Endoscopic ultrasound-guided pancreatic duct drainage

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Abstract Endoscopic transpapillary or transanastomotic pancreatic duct drainage (PD) is the mainstay of drainage in symptomatic pancreatic duct obstruction or leakage. However, transpapillary or transanastomotic PD can be technically difficult due to the tight stricture or surgically altered anatomy (SAA), and endoscopic ultrasound (EUS)-guided PD (EUS-PD) is now increasingly used as an alternative technique. There are two approaches in EUS-PD: EUS-guided rendezvous (EUS-RV) and EUS-guided transmural drainage (EUS-TMD). In cases with normal anatomy, EUS-RV should be the first approach, whereas EUS-TMD can be selected in cases with SAA or duodenal obstruction. In our literature review, technical success and adverse event rates were 78.7% and 21.8%, respectively. The technical success rate of EUS-RV appeared lower than EUS-TMD due to the difficulty in guidewire passage. In future, development of dedicated devices and standardization of EUS-PD procedure are necessary.

Keywords: Endoscopic ultrasound, pancreatic duct obstruction, rendezvous, transmural drainage

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INTRODUCTION

While endoscopic or surgical drainage is available for the management of symptomatic pancreatic duct obstruction or leakage, endoscopic transpapillary (or trans-anastomotic) drainage is often selected as a first-line treatment because of its less invasiveness.[1] However, endoscopic drainage can be technically or anatomically difficult in some cases such as complete pancreatic duct obstruction in chronic pancreatitis, a disconnected duct syndrome after severe acute pancreatitis or pancreatic trauma, duodenal stricture and surgically altered anatomy (SAA). In those difficult cases, surgical,[2] or rarely percutaneous,[3] pancreatic duct drainage (PD) is performed as an alternative method. Recent development of interventional endoscopic ultrasound (EUS)[4] allows an access to various regions such as the biliary tract, pancreatic fluid collections, abdominal abscess and the pancreatic duct, even if endoscopic retrograde cholangiopancreatography (ERCP) is difficult.

Access to the pancreatic duct under EUS guidance was reported as EUS-guided pancreatography after failed ERCP, in 1995 by Harada *et al*.[5] EUS-guided PD (EUS-PD) was first reported as rendezvous (RV) and transmural drainage (TMD) in 2002.[6] Since then, many studies have been published on EUS-PD, with most of these being case reports or case series since EUS-PD is one of the most technically difficult interventional EUS procedures. In this review, we describe a literature review, technical tips, and hurdles and propose an algorithm for EUS-PD.

Access this article online	
Quick Response Code:	Website: www.saudijgastro.com
	DOI: 10.4103/sjg.SJG_474_18

How to cite this article: Nakai Y, Kogure H, Isayama H, Koike K. Endoscopic ultrasound-guided pancreatic duct drainage. Saudi J Gastroenterol 2019;25:210-7.

INDICATIONS

The indications and contraindications of EUS-PD are summarized in Table 1. The indications for endoscopic PD are pancreatic duct obstruction and pancreatic leakage and disconnected pancreatic duct syndrome. EUS-PD is often attempted after failed ERCP due to various reasons. In cases with normal anatomy, EUS-PD should be attempted after failed ERP. In cases with difficulty due to anatomical reasons such as duodenal obstruction and SAA, EUS-PD can be considered as a first-line treatment option. The contraindications of EUS-PD include no visualization of the pancreatic duct under EUS, intervening vessels, severe coagulopathy and an unstable general condition for endoscopic procedures. In cases with massive ascites, EUS-PD has a risk of pancreatic fistula and peritonitis, and the indications of EUS-PD should be determined carefully in those patients with ascites.

PROCEDURE VARIATIONS

There are two approaches for EUS-PD: transpapillary (or transanastomotic) RV [EUS-RV, Figure 1] and TMD [EUS-TMD, Figure 2]. The latter included EUS-guided pancreatico-enterostomy and transenteric antegrade stenting.

Table 1: Indications and contraindications of endoscopic ultrasound-guided pancreatic duct drainage

Indications
Chronic pancreatitis with pancreatic duct obstruction
Anastomotic stricture at pancreatico-jejunostomy
Pancreatic fistula
Pancreatic duct disruption due to severe acute pancreatitis
Failed pancreatic duct cannulation
Contraindications
Failed visualization of pancreatic duct
Intervening vessels
Severe coagulopathy
Unstable conditions unfit for endoscopic interventions

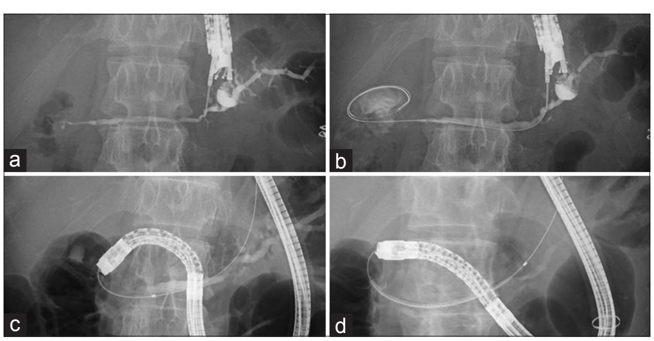

Figure 1: EUS-guided rendezvous in patient with pancreatic divium and surgically altered anatomy. (a) Puncture and pancreatogram. (b) Guidewire passage through the minor papilla into the duodenum. (c) Balloon enteroscope insertion and cannulation over the rendezvous guidewire. (d) Pancreatic stent placement across the minor papilla

In cases with an accessible ampulla or anastomosis, EUS-RV can be selected. EUS-RV is performed as follows: puncture of the pancreatic duct, pancreatogram, guidewire insertion through the ampulla or the anastomosis, scope exchange, ERP using the RV guidewire, and PD. Devices for EUS-TMD should be readily available even if EUS-RV is planned because guidewire passage can be technically impossible during EUS-RV.

In cases with an inaccessible ampulla or anastomosis, or in cases after failed guidewire passage during EUS-RV, EUS-TMD can be performed. The procedure is quite similar to EUS-RV until the step of guidewire insertion: puncture of the pancreatic duct, pancreatogram, guidewire insertion to the pancreatic duct, fistula (and/or stricture) dilation and TMD placement. TMD can be pancreatico-enterostomy (antegrade, retrograde) or transpapillary (or transanastomotic) pancreatico-enterostomy.[4] The former is to put a stent between the pancreatic duct and the gastrointestinal lumen, and the latter is to push the stent end further into the small intestine through the ampulla or the anastomosis.

TECHNICAL ASPECTS OF EUS-PD

The details of EUS-PD procedure are well-summarized in two review articles.[7,8] Due to the small size of the pancreatic duct with side branches and the stricture, the key to successful EUS-PD is puncture of the pancreatic duct and

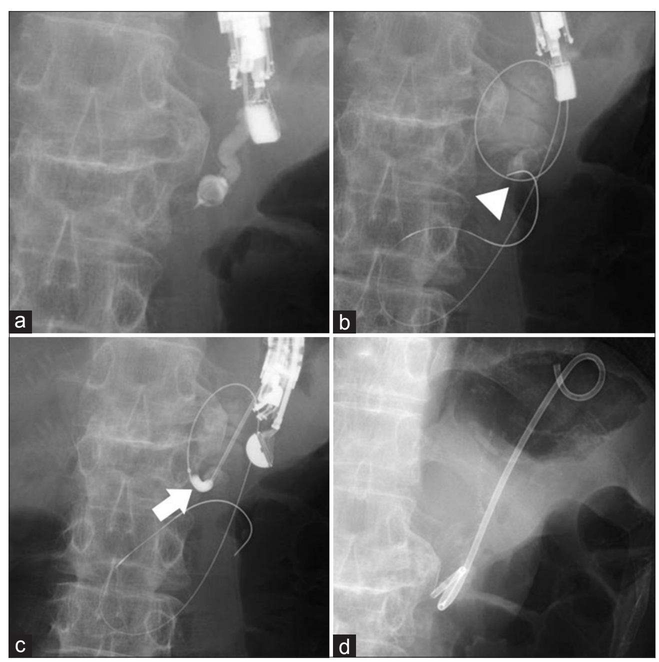

Figure 2: EUS-guided transmural pancreatic duct drainage. (a) Puncture and pancreatogram. (b) Guidewire passage through the anastomosis (arrowhead). (c) Balloon dilation of the pancreatico-jejunostomy (arrow). (d) Transmural stent placement between the jejunum and the stomach

guidewire manipulation. As recommended by Itoi *et al.*,[7] the use of a 19-gauge fine needle aspiration (FNA) needle with a sharp tip (EZ Shot 3 Plus; Olympus Medical Systems, Tokyo, Japan) and a 0.025-inch guidewire with a flexible tip (VisiGlide2; Olympus Medical Systems) are routinely used in our institution. A 22-gauge needle in combination with a smaller (0.018- or 0.021-inch) guidewire can be used in cases with a small pancreatic duct, but small guidewires are difficult to manipulate even after successful pancreatic duct puncture, and we use a 19-gauge needle even in cases with a nondilated pancreatic duct. Guidewire shearing at the needle tip can occur during guidewire manipulation. To avoid guidewire shearing, gentle guidewire manipulation is mandatory. Guidewire shearing occurs when the guidewire is pulled back. The guidewire should not be just pushed and pulled back and forth to avoid shearing, and the rotation of guidewire with tactile feedback is essential to get into the pancreatic duct and pass the stricture. When there is resistance during the guidewire manipulation, the needle tip should be adjusted, either by pulling slightly back to the pancreatic parenchyma as described in EUS-BD[9] or by releasing the lure lock of the FNA needle, which may change the direction of the bevel of the needle tip.

The selection of the puncture site is also important. Preprocedure contrast-enhanced computed tomography (CT) and/or magnetic resonance imaging (MRI)/magnetic retrograde cholangiopancreatography (MRCP) are recommended for planning EUS-PD. The size and configuration of the pancreatic duct, the presence of the pancreatic duct stricture and/or pancreatic stones, as well as the presence of intervening vessels should be evaluated. Coronal images of CT scan in addition to the axial images are also helpful to figure out the pancreatic duct configuration. Given the difficulty in guidewire manipulation, the puncture site should be selected based on the distance to the stricture and the angle of the needle and the pancreatic duct in addition to the size of the duct. When the needle and the pancreatic duct are perpendicular, guidewire manipulation and subsequent device insertion can be technically difficult. Therefore, prior to the puncture of the pancreatic duct, the scope and needle angle should be evaluated on fluoroscopy. In SAA patients with gastrectomy, the puncture site is quite limited depending on the size of the remnant stomach. The distance of the pancreas and the stomach should be evaluated on preprocedure CT and MRI. Once the EUS scope is inserted, the stomach is pushed against the pancreas and two organs appear close to each other on EUS but if the pancreatic duct is punctured at the region where the stomach and pancreas are far apart, subsequent device insertion can be extremely difficult and guidewire loss may occur.

Track dilation is performed for EUS-TMD. For track dilation, both cautery and noncautery dilators are available. Tapered noncautery dilators are preferred for track dilation during EUS-PD. A balloon catheter[10] and/or a bougie dilator[11] are used for initial dilation method in our institutions. Cautery dilators may have a risk of bleeding and pancreatitis, and only coaxial cautery dilators should be used. In cases with severe chronic pancreatitis, both the pancreatic parenchyma and the pancreatic duct wall are hard and the use of cautery dilators might be necessary if noncautery dilators cannot be advanced into the pancreatic duct. When track dilation or device insertion is impossible, crossover to EUS-RV should be considered when available.

CLINICAL OUTCOMES OF EUS-PD IN THE LITERATURE

Previous reports of EUS-PD including both RV and TMD are summarized in Table 2. A total of 517 procedures from 33 studies were reviewed, and the technical success rate was 78.7% and the adverse event rate was 21.8%.

The technical success rate of EUS-PD appeared to be lower than that of EUS-BD (>90%).[12,13] Of 33 studies, EUS-RV was performed in 12 studies, EUS-TMD in 11 studies, and both in 10 studies. When EUS-RV in 12 studies and EUS-TMD in 11 studies were compared, the technical success rates were 55.6% versus 93.8% ($P < 0.01$), respectively. Shah *et al.*[14] reported that the initial technical success rates of EUS-RV and EUS-TMD were only 50% and 63%, respectively, but the overall technical success rates increased to 56% and 71% after crossover to EUS-TMD or EUS-RV. EUS-RV appears technically more difficult because of the necessity to guidewire passage and scope exchange. Technical failure is most common in guidewire manipulation during EUS-RV for biliary indications.[15,16] Therefore, crossover to EUS-TMD should be considered if guidewire passage is impossible.

The adverse event rate of EUS-PD appeared similar to that of EUS-BD (≈20%).[12,13] Adverse events related to EUS-PD include abdominal pain, pancreatitis, pancreatic leakage, peripancreatic fluid collection, peritonitis, stent dislocation, bleeding and perforation. In EUS-PD, puncture and, sometimes, track dilation through the pancreatic parenchyma are necessary, and most patients who need PD are prone to pancreatitis due to pancreatic duct hypertension. Thus, pancreatitis, pancreatic leakage, and subsequent fluid collection can occur after EUS-PD. Monitoring of physical examination in combination with laboratory tests are recommended, and we routinely perform CT scan on the next day of the procedure to evaluate those possible adverse events.

Table 2: Review of endoscopic ultrasound-guided pancreatic duct drainage

Author	Year	Study design	*n*	Reason for EUS-PD	Procedure	Technical success	Adverse events	Details of adverse events
Bataille and Deprez[6]	2002	Case report	1	Failed ERP	RV	100.0%	0	
Francois *et al.*[32]	2002	Case series	4	Failed ERP	TMD	100.0%	25.0%	Stent dislocation
Kahaleh *et al.*[33]	2003	Case series	2	SAA	TMD	100.0%	50.0%	Bleeding
Mallery *et al.*[34]	2004	Case series	4	Failed ERP, SAA	RV	25.0%	25.0%	Fever
Will *et al.*[35]	2005	Case report	1	Failed ERP	RV	100.0%	0	
Kahaleh *et al.*[36]	2007	Retrospective	13	Failed ERP, SAA	TMD	76.9%	15.4%	Bleeding, perforation
Papachristou *et al.*[37]	2007	Case series	2	Failed ERP, SAA	RV	100.0%	NA	
Tessier *et al.*[38]	2007	Retrospective	36	Failed ERP, SAA	TMD	91.7%	13.9%	Pancreatitis, hematoma
Will *et al.*[39]	2007	Prospective	12	Failed ERP, SAA	RV, TMD	69.2%	42.9%	Pain, bleeding, perforation
Keenan *et al.*[40]	2007	Case report	1	Failed ERP	RV	100.0%	0	
Gleeson *et al.*[41]	2007	Case report	1	Failed ERP	RV	100.0%	0	
Saftoiu *et al.*[42]	2007	Case report	1	Failed ERP	RV	100.0%	0	
Brauer *et al.*[43]	2009	Prospective	8	Failed ERP	RV, TMD	87.5%	0	
Kinney *et al.*[44]	2009	Retrospective	9	SAA	RV	44.4%	11.1%	Fever
Barkay *et al.*[45]	2010	Retrospective	12	Failed ERP	RV	33.3%	9.5%	
Cooper *et al.*[46]	2010	Case report	1	Failed ERP	RV	100.0%	0	
Ergun *et al.*[47]	2011	Retrospective	20	Failed ERP, SAA	RV, TMD	90.0%	10.0%	Bleeding, fluid collection
Itoi *et al.*[48]	2011	Case series	2	SAA	RV	100.0%	50.0%	Fluid collection
Kikuyama *et al.*[49]	2011	Retrospective	5	SAA	RV, TMD	100.0%	NA	
Shah *et al.*[14]	2012	Retrospective	25	Failed ERP, SAA	RV, TMD	54.5%	16.0%	Pancreatitis, pneumoperitoneum
Vila *et al.*[50]	2012	Retrospective	19	Details unknown	RV, TMD	57.9%	26.3%	
Fujii *et al.*[51]	2013	Retrospective	43	Failed ERP, SAA	TMD	74.4%	37.2%	Pain, pancreatitis, abscess, retained guidewire
Kurihara *et al.*[52]	2013	Retrospective	17	Failed ERP, SAA	RV, TMD	88.2%	5.9%	Aneurysm
Takikawa *et al.*[53]	2013	Case report	1	SAA	RV	100.0%	0	
Will *et al.*[54]	2015	Retrospective	94	Failed ERP, SAA	RV, TMD	56.6%	21.6%	Bleeding, pancreatitis, abscess, fluid collection, perforation, retention cyst, aspiration, ulcers
Oh *et al.*[25]	2016	Retrospective	25	Failed ERP, SAA, GOO	TMD	100.0%	20.0%	Pain, bleeding
Nakai *et al.*[55]	2016	Case report	1	SAA	TMD	100.0%	100.0%	Stent dislocation
Tyberg *et al.*[56]	2017	Retrospective	80	Failed ERP, SAA	RV, TMD	88.8%	20.0%	Pancreatitis, fluid collection, pain, leakage, perforation, bleeding
Chen *et al.*[19]	2017	Retrospective	40	SAA	RV, TMD	92.5%	37.5%	Pain, abscess, ulcer
James *et al.*[18]	2018	Retrospective	5	Failed ERP	TMD	100.0%	0	
Matsunami *et al.*[23,24]	2018	Retrospective	30	Failed ERP, SAA	TMD	100.0%	23.3%	Pain, pancreatitis, bleeding
Uchida *et al.*[57]	2018	Retrospective	15	Failed ERP, SAA	TMD	86.7%	26.7%	Peritonitis, stent dislocation, bleeding
Overall						78.7%	21.8%	

EUS-PD: Endoscopic ultrasound guided pancreatic duct drainage; ERP: Endoscopic retrograde pancreatography; RV: Rendezvous; TMD: Transmural drainage; SAA: Surgically altered anatomy; GOO: Gastric outlet obstruction; NA: Not available

As shown in Table 2, most reports were retrospective including case reports and case series, and therefore publication bias might exist. Of note, the technical success and adverse event rates varied significantly even by experts. Therefore, EUS-PD should be performed in expert centers where support from interventional radiologists, surgeons and anesthesiologists is readily available.

ALTERNATIVE APPROACH TO EUS-PD

Alternative approach to endoscopic drainage is limited for PD compared with biliary drainage. ERCP is the mainstay because of its less invasiveness and, if ERCP failed either technically or clinically, surgical procedure is often performed. However, surgical procedures such as Frey procedure for chronic pancreatitis can be invasive. Reoperation in those with SAA can be technically difficult. While biliary drainage can be performed surgically, percutaneously or endoscopically (ERCP and EUS), percutaneous PD is not routinely performed.[3] Therefore, EUS-PD can be a less invasive alternative approach when ERCP approach fails. However, long-term data of EUS-PD are limited. As previously reported in transpapillary pancreatic duct stent placement, severe pancreatic duct stricture can be refractory to endoscopic stent placement[1] and may need surgical drainage. EUS-guided TMD can adversely affect the surgical procedures because of its inflammation and adhesion. Therefore, the advantages and disadvantages of EUS-guided TMD and surgery should be discussed with patients prior to the procedure. In addition, as described above, percutaneous approach is uncommon for PD. When EUS-BD fails after failed ERCP, percutaneous transhepatic biliary drainage can be a salvage technique.[12] However, if PD cannot be achieved, that is, successful pancreatic duct access but failed stent placement, pancreatic leakage may occur and surgical salvage might be necessary.

ALGORITHM FOR MANAGEMENT OF PANCREATIC DUCT OBSTRUCTION

Our proposal for management of pancreatic duct obstruction is shown in Figure 3. In cases with normal anatomy, EUS-RV followed by transpapillary pancreatic stent placement should be attempted first. If guidewire passage fails due to the pancreatic duct stricture or pancreatic stones, EUS-TMD can be temporarily performed. Guidewire passage can be attempted later through the pancreatico-enterostomy after fistula maturation as a two-step procedure similar to EUS-guided antegrade stone treatment.[17] If the reason for failure is pancreatic stone impaction, extracorporeal shock wave lithotripsy (ESWL) might be useful, and lithotripsy using a peroral pancreatoscopy through the pancreatico-enterostomy was also reported.[18] Guidewire passage can be technically successful after lithotripsy for impacted pancreatic stones [Figure 4], or PD might be even unnecessary in cases without pancreatic duct strictures.

In cases with SAA, it is still unclear whether we should perform enteroscopy-assisted ERCP or EUS-PD first, and EUS-RV or EUS-TMD first when EUS-PD is performed. There was one retrospective, comparative study of EUS-PD and enteroscopy-assisted ERCP for pancreatic indications in patients after Whipple surgery.[19] A total of 75 procedures (40 EUS-PD and 35 enteroscopy-assisted ERCP) were evaluated, and technical and clinical success rates were significantly higher in EUS-PD: technical success rates of 92.5% and 20% and clinical success rates of 87.5% and 23.1% in EUS-PD and enteroscopy-assisted ERCP, respectively. However, adverse events were more common in EUS-PD: 35% and 2.9%. Technical success rates of enteroscopy-assisted ERCP might vary according to previous surgery and indications (benign vs. recurrent malignancy), and a large-scale data are warranted comparing EUS-PD and enteroscopy-assisted ERCP. While transpapillary or transanastomotic stent placement using enteroscopy-assisted ERCP allows physiological pancreatic juice flow, the insertion of enteroscope can be technically difficult or even impossible. Thus, long-term stent exchange for severe pancreatic duct stricture is necessary; reintervention might be less time-consuming and technically easier in EUS-TMD due to its better access to the site of pancreatic stents than in enteroscopy-assisted ERCP.

FUTURE RESEARCH

Most reports of EUS-PD were small, retrospective studies, and obviously we need more data of EUS-PD in prospective studies.[20] Even though EUS-PD has been increasingly reported, the procedure is far from standardization. The consensus guidelines of interventional EUS were recently published,[21] but the evidence levels are low to very low in most statements on EUS-PD. Given the low technical success rate and relatively high adverse event rate, a training model of EUS-PD should be established[22] and a learning curve should be clarified.

The major limitation of EUS-PD is the lack of dedicated devices. For standardization of EUS-PD procedures, development of dedicated devices is essential, but most devices currently used during EUS-PD are originally developed for EUS-FNA and ERCP. Recently, encouraging

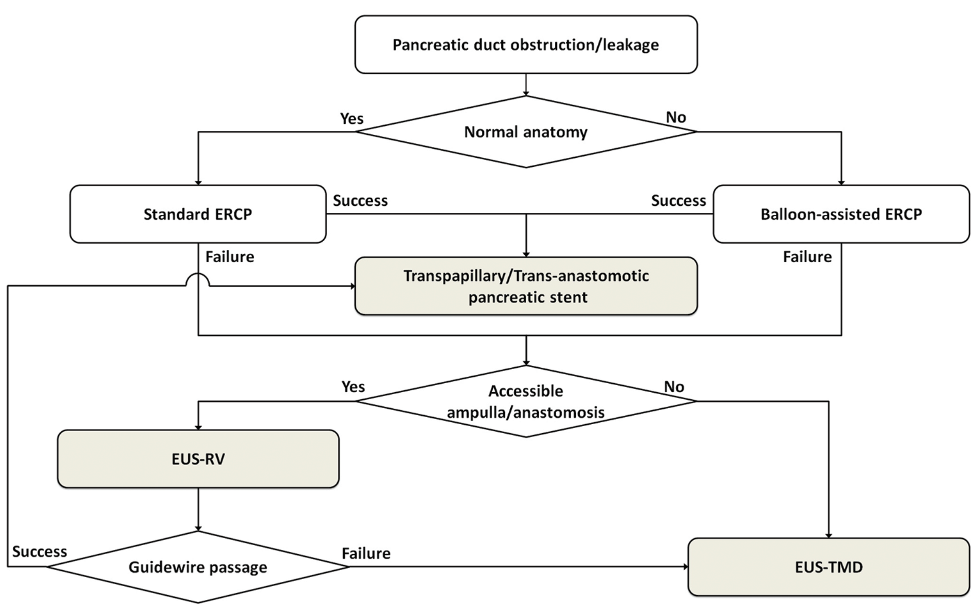

Figure 3: Algorithm to pancreatic duct obstruction/leakage. EUS: endoscopic ultrasound; RV: Rendezvous; TMD: Transmural drainage

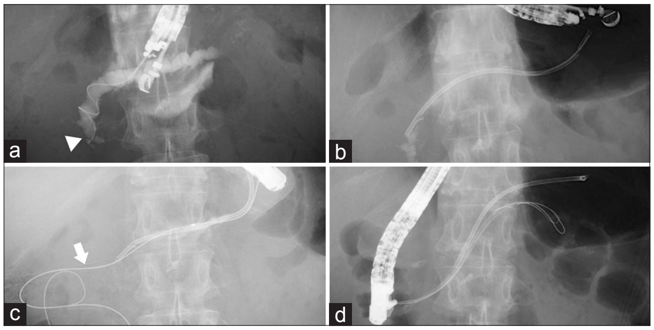

Figure 4: Successful transpapillary drainage after EUS-guided transmural pancreatic duct drainage and ESWL in a case with calcified chronic pancreatitis. (a) EUS-guided rendezvous was attempted but the guidewire passage failed due to stone impaction (arrowhead). (b) EUS-guided transmural pancreatic duct stent was placed. (c) Guidewire passage through the minor papilla (arrow) was eventually successful through pancreatico-gastrostomy route after ESWL. (d) A pancreatic stent was placed across the minor papilla using the rendezvous technique. ESWL: Extracorporeal shock wave lithotripsy

long-term outcomes of a dedicated plastic stent[23,24] were reported. In addition, Oh *et al*.[25] reported the feasibility of covered metal stents in EUS-PD. The use of covered metal stents has been investigated in ERCP approach.[26,27] While its large diameter appears to have an advantage of better stricture resolution, a covered metal stent placed in the pancreatic duct can potentially occlude side branches of the pancreatic duct and tissue hyperplasia at the proximal stent end is a concern. Therefore, long-term outcomes should be further evaluated to justify the routine use of covered mental stents in EUS-PD.

EUS-guided biliary drainage, which was first introduced as an alternative biliary drainage, is now used as a port for more complex procedures such as antegrade stone extraction,[28] peroral cholangioscope for lithotripsy,[29,30] or tumor ablation.[31] On the other hand, the indications of EUS-PD are still limited for drainage alone. There are some reports on pancreatoscopy for lithotripsy and stone extraction through EUS-PD fistula.[18] In future, EUS-PD can be used as a port to the pancreas for the management of various pancreatic diseases such as difficult pancreatic stones, guidewire passage through the stricture, tumor diagnosis, and ablation once EUS-PD procedures are established and standardized.

SUMMARY

In summary, EUS-PD should be considered as an alternative method for PD after failed ERCP. However, it is technically demanding, especially guidewire passage during EUS-RV, with a technical success rate of 78.7% and adverse event rate of 21.8%, even when done by experts. Although EUS-PD fistula can potentially be used for advanced procedures such as lithotripsy and tumor ablation, standardization of the procedures and development of dedicated devices are mandatory.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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