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Effectiveness and Safety of Enteroscopy-Assisted ERP-Guided Versus EUS-Guided Pancreatic Duct Drainage for Pancreaticojejunostomy Strictures: A Multicenter Observational Study

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ABSTRACT

Objectives: Enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage (eERP-PDD) and endoscopic ultrasound-guided pancreatic duct drainage (EUS-PDD) are minimally invasive alternatives to surgery for pancreaticojejunostomy stricture (PJS); however, comparative data remain limited. We compared the effectiveness and safety of these approaches and identified factors associated with technical failure.

Methods: This multicenter retrospective study included 88 patients (111 procedures) who underwent endoscopic intervention for PJS at 13 Japanese tertiary centers. We compared clinical outcomes between eERP-PDD and EUS-PDD. The primary outcome was technical success; secondary outcomes included clinical success, procedure time, and adverse events (AEs). Propensity-score overlap weighting was used to adjust for baseline differences.

Results: As initial treatment, 77 patients underwent eERP-PDD and 11 underwent EUS-PDD. After adjustment, EUS-PDD achieved higher technical success (eERP-PDD, 28% vs. EUS-PDD, 71%; $p = 0.012$) and clinical success (22% vs. 71%; $p = 0.003$), with shorter procedure time (76 min vs. 41 min; $p = 0.001$). AE incidence was higher with EUS-PDD before

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adjustment (5% vs. 27%; $p = 0.039$) but comparable after adjustment (7% vs. 29%; $p = 0.15$); all AEs resolved with conservative management. Age < 75 years, male sex, and main pancreatic duct (MPD) diameter ≥ 5 mm were independently associated with eERP-PDD failure.

Conclusions: EUS-PDD demonstrated higher technical and clinical success than eERP-PDD for PJS, with comparable safety after adjustment. An MPD diameter ≥ 5 mm was associated with eERP-PDD failure. An MPD-based algorithm is proposed: eERP-PDD for MPD < 5 mm with EUS-PDD as salvage, and EUS-PDD for MPD ≥ 5 mm. This algorithm is hypothesis-generating and requires prospective validation.

1 | Introduction

Pancreaticoduodenectomy is an established surgical treatment for periampullary tumors. Pancreaticojejunostomy stricture (PJS) occurs in 1.4%–11.4% of patients [1] and can cause abdominal pain, recurrent pancreatitis, and pancreatic fistula, often requiring intervention [2–6].

Enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage (eERP-PDD) is a less invasive alternative to surgical revision; however, altered postoperative anatomy limits the technical success rate to 8%–50% [7–10], mainly due to difficulty in reaching the target, identifying the pancreaticojejunostomy site, and cannulating the pancreatic duct.

Endoscopic ultrasound-guided pancreatic duct drainage (EUS-PDD) is a promising alternative [11–15]. By enabling direct puncture and drainage of the pancreatic duct under EUS guidance from the stomach or small intestine, EUS-PDD can overcome limitations of eERP-PDD related to postoperative anatomy. A 2021 systematic review reported a pooled technical success rate of 81.4%; however, EUS-PDD was associated with an adverse event (AE) rate of 21%, including potentially serious complications such as perforation, bleeding, and severe pancreatitis [16].

Two comparative studies have evaluated eERP-PDD and EUS-PDD for PJS. An international multicenter study demonstrated higher technical and clinical success with EUS-PDD [17], and a systematic review also favored EUS-guided approaches [18]. However, both studies reported higher AE rates with EUS-PDD. Because these investigations were retrospective and included heterogeneous cohorts with baseline differences, the certainty of their comparative conclusions remains limited. Consequently, the optimal treatment strategy for PJS remains unclear, particularly regarding selection criteria between the two procedures and predictors of technical failure in real-world practice.

We hypothesized that the technical success of eERP-PDD and EUS-PDD may differ according to patient anatomy and procedural feasibility. Therefore, this multicenter retrospective study compared the two modalities using complementary analytic approaches: a per-patient analysis reflecting real-world initial treatment selection and a per-procedure analysis evaluating intrinsic technical performance of the procedures. We also sought to identify factors associated with procedural failure to inform clinical decision-making for PJS.

2 | Methods

2.1 | Study Design

This multicenter retrospective cohort study was conducted by the Therapeutic Endoscopic UltraSonography (TEUS) study group at 13 Japanese referral centers. Data from consecutive patients who underwent endoscopic interventions for PJS were extracted from institutional records.

This study complied with the Declaration of Helsinki and was approved by the Institutional Review Board of Hyogo Medical University (approval no. 4050) and all participating centers. Informed consent for data use was obtained via an opt-out process.

2.2 | Patient Selection

Patients who underwent eERP-PDD or EUS-PDD for PJS between April 1, 2011, and October 31, 2021 were included. Inclusion criteria were: (i) age ≥ 20 years; (ii) PJS after pancreaticoduodenectomy; and (iii) PJS-related symptoms (abdominal pain and/or recurrent pancreatitis) and/or imaging findings (pancreatic duct dilation). Exclusion criteria were prior endoscopic or surgical treatment for PJS and active malignancy.

2.3 | Interventions

All procedures were performed on an inpatient basis under deep sedation. The choice of intervention was left to the endoscopist's discretion, without standardized protocols across institutions. Participating centers were high-volume tertiary institutions with substantial pancreatobiliary expertise; the median annual volume of endoscopic retrograde cholangiopancreatography (ERCP) in surgically altered anatomy was 35 cases (interquartile range [IQR], 25–80) per center, and that of EUS-guided drainage (EUS-guided biliary drainage and EUS-PDD) was 30 cases (IQR, 15–47.5) per center. When intervention failed, management options included repeated attempts, alternative endoscopic approaches, surgery, or conservative care.

2.4 | eERP-PDD

eERP-PDD was performed using a double-balloon, single-balloon, or conventional forward- or side-viewing endoscope, at the endoscopist's discretion. After insertion into the afferent

limb and identification of the PJS, pancreatic duct access was attempted using standard ERCP techniques. After cannulation, the stricture was dilated using a bougie and/or balloon dilator, followed by placement of a plastic stent across the stricture. Stent size and length were selected according to duct diameter and stricture severity (Figure 1).

2.5 | EUS-PDD

EUS-PDD was performed using a convex echoendoscope. After confirming the absence of intervening vessels on Doppler, the pancreatic duct was punctured using a fine-needle aspiration needle under EUS guidance. Needle/guidewire selection was based on duct diameter and puncture difficulty (19-gauge needle with a 0.025-in. guidewire or 22-gauge needle with a 0.018-in. guidewire). After pancreatography, a guidewire was advanced into the duct, and one of three approaches was performed: pancreaticogastrostomy, transgastric antegrade stenting, or rendezvous technique (Figure 2 and Figure S1).

2.6 | Exposure and Outcomes

Patients were categorized as EUS-PDD (exposure) and eERP-PDD (control). The primary outcome was technical success; secondary outcomes were clinical success, procedure time, and AEs. Technical success required completion of three steps: endoscope insertion, pancreatic duct access, and definitive treatment. Endoscope insertion was defined as reaching the PJS in eERP-PDD and visualizing the pancreatic duct in EUS-PDD. Pancreatic duct access was defined as successful guidewire placement. Definitive treatment was defined as either (i) successful stent placement in the intended position per the planned approach, with fluoroscopic confirmation of contrast drainage from the main pancreatic duct (MPD), or (ii) balloon dilation alone with complete resolution of the anastomotic waist on fluoroscopy and no need for further intervention. Balloon dilation followed by failed stent placement was classified as technical failure. Clinical success was defined as (i) resolution or marked improvement of PJS-related symptoms (abdominal pain, recurrent pancreatitis, or PJS-related pancreatic fistula) within 14 days after the procedure, and (ii) radiologic improvement on CT or MRI within the same period, demonstrated by reduced MPD dilatation, decreased peripancreatic inflammation, or resolution/reduction of pancreatic fistula or fluid collection. AEs were defined as procedure-related complications within 14 days and graded by the AGREE criteria [19]; events beyond 14 days were excluded.

2.7 | Statistical Analyses

Associations between exposure and outcomes were evaluated in two analytic cohorts: per-patient and per-procedure. The

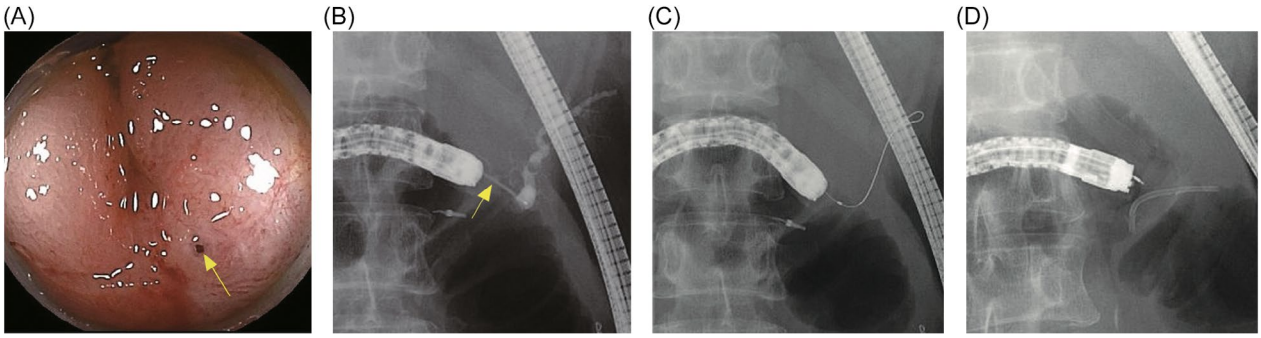

FIGURE 1 | eERP-PDD procedure for PJS. (A) Endoscopic view showing a pinhole-like opening at the pancreaticojejunostomy site (yellow arrow). (B) Pancreatogram demonstrating a dilated main pancreatic duct upstream of the stricture (yellow arrow). (C) Fluoroscopic image showing a 0.025-in. guidewire advanced across the stricture. (D) Fluoroscopic image showing placement of a 7-Fr plastic stent across the stricture. eERP-PDD, enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage; PJS, pancreaticojejunostomy stricture.

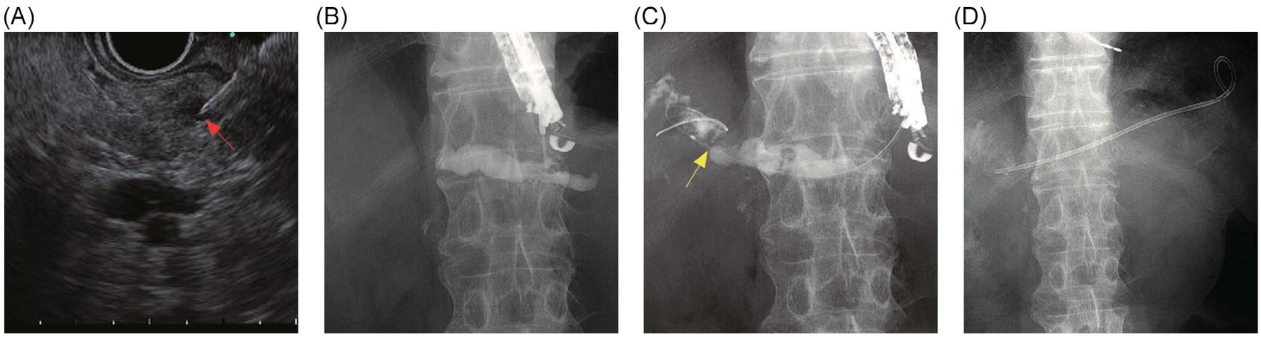

FIGURE 2 | EUS-PDD procedure (transgastric antegrade stenting) for PJS. (A) Endoscopic ultrasound image showing puncture of the dilated main pancreatic duct from the stomach (red arrow). (B) Pancreatogram showing a dilated main pancreatic duct. (C) Fluoroscopic image showing a 0.025-in. guidewire advanced across the stricture (yellow arrow) and coiled in the jejunum. (D) Fluoroscopic image showing antegrade placement of a 7-Fr plastic stent across the stricture, bridging the stomach and jejunum. EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; PJS, pancreaticojejunostomy stricture.

primary analysis was per-patient, reflecting real-world initial treatment selection; the complementary per-procedure analysis assessed intrinsic technical performance, including crossover and repeat procedures.

To adjust for baseline imbalances between eERP-PDD and EUS-PDD, we used propensity score (PS) overlap weighting, which emphasizes patients with PSs around 0.5 and achieves exact mean balance for covariates in the PS model [20, 21]. PSs for patients receiving EUS-PDD were estimated by logistic regression, including the following covariates: age, sex, performance status ≥ 1, indication of acute pancreatitis, Child's reconstruction, and MPD diameter. Patients were weighted by PS (for the eERP-PDD group) or $1-\text{PS}$ (for the EUS-PDD group), reducing the influence of extreme PS values and improving precision compared with inverse probability weighting [20, 21]. Compared with PS matching, overlap weighting preserves the full sample size and provides a stable estimate of the average treatment effect. Risk differences and 95% confidence intervals (CIs) were calculated for all outcomes.

Multivariable logistic regression was performed to identify risk factors for technical failure of eERP-PDD. In the multivariable model, the following variables were included based on clinical relevance: age <75 years, sex, indication of acute pancreatitis, MPD diameter ≥ 5 mm, and Child's reconstruction [22–25]. Results are presented as odds ratios (ORs). Multivariable analysis was not performed for EUS-PDD because of the small number of technical failures.

Continuous variables are reported as medians with interquartile ranges (IQRs), whereas categorical variables are reported as counts and percentages. Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables using Fisher's exact or chi-square tests. Statistical significance was set at $p < 0.05$ (two-tailed). All analyses were performed using Stata MP19 (StataCorp, College Station, TX, USA).

3 | Results

3.1 | Initial Endoscopic Treatments for PJS (Per-Patient Analysis)

Among 88 patients, 77 underwent eERP-PDD and 11 underwent EUS-PDD as the initial endoscopic treatment (Figure 3). Baseline characteristics are shown in Table 1. Acute pancreatitis was the most common indication in both groups (eERP-PDD, 68% vs. EUS-PDD, 45%), and Child's reconstruction was predominant (90% vs. 64%). The median MPD diameter was larger in the EUS-PDD group (5.5 mm vs. 6.6 mm; $p = 0.023$).

Before PS overlap weighting, the technical success rate did not differ significantly (eERP-PDD, 42% vs. EUS-PDD, 73%; $p = 0.052$), although the point estimate difference was 31%. The endoscope insertion rate was comparable, whereas the pancreatic duct access rate was higher in the EUS-PDD group (42% vs. 82%; $p = 0.012$). The clinical success rate was also higher in the EUS-PDD group (40% vs. 73%; $p = 0.043$). Among cases with successful stent placement, the clinical success rate was similar between the two groups. The AE incidence was higher with EUS-PDD (5% vs. 27%; $p = 0.039$). All AEs

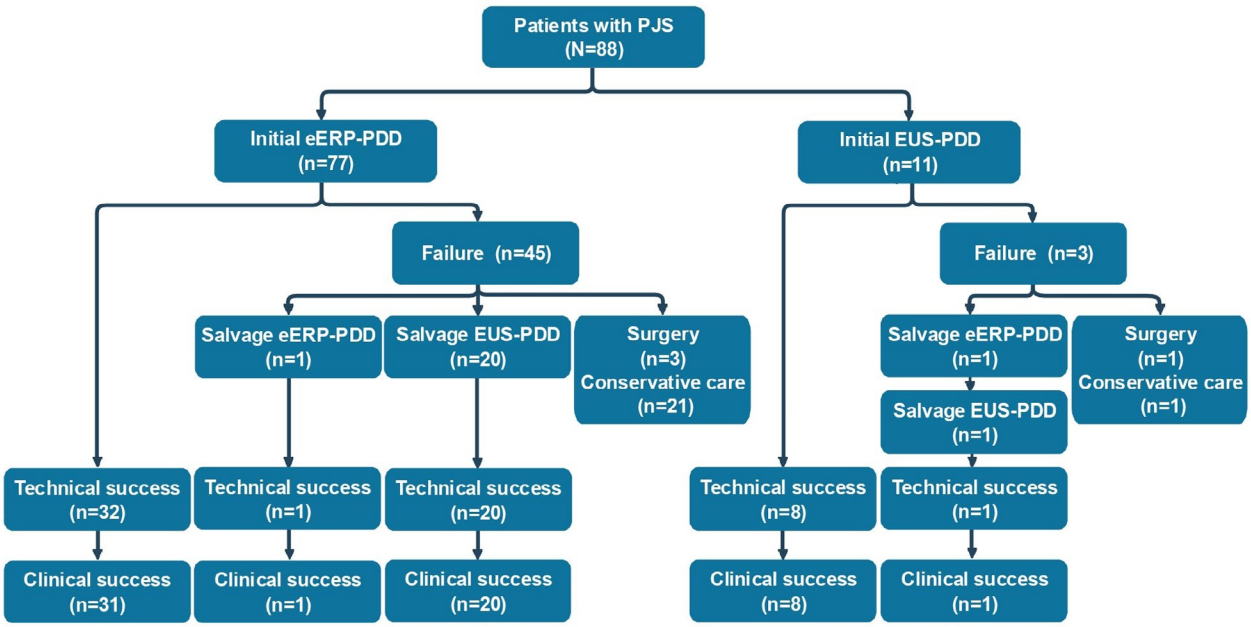

FIGURE 3 | Flow diagram of patient allocation and treatment outcomes. The diagram shows the initial endoscopic treatment (per-patient analysis) and subsequent endoscopic salvage procedures (included in the per-procedure analysis). After failure of the initial approach, patients underwent endoscopic salvage procedures, surgery, or conservative management. One patient initially treated with EUS-PDD required sequential salvage procedures (eERP-PDD followed by EUS-PDD) to achieve technical success. Patients who underwent surgery or conservative management were excluded from the per-procedure analysis because no further endoscopic procedures were performed. eERP-PDD, enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage; EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; PJS, pancreaticojejunostomy stricture.

TABLE 1 | Characteristics of patients who underwent initial endoscopic treatment (per-patient analysis).

Variables	Total ($n=88$)	eERP-PDD ($n=77$)	EUS-PDD ($n=11$)	p
Age, years, median (IQR)	67.5 (60–75)	67 (59–75)	68 (65–75)	0.61
Sex, male	51 (58%)	44 (57%)	7 (64%)	0.68
Performance status ≥1	4 (5%)	3 (4%)	1 (9%)	0.42
Indication				0.21
Acute pancreatitis	57 (65%)	52 (68%)	5 (45%)	
Abdominal/back pain	11 (12%)	8 (10%)	3 (27%)	
Dilated MPD	11 (12%)	10 (13%)	1 (9%)	
Pancreatic fistula	7 (8%)	5 (6%)	2 (18%)	
Others	2 (2%)	2 (3%)	0 (0%)	
Type of reconstruction				0.019
Child	76 (86%)	69 (90%)	7 (64%)	
Whipple	1 (1%)	1 (1%)	0 (0%)	
Imanaga	3 (3%)	3 (4%)	0 (0%)	
Unknown	8 (9%)	4 (5%)	4 (36%)	
MPD diameter, mm, median (IQR)	5.8 (4.1–7.0)	5.5 (4.0–6.6)	6.6 (4.8–8.6)	0.023
Days from surgery to endoscopic treatment, days, median (IQR)	1402 (568–2181)	1402 (575–2178)	1455.5 (447.5–3132)	0.94

Abbreviations: eERP-PDD, enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage; EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; IQR, interquartile range; MPD, main pancreatic duct.

were AGREE Grades I–IIIa and resolved with conservative management (Table 2).

Table 3 summarizes outcomes after PS overlap weighting. After adjustment, baseline variables were well balanced (Table S1). In the per-patient analysis, the technical success rate was higher with EUS-PDD (eERP-PDD, 28% vs. EUS-PDD, 71%; difference, 42%; 95% CI, 9%–76%; $p=0.012$). The clinical success rate was also higher with EUS-PDD (22% vs. 71%; difference, 48%; 95% CI, 16%–80%; $p=0.003$). Procedure time was shorter with EUS-PDD (76 min vs. 41 min; difference, −35 min; 95% CI, −56 to −14 min; $p=0.001$). The AE incidence did not differ significantly between the groups (7% vs. 29%; difference, 22%; 95% CI, −8%–51%; $p=0.15$).

3.2 | Cumulative Endoscopic Treatments for PJS (Per-Procedure Analysis)

A total of 111 procedures were performed in 88 patients (eERP-PDD, 79; EUS-PDD, 32) (Table S2). Outcomes before PS overlap weighting were generally consistent with the per-patient analysis (Table S3). Three EUS-PDD procedures were technically unsuccessful; their characteristics are shown in Table S4. After PS overlap weighting, baseline variables were well balanced (Table S5). In the per-procedure analysis, technical and clinical success rates were significantly higher with EUS-PDD, whereas the AE incidence and procedure time were comparable between the groups (Table 3). Procedural details are provided in Tables S6 and S7.

3.3 | Risk Factors for Technical Failure in eERP-PDD

In the per-patient initial treatment analysis, multivariable logistic regression identified age < 75 years (OR, 8.76; 95% CI, 2.45–31.3; $p=0.001$), male sex (OR, 3.42; 95% CI, 1.12–10.3; $p=0.029$), and MPD diameter ≥ 5 mm (OR, 4.23; 95% CI, 1.32–13.5; $p=0.015$) as independent predictors of eERP-PDD technical failure. These factors were similarly associated with technical failure in the per-procedure cumulative treatment analysis (Table 4).

4 | Discussion

In this multicenter retrospective study comparing eERP-PDD and EUS-PDD for PJS, we conducted a per-patient analysis of initial treatment as the primary analysis and adjusted for baseline differences using PS overlap weighting. EUS-PDD achieved significantly higher technical and clinical success than eERP-PDD. Although the AE incidence was significantly higher with EUS-PDD before adjustment, it was comparable after PS overlap weighting. Multivariable analysis identified age < 75 years, male sex, and MPD diameter ≥ 5 mm as independent risk factors for eERP-PDD technical failure.

In our study, eERP-PDD showed low technical success (42% unadjusted; 28% adjusted), consistent with prior reports (8%–50%) [7–10, 26]. Although less invasive than surgical revision with a favorable safety profile, several factors may limit technical success. Most failures occurred during pancreatic duct access

TABLE 2 | Clinical outcomes of initial endoscopic treatment (per-patient analysis).

Clinical outcomes before propensity score overlap weighting			
Outcomes	**eERP-PDD ($n=77$)**	**EUS-PDD ($n=11$)**	***p***
Technical success, *n* (%)	32 (42%)	8 (73%)	0.052
Success of endoscope insertion, *n* (%)	76 (99%)	11 (100%)	0.70
Success of pancreatic duct access, *n* (%)	32 (42%)	9 (82%)	0.012
Clinical success, *n* (%)	31 (40%)	8 (73%)	0.043
Clinical success after technical success, *n* (%)	31/32 (97%)	8/8 (100%)	>0.95
Procedure time, min; mean (SD)	75 (43)	39 (24)	0.008
Adverse events, *n* (%)	4 (5%)	3 (27%)	0.039
AGREE (Grades I/II/IIIa/IIIb/IV/V)	2/2/0/0/0/0	1/1/1/0/0/0	
Abdominal pain, *n*	0	1	
Fever, *n*	1	0	
Elevation of pancreatic enzyme, *n*	1	0	
Acute pancreatitis (mild), *n*	1	1	
Peritonitis (mild), *n*	0	0	
Perforation, *n*	1	0	
Others, *n*	0	1[a]	

Abbreviations: AGREE, adverse events in gastrointestinal endoscopy; eERP-PDD, enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage; EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; SD, standard deviation.
[a]Transient oxygen desaturation during the procedure.

TABLE 3 | Clinical outcomes after propensity score overlap weighting.

Outcomes	eERP-PDD	EUS-PDD	Difference (95% CI)	*p*
Initial endoscopic treatment (per-patient analysis)				
Technical success, %	28%	71%	42% (9%–76%)	0.012
Clinical success, %	22%	71%	48% (16%–80%)	0.003
Procedure time, min; mean (SD)	76 (47)	41 (23)	−35 (−56 to −14)	0.001
Adverse events, %	7%	29%	22% (−8% to 51%)	0.15
Cumulative endoscopic treatment (per-procedure analysis)				
Technical success, %	37%	91%	55% (39%–70%)	<0.001
Clinical success, %	35%	91%	56% (41%–71%)	<0.001
Procedure time, min; mean (SD)	75 (45)	62 (43)	−13 (−31 to 6)	0.17
Adverse events, %	10%	17%	7% (−8% to 22%)	0.38

Note: Outcomes are shown for the per-patient analysis (initial endoscopic treatment per patient) and the per-procedure analysis (all procedures, including repeated and crossover procedures).
Abbreviations: CI, confidence interval; eERP-PDD, enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage; EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; SD, standard deviation.

rather than endoscope insertion or stent placement [7, 11, 17]. Our results suggest that while double-balloon endoscopy, used in most patients (89%), can facilitate access to the target in surgically altered anatomy, identification of the PJS site and successful pancreatic duct cannulation remain major challenges. The pancreaticojejunal anastomosis is often tangential to the endoscopic view and may be obscured by intestinal folds, making precise identification of the anastomotic orifice difficult. Moreover, the narrow postoperative jejunal lumen can prevent a stable working space, leading to unstable cannulation. Unlike bile, transparent pancreatic juice is difficult to distinguish from surrounding intestinal fluid, further complicating orifice identification [27]. These difficulties are likely greater in severe strictures, where the orifice may be

TABLE 4 | Risk factors for technical failure in patients with eERP-PDD.

Variables	Odds ratio	(95% CI)	*p*
Initial endoscopic treatment (per-patient analysis)			
Age < 75 years	8.76	(2.45–31.3)	0.001
Sex, male	3.42	(1.12–10.3)	0.029
Indication: acute pancreatitis	1.24	(0.39–3.95)	0.71
MPD diameter ≥ 5 mm	4.23	(1.32–13.5)	0.015
Child's reconstruction	0.96	(0.18–5.99)	0.97
Cumulative endoscopic treatments (per-procedure analysis)			
Age < 75 years	8.82	(2.47–31.5)	0.001
Sex, male	3.30	(1.10–9.86)	0.033
Indication: acute pancreatitis	1.38	(0.44–4.28)	0.58
MPD diameter ≥ 5 mm	4.82	(1.52–15.3)	0.008
Child's reconstruction	0.93	(0.17–5.03)	0.93

Note: Per-patient analysis is based on the initial eERP-PDD per patient; per-procedure analysis includes all eERP-PDD procedures, including repeat and crossover procedures.
Abbreviations: CI, confidence interval; eERP-PDD, enteroscopy-assisted endoscopic retrograde pancreatography-guided pancreatic duct drainage; MPD, main pancreatic duct.

pinhole-like or completely obscured. A dilated MPD (≥ 5 mm) may reflect high-grade obstruction, which could explain the association between larger MPD diameter and eERP-PDD failure in our study. Several adjunctive techniques may help localize the PJS site. Indigo carmine chromoendoscopy can highlight areas of dye dilution from pancreatic juice outflow [28]. Texture and color enhancement imaging (TXI) may accentuate subtle mucosal texture and color changes to detect scar-like or concealed orifices [29]. Gel immersion endoscopy may open intestinal folds and stabilize the visual field. When combined with a transparent long cap, it enables visualization of pancreatic juice flow based on contrast between the transparent juice and viscous gel, potentially aiding identification of the anastomotic orifice [30]. Although not yet standardized, these approaches are practical options when PJS site localization is difficult.

The higher pancreatic duct access rate with EUS-PDD likely reflects direct visualization and puncture of the pancreatic duct, thereby bypassing surgically altered anatomy [17, 31]. This advantage is particularly relevant when PJS identification or pancreatic duct cannulation is difficult—the main causes of failed pancreatic duct access with eERP-PDD. EUS-PDD also showed high salvage success: all 21 patients who underwent EUS-PDD after eERP-PDD failure achieved technical success (100%). This salvage success is consistent with previous reports [16, 32–36]. In a systematic review by Basiliya et al. [18], EUS-PDD was successful in 86% of patients after failed eERP-PDD. These findings support EUS-PDD as an effective option to overcome technical limitations of eERP-PDD. Notably, when successful stent placement was achieved, clinical success was similarly high with both approaches (eERP-PDD, 97% vs. EUS-PDD, 100%), indicating that the key difference is technical rather than therapeutic.

EUS-PDD was associated with a higher AE incidence before adjustment; however, all events resolved with conservative management. Thus, although EUS-PDD may carry higher AE risk, it appears manageable and should be weighed against its superior technical success. After PS overlap weighting, the difference in AE incidence between EUS-PDD and eERP-PDD was no longer statistically significant (eERP-PDD, 7% vs. EUS-PDD, 29%; $p = 0.15$). This finding suggests that the initially observed higher AE rate in EUS-PDD may be partially attributable to patient selection factors rather than the procedure itself. When baseline characteristics are balanced, the risk–benefit profile of EUS-PDD may be more favorable than initially apparent, supporting its consideration for PJS.

Identifying risk factors for eERP-PDD failure may aid clinical decision-making. In our study, MPD diameter ≥ 5 mm was associated with eERP-PDD failure. A dilated MPD often reflects severe anastomotic strictures, making identification of the PJS site particularly challenging. In contrast, EUS-PDD provides direct access to the dilated MPD regardless of stricture severity. Moreover, ductal dilation facilitates guidewire looping and stable guidewire anchoring, improving procedural stability during tract dilation and stent placement. Thus, MPD diameter may help guide initial treatment selection. eERP-PDD may be suitable for patients with a smaller MPD diameter given its favorable safety profile, whereas EUS-PDD may be preferred for patients with dilated MPD when performed by experienced endoscopists [16]. Accordingly, we propose an MPD diameter-based strategy: eERP-PDD as the initial approach for MPD < 5 mm, with EUS-PDD as salvage after failure; and EUS-PDD as the initial approach for MPD ≥ 5 mm at centers with expertise in EUS-guided interventions.

Although EUS-PDD achieved high technical success in our cohort and may appear acceptable as a first-line approach, we do not recommend it as a universal initial modality. First, predictors of EUS-PDD failure could not be reliably assessed because only three procedures were unsuccessful ($n = 3$). Second, EUS-PDD is highly operator-dependent, and outcomes from experienced tertiary centers may not be generalizable to lower volume institutions. Therefore, our proposed algorithm should be considered hypothesis-generating and intended to support initial treatment selection in real-world practice. With ongoing device development and procedural standardization, EUS-PDD may become a first-line therapy in the future. Prospective studies are needed to validate this algorithm and identify predictors of EUS-PDD failure.

Our study has several limitations. First, the retrospective design and the relatively small EUS-PDD sample limit generalizability. Although PS overlap weighting adjusted for baseline differences, residual confounding and selection bias cannot be excluded. Second, treatment selection (eERP-PDD vs. EUS-PDD) and procedural techniques were left to individual endoscopists without standardized protocols, potentially influencing outcomes. Third, all 13 centers were high-volume Japanese tertiary referral institutions with substantial pancreatobiliary expertise; therefore, outcomes—particularly for EUS-PDD—may not be generalizable to lower volume centers with less experience in EUS-guided

interventions. Finally, we assessed only short-term outcomes; long-term outcomes, including late complications, stricture recurrence, and reintervention rates, were not evaluated. Notably, EUS-PDD may facilitate reintervention because, once a fistulous tract matures, subsequent procedures may be performed using a standard gastroscope or duodenoscope without balloon-assisted enteroscopy, potentially simplifying long-term management. Despite these limitations, our study provides real-world comparative data on endoscopic strategies for PJS and proposes a practical, hypothesis-generating approach to patient selection.

In conclusion, EUS-PDD demonstrated higher technical and clinical success than eERP-PDD for PJS, with comparable safety after adjustment. An MPD diameter ≥ 5 mm was associated with technical failure of eERP-PDD. Based on these findings, we propose an MPD diameter–based algorithm: eERP-PDD for MPD < 5 mm with EUS-PDD as salvage, and EUS-PDD may be considered for MPD ≥ 5 mm. This algorithm is hypothesis-generating and requires prospective validation.

Author Contributions

S.O., H.S., and M.N.: study concept and design. H.S.: obtained funding. S.O., Y.F., K.M., M.Ka., M.S., N.F., H.K., S.U., T.O., M.T., R.N., K.N., A.S., S.S., O.I., K.K., M.Ko., Y.I., A.O., N.F., T.T., and T.M.: acquisition of the data. S.O., H.S., and M.N.: Analysis and interpretation of the data. S.O., H.S., and M.N.: drafting of the manuscript. K.M., M.S., H.K., T.O., M.T., A.S., O.I., K.K., Y.I., N.F., T.M., and M.Ki.: editing and critical revision of the manuscript for important intellectual contents. M.Ki.: study supervision. All authors: approval of the final version of the manuscript.

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Ethics Statement

Approval of the Research Protocol by an Institutional Review Board: This multicenter retrospective observational study was approved by the institutional review boards of all participating institutions (Hyogo Medical University, approval number: 4050).

Registry and Registration Number of the Study/Trial: N/A. This study was not registered in any clinical trial registry.

Animal Studies: N/A. No animal experiments were conducted for this research.

Consent

Owing to the retrospective design of the study, written informed consent was not obtained from all individual participants. Instead, study information was disclosed publicly, and patients were provided with the opportunity to opt out in accordance with institutional and national ethical guidelines.

Conflicts of Interest

M.Ki. is Editor-in-Chief of Digestive Endoscopy. M.T. is an Associate Editor of Digestive Endoscopy. Other authors declare no conflicts of interest for this article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Schematic illustration of EUS-PDD for PJS. (A) Pancreaticogastrostomy: After looping the guidewire within the main pancreatic duct, the puncture tract was dilated using a bougie and/or balloon dilator; an electrocautery dilator was used when needed. A plastic stent was then placed between the stomach and the main pancreatic duct. (B) Transgastric antegrade stenting: The guidewire was advanced across the PJS into the jejunum. The PJS was dilated using a bougie and/or balloon dilator. A plastic stent was then placed antegrade across the PJS, bridging the stomach and jejunum. (C) Rendezvous technique: After guidewire passage across the PJS, the echoendoscope was exchanged for a forward- or side-viewing endoscope. The pancreatic duct was then cannulated over or alongside the guidewire, followed by stricture dilation and stent placement. EUS-PDD, endoscopic ultrasound-guided pancreatic duct drainage; PJS, pancreaticojejunostomy stricture. **Table S1:** Covariate balance before and after propensity score overlap weighting (per-patient analysis). **Table S2:** Characteristics of patients who underwent endoscopic treatment (per-procedure analysis). **Table S3:** Clinical outcomes of cumulative endoscopic treatment before propensity score overlap weighting (per-procedure analysis). **Table S4:** Summary of unsuccessful EUS-PDD procedures. **Table S5:** Covariate balance before and after propensity score overlap weighting (per-procedure analysis). **Table S6:** EUS-PDD procedure details. **Table S7:** eERP-PDD procedure details.