Previous studies suggested that 200 and 100 precuts are required to achieve high success and low bleeding rates, respectively.^{27, 36}

If guidewire inadvertently enters the pancreatic duct during standard biliary cannulation, DGW technique or cannulation over a pancreatic duct stent can be used as the next-line modality before precut. DGW technique is performed by placing the first guidewire in the pancreatic duct followed by selective biliary cannulation with a second guidewire. The first guidewire not only acts as a landmark but also facilitates cannulation by straightening the duodenal portion of the common channel. There were 3 RCTs evaluating DGW technique in difficult cannulation.^{12, 14, 16} The pooled success rate of DGW was 58% (range, 47%-79%),^{8, 12, 14, 16} the success rate was comparable with precut^{16, 36} and was similar to attempts at persistent cannulation¹². The pooled PEP rate of DGW was 22% (range, 17%-38%),^{12, 14, 16} the rate of PEP was comparable with that of persistent cannulation^{8, 12} or precut using the fistulotomy technique¹⁴, but was higher than that of precut using the transpancreatic technique¹⁶. A complementary technique to DGW with comparable efficacy and safety is to place a pancreatic stent after inadvertent access to the pancreatic duct, followed by biliary cannulation over the stent.¹⁷ If DGW technique or cannulation over a pancreatic duct

stent still fails to achieve biliary access, precut over the pancreatic stent or transpancreatic septotomy can be used as the next-line modality.

5. All precut techniques achieve a high biliary access rate. Needle-knife fistulotomy may be associated with fewer adverse events.

Evidence level: I-B

Recommendation grade: A

Voting on recommendation: A, 56%; B, 38%; C, 6%; D, 0%; E, 0%

Precut techniques include needle-knife papillotomy (NKP),³⁷ needle-knife fistulotomy (NKF),³⁸ and transpancreatic septotomy (TPS)³⁹. NKP starts cutting from the papillary orifice toward the 11 o'clock direction.³⁷ By contrast, NKF³⁸ starts at 3 to 5 mm above the papillary orifice in the same direction as NKP; therefore, NKF may be easier to perform when the intraduodenal segment of the bile duct is long or prominent. In TPS, after superficial or deep cannulation of the pancreatic duct is achieved, a sphincterotome is inserted into the pancreatic duct and cuts the septum between bile and pancreatic ducts toward the 11 o'clock direction.³⁹

For NKF, NKP, and TPS, the initial success rates were 75.7% to 100%, 73.4% to 84.2%, and 95.8% to 100%, respectively^{38, 40-42} (Table 3). An RCT demonstrated comparable success rate between NKF and NKP after failed standard cannulation; the primary success rates were 75.7% and 73.4%, and the cumulative success rates after repeat cannulation at 48 to 72 hours were 90.5% and 88.6%, respectively.³⁸ Two RCTs showed that TPS had higher primary success rate than NKP (100% vs 77%, $p=0.01$ ⁴³ and 95.9% vs 84.2%, $p = 0.018$ ⁴², respectively).

Unlike NKP and TPS, NKF does not involve the pancreatic orifice. An RCT demonstrated that NKF had a lower risk of PEP than NKP (0% vs 7.6%, $p < 0.05$).³⁸ Subgroup analysis of a meta-analysis revealed that NKF significantly decreased the risk of PEP (OR 0.27; 95% CI, 0.09-0.82) with an absolute risk reduction of 5% (95% CI, 1%-10%), whereas NKP did not (OR 0.89; 95% CI, 0.41-1.92).³⁴ In a retrospective study NKF had lower PEP rate than the others; the PEP rates of NKF, NKP, and TPS were 2.6%, 21%, and 22.4%, respectively ($p = 0.001$).⁴⁰ Therefore, if the pancreatic duct can be cannulated, a pancreatic stent should be placed before NKP to guide the precut and to reduce PEP risk; a retrospective study showed that precutting over a pancreatic stent achieved a higher success rate and a lower adverse event rate.^{20, 44} The stent should be left in place after ERCP; in an RCT the risk of

PEP with stent in place versus stent removal after precut over the stent was 4.3% versus 21.3% ($p=0.027$).³² It is also reasonable to leave a pancreatic stent after TPS for prophylaxis of PEP.²⁰ There was no significant difference in the rates of bleeding and perforation among the 3 techniques (Table 3).^{38, 40-42}

Collectively, all precut techniques performed in the setting of difficult cannulation had success rates of 70% to 90% with similar bleeding and perforation rates. NKF had lower PEP rate than other precut techniques.

6. In patients with Billroth II anatomy, both side-viewing and conventional forward-viewing endoscopes may achieve comparable biliary access. The use of side-viewing endoscopes may be associated with a higher risk of perforation.

Evidence level: I-B

Recommendation grade: A

Voting on recommendation: A, 62.5%; B, 37.5%; C, 0%; D, 0%; E, 0%

In Billroth II anatomy, the papilla can be accessed by either side-viewing or forward-viewing endoscopes because the afferent limb is relatively short. The main

challenge is duodenal intubation with side-viewing duodenoscopes, and cannulation without an elevator with forward-viewing endoscopes. A longitudinal case series that included 713 patients with Billroth II anatomy undergoing ERCP showed that the success rates of duodenal intubation with side-viewing endoscopes was 84%, with an overall perforation rate of 1.8%.⁴⁵ The overall failure rate decreased from 54% in the first 5 years to 12% to 22% in the subsequent 25 years.⁴⁵ A small RCT comparing side-viewing and forward-viewing endoscopes in 45 patients with Billroth-II anatomy showed no significant difference in the overall success rate (68% and 87%, respectively).⁴⁶ The main reasons for failure with side-viewing endoscopes were jejunal perforation (18%), failure to reach the papilla (9%), and severe abdominal pain (4.5%). Once the papilla could be reached, side-viewing endoscopes achieved cannulation in all patients. This study raises concerns about using side-viewing endoscopes as it carried a higher risk of jejunal perforation compared with forward-viewing endoscopes (18% vs 0%, $p < 0.05$).⁴⁶ However, the rate of jejunal perforation of this study was higher than those of other reports (0.7%-10.2%).^{45, 47} The higher perforation risk might be attributed to the longer tip of the earlier duodenoscopes, and this risk may have become lower with the evolution of endoscope design.⁴⁵ In addition, device-assisted enteroscopy using short single-balloon or

double-balloon enteroscopes can also be used in Billroth II anatomy with a high success rate.⁴⁸

7. In surgically altered anatomy, particularly Roux-en-Y anastomosis, device-assisted enteroscopy may facilitate access to the papilla or bilio-enteric anastomosis.

Evidence level: I-A

Recommendation grade: A

Voting on recommendation: A, 81%; B, 19%; C, 0%; D, 0%; E, 0%

Compared with Billroth II anatomy, Whipple's procedure or Roux-en-Y anastomosis poses greater challenges in endoscope intubation and biliary cannulation.^{49, 50} Identifying the afferent limb and reaching the biliary orifice can be challenging and potentially complicated by mucosal tears or even perforation. Unfavorable angles may render cannulation difficult.

Device-assisted enteroscopy represents a breakthrough in biliary access for patients with surgically altered anatomy. Shah et al reported a large multicenter U.S. series using single-balloon, double-balloon, and rotational overtube-assisted

enteroscopy for ERCP in patients with surgically altered anatomy.⁵¹ The largest patient subsets were post Roux-en-Y gastric bypass and Whipple procedure (intact papilla) followed by non-transplant Roux-en-Y hepaticojejunostomy. Overall, ERCP was successful in 63% of patients. The success rate increased to 88% when the biliary orifice was reached. Enteroscopy success was comparable among the 3 techniques.⁵¹ In a more recent series, double-balloon enteroscopy-assisted ERCP was successful in 95% of patients with prior Roux-en-Y.⁵² Studies involving single balloon endoscopy-ERCP in patients with Roux-en-Y gastric bypass, hepaticojejunostomy or Whipple procedure (15 trials, 461 patients) were assessed in a recent meta-analysis. Overall, enteroscopy success was 80.9% and procedural success was 61.7%, with adverse events occurring in 6.5% of patients.⁵³

Besides device-assisted enteroscopy, direct puncture into bile duct under EUS guidance provides biliary access without the need to access the papilla or bilio-enteric anastomosis (see statement 8). Alternatively, ERCP can be performed in an antegrade fashion through a transcutaneous gastrostomy into the remnant stomach using a duodenoscope. Gastrostomy can be created either by laparoscopy (laparoscopy-assisted ERCP)⁵⁴ or by first using EUS to puncture and insufflate the remnant stomach followed by direct percutaneous puncture^{55, 56}. Case series showed a

success rate exceeding 90% with this approach,⁵⁴⁻⁵⁶ supporting that transgastric ERCP is a valuable addition to biliary endoscopists' armamentarium for managing patients with surgically altered anatomy.

8. EUS-guided biliary access is a viable method for drainage of an obstructed system when cannulation via the papilla is unsuccessful by conventional methods, or if the papilla is not accessible.

Evidence level: I-A

Recommendation grade: A

Voting on recommendation: A, 81%; B, 19%; C, 0%; D, 0%; E, 0%

Endoscopic ultrasound-guided biliary access has emerged as a viable alternative when ERCP fails. After EUS-guided puncture of intrahepatic or extrahepatic bile ducts from the stomach or duodenum, subsequent biliary therapy can be performed either by transluminal or antegrade approaches, or by rendezvous technique. As the access site is removed from the papilla, this technique can be applied in patients with duodenal stenosis or surgically altered anatomy. Two recent meta-analyses showed

that endoscopic ultrasound-guided biliary drainage (EUS-BD) can achieve success rates of 90% with adverse event rates around 20%.^{57, 58}

9. Where both EUS-guided biliary access routes are possible, the transduodenal approach when appropriate, appears to be safer than transgastric access.

Evidence level: II-B

Recommendation grade: B

Voting on recommendation: A, 81%; B, 19%; C, 0%; D, 0%; E, 0%

Transgastric and transduodenal routes can be used for EUS-guided biliary access.^{59, 60} The success and adverse event rates of the 2 access routes are summarized in Table 4. A review comparing these 2 access routes in published studies with 25 or more cases, including 211 transduodenal and 138 transhepatic cases, found that the adverse event rate was higher with the transhepatic route (21.7% vs 9.9%, $p < 0.01$).⁶¹ A recent RCT that compared EUS-guided hepaticogastrostomy (EUS-HGS) and EUS-guided choledochoduodenostomy (EUS-CDS) in patients with malignant distal biliary obstruction found that the 2 approaches were comparable in terms of

technical success (96% vs 91% respectively, $p=0.609$), quality of life scores, and survival ($p=0.603$). EUS-HGS seemed to have a higher clinical success rate (91% vs 77%, $p=0.234$) and a higher immediate adverse event rate (20% vs 12.5%, $p=0.702$) than EUS-CDS, but the differences were not statistically significant.⁶² A recent meta-analysis showed that the transduodenal route was safer than the transgastric route (pooled OR for adverse events 0.4; 95% CI, 0.18-0.87).⁵⁸ In another meta-analysis, the pooled OR for adverse events for transduodenal versus transgastric route was 0.61 (95% CI, 0.36-1.03).⁵⁷ The higher adverse event rate of HGS, most notably bile leak, may be attributed to the longer distance between the puncture site and the bile duct through liver parenchyma. Furthermore, stent is placed in the common bile duct with CDS but in the intrahepatic bile duct with HGS; segmental cholangitis from obstruction of side branches may occur with HGS.⁶³

10. EUS-guided biliary drainage may be performed with high success and an acceptable adverse event rate, in experienced hands.

Evidence level: I-A

Recommendation grade: A

Voting on recommendation: A, 77%; B, 23%; C, 0%; D, 0%; E, 0%

A retrospective analysis comparing ERCP and EUS-BD after failed ERCP for biliary drainage in cases of malignant distal biliary obstruction found that the 2 approaches were comparable with respect to success of stent placement (94.23% vs 93.26%), adverse events (8.65% vs 8.65%), and procedure time.⁶⁴ The risk of pancreatitis appeared to be lower with EUS-BD compared with ERCP (0% vs 4.8%, $P=0.059$).⁶⁴ Although case series of EUS-BD performed by experienced endoscopists suggested EUS-BD is comparable with ERCP in terms of short-term outcomes, EUS-BD is less successful and more risky when performed by inexperienced endoscopists. A Spanish national survey on EUS-BD conducted in hospitals with an experience of fewer than 20 procedures showed that EUS-BD was technically successful in only 68.9% of 73 patients with an adverse event rate of 22.6%.⁶⁵ Another single-center retrospective study also observed a higher adverse event rate among the first 50 cases.⁶⁶ Taken together, EUS-BD is still relatively nascent and should only be performed by expert endoscopists experienced in this procedure. In experienced hands, EUS-BD is a safe and effective salvage procedure for endoscopic biliary drainage when transpapillary biliary access has failed or is impossible.^{59, 60, 67}

11. Percutaneous transhepatic access is a viable method of biliary intervention when endoscopic methods fail or are not appropriate.

Evidence level: I-B

Recommendation grade: A

Voting on recommendation: A, 81%; B, 13%; C, 6%; D, 0%; E, 0%

In patients with a dilated biliary tract from biliary obstruction, percutaneous transhepatic puncture of the bile duct is widely used to achieve biliary access when ERCP fails.⁶⁸ After biliary access is achieved, drainage can be performed by placing an external catheter or an internal stent, or by passing a guidewire into the duodenum for subsequent rendezvous procedure using a duodenoscope or an enteroscope where applicable.

The technical success rate of this method approaches 100% in cases with dilated bile ducts and is expected to exceed 70% with non-dilated bile ducts.⁶⁹

Although mild bleeding after transhepatic puncture is common and usually self-limiting, severe bleeding may occur. In a nationwide audit in Japan, the rate of

severe bleeding requiring transfusion and/or arterial embolization after percutaneous transhepatic biliary drainage (PTBD) was 2.3% among 34,606 cases.⁷⁰

12. Percutaneous transhepatic and EUS-guided biliary access appear comparable in terms of efficacy, and may be appropriate in surgically altered anatomy.

Evidence level: I-B

Recommendation grade: A

Voting on recommendation: A, 56%; B, 31%; C, 13%; D, 0%; E, 0%

A retrospective study comparing EUS-BD and PTBD in patients with distal biliary obstruction and failed ERCP found that the clinical success rates were comparable (86.4% vs 92.2%, $p=0.4$), but PTBD had a higher rate of adverse events during the index and re-intervention procedures compared with EUS-BD (70.6% vs 18.2%, $p<0.001$).⁷¹ In an RCT comparing PTBD ($n=12$) and EUS-BD ($n=13$) in patients with malignant biliary obstruction and failed ERCP, technical and clinical success were achieved in all patients without significant differences in the adverse event rate and cost.⁷² However, given limited sample size the study may not have

been adequately powered to show a difference. A recent RCT evaluating patients with malignant distal biliary obstruction and inaccessible papilla also found that PTBD (n=32) and EUS-BD (n=34) had comparable rates of technical (96.9% vs 94.1%) and functional success (87.1% vs 87.5%), but patients undergoing EUS-BD had fewer adverse events (8.8 % vs 31.2%, p=0.022) and re-interventions (25% vs 54.8%, p=0.015).⁷³ However, it should be cautioned that those studies were conducted in referral centers by expert endoscopists experienced in EUS-BD, and thus the results may not be directly generalizable to other settings; it is important to consider availability of expertise when choosing between percutaneous and EUS-guided access. Collectively, EUS-guided and percutaneous transhepatic biliary access have comparable technical and functional success rates; EUS-guided access may carry a lower adverse event rate in experienced hands. The possible choices of endoscopes and access routes for biliary access in various scenarios of difficult biliary access are summarized in Table 5.

13. In the presence of significant duodenal stenosis, endoscopic balloon dilation and/or enteral stenting followed by standard biliary cannulation may be considered.

EUS-guided or percutaneous biliary access techniques are alternative first-line approaches.

Evidence level: III

Recommendation grade: C

Voting on recommendation: A, 75%; B, 19%; C, 6%; D, 0%; E, 0%

When the papilla is not accessible due to duodenal stenosis, balloon dilation of the stenosis or/and duodenal stenting may enable passage of a duodenoscope and subsequent biliary access. The success rate of dilation varied from 0 to 87% in previous studies.⁷⁴⁻⁷⁶ Identifying the papilla can be challenging due to post-dilation bleeding.⁷⁴ Dilation also carries a risk of perforation; one study reported perforation in 1 of 16 patients after dilation of duodenal stenosis for access to papilla.⁷⁶ If dilation alone is insufficient, further placement of a self-expanding metal stent (SEMS) may allow passage of the duodenoscope.^{74,76} Mutignani et al reported that duodenoscope passage through the duodenal SEMS was successful in 63 of 64 patients without stent displacement after biliary drainage.⁷⁴ Placement of a SEMS also palliates symptomatic obstruction from duodenal stenosis.⁷⁵

EUS-guided and percutaneous transhepatic biliary accesses are alternative approaches in cases with significant duodenal stenosis. Both approaches directly puncture the bile duct, obviating the need to access the papilla. A multicenter retrospective study suggested that in patients with prior duodenal SEMS placement and biliary obstruction, biliary SEMS insertion via EUS-BD may be associated with a longer stent patency compared with the transpapillary route, likely due to food impaction in the duodenal SEMS.⁷⁷ Although there has been no prospective study comparing biliary access after dilation of duodenal stricture with/without stenting versus EUS-guided or percutaneous transhepatic biliary access, the latter might be preferable if the duodenal stenosis does not cause significant obstruction requiring palliation.

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Table 1 Classification of evidence levels, recommendation grades, and voting on recommendation²

Level/grade	Description
Evidence level	
I-A	Evidence from meta-analysis of randomized, controlled trials
I-B	Evidence from at least one randomized, controlled trial
II-A	Evidence from at least one controlled study without randomization
II-B	Evidence from at least one other type of quasi-experimental study
III	Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both
Recommendation grade	
A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendation from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
Voting on recommendation	
A	Accept completely
B	Accept with some reservation
C	Accept with major reservation
D	Reject with reservation
E	Reject completely

Table 2 Definition and incidence of difficult cannulation in randomized controlled trials

First author (year)	Definition of difficult cannulation	No. of difficult cannulation/no. of eligible subjects	Randomly assigned intervention (N)
Maeda S (2003) ⁸	>10 min	53/107 (49.5%)	DGW (27) PC (26)
Tang SJ (2005) ⁹	>12 min (7 by trainee and 5 by faculty)	62/642 (9.7%)	NKP (32) PC (30)
Zhou PH (2006) ¹⁰	>10 min >3 PD cannulation	91/948 (9.6%)	NKP (43) PC (48)
Cennamo V (2009) ¹¹	>5 min >3 PD cannulation	146/842 (17.3%)	NKP (36) PC (110)
Herreros de Tejada A (2009) ¹²	>5 attempts	188/845 (22.2%)	DGW (97) PC (91)
Manes G (2009) ¹³	>10 min >5 PD injection	158/1654 (9.6%)	Early NKF (80) Late NKF (78)
Ito K (2010) ¹⁹	>5 attempts	108/1451 (7.4%)	PD stent (35) No stent (35)
Angsuwatcharakon P (2012) ¹⁴	>15 min (5 by trainee 10 min by faculty)	44/426 (10.3%)	DGW (23) NKF (21)
Coté GA (2012) ¹⁷	>6 min >3 PD injection or cannulation	87/442 (19.7%)	DGW (42) PD stent (45)
Lee TH (2012) ¹⁸	>10 min >5 PD cannulation >10 attempts	101/1522 (6.6%)	PD stent (50) No stent (51)
Swan MP (2013) ¹⁵	>10 min* >10 attempts* >4 PD cannulation*	73/464 (15.7%)	NKP (39) PC (34)
Yoo YW (2013) ¹⁶	>10 attempts >10 min	71/1349 (5.2%)	DGW (34) TPS (37)
Zang J (2014) ⁴²	>10 min >5 PD cannulation	164/1181 (13.9%)	TPS (73) NKP (76)
		Total	1346/11873 (11.3%)

min, minute; PD, pancreatic duct ; DGW, double guidewire technique; NKP, needle knife

papillotomy; PC, persistent standard cannulation; PD, pancreatic duct; TPS, transpancreatic

septotomy

*By trainee and faculty: >5 minutes, >5 attempts, >2 PD cannulation, respectively.

Table 3 Success and adverse event rates of the 3 precut techniques in patients with failed standard cannulation

First author (year)	Study design	Technique	Initial success	Success after second attempt	Pancreatitis	Bleeding	Perforation
Katsinelos P (2012) ⁴⁰	Retrospective	NKF	92.3%	98.7%	2.6%	5.2%	0%
		NKP	83.7%	97.7%	21%	3.9%	0.8%
		TPS	100%	NA	22.4%	0%	0%
			(p - NS)	(p - NS)	(p<0.05)	(p - NS)	(p - NS)
Horiuchi A (2007) ⁴¹	Retrospective	NKF	100%	NA	0%	0%	0%
		NKP	90%	100%	3.3%	6.7%	0%
		TPS	95.8%	100%	2.1%	0%	0%
			(p - NS)	(p - NS)	(p - NS)	(p - NS)	(p - NS)
Mavrogiannis C (1999) ³⁸	RCT	NKF	75.7%	90.5%	0%	6.8%	2.7%
		NKP	73.4%	88.6%	7.6%	5.1%	2.5%
			(p - NS)	(p - NS)	(p<0.05)	(p - NS)	(p - NS)
Catalano MF (2004) ⁴³	RCT	NKP	75%	NA	12.5%	6.3%	0%
		TPS	94%	NA	3.2%	0%	0%
			(p-NS)		(p-NS)	(p-NS)	
Zang J (2014) ⁴²	RCT	NKP	84.2%	NA	6.6%	3.9%	0%
		TPS	95.9%	NA	6.8%	1.4%	0%
			(p<0.05)		(p - NS)	(p - NS)	(p - NS)

NKF, needle knife fistulotomy; NKP, needle knife papillotomy; TPS, transpancreatic septotomy; NA, not available; NS, not significant; RCT, randomized controlled trial.

ACCEPTED MANUSCRIPT

Table 4 Comparison of transgastric and transduodenal routes for EUS-guided biliary access

First author (year)	Design	Transgastric vs transduodenal	
		Success, n (%)	Adverse events, n (%)
Dhir V (2013) ⁷⁸	Retrospective 17/18	16 (94.1%) vs 18 (100%)	Bile leak: 2 (11.7%) vs 0 Pneumoperitoneum: 2 (11.7%) vs 0
Dhir V (2014) ⁶¹	Retrospective 36/32	34 (94.4%) vs 31 (96.8 %)	11 (30.5%) vs 3 (9.3%)*
Kawakubo K (2014) ⁵⁹	Retrospective 20/44	19 (95%) vs 42 (95%)	6 (30%) vs 6 (14%)
Poincloux L(2015) ⁶⁶	Retrospective 71/30	66 (94.3 %) vs 27 (93.1%)	10 (14.1%) vs 2 (6.7%)
Artifon E (2015) ⁶²	Prospective 25/24	22 (91%) vs 17 (77%)	5 (20%) vs 3 (12.5%)

*P<0.05.

Table 5 Choice of endoscopes and access routes in various scenarios of difficult biliary access

	Difficult cannulation in normal anatomy	Billroth II anatomy	Roux-en-Y anastomosis
Duodenoscope	Yes	Yes	No
Forward-viewing upper endoscope	No	Yes	No
Device-assisted enteroscope	No	Yes (in a long afferent limb)	Yes
EUS-guided biliary drainage	Yes	Yes	Yes
Percutaneous biliary drainage	Yes	Yes	Yes

ACRONYMS:

ERCP: endoscopic retrograde cholangiopancreatography

PEP: post-ERCP pancreatitis

DGW: double guidewire

RCT: randomized controlled trial

EUS: endoscopic ultrasound

RR: relative risk

OR: odds ratio

CI: confidence interval

NKP: needle knife papillotomy

NKF: needle knife fistulotomy

TPP: transpancreatic precut

NSAID: nonsteroidal anti-inflammatory drug

EUS-BD: endoscopic ultrasound-guided biliary drainage

EUS-HGS: endoscopic ultrasound-guided hepaticogastrostomy

EUS-CDS: endoscopic ultrasound-guided choledochoduodenostomy

PTBD: percutaneous transhepatic biliary drainage

SEMS: self-expanding metal stent

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1. Wei-Chih Liao, Phonthep Angsuwatcharakon, Hiroyuki Isayama: conception and design; drafting of initial statements; review/revision/voting on statements; drafting of the article.
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