Endoscopic endgame for obstructive pancreatopathy: outcomes of anterograde EUS-guided pancreatic duct drainage. A dual-center study CME

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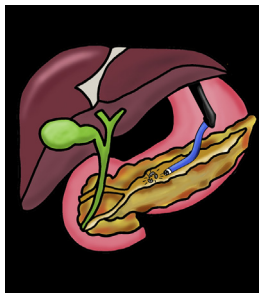
GRAPHICAL ABSTRACT



Background and Aims: Anterograde endoscopic ultrasound-guided pancreatic duct drainage (EUS-PDD) refers to transmural drainage of the main pancreatic duct via an endoprosthesis passed anterograde through the gastric (or intestinal) wall. Anterograde EUS-PDD is a rescue procedure for recalcitrant cases of benign obstructive pancreatopathy.

Methods: We conducted a dual-center retrospective chart review of 28 patients (mean age, 59 years; 50% female) who underwent attempted anterograde EUS-PDD between April 2016 and September 2019 for chronic pancreatitis (CP) (93%) or pancreaticojejunostomy stenosis (PJS) after Whipple resection (7%). The study endpoint was achievement of transpapillary/transanastomotic drainage (definitive therapy).

Results: Gastropancreaticoenterostomy (ring drainage, definitive therapy) was successfully performed during the index procedure in the 2 patients with PJS (technical success, 100%). Clinical success was 100% in the 2 ring drainage recipients during a mean 18-month follow-up period. The remaining 26 patients with CP underwent attempted pancreaticogastrostomy (PG) with 81% technical success, 75% clinical success, and 15% adverse events (AEs). Repeat endoscopic transmural interventions were performed in the 15 patients with clinical success after PG creation. Definitive therapy transpired in all 15 patients after a median 1 repeat procedure per patient. Clinical success after definitive therapy was maintained in all 15 patients (100%) during a median 4.5-month follow-up.

Conclusions: In agreement with previous studies, our study showed mild to moderately high rates of technical failure (19%), clinical failure (25%), and AEs (15%) during index drainage (PG creation). Among patients with CP with both technical and clinical success after index PG creation (n = 15), 100% definitive therapy was achieved and clinical outcomes were excellent (100% clinical success, 0% AEs). (Gastrointest Endosc 2020;92:1055-66.)

(footnotes appear on last page of article)

BACKGROUND AND AIMS

Benign obstructed pancreatic ductal systems are generally managed using a step-up approach of medical therapy, endoscopy, and surgery.[1] Overarching goals of treatment are pain relief, morbidity reduction, and preservation of pancreatic function.[2,3] The advent of therapeutic endosonography has broadened the repertoire of endoscopic interventions that may be attempted before surgery. Endoscopic ultrasound-guided pancreatic duct drainage (EUS-PDD) can be used as a rescue procedure after technical failure of endoscopic retrograde pancreatography (ERP) and can serve as an alternative to enteroscopy-assisted endoscopic retrograde pancreatography (EA-ERP) in cases of surgically altered anatomy.[4] EUS-PDD is an umbrella term that encompasses EUS-guided rendezvous-assisted ERP and anterograde EUS-PDD. Rendezvous-assisted ERP consists of transmural puncture and pancreatography, followed by anterograde transpapillary/transanastomotic guidewire passage to facilitate main pancreatic duct (MPD) cannulation via ERP. Anterograde EUS-PDD refers to transmural anterograde passage of an endoprosthesis directly into the MPD (ie, pancreaticogastrostomy, pancreaticoenterostomy, and gastropancreaticoenterostomy [also known as ring drainage]). Anterograde EUS-PDD is technically challenging and relatively high risk compared with other endoscopic MPD drainage modalities. It should be reserved as a salvage procedure for nonsurgical candidates (and for patients who decline surgery), after technical failure and/or infeasibility of ERP and rendezvous-assisted ERP (or EA-ERP in altered anatomy). Chronic pancreatitis (CP), anastomotic pathology in surgically altered anatomy (eg, pancreaticojejunostomy stenosis [PJS]), and disconnected pancreatic duct syndrome are among the most frequently cited clinical indications for anterograde EUS-PDD.[4-14]

Long-term outcomes of anterograde EUS-PDD are not fully known at this time. The available literature is relatively sparse and mostly single-center retrospective studies with small sample sizes. Reasons for this knowledge gap include the rarity and relative novelty of this procedure (ie, initial description by François in 2002).[7] The aim of our retrospective dual-center study is to report the long-term technical and clinical outcomes of anterograde EUS-PDD, including the endpoint for endoscopic transmural (anterograde) therapy.

METHODS

We conducted a dual-center retrospective study of patients with obstructive pancreatopathy due to CP (n = 26) or PJS after Whipple surgery (n = 2), who underwent anterograde EUS-PDD at 2 tertiary care centers in the United States between April 2016 and September 2019. Anterograde EUS-PDD was our umbrella term for EUS-guided pancreaticogastrostomy (PG) and EUS-guided gastropancreaticoenterostomy (ring drainage). One advanced endoscopist per institution performed the procedures. A uniform set of inclusion criteria existed within the 2 centers (West Virginia University Medicine and University of North Carolina Medical Center). The indication for pancreatic ductal drainage was relief of symptomatic benign pancreatic ductal hypertension, suspected because of pancreatic pain or recurrent acute pancreatitis occurring in the setting of a dilated MPD. The exception was a single case of PG attempted in a nondilated MPD (2 mm, body of pancreas) in a patient with CP and an obstructing MPD stone, which resulted in technical failure. A previous attempt at both ERP and rendezvous-assisted ERP was mandatory before attempting PG in normal anatomy. A previous attempt at EA-ERP was necessary before attempting gastropancreatoenterostomy (ring drainage) in post-Whipple anatomy. Last, before attempting PG or ring drainage, patients had to be deemed suboptimal surgical candidates (after surgical consultation) or the patients provided informed refusal of surgery.

PG was attempted in the CP study arm (n = 26) after technical failure of ERP and rendezvous-assisted ERP. Repeat endoscopy session(s) occurred until attainment of transpapillary drainage. Ring drainage was attempted in the PJS study arm (n = 2) after technical failure of EA-ERP. The endoscopic endpoint in both study arms was definitive therapy, defined as transpapillary drainage (normal anatomy) or transanastomotic drainage (surgically altered anatomy). In the PG cohort, 8 patients were previously reported in single-center studies at our respective institutions.[15,16] This study was approved by the Institutional Review Boards for Human Research and complied with Health Insurance Portability and Accountability Act regulations at each participating institution.

Technical success, clinical success, and other collected data

Data collection was categorized according to index and repeat drainage procedures. No repeat procedures were necessary in the PJS study arm (ie, definitive therapy occurred during the index endoscopy), whereas repeat endoscopy occurred after all clinically successful PGs (CP arm). If definitive therapy was not achieved during a repeat endoscopy session, the goal was PG stent exchange (ie, PG aperture widening). A variety of endoscopic techniques were used during repeat endoscopy session(s) to achieve definitive therapy, including ERP, rendezvous-assisted ERP, transmural (anterograde) pancreatoscopy with electrohydraulic lithotripsy (TMP-EHL), and/or anterograde transpapillary stent insertion. Follow-up was recorded for all patients after their final procedure, regardless of outcome, by way of chart review, clinic visits, and/or telephone calls.

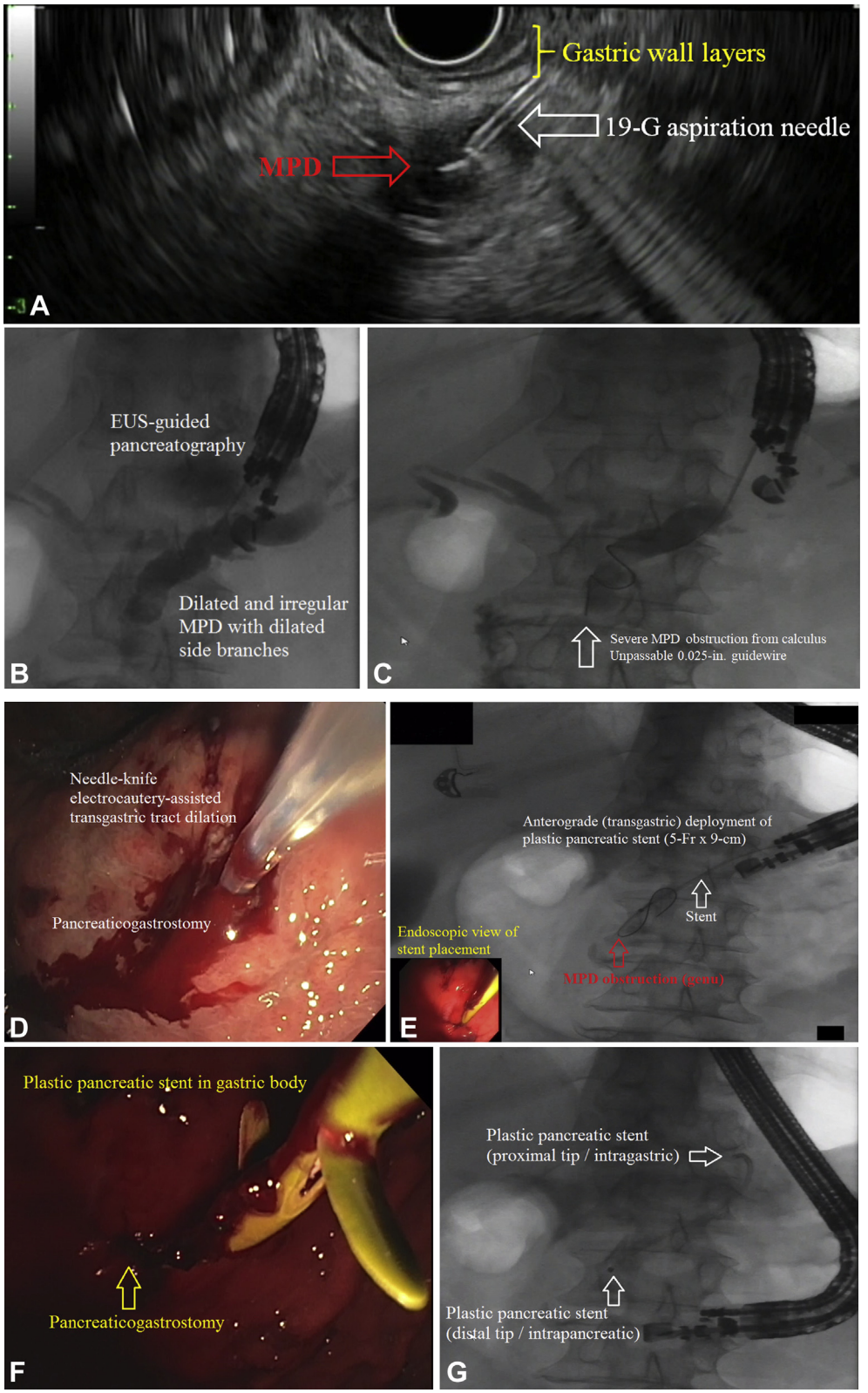


Figure 1. A, Endosonographic view of EUS-guided transgastric MPD access. A 19-gauge aspiration needle is accessing the dilated main pancreatic duct (MPD; 10.5 mm) in the body of the pancreas. **B**, Fluoroscopic view of EUS-guided transgastric pancreatography. A filling defect is present in the genu of the pancreas. The proximal MPD is irregular and dilated to 10.5 mm in the body of the pancreas. Multiple irregular side branches are present. **C**, Fluoroscopic view of attempted transgastric (anterograde) guidewire passage. The 0.635-mm (0.025-inch) guidewire is unable to traverse a high-grade MPD obstruction located in the genu. Rendezvous-assisted endoscopic retrograde pancreatography is no longer an option. **D**, Endoscopic view of needle-knife cautery-assisted transmural tract dilation in preparation for anterograde guidewire-assisted pancreatic stent passage. (*legend continued on next page*)

Technical success was broadly defined as completion of the intended procedure. A technically successful index drainage procedure was completion of PG in the CP arm and completion of ring drainage in the PJS arm. A technically successful repeat procedure (CP arm) consisted of either PG stent exchange, definitive therapy, or an endoscopic technique that facilitated future definitive therapy (eg, TMP-EHL). Clinical success was defined as partial to complete pain relief. Pain relief was defined subjectively by the patients using a scale of no relief, partial relief, and complete relief. Among patients who achieved clinical success, change in pre- and postprocedure narcotic usage was recorded. Adverse events (AEs) were recorded for all index and repeat procedures. AE severity was graded according to the American Society for Gastrointestinal Endoscopy (ASGE) lexicon for endoscopic AEs.[17]

Procedures

EUS-guided pancreaticogastrostomy. PG was attempted on 26 patients with CP and high-grade or complete distal MPD. Complete endosonographic examination of the pancreas was performed before the intended intervention. EUS-guided transgastric MPD access was obtained using a 19-gauge aspiration needle (Fig. 1A). EUS-guided pancreatography consisted of contrast medium (dilated 1:1 with sterile water) injected through the indwelling 19-gauge needle under fluoroscopy (Fig. 1B). A 0.635-mm (0.025-inch) (or 0.889 mm [0.035-inch]) straight or angled guidewire was advanced through the 19-gauge aspiration needle, into the MPD, and toward the head of the pancreas (Fig. 1C). If the guidewire was unable to traverse the papilla/anastomosis, PG was attempted.

To perform PG, the aspiration needle was exchanged over-the-wire in either a noncautery-assisted (ie, biliary balloon dilator) or a cautery-assisted transmural tract dilator (ie, needle knife, cystotome). The dilator was advanced through the gastric wall, pancreatic parenchyma, and into the MPD (Fig. 1D). Noncautery-assisted transmural tract dilation was usually attempted before cautery-assisted tract dilation. A biliary dilation balloon was the noncautery-assisted dilator of choice (Hurricane RX biliary balloon dilatation catheter; Boston Scientific, Marlborough, Mass, USA). The balloon length measured 4 cm and the inflated outside diameter was 4 mm. The dilation balloon catheter outside diameter was 5.8F; therefore, it was mostly used before deployment of a transmural stent with an outside diameter greater than 5F. When the biliary balloon dilator could not be wholly passed into the MPD, due to resistance against the catheter, cautery-assisted tract dilation was performed using either a needle knife (5-mm needle tip length; NeedleCut3V Needle Knife; Olympus, Center Valley, Pa, USA) or a cystotome (Cystotome Cystoenterostomy Needle Knife; Cook Medical, Winston-Salem, NC, USA). There were 2 main exceptions to our tract dilation strategy. In patients with a mildly dilated MPD (eg, 5 mm), into which we planned to insert a 3F plastic pancreatic stent, we used the 19-gauge aspiration needle as the transmural tract dilator. The rationale is that a 19-gauge aspiration needle is approximately the same diameter as a 3F plastic stent. The second exception was that cautery-assisted tract dilation was sometimes used as first-line therapy in patients with significantly fibrotic and/or calcified pancreatic parenchyma.

After successful transmural tract dilation, anterograde transmural insertion of 1 or 2 pancreatic stent(s) occurred (Fig. 1E). The final PG consisted of transmural stent(s); the distal stent tip(s) within the MPD, and the proximal tip(s) within the gastric lumen (Fig. 1F and G). The transmural endoprostheses used were either straight or pigtail pancreatic stents. Straight plastic pancreatic stents with a leading barb (Advanix pancreatic stent; Boston Scientific) were deployed with the leading barb in the MPD. The leading barb tip was deployed within the MPD because distal stent tip spontaneous migration (dislodgement) was thought to be more likely than proximal tip migration (because there is less space in the MPD to accommodate the stent tip, as opposed to the gastric lumen). Single-pigtail plastic pancreatic stents with a leading barb (Zimmon pancreatic stent; Cook Medical, Winston-Salem, NC, USA) were deployed with the pigtail of the stent either in the MPD or in the gastric lumen. Double-pigtail plastic pancreatic stents (DPPSs; Zimmon pancreatic stent; Cook Medical) were also used for PG creation.

EUS-guided gastropancreaticoenterostomy (ring drainage). Ring drainage is appropriate for cases of inaccessible papillae and/or anastomoses with incomplete obstruction. We reserved ring drainage for the 2 patients with surgically altered anatomy (eg, Whipple anatomy) resulting in inaccessible pancreaticojejunostomies. Ring drainage is almost identical to PG, except transanastomotic guidewire passage occurs. The guidewire is advanced through the pancreaticojejunostomy and coiled into the bowel lumen. Anterograde transmural stent passage occurs, but the distal end of the stent is advanced across the anastomosis and into the bowel lumen. The final gastropancreaticoenterostomy consists of the distal stent tip located within the bowel lumen and the proximal stent

The fibrotic pancreatic parenchyma was too hardened for successful noncautery-assisted tract dilation. **E**, Fluoroscopic view of anterograde deployment of a plastic pancreatic stent (5F × 9 cm) via the pancreaticogastrostomy (PG). The distal end of the stent is placed as far as the MPD obstruction in the genu of the pancreas. Endoscopic view of transgastric pancreatic stent deployment (thumbnail). **F**, Endoscopic view of the proximal end of the plastic pancreatic stent protruding into the gastric lumen via the PG. **G**, Fluoroscopic image of the successfully placed plastic pancreatic stent traversing the PG. The distal and proximal tips of the stent are labeled.

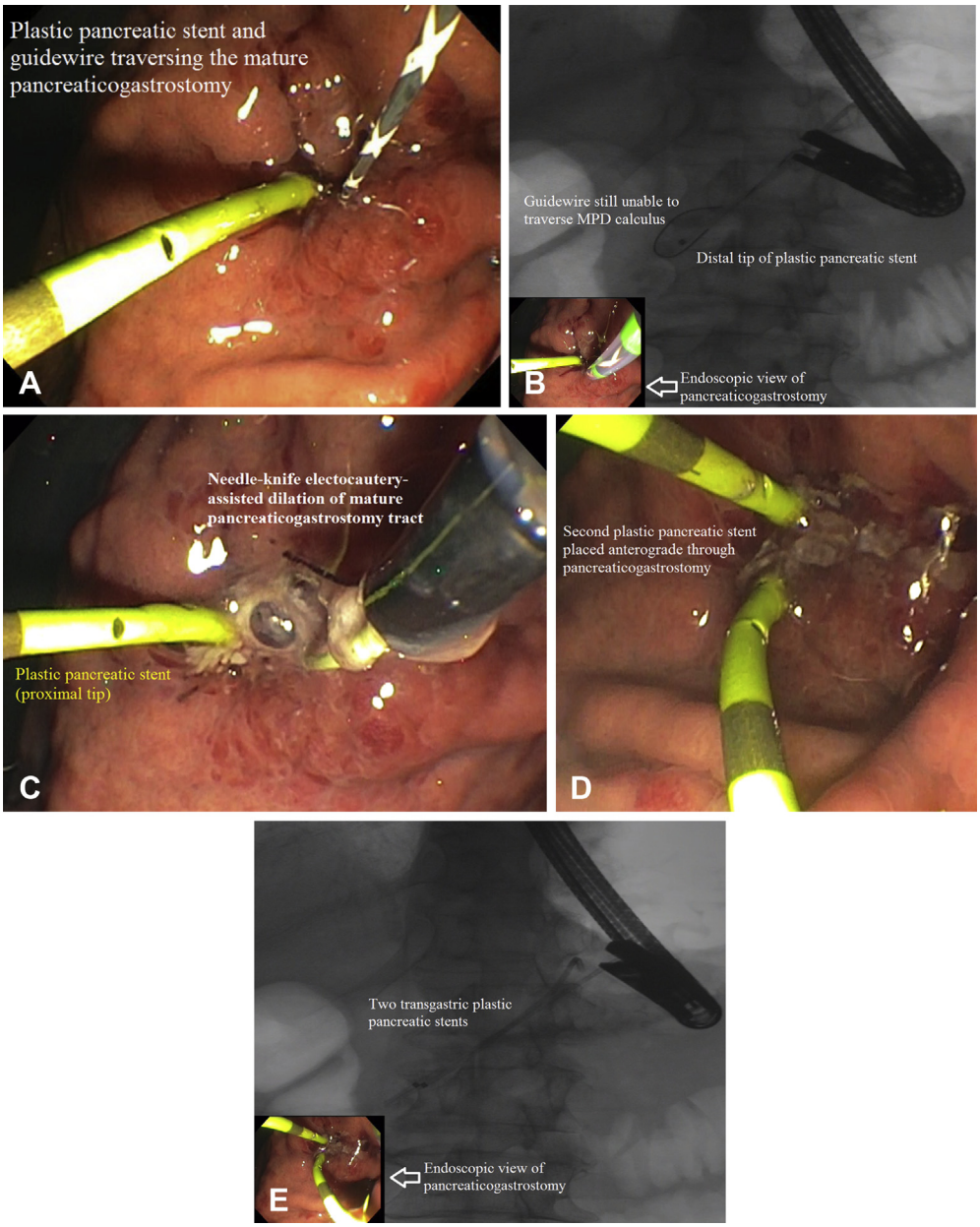


Figure 2. **A**, Second endoscopy session performed 2 months after the index procedure. Endoscopic view of a 5F × 9 cm plastic pancreatic stent (newly exchanged) and a 0.635-mm (0.025-inch) guidewire traversing the mature pancreaticogastrostomy (PG). **B**, Fluoroscopic view of the guidewire still unable to pass the main pancreatic duct (MPD) calculus located in the genu. **C**, Endoscopic view of needle-knife electrocautery-assisted dilation of the PG in preparation for anterograde guidewire-assisted passage of a second plastic pancreatic stent. **D**, Endoscopic view of a second plastic pancreatic stent successfully placed through the PG. **E**, Fluoroscopic view of both plastic pancreatic stents traversing the PG.

tip within the gastric lumen (definitive therapy). DPPSs were used for each ring drainage and were considered ideal stents for this drainage procedure, as each pigtail was able to curl within the lumen of the intestine and stomach. Ring drainage with a DPPS may theoretically reduce the risk of stent-induced pancreatic ductal injury from a lodged stent tip within the wall of the MPD.

Postprocedural management (after the index procedure). After the index transmural pancreatic endotherapy (ie, anterograde EUS-PDD) occurs, we routinely administer 3 days of postprocedural antibiotics, with gram-negative and anaerobic coverage. Longer courses of antimicrobials are prescribed after technical failure of anterograde EUS-PDD (eg, if the gastric wall is punctured, without transmural stent placement). The intention of prophylactic antimicrobials is prevention of perigastric abscess and/or pancreatic sepsis. We do not routinely use postprocedure rectal indomethacin or hydration in our patients with advanced CP, who we consider low risk for post-ERCP pancreatitis, because the pancreas is already fibrotic.

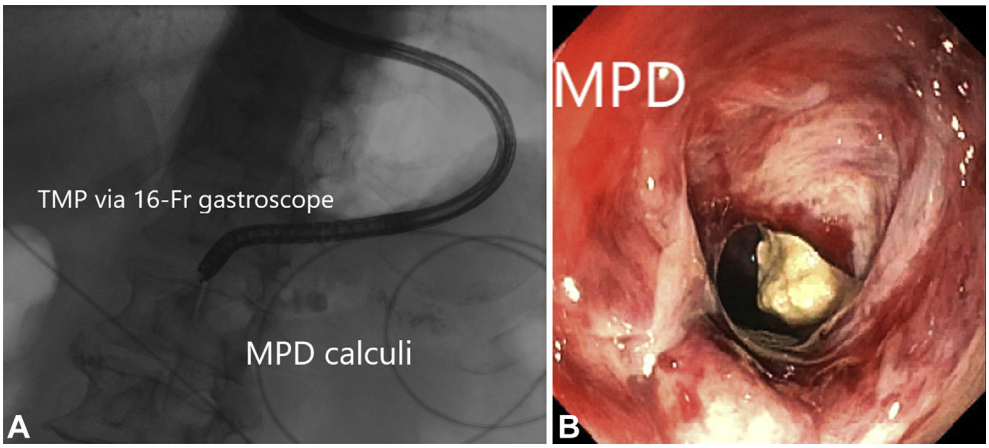


Figure 3. A, Fluoroscopic view of transmural pancreatography (TMP) using a 16F gastroscope inserted through the PG. Shadows from main pancreatic duct (MPD) calculi are visible. **B**, Anterograde transmural endoscopic view of the MPD with a stricture and an obstructing calculus before retrieval.

TABLE 1. Demographic and preprocedural information

Patient characteristics	Attempted anterograde EUS-PDD (n = 28)
Age (years), mean ± SD	59 ± 16
Female	14 (50)
Charlson Comorbidity Index, median (IQR)	3 (2-5)
Indication	
Chronic pancreatitis	26 (93)
Alcohol	19 (73)
Idiopathic	4 (15)
Recurrent choledocholithiasis	3 (12)
Stone(s)	12 (46)
Stricture(s)	10 (39)
Both	4 (15)
Pancreaticojejunostomy stenosis (Whipple anatomy)	2 (7)
Chronic narcotic therapy (preprocedure)	17 (61)
Pancreatic enzyme supplementation (preprocedure)	23 (82)
Main pancreatic duct diameter (mm), median (IQR)	6 (5-8)

Values are number (%) unless otherwise stated.
EUS-PDD, EUS-guided pancreatic duct drainage; *SD*, standard deviation; *IQR*, interquartile range.

Postprocedural indomethacin is administered for cases of obstructive pancreatopathy without CP (eg, PJS after Whipple resection). We often perform anterograde EUS-PDD as an outpatient procedure. Our outpatients are only admitted to the hospital if there is clinical suspicion for an AE.

Repeat endoscopy and definitive therapy. In patients with clinical success after index PG, endoscopic procedures were repeated electively until attainment of transpapillary drainage (definitive therapy). If definitive therapy was not accomplished during a repeat procedure, we performed elective PG stent exchange. The index (or previously placed) PG stent was exchanged for a new wider caliber transmural stent, or additional stent(s) were inserted parallel to the original stent to achieve a wick effect (Fig. 2A-E). TMP-EHL was performed during some repeat procedures for MPD stone disimpaction/definitive therapy (Fig. 3A and B). In 1 case, a 16F gastroscope was inserted through the PG, into the MPD, for intraductal stone clearance with a basket (Fig. 3A and B). All other cases of TMP-EHL consisted of anterograde transmural passage of a digital cholangiopancreatoscope (SpyGlass DS; Boston Scientific), followed by intraductal EHL, via a 1.9F bipolar electrohydraulic lithotripter probe (Autolith Touch; Boston Scientific), passed through the working channel of the cholangiopancreatoscope. Shocks were applied at 80 to

TABLE 2. Index anterograde EUS-PDD outcomes

Procedural variables	Attempted anterograde EUS-PDD (n = 28)	Technical success	Clinical success	Adverse events
Anterograde EUS-PDD	28	23 (82)	17 of 22 (77)*	4 (14)
Pancreaticogastrostomy	26	21 (81)	15 of 20 (75)	4 (15)
Gastropancreatoenterostomy (ring drainage)	2	2 (100)	2 (100)	0
Cautery-assisted transmural tract dilation	18 (64)	13 (72)		3 (17)
Needle knife	12	9 (75)		2 (17)
Cystotome (needle knife and ring electrode)	5	4 (80)		
ECE-LAMS (10 mm)	1	0		1 (100)
Noncautery-assisted transmural tract dilation	10 (36)	10 (100)		1 (10)
Balloon dilation	8	8 (100)		
No dilation	2	2 (100)		1 (50)
Transmural stent characteristics				
Straight plastic pancreatic stent	10 (36)	8 (80)		3 (75)
Single-pigtail plastic pancreatic stent	8 (28)	7 (87)		
Double-pigtail plastic pancreatic stent	8 (28)	7 (87)		
Biliary FCSEMS (10 mm × 6 cm)	1 (4)	1 (100)		
ECE-LAMS (10 mm)	1 (4)	0		1 (25)
Plastic stent dimensions				
Diameter (cm), median (IQR)	5 (5-7)			
Length (cm), median (IQR)	11.5 (9-15)			

Values are number (%) unless otherwise stated.

EUS-PDD, Endoscopic ultrasound-guided pancreatic duct drainage; *ECE-LAMS*, electrocautery-enhanced lumen-apposing metal stent; *FCSEMS*, fully covered self-expanding metal stent; *IQR*, interquartile range.

*The total number for clinical success excludes a single patient who underwent a technically successful EUS-guided pancreaticogastrostomy but who died 1 week later from an unrelated disease (vascular disease).

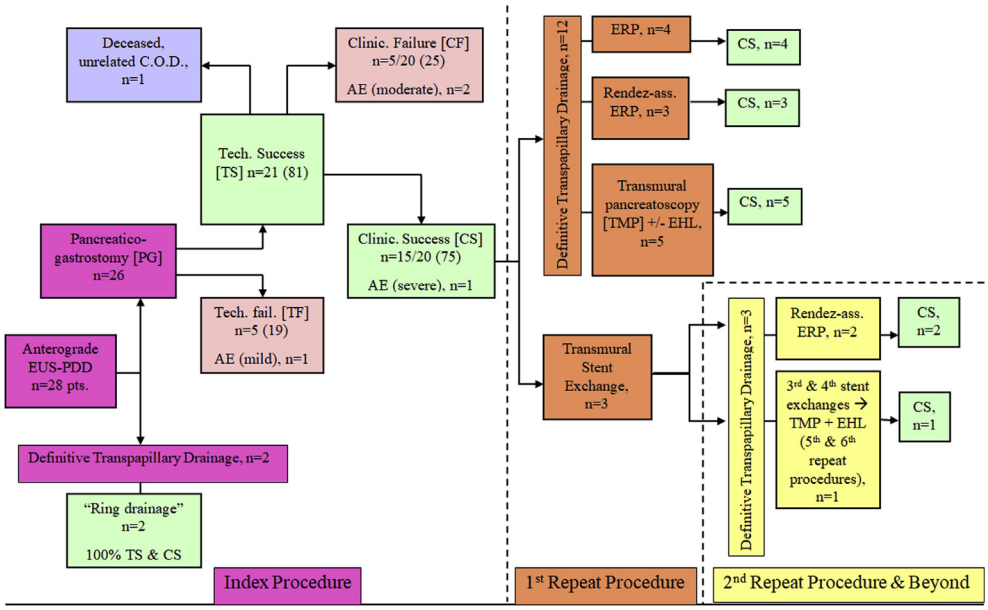


Figure 4. Endoscopy flowchart demonstrating the procedural pathway to definitive therapy (transpapillary/transanastomotic drainage) among the original 28-patient cohort. *C.O.D.*, Cause of death; *ERP*, endoscopic retrograde pancreatography; *EUS-PDD*, endoscopic ultrasound-guided pancreatic duct drainage; *TMP*, transmural (anterograde) pancreatoscopy; *EHL*, electrohydraulic lithotripsy.

100 J, with 10 to 20 shocks per pulse, as previously reported.[18] Other procedural modalities used to achieve definitive therapy during repeat endoscopy included ERP, rendezvous-assisted ERP, and anterograde transpapillary stent insertion.

Statistical analysis

Categorical variables are reported as percentages, and quantitative variables are reported either as means ± standard deviation or medians with interquartile range (IQR). Statistical analysis was performed using Microsoft Excel 2010 (Microsoft Corporation, Redmond, Wash, USA).

RESULTS

Demographic and preprocedural information

Twenty-eight patients (14 females, 14 males) underwent attempted anterograde EUS-PDD during the study period (Table 1). The mean patient age was 59 ± 16 years. Procedural indications included obstructive pancreatopathy due to CP (n = 26, 93%) and PJS after Whipple resection (n = 2, 7%). Causes of CP (n = 26) included alcohol (n = 19), idiopathic (n = 4), and recurrent choledocholithiasis (n = 3). The cause of MPD obstruction in the CP cohort (n = 26) was either stone (n = 12), stricture (n = 10), or both (n = 4). Among the entire patient cohort (n = 28), 17 of 28 (61%) patients were on preprocedural chronic narcotic therapy, and 23 of 28 (82%) patients were on pancreatic enzyme supplementation. Median MPD diameter at the index drainage procedure was 6 mm (IQR, 5-8 mm). PG was attempted on the 26 patients with CP, and ring drainage was attempted on the 2 patients with PJS.

Index anterograde EUS-PDD outcomes (PG and ring drainage cohorts)

Transmural MPD access was attempted using a 19-gauge needle (n = 28, 100%) and a 0.635-mm (0.025-inch) guidewire (n = 24, 86%) or a 0.889-mm (0.035-inch) guidewire (n = 4, 14%). Cautery-assisted transmural tract dilation was used in 18 patients (64%) versus noncautery-assisted tract dilation in 10 patients (36%) (Table 2). Various transmural stents were attempted and/or used during the index drainage, including straight, single-pigtail, and double-pigtail pancreatic plastic stents. Median plastic pancreatic stent dimensions were 5F × 11.5 cm (IQR, 5-7F × 9-15 cm). One 10 mm × 6 cm biliary fully covered self-expanding metal stent was successfully used during index PG, and one 10-mm electrocautery-enhanced lumen-apposing metal stent (ECE-LAMS) failed to create the PG.

The PG study arm experienced 81% technical success (n = 21 of 26), 75% clinical success (n = 15 of 20), and 15% AEs (n = 4 of 26) (Fig. 4 and Table 2). Technical failure occurred in 5 patients due to inability to effectively dilate the transmural tract and/or insert and correctly position the transmural PG stent, after successful EUS-guided pancreatography and anterograde transmural guidewire insertion. Three patients had clinical failure after PG, without AEs, due to noncompliance with procedural follow-up (n = 2) and lack of response to index PG (n = 1); transmural stents were removed in these patients. A 93-year-old patient died 1 week after successful PG, due to unrelated vascular disease.

Four AEs occurred during or soon after the index PG procedure. One patient had technically successful PG with a severe AE due to intraprocedural transection of a branch of the left gastric artery, resulting in luminal hemorrhage, requiring blood transfusion and intensive care unit admission. Hemorrhage resolved with embolization by an interventional radiologist, and this patient ultimately went on to clinical success. One patient experienced a mild AE related to a symptomatic (contained) microperforation after technical failure of PG. The technical failure was maldeployment of a 10-mm ECE-LAMS into a severely dilated MPD (20 mm). The patient awoke with postprocedural abdominal pain, and a subsequent CT scan showed extraluminal air foci from attempted transmural drainage. The patient recovered quickly with supportive care and oral antimicrobials.

Two patients experienced moderate AEs and clinical failure due to postprocedural PG stent migration, resulting in leakage of a small amount of gastric and/or pancreatic secretions into the abdominal cavity. In both patients, the distal (intraductal) tip of the indwelling PG stent migrated outside the MPD and into the abdominal cavity, whereas the proximal stent tip remained within the stomach lumen. The (migrated) stent types were a 3F × 11 cm straight plastic pancreatic stent with a leading barb and a 5F × 9 cm straight plastic pancreatic stent with a leading barb. Both stents were deployed with the leading barb tip within the MPD. Both cases of spontaneous stent migration were detected via CT scan ordered 1 to 2 days after PG creation for workup of postprocedural abdominal pain. CT findings in both cases included focal peripancreatic mesenteric stranding at the puncture site. A small collection of peripancreatic fluid was present in 1 case, which had resolved spontaneously on follow-up CT 2 weeks later. Stents were retrieved endoscopically in both cases, and patients were prescribed 1 week of prophylactic antimicrobial therapy. Both patients recovered rapidly and were discharged from the hospital within 2 days of endoscopic stent extraction.

Technical success of ring drainage in the PJS study arm was 100% (n = 2) without AEs (0%). The ring drainage recipients were followed for 1 and 2 years after definitive therapy (mean, 18 months follow-up). Partial pain relief occurred in both patients (100% clinical success). One patient (50%) was on a chronic narcotic medicine before the procedure. After achieving definitive therapy, this narcotic was discontinued. Given this patient's excellent response to transanastomotic drainage,

the gastropancreatoenterostomy stent was removed 7 months after definitive drainage, and no symptoms recurred. Stent exchange versus stent removal was offered to the second ring drainage recipient; however, this patient was elderly (83 years old) and declined any further endoscopic procedures. This patient remains well on 1-year follow-up.

Repeat endoscopy and definitive therapy (PG cohort)

The 15 patients with clinical success after PG underwent elective repeat procedures occurring a median 1.5 months later (IQR, 1-2 months) (Fig. 4). All 15 patients received definitive therapy (100% technical success), after a median of 1 repeat procedure (IQR, 1; range, 1-5). Definitive therapy was accomplished during the first repeat procedure (n = 12 of 15, 80%), second repeat procedure (n = 2 of 15, 13%), or via multiple repeat procedures (n = 1 of 15, 7%) (Fig. 4). TMP-EHL was used to facilitate and/or accomplish definitive therapy in 40% (n = 6 of 15). Definitive therapy was attained in the remaining patients using rendezvous-assisted ERP (33%, n = 5 of 15) and ERP (27%, n = 4 of 15). Among the 15 patients with long-term clinical success in the PG cohort, 11 of 15 (73%) patients were on chronic narcotics before PG creation. During clinical follow-up (median, 4.5 months follow-up after definitive therapy), narcotics were discontinued or dosing was tapered in 6 of 11 (55%) patients. However, clinical success was 100% in terms of achieving partial or complete pain relief (n = 15 of 15). No AEs occurred during a median 4.5 months (IQR, 3-7.75 months) follow-up in this definitive therapy cohort.

DISCUSSION

Anterograde EUS-PDD is a rarely performed procedure with a relative paucity of data, especially in comparison with ERP drainage. Most studied on anterograde EUS-PDD are focused on the index drainage procedure, with less information on long-term follow-up. A recent review article on anterograde EUS-PDD with transmural stent placement (ie, PG) identified 13 available studies involving 155 attempted procedures.[16] Technical success, defined as successful transmural stent placement on initial or repeat attempt, was 89% (n = 138 of 155).[4,5,7-12,19,20] Clinical success, defined as partial or complete resolution of symptoms or the clinical problem, was 87% (n = 127 of 146).[4,5,7,9,10,13,19,20] AEs occurred in 12% (n = 12 of 103) of intervention attempts, including abdominal pain (n = 4), bleeding (n = 3), pancreatitis (n = 2), pseudocyst (n = 2), and perforation (n = 1).[5,7-9,11,12,19,20] More recently, Dalal et al[21] reported a single-center retrospective experience with 21 patients who underwent PG (n = 18) and pancreaticoenterostomy (n = 3), with technical success (17 of 21, 81%), clinical success (16 of 21, 76%), and AEs (6 of 21, 29%). Spontaneous stent migration accounted for 2 (33%) of the delayed AEs.

The purpose of our study was to provide a longitudinal view of our patients who underwent attempted anterograde EUS-PDD. Our study population was divided into 2 study arms: attempted gastropancreaticoenterostomy (ring drainage) for PJS after Whipple resection (n = 2) and attempted PG for CP (n = 26). Ring drainage was completed with 100% technical success, 100% clinical success, and 0% AEs. Moreover, ring drainage was accomplished during the index procedure, meaning that definitive therapy (transanastomotic drainage) was immediately achieved. Clinical follow-ups of 1 and 2 years were available for these 2 patients, and pain relief endured with 1 ring drain (stent) removed 7 months after placement and with 1 ring drain left in situ (per patient preference). No conclusions can be drawn from the ring drainage study arm because of the tiny sample size (n = 2); however, we hypothesize that our excellent clinical success is multifactorial. First, ring drainage creates an MPD dual-drainage system (ie, PG and pancreaticoenterostomy), thereby enhancing pancreatic secretion outflow. Second, the underlying pathophysiology of PJS differs from CP. In PJS, the problem is focal (ie, stenotic anastomosis), compared with CP, a chronic inflammatory condition with a complex multifactorial pain pathway (ie, MPD hypertension is one of several pain mechanisms in CP).[22] The focal nature of PJS may explain why definitive therapy was accomplished during the index procedure, as opposed to during repeat endoscopy session(s) after index PG. Anterograde transanastomotic guidewire passage through a stenotic pancreaticojejunostomy is easier to perform than anterograde transpapillary guidewire passage through an MPD filled with stones and strictures in cases of CP. Moreover, achievement of transanastomotic guidewire passage enables application of a greater amount of guidewire tension, thereby facilitating anterograde (transmural) stent deployment.

Regarding long-term stent management in cases of ring drainage, we hypothesize that patients may be able to tolerate a longer duration with an indwelling stent, given the dual outflow points for pancreatic secretions. In addition, ring drainage might carry a decreased risk of stent-induced ductal injury because both stent tips are located in the intestinal and gastric lumens. This may explain why our 83-year-old patient who refused removal of her ring drain remained asymptomatic 1 year after stent insertion.

Outcomes from our PG study arm (n = 26) were analyzed according to the index procedure (PG) and the repeat procedures that ensued until definitive therapy (transpapillary drainage). Our study showed mild to moderately high rates of technical failure (19%, n = 5 of 26), clinical failure (25%, n = 5 of 20), and AEs (15%, n = 4 of 26) during index PG, which is comparable

with previous studies (Table 2).[16] Technical failure occurred in 5 patients due to inability to effectively dilate the transmural tract and/or insert and correctly position the transmural PG stent. In the PG study arm, 65% (n = 17 of 26) received cautery-assisted transmural tract dilation with 71% (n = 12 of 17) PG technical success; whereas 35% (n = 9 of 26) had noncautery-assisted transmural tract dilation with 100% (n = 9 of 9) PG technical success. The difference in PG technical success between methods of transmural tract dilation (71% vs 100%) might indicate that noncautery assistance is more effective, but a major confounder exists. Fibrotic and calcified pancreatic parenchyma and duct walls do not readily dilate via balloon; instead, thermal energy in the form of a needle knife or cystotome may be required for transmural tract dilation.

Transmural tract dilation and stent deployment are the most technically challenging aspects of PG creation because of the limited length of guidewire that can be inserted into the obstructed/disconnected MPD, and therefore the limited guidewire tension that can be maintained without losing access. Moreover, the dilator and endoprosthesis must traverse the gastric wall and fibrotic pancreatic parenchyma, both of which create resistance to catheter passage. To troubleshoot the inherent challenges of transmural tract dilation and stent insertion, Hayat et al[23] have proposed using a small-caliber angioplasty balloon dilator (diameter, 3.5 mm; sheath 4F), passed over a 0.457-mm (0.018-inch) guidewire, for transmural tract dilation, followed by transmural deployment of a 3F single-pigtail endoprosthesis. Using this technique, Hayat et al[23] achieved technical success in 7 out of 8 (88%) patients undergoing PG in the setting of disconnected pancreatic duct syndrome (n =4), PJS after Whipple resection (n = 3), and CP (n = 1).

Almost half of the clinical failures (40%, n = 2 of 5) after index PG were attributed to PG stent migration (n = 2 [AEs]), which underscores the fact that no PG-specific stent is commercially available. Antimigratory flaps or pigtail stent design are the safety mechanisms that we rely upon to prevent PG stent migration. In our PG cohort, both cases of stent migration occurred with use of straight plastic pancreatic stents with a leading barb, whereas no cases of stent migration occurred using pigtail stents. This might suggest that the pigtail design is inherently more stable for prevention of stent migration (better anchoring effect). The remaining clinical failures (60%, n = 3 of 5) occurred after successful PG creation and were not associated with AEs. Two patients were noncompliant with follow-up and continued to consume alcohol; their pancreatic pain recurred with PG stents in situ (n = 2). These 2 cases show the importance of preprocedural patient selection. The last patient experienced no pain relief whatsoever after index PG (n = 1). This case serves as a reminder that MPD hypertension does not contribute to pain in every patient with CP with a dilated MPD.

Elective repeat endoscopy was performed on the 15 patients whose index PG was technically successful, clinically successful, and free of AEs (Fig. 4). A median 1.5-month interval (IQR, 1-2 months) occurred between the index PG and the first repeat endoscopy. The goal of performing repeat endoscopy was to achieve definitive therapy. The alternative strategy would have been to leave the PG stent(s) in situ (ie, destination therapy), with on-demand stent exchanges for pain recurrence. We prefer definitive to destination therapy because the patient can be transitioned back to standard-of-care ERP for his or her future needs after achieving transpapillary drainage. Our 1- to 2-month interval from index to repeat endoscopy allowed for PG fistula maturation. A mature fistula tract enabled use of more aggressive transmural techniques (eg, TMP-EHL to achieve definitive therapy), without risk of pancreatic leak or gastric perforation.

Definitive therapy was ultimately attained in the 15 patients in the PG cohort who underwent repeat endoscopy (100%, n = 15 of 15). Clinical success was seen in 100% (n = 15 of 15), over a median 4.5-month follow-up period, and chronic narcotic usage was discontinued or tapered in 6 of 11 (55%) patients who were prescribed narcotics before the procedure. Outstanding clinical success is not surprising because only the patients who responded to index PG were selected for repeat endoscopy. Definitive therapy was achieved during the first repeat endoscopy in 80% of this cohort (n = 12 of 15). Among the 12 patients who achieved definitive therapy during the first repeat endoscopy, use of TMP-EHL was responsible for 42% (n = 5 of 12). The remaining 58% (n = 7 of 12) had either successful ERP (n = 4) or rendezvous-assisted ERP (n = 3) during the first repeat endoscopy. No difference in clinical success occurred among recipients of definitive transpapillary drainage via ERP compared with rendezvous-assisted ERP. Definitive therapy after only 1 repeat endoscopy may have occurred for the following reasons. Restoration and redirection of MPD secretory flow after the index PG may have redistributed or drained intraductal calculi, thereby lessening the severity of MPD impaction. The distal tip of the transmural stent may have also mechanically degraded intraductal calculi over time.

Three recipients of successful index PG (20%, n = 3 of 15) did not achieve definitive therapy during the first repeat endoscopy, due to high-grade distal MPD obstruction prohibiting transpapillary drainage (Fig. 4). In these patients, definitive therapy occurred during the second repeat endoscopy (13%, n = 2 of 15) and sixth repeat endoscopy (7%, n = 1 of 15) (Fig. 4). The interval strategy was transmural stent exchange as a bridge to definitive therapy. Additional transmural plastic stent(s) were placed parallel to the original transmural stent, with or without replacement of the original stent. The idea of inserting additional stents across the PG was 2-fold. First, larger stent diameter is recommended by United European

Gastroenterology for management of MPD strictures, because a wider stent diameter has been shown to decrease hospitalization rates for pancreatic pain episodes.[1,24] Second, increasing the number of transmural stents increases the potential space around each stent and decreases the pancreaticogastric pressure gradient, thereby promoting the wick effect (ie, the phenomenon of clinical success occurring in the setting of stent occlusion).[25]

Limitations of our study include its retrospective design, lack of a control group (noncomparative study), and its nonvalidated patient-reported subjective scale for measuring clinical success. Although we were able to measure changes in pre- and postprocedural narcotic usage, our study was limited by a lack of other available objective outcome markers. We encourage future prospective studies to include more objective parameters, such as a validated quality-of-life scale and change in number of hospitalizations (preprocedure vs postprocedure). Another limitation of our study is that there is some heterogeneity in the procedural techniques because the procedures were completed at the discretion of 2 advanced endoscopists at different institutions. However, these procedures were undertaken by 2 veteran advanced endoscopists with expertise in therapeutic EUS. Anterograde EUS-PDD should not be attempted by inexperienced and/or low-volume endoscopists. Relative strengths of this study include its collaborative nature (ie, dual center) and a relatively large sample size (n = 28). For perspective, the largest available study to date is a multicenter study (4 centers) with anterograde EUS-PDD used in 51 patients.[14]

CONCLUSIONS

Anterograde EUS-PDD is an endoscopic salvage procedure and an alternative to surgery for nonsurgical patients experiencing morbidity related to obstructive pancreatopathy. We recommend careful patient selection and counseling before attempting anterograde EUS-PDD. Patients with inaccessible anastomosis (or papilla) should be told that ring drainage is definitive therapy. Patients with CP with impassable papillae must know that PG creation is not the recommended endpoint under most circumstances. PG should be attempted as a step toward definitive therapy, and at least 1 repeat endoscopy may be required to achieve transpapillary drainage. Transpapillary drainage (definitive therapy) is the endoscopic endpoint because once attained, future procedural care can be reverted to standard ERP, a much more widely available and reliable pancreatic drainage modality.

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Abbreviations: AE, adverse event; CP, chronic pancreatitis; EA-ERP, enteroscopy-assisted endoscopic retrograde pancreatography; ECE-LAMS, electrocautery-enhanced lumen-apposing metal stent; ERP, endoscopic retrograde pancreatography; EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; IQR, interquartile range; MPD, main pancreatic duct; PG, pancreaticogastrostomy; PJS, pancreaticojejunostomy stenosis; TMP-EHL, transmural (anterograde) pancreatoscopy with electrohydraulic lithotripsy.

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