Postoperative pancreatic fistulas (POPFs) are common adverse events that occur after pancreatic surgery. Endoscopic ultrasonography (EUS)-guided drainage (EUS-D) is a first-line treatment, similar to that for pancreatic fluid collection (PFCs) after acute pancreatitis. However, some POPFs do not develop fluid collections depending on the presence or location of the surgical drain, whereas others develop fluid collections, such as postoperative fluid collections (POPFCs). Although POPFCs are similar to PFCs, the strategy and modality for POPF management need to be modified according to the presence of fluid collections, surgical drains, and surgical type. As discussed for PFCs, the indications, timing, and selection of interventions or stents for EUS-D have not been fully elucidated for POPFs. In this review, we discuss the management of POPFs and POPFCs in comparison with PFCs due to acute pancreatitis and summarize the topics that should be addressed in future studies.

Keywords: Drainage; Endosonography; Pancreatic fistula; Postoperative complications

INTRODUCTION

Pancreatic fluid collections (PFCs), which can complicate the clinical course of acute pancreatitis, have been managed by surgical or percutaneous interventions. Endoscopic ultrasonography (EUS)-guided drainage (EUS-D) is often used as a first-line treatment for PFCs. However, clarity is lacking regarding topics such as endoscopic vs. percutaneous drainage (PCD), the timing of interventions, and management of pancreatic leakage or disconnected pancreatic duct syndrome to prevent PFC recurrence.1-3

Postoperative pancreatic fistulas (POPFs), or postoperative pancreatic fluid collections (POPFCs) in cases with fluid collection, are common adverse events (AEs) that occur after pancreatic surgery with the reported incidences of up to 25% in pancreaticoduodenectomy4 and 43% in distal pancreatectomy.5
Prevention of POPFs by surgical interventions such as pancreatic stents and fibrin sealants has been investigated with conflicting data. Similar to PFCs after acute pancreatitis, POPFs or POPFCs may be resolved with conservative treatment alone, but persistent pancreatic fistulas and fluid collections can lead to severe consequences such as bleeding and infection, and require intervention in some cases. However, the indications, timing, and selection of these interventions have not been fully elucidated. In this review, we discuss the management of POPFs and POPFCs in comparison with PFCs due to acute pancreatitis and summarize the topics that should be addressed in future studies. This review was conducted within the WON and pERipancreatic FIUId collection (WONDERFUL) consortium, which consists of expert endoscopists, gastroenterologists, interventional radiologists, and epidemiologists at high-volume centers in Japan.

DEFINITION, GRADING, AND CLASSIFICATION OF POPF

The definition and grading of POPF were proposed by the International Study Group on Pancreatic Fistula Definition in 2005, and updated in 2016. POPF is defined as an abnormal communication between the pancreatic ductal system and another epithelial surface containing pancreas-derived, enzyme-rich fluid. In the updated POPF grading, POPFs were graded as grade B and grade C biochemical leaks (Fig. 1). If any non-surgical drainage, either percutaneous or endoscopic, was performed, POPF was graded as grade B. In cases of reoperation, organ failure, or mortality, the grade was C.

Owing to the increasing numbers of endoscopic interventions, as discussed below, an endoscopy-oriented classification was proposed by Mutignani et al. (Table 1). Leak types are classified into three categories: type I (leakage from the small side branches or the very distal end of the pancreatic duct), type II (leakage from the main pancreatic duct, with disconnected/disrupted pancreatic duct syndrome), and type III (leakage after pancreatectomy).

Type I pancreatic leakage or fistula occurs after pancreatic parenchymal injury and can be managed by bridging the pancreatic duct with a stent.

<table>
<thead>
<tr>
<th>Leakage</th>
<th>Subtype</th>
<th>Endoscopic interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Head (IH)</td>
<td>Bridging stent or NPD</td>
</tr>
<tr>
<td>Body (IB)</td>
<td>Bridging stent or NPD</td>
<td></td>
</tr>
<tr>
<td>Tail (IT)</td>
<td>Bridging stent if duct caliber allows or cyanoacrylate/fibrin glue/other polymer injection at pancreatic tail/fistulous tract</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Open proximal stump (IIO)</td>
<td>Bridging stent or NPD or extrapancreatic transpapillary protruding stent</td>
</tr>
<tr>
<td>Closed proximal stump (IIC)</td>
<td>EUS + transmural drain of fluid collection from the distal gland into stomach/intestine or EUS-guided pancreaticogastrostomy or conversion to open + bridging stent/NPD</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Proximal (IIIP)</td>
<td>Transpapillary protruding stent to drain the collection</td>
</tr>
<tr>
<td>Distal (IIID)</td>
<td>Drain the CBD and the jejunum at the level of anastomosis EUS for transmural drain of peripancreatic collections or pancreaticogastrostomy</td>
<td></td>
</tr>
</tbody>
</table>

NPD, nasopancreatic drain; EUS, endoscopic ultrasonography; CBD, common bile duct.
creatic stent. In cases of type II leakage or fistulae, the treatment strategy may differ depending on the stump. When the stump is open (type IIO), pancreatic duct drainage is necessary owing to the absence of fluid collection. In contrast, EUS-D can be performed when the stump is closed and fluid collection is present (type IIC). Finally, type III was sub-classified as type IIIP (leakage after distal pancreatectomy) or type IIID (leakage after pancreatecoduodenectomy). Although transpapillary drainage has been described as the treatment of choice, EUS-D is increasingly utilized for both types IIIP and IIID. Type IIID leakage differs from other types because it is caused by anastomotic leakage and includes both pancreatic and intestinal juice leakages. This endoscopy-oriented classification helps understand the pathophysiology of POPF and make an informed decision regarding treatment options; however, treatment outcomes based on this classification require validation.

WHAT ARE THE INDICATIONS OF DRAINAGE?

While POPFCs occur in 20% to 40% of cases after pancreatic surgery, only 9% to 11% of POPFCs require interventions, suggesting that most POPFCs can be managed conservatively through techniques such as prolonged period of fasting, total parenteral nutrition, and somatostatin analogs. The indications for intervention for POPFCs are similar to those for PFCs after acute pancreatitis. The most common indications are clinical symptoms such as infection, pain, enlargement of fluid collection, and persistent discharge with high levels of pancreatic enzymes.

The indication for drainage according to fluid collection size has not been established, but the size of most POPFCs undergoing interventions is larger than 5 to 6 cm in most reports. However, in cases with in-dwelling surgical drainage, the size of POPFCs can be small, or there might be no collection in cases with external POPFs, which still require intervention. Thus, it may be difficult to set a POPFC size threshold to indicate drainage.

Although infection is one of the major indications for interventions for POPFCs, the infection rates by positive culture of fluid vary from 30% to 91%. Common bacteria found in culture were *Klebsiella* spp., *Enterococcus* spp., *Enterobacter* spp., and *Pseudomonas* spp.; however, Candida spp. were also detected. Thus, empirical antibiotics should be administered first, but escalation or de-escalation should be considered according to the culture results, including fungal infections. One study suggested that the computed tomography (CT) value could predict the presence of infection, which may help identify patients who require interventions. The exploration of biomarkers, such as procalcitonin, is needed to reliably detect infected POPFCs.

WHICH IS BETTER FOR MANAGEMENT OF POPFCS, PERCUTANEOUS OR ENDOSCOPIC?

In cases of POPFCs, owing to the invasiveness of surgical management, noninvasive treatments such as total parental nutrition, jejunal feeding, and antibiotics are preferred. Recently, less invasive drainage has been increasingly utilized and there are two approaches in less invasive approach to POPFCs by PCD or EUS-D.

In PCD, the POPFCs are punctured under CT or transabdominal ultrasonography guidance, and percutaneous external drainage is performed. In EUS-D, POPFCs are punctured under EUS guidance and internally drained using plastic and/or metal stents, and lumen-apposing metal stents (LAMSs) are placed. Temporary external naso-POPFC drainage can be used for irrigation (Fig. 2). While external drainage can be removed in EUS-D, it needs to be maintained until the resolution of POPF in PCD and can impair the quality of life with a risk of continuous external pancreatic fistula.

In a systematic review and meta-analysis comparing EUS-D and PCD, technical and clinical successes were achieved in 94% and 87% of cases, respectively, with AE and recurrence rates of 14% and 9%, respectively. When EUS-D was compared to PCD, the technical success rate was not significantly different with odds ratio (OR) of 0.94 (95% confidence interval [CI], 0.14–0.62). However, the clinical success rate was higher with an OR of 1.90 (95% CI, 0.95–3.81) and AE rate was lower with an OR of 0.69 (95% CI, 0.24–1.98) in EUS-D, though without statistical significance. The length of hospital stay was significantly shorter (mean difference, 3.84 days in EUS-D). As a long-term outcome, the recurrence rate was similar with OR of 1.12 (95% CI, 0.27–4.76).

Comparison between EUS-D and PCD for PFCs after acute pancreatitis was also reported. In a meta-analysis of endoscopic drainage compared to PCD in cases with PFCs after acute pancreatitis, a relative risk (RR) of clinical success was 0.40 (95% CI, 0.26–0.61), suggesting the superiority of endoscopic drainage. The length of hospital stay was shorter in the endoscopic drainage group, with a mean difference of 8.97 days. In contrast, RRs of technical success, AE, and recurrence did not differ significantly with RRs of 1.50 (95% CI, 0.52–4.37), 0.77...
clinical outcomes were quite similar in POPFCs and PFCs after acute pancreatitis; the clinical success rate was higher with a shorter length of hospital stay in EUS-D. Furthermore, the risk of pancreatic fistula is reportedly higher in PCD than in EUS-D for PFCs after acute pancreatitis. As surgical drainage is sometimes left in place at the time of POPF diagnosis, internal drainage via EUS-D is preferred over PCD to avoid persistent pancreatic fistula. In terms of anatomy, while EUS-D is used for centrally located PFCs close to the stomach or duodenum, PCD works better for peripherally located PFCs.

In summary, EUS-D should be selected as a first-line treatment for POPFCs rather than PCD when it is technically and anatomically feasible because it might be associated with a higher clinical success rate and shorter hospital stay, as shown in PFCs after acute pancreatitis.

**WHICH STENT IS SUITABLE FOR EUS-GUIDED DRAINAGE?**

Currently, electrocautery-enhanced LAMSs are widely used in various EUS-guided procedures such as EUS-guided gallbladder drainage and PFC drainage. An electrocautery-enhanced system allows a single-step procedure, and a large-diameter LAMS may facilitate the drainage of infected fluid or necrotic tissues as well as direct endoscopic necrosectomy for massive WON lesions. The role of LAMS in the management of PFCs after acute pancreatitis has been investigated in comparison to that of conventional plastic stents (PS). In a head-to-head comparison between LAMS and PS for EUS-guided drainage of PFC after acute pancreatitis, technical and clinical success rates did not differ between two stents but the AE rate was lower in LAMS. In another meta-analysis, clinical outcomes of LAMS and PS for walled-off necrosis did not differ significantly, other than shorter procedure time in LAMS. In EUS-D for POPFCs, 7 to 10 Fr PS are mainly used but a few recent studies evaluated the safety and effectiveness of LAMS for POPFCs (Table 2). Technical and clinical success rates ranged from 87.2% to 100% and 78.7% to 93.0%, respectively, in EUS-D using LAMS, and AE rates were higher than 10%. Evidence comparing LAMS and PS in the context of POPFC treatment of POPFCs are scarce. One retrospective study compared LAMS and PS in EUS-D,
which did not show the superiority of LAMS. The clinical success rates were 87% and 100% (p=0.997), and the AE rates were 14.5% and 4.6% (p=0.114) in the LAMS and PS groups, respectively. The recurrence rate was higher in the LAMS group (12%) than in the PS group (2.3%), although the difference was not statistically significant (p=0.114). A study by Fujimori et al. suggested that LAMS might be associated with a shorter length of hospital stay. Notably, technical success rates of EUS-D using LAMS were lower in cases after pancreaticoduodenectomy: 73.7% after pancreaticoduodenectomy and 96.4% after distal pancreatectomy (p=0.02). Technical failure was due to the distance between the POPFC and the luminal wall, which might be longer in cases after pancreaticoduodenectomy. As LAMS are not feasible in cases with POPFCs that are distant from the gastrointestinal lumen, stent selection might be affected by the type of surgery and the subsequent distance between the POPFC and the luminal wall.

One of the advantages of large-bore LAMS is that it can facilitate the drainage of PFC contents as well as access for direct endoscopic necrosectomy, if necessary. Direct endoscopic necrosectomy is performed as a step-up approach in cases of walled-off necrosis following necrotic pancreatitis. The rate of endoscopic necrosectomy might differ according to the solid component within PFCs but was reported to be 40% to 50% in cases with large walled-off necrosis. Meanwhile, the rate of direct endoscopic necrosectomy for POPFCs ranged from 0 to 33.3%. While the rate of necrosectomy was 7.0% to 33.3% in four studies with EUS-D using PS, it was 0% to 14.5% in three studies with EUS-D using LAMS. Although inter-study comparison is difficult, the use of LAMS might allow better drainage and reduce the necessity of endoscopy.

In summary, the superiority of LAMS over PS has not been demonstrated in POPFCs, and further evidence is required. In walled-off necrosis after acute pancreatitis, LAMS is increasingly utilized, but a potential risk of bleeding by LAMS placement longer than three to four weeks has been suggested. To reduce the risk of bleeding, exchange from LAMS to PS is recommended, or coaxial PS placement through LAMS is also investigated. If LAMS is to be used in POPFCs, the risk of bleeding and the role of coaxial PS should be evaluated.

### WHEN SHOULD WE INTERVENE?

The timing of interventions for the PFCs after acute pancreatitis has long been discussed. Although delayed interventions were reportedly associated with low mortality, the role of early interventions is increasingly being discussed with conflicting data. A recent randomized controlled trial of immediate drainage for necrotizing pancreatitis did not demonstrate its superiority over delayed drainage. However, early interventions are clinically needed for the deterioration of infection in PFCs. While some studies have reported that early (<4 weeks) interventions are associated with increased AEs, recent studies have focused on encapsulation of PFCs, rather than the timing itself. Although encapsulation is often seen after four weeks of acute pancreatitis onset, it can sometimes occur within four weeks and early interventions can be safe and feasible in cases with encapsulated PFCs.

However, the appropriate timing of interventions for POPFCs has not yet been established. While some POPFCs can be managed conservatively, adverse consequences, such as infection and bleeding, may occur in refractory POPFCs. In a comparative study of early versus delayed rescue surgery, early surgery might decrease mortality but there is no established consensus on the indication and appropriate timing of invasive surgery. Although EUS-guided drainage, a less invasive alternative to surgery, has the potential advantages of early clinical response and shorter hospital stay, it is still associated with procedure-related AEs. Given the low invasiveness of EUS-D and its

### Table 2. EUS-guided drainage of postoperative pancreatic fluid collections using lumen-apposing metal stents

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>LAMS type</th>
<th>LAMS size (mm)</th>
<th>Technical success (%)</th>
<th>Clinical success (%)</th>
<th>Adverse event (%)</th>
<th>Mean stent duration (day)</th>
<th>Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mudireddy et al.</td>
<td>2018</td>
<td>47</td>
<td>Axios</td>
<td>10, 15</td>
<td>93.6</td>
<td>89.3</td>
<td>10.6</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>2019</td>
<td>62</td>
<td>Axios</td>
<td>10, 15</td>
<td>96.8</td>
<td>91.9</td>
<td>12.9</td>
<td>46.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Storm et al.</td>
<td>2020</td>
<td>75</td>
<td>Axios</td>
<td>10</td>
<td>100</td>
<td>93.0</td>
<td>25.3</td>
<td>48</td>
<td>5.3</td>
</tr>
<tr>
<td>Oh et al.</td>
<td>2022</td>
<td>47</td>
<td>Spaxus</td>
<td>8, 10</td>
<td>87.2</td>
<td>78.7</td>
<td>12.8</td>
<td>47.3</td>
<td>2.1</td>
</tr>
</tbody>
</table>

EUS, endoscopic ultrasonography; LAMS, lumen-apposing metal stent.

Median stent duration: a) early (<30 days) drainage and b) delayed (>30 days) drainage.
internal drainage, the threshold for EUS-D may be lower than that for surgery or PCD. As discussed in EUS-D for PFCs after acute pancreatitis, the timing of drainage for POPFCs is being increasingly reported; however, there are some differences between PFCs after acute pancreatitis and POPFCs. First, there is adhesion around the POPFCs due to surgical procedures, which may allow for safe EUS-D, even in the early post-surgery phase. Two retrospective studies focused on the safety of early EUS-D, and early and delayed drainage were comparable in terms of safety. Storm et al. compared clinical outcomes in acute (<2 weeks), early (<4 weeks), and delayed EUS-D for POPFCs and found no significant differences in clinical success (95%, 93%, and 94%, respectively) and AEs (21.4%, 15.0%, and 30.3%, respectively). Furthermore, necrosectomy is less often required during early EUS-D. In our meta-analysis of 235 cases of POPFCs, there were no significant differences in clinical success and AE between early and delayed EUS-D, although all studies included in the analysis were retrospective.

Oh et al. evaluated clinical outcomes according to the presence of encapsulation in addition to the timing of EUS-D. Technical success, clinical success, and AE rates were also similar between early and delayed interventions. In this study cohort, encapsulation described as “walled-off fluid collection” was observed in 81.3%; encapsulation developed in 43.8% within 14 days and in additional 37.5% between 14 and 28 days. Clinical outcomes did not differ according to encapsulation; the clinical success rates were 97.4% and 88.9% for POPFCs with and without encapsulation, respectively, and the median time to resolution of POPFCs was 23.5 days in both groups. There were two instances of bleeding (4.2%) in the study cohort, and the time to EUS-D was 7 and 9 days after surgery in cases with bleeding. However, the presence or absence of encapsulation was not mentioned in the bleeding cases. In cases without encapsulation, PCD, which is a relatively sterile procedure compared with EUS-D, might be preferred to avoid contamination. However, a comparative study by Tamura et al. revealed technical success, clinical success, and AEs were comparable between EUS-D by nasocystic drainage and EUS-D with PCD in this setting. Furthermore, the time to resolution and length of hospital stay were shorter with EUS-D, suggesting its superiority, even in POPFCs without encapsulation. While encapsulation is emphasized in PFCs after acute pancreatitis to determine the timing of interventions, it is still unclear whether encapsulation of POPFCs might favorably affect the clinical outcomes, especially the safety, of early drainage in POPFCs. Further prospective studies are warranted to confirm the appropriate timing of interventions for POPFCs.

ARE POPFS WITH AND WITHOUT FLUID COLLECTION DIFFERENT?

In contrast to PFCs after acute pancreatitis, POPFs may or may not develop fluid collection, because the surgical drain may be kept in place at the time of POPF occurrence. EUS-guided internalization of external pancreatic fistulas has been reported in some case series. EUS-guided pancreaticogastrostomy, EUS-guided drainage of the PCD tract, or EUS-assisted rendezvous technique (Fig. 3) can be utilized according to the anatomy, such as the presence of a dilated pancreatic duct (Table 3). First, EUS-D can be performed by artificial fluid collection via saline injection through a surgical drain. If artificial fluid collection cannot be performed, direct transmural drainage of the fistula tract is an option when the surgical drainage tip can be visualized using EUS. If direct fistula tract drainage is difficult because of an invisible drain tip or insufficient traction force, rendezvous techniques with a percutaneous approach can be alternatives. In the “outside-in” technique, the enteric wall is punctured by a trans-jugular portosystemic shunt needle via the percutaneous route under fluoroscopic guidance, then a guidewire is inserted and grasped by an endoscope. Transmural stents were inserted endoscopically over the guidewire after tract dilation. In the “inside-out” technique, the fistula tract is punctured under EUS guidance, followed by insertion of a guidewire into the fistula tract. The guidewire is caught by a basket catheter via the percutaneous route; subsequently, transmural stents are inserted into the fistula tract endoscopically. Finally, when the aforementioned techniques are unavailable and/or the remnant pancreatic duct has sufficient diameter, EUS-guided pancreatic duct drainage can be selected.

A multicenter retrospective study compared the clinical outcomes of POPFs with or without fluid collections. Among 2,184 cases with pancreatic resection, 196 cases (132 with fluid collection and 64 without fluid collection) developed POPFs and underwent interventions. Notably, systemic inflammatory changes, such as C-reactive protein levels, were higher in POPFs with fluid collection (POPFCs). Regarding interventional procedures, PCD was the most often performed (45%), followed by EUS-D (30%), in POPFs with fluid collection. Surgical drainage (64%), EUS-D (16%), and surgery (16%) were performed for POPFs without fluid collection. The clinical success rates of...
EUS-D were the highest in POPFs with fluid collection (85%) and POPFs without fluid collection (90%). Notably, the median time to resolution was shorter with EUS-D than with the other modalities. In POPFs with fluid collection, EUS-D required a median of 8 days, compared to 25 days for PCD. In cases of POPFs without fluid collection, it was 4.5 days in EUS-D and 51 days for EUS-D and surgical drainage, respectively.

Thus, EUS-D should be the first-line treatment for POPFs with and without fluid collection, although advanced techniques may be necessary for POPFs without fluid collection.

**Table 3. Complex endoscopic interventions for postoperative pancreatic fistula without fluid collection**

<table>
<thead>
<tr>
<th>Intervention</th>
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<tbody>
<tr>
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</tr>
<tr>
<td>EUS-guided direct fistula tract drainage</td>
</tr>
<tr>
<td>Endoscopic rendezvous with percutaneous route</td>
</tr>
<tr>
<td>Outside-in</td>
</tr>
<tr>
<td>Inside-out</td>
</tr>
<tr>
<td>EUS-guided pancreaticoenterostomy</td>
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**Fig. 3.** Endoscopic ultrasonography (EUS)-assisted rendezvous for postoperative pancreatic fistula without fluid collection after distal pancreatectomy with pancreatic divisum. (A) A limited fluid collection around the surgical site seen on computed tomography (CT). (B) Surgical drain left in place on CT. (C) After failed minor papilla cannulation, the pancreatic duct was punctured under EUS-guidance for rendezvous technique. (D) Successful minor papilla cannulation by EUS-assisted rendezvous. (E) A pancreatic stent was placed. (F) Endoscopic image of a pancreatic stent through the minor papilla.

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</tbody>
</table>

EUS, endoscopic ultrasonography.

**DOES TRANSPAPILLARY DRAINAGE BY ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PLAY A ROLE?**

Transpapillary pancreatic drainage by endoscopic retrograde cholangiopancreatography (ERCP) can be an option for POP-FCs due to pancreatic disruption or leak after distal pancreatectomy (Table 1) but was less frequently reported than EUS-D.66-62 Technical and clinical success rates were reportedly 75% to 100% and 68% to 100%, respectively, without significant AEs. As reported in ERCP for postoperative bile leakage, there are some treatment options, such as pancreatic sphincterotomy, nasopancreatic duct tube placement, PS placement, or a combination of these. Although postoperative bile leak can often be managed by endoscopic biliary sphincterotomy alone, pancreatic sphincterotomy is insufficient, and pancreatic drainage is necessary for POPF because of the higher intraductal pressure of the pancreas.12 In general, in cases with pancreatic leak on pancreatography, bridging the leak is recommended. However,
in a limited number of case studies, there were no significant differences among the procedures. Due to its direct intervention in pancreatic duct leaks, recurrence was only reported in one case with pancreatic stent occlusion, which might be an advantage over EUS-D or PCD for POPFCs.

As discussed above, EUS-D using LAMS can be technically difficult in cases of POPFs after pancreaticoduodenectomy, and ERCP may play a role in this setting. However, conventional ERCP is not technically possible owing to the surgically altered anatomy, and balloon enteroscope-assisted ERCP (BE-ERCP) is necessary. Data on BE-ERCP are limited, but the technical success rates of BE-ERCP for pancreatic indications are not as high as those for biliary indications. Thus, expertise in both BE-ERCP and EUS-guided pancreatic duct drainage is important for managing cases after pancreaticoduodenectomy.

In PFCs after acute pancreatitis, the role of combined EUS-D and transpapillary drainage has also been discussed, especially in patients with pancreatic duct disruption or disconnected pancreatic duct syndrome who are at high risk of recurrence.

In cases with infected PFCs, EUS-D can be performed first, and after the infection is resolved, a transpapillary approach can manage pancreatic duct processes such as pancreatic leakage or pancreatic duct stricture. A direct comparison between EUS-D and transpapillary drainage for POPFs has not been reported thus far; however, the combination of EUS-D and transpapillary drainage might also play a role in cases with continuous POPFs.

**PROPOSAL FOR STRATEGY OF POPF MANAGEMENT**

The selection of interventions for POPF depends on the presence of fluid collection, the type of pancreatic surgery, and the presence of a surgical drain. The proposed strategy for POPF management is illustrated in Figure 4. First, in cases of fluid collection, EUS-D can be selected because of its anatomical and technical feasibility. Second, in the case with distal pancreatectomy, ERCP is the next step. If these methods fail, EUS-guided approaches, such as drainage of the fistula tract or rendezvous,

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**Fig. 4.** A proposal for strategy of postoperative pancreatic fistula. BE-ERCP, balloon endoscope-assisted endoscopic retrograde cholangiopancreatography; DP, distal pancreatectomy; ERCP, endoscopic retrograde cholangiopancreatography; EUS-D, endoscopic ultrasonography-guided drainage; EUS-PDD, EUS-guided pancreatic duct drainage; EUS-RV, EUS-assisted rendezvous; MPD, main pancreatic duct; PD, pancreaticoduodenectomy; POPF, postoperative pancreatic fistula. EUS-guided drainage of artificially created fluid collection or direct fistula tract drainage. EUS-guided rendezvous via the percutaneous route. EUS-guided rendezvous with ERCP or BE-ERCP.
can be attempted. However, conventional ERCP is difficult, and EUS-guided approaches such as pancreatic duct drainage and fistula tract drainage are the next steps, depending on the presence of pancreatic duct dilation and surgical drainage. If experts are available, BE-ERCP can be attempted with or without EUS-assisted rendezvous. If all the endoscopic procedures fail, percutaneous drainage or surgery should be considered. As both EUS-guided pancreatic duct drainage or rendezvous and BE-ERCP require expertise and have potential risks of AEs, our proposed strategy should be modified according to the local expertise and each patient’s condition.

CONCLUSIONS

POPFs are common AEs that occur after pancreatic surgery and may require intervention. As demonstrated for PFCs after acute pancreatitis, EUS-D may be preferred because of its high clinical success rate and shorter hospital stay. However, the clinical evidence of POPFs is still limited compared to that of PFCs after acute pancreatitis. The indications and timing of the intervention and stent selection in EUS-D for POPFs or POPFCs require further investigation.

Conflicts of Interest

Yousuke Nakai received research grants from Boston Scientific Japan and HOYA Corporation, and honoraria from Boston Scientific Japan, Fujifilm Corporation, and Olympus Corporation. Hiroyuki Isayama received research grants from Boston Scientific Japan, Fujifilm Corporation, Fujifilm Health Care Corporation, Gadelius Medical KK, and Zeon Medical Inc., and honoraria from Boston Scientific Japan, Fujifilm Corporation, Taewoong Medical Devices, Olympus Corporation, Century Medical Inc., and Cook Medical. Ichiro Yasuda received honoraria from Gadelius Medical KK, Medicos Hirata, and Olympus Corporation. The other authors have no potential conflicts of interest to declare.

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