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Impact of disconnected pancreatic duct syndrome on endoscopic ultrasound-guided drainage of pancreatic fluid collections

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ABSTRACT

Background Endoscopic intervention for pancreatic fluid collections (PFCs) with disconnected pancreatic duct syndrome (DPDS) has been associated with failures and increased need for additional endoscopic and non-endoscopic interventions. The primary aim of this study was to determine the outcomes of endoscopic ultrasound (EUS)-guided transmural drainage of PFCs in patients with DPDS.

Methods In patients undergoing EUS-guided drainage of PFCs from January 2013 to January 2018, demographic profiles, procedural indications and details, adverse events, outcomes, and subsequent interventions were retrospectively collected. Overall treatment success was determined by PFC resolution on follow-up imaging or stent removal without recurrence.

Results EUS-guided drainage of PFCs was performed in 141 patients. DPDS was present in 57 of them (40 %) and walled-off necrosis was the most frequent type of PFC (55 %). DPDS was not associated with lower clinical success, increased number of repeat interventions, or increased time to PFC resolution. Patients with DPDS were more likely to be treated with permanent transmural plastic double-pigtail stents (odds ratio [OR] 6.4; 95 % confidence interval [CI] 2.5 – 16.5; $P < 0.001$). However, when stents were removed, DPDS was associated with increased PFC recurrence after stent removal (OR 8.0; 95 %CI 1.2 – 381.8; $P = 0.04$).

Conclusions DPDS frequently occurs in patients with PFCs but does not negatively impact successful resolution. DPDS is associated with increased PFC recurrence after stent removal.

Introduction

Inflammatory pancreatic fluid collections (PFCs) result from pancreatic injury and are defined by the 2012 Revised Atlanta Criteria based on the duration of the fluid collection and the presence of necrosis [1]. In up to 44 % of cases of severe acute pancreatitis, injury to the main pancreatic duct (MPD) occurs [2]. Disconnected pancreatic duct syndrome (DPDS) is a condition where the MPD is completely disrupted and a viable upstream pancreatic segment continues to secrete pancreatic enzymes that do not drain into the duodenum. DPDS can result in symptomatic persistent or recurrent fluid collections and recurrent pancreatitis if not appropriately managed (▶ **Fig. 1**). The true prevalence of DPDS is unknown, but it has been reported to occur in 16 % – 23 % of patients with PFCs and/or pancreatic fistulas [2 – 4]. DPDS should be suspected in individuals with persistent or recurrent fluid collections, but requires confirmation with imaging. Prompt diagnosis and treatment is warranted, as DPDS and its sequelae are associated with pancreaticocutaneous and pancreaticopleural fistulas [2].

Endoscopic drainage of symptomatic PFCs has been demonstrated to have similar rates of clinical success and adverse

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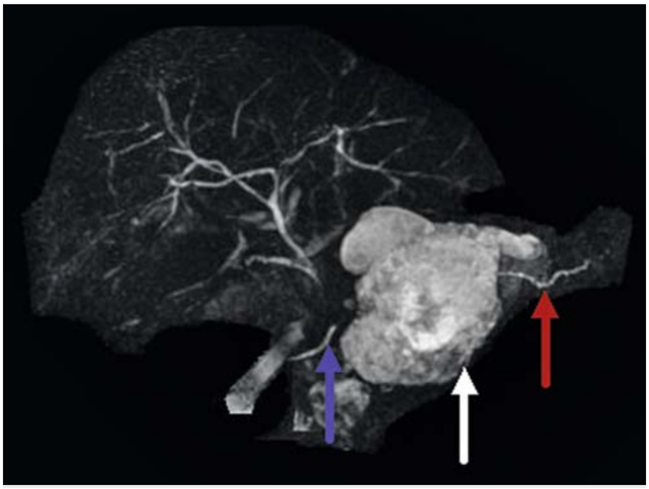

▶ **Fig. 1** Magnetic resonance imaging cholangiopancreatography (MRCP) image showing a disconnected pancreatic duct (DPD) as evidenced by complete cut-off of the main pancreatic duct (blue arrow). An upstream viable main pancreatic segment (red arrow) can be seen directly communicating with the pancreatic fluid collection (white arrow).

events, with the added advantage of reduced hospital stay and costs, when compared to surgical intervention [5]. EUS-guided transmural drainage, specifically, has emerged as the endoscopic technique of choice owing to its ability to identify PFCs without a readily identifiable subepithelial bulge, characterize the amount of solid necrosis within a collection, and facilitate selection of optimal cystenterostomy sites while avoiding intervening vessels [6]. EUS-guided transmural drainage has led to improved technical success rates and reduced procedural adverse events when compared to conventional transmural drainage [7].

Despite endoscopic advancements, the treatment and impact of DPDS in patients with PFCs remains unclear. For patients with DPDS, standalone transpapillary drainage via endoscopic retrograde cholangiopancreatography (ERCP) has been associated with failure rates as high as 74 % and increased PFC recurrence [3, 8], while endoscopic transmural drainage has been associated with lower rates of failure and PFC recurrence as low as 20 % [9]. Furthermore, in patients with PFCs undergoing transmural drainage, transpapillary drainage has not been found to have an additional benefit, even in patients with pancreatic duct leak or disruption [10].

DPDS is often unrecognized in patients with PFCs, and data on its impact on the successful treatment of PFCs via EUS-guided transmural drainage are limited. Prior data investigating endoscopic management of PFCs in patients with DPDS are heterogeneous, with studies including the use of both conventional non-EUS and EUS-guided transmural drainage, performed at a time during which endoscopic techniques for EUS-guided drainage were undergoing refinement [11 – 14]. A variety of stents, including self-expanding metal stents (SEMSs), which are no longer routinely used at our institution for PFC drainage, were also included in these studies.

The primary aim of this study was to compare the rates of resolution and recurrence of PFCs treated with EUS-guided transmural drainage in patients with DPDS compared with those without DPDS.

Methods

This is a single-center retrospective cohort study including consecutive patients who underwent EUS-guided transmural drainage for PFCs secondary to acute pancreatitis from January 2013 to January 2018 at Mayo Clinic, Rochester, Minnesota, USA. Data on patient demographics, procedural indications and details, adverse events, and subsequent interventions were collected. Overall treatment success was determined by PFC resolution on follow-up imaging or stent removal without recurrence. This study was approved by the Mayo Clinic Institutional Review Board (IRB# 18 – 007238).

Patients

A Mayo Clinic hospital and endoscopy database was searched to identify patients who underwent EUS-guided transmural drainage for PFCs from January 2013 to January 2018. Exclusion criteria consisted of the following: age less than 18; postoperative fluid collections; non-pancreatic abdominal fluid collections; malignancy-associated PFC; patients undergoing only transpapillary stenting; index drainage occurring at an outside institution; PFC drainage not using EUS; PFC drainage not using lumen-apposing metal stents (LAMSs) or plastic double-pigtail stents; patients with an existing percutaneous drain at the time of index endoscopic intervention; and incomplete records or loss to follow-up prior to PFC resolution.

The presence of a disconnected pancreatic duct (DPD) is routinely assessed with expert radiologic review of endoscopic retrograde pancreatography (ERP), magnetic resonance cholangiopancreatography (MRCP), computed tomography (CT), or EUS. Patients were diagnosed with a DPD either around the time of the index drainage procedure or on subsequent imaging after the use of several of the above imaging modalities. Patients with only a disrupted, but not disconnected, duct were not considered to have DPDS.

The outcomes of patients with DPDS were compared with those without DPDS. Patients with an equivocal DPD were excluded from the DPDS analysis.

Imaging

Pre-intervention abdominal cross-sectional imaging and follow-up imaging 2 – 4 weeks after the index endoscopy were obtained. If a DPD was suspected, but not confirmed on review of initial cross-sectional imaging, ERP images were reviewed to confirm the DPD.

Endoscopic technique and subsequent interventions

All patients underwent EUS-guided transmural drainage using a therapeutic linear echoendoscope, as has been previously described [15] (▶ **Fig. 2**). The choice of stent was left to the discretion of the performing endoscopist. In general, if a PFC was lar-

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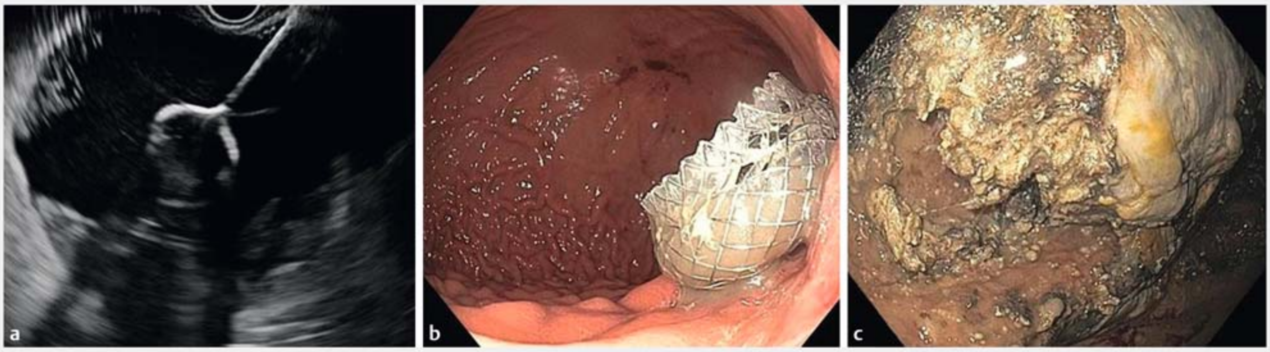

▶ **Fig. 2** Images of endoscopic ultrasound (EUS)-guided drainage of walled-off necrosis with a lumen-apposing metal stent (LAMS) showing: **a** deployment of the inner flange of the LAMS under EUS guidance; **b** endoscopic appearance post-LAMS deployment; **c** necrotic material within the cavity.

ger or contained more solid debris, a LAMS was more routinely employed. However, proximity of the PFC to vasculature or use of a transduodenal approach were additional influential factors affecting stent selection when treating walled-off necrosis (WON).

For placement of plastic double-pigtail stents or non-cautery-enhanced LAMSs, a 19-gauge EUS needle was used to puncture the PFC in a perpendicular fashion if the distance was less than 10 mm. A 0.035-inch guidewire was then advanced and coiled within the cyst. The tract was dilated with a balloon, with placement of stents thereafter. Cautery-enhanced LAMSs were placed either using the aforementioned technique without the need for dilation of the cystenterostomy tract, or were placed with direct puncture using electrocautery.

The index drainage route was dependent on the PFC location and accessibility via transgastric vs. transduodenal approach. In select cases, the multiple transluminal gateway technique (MTGT) was performed at the index endoscopy. On occasion, patients with persistent symptomatic PFCs were managed with additional transmural drainage using the alternative drainage route and were treated as cross-overs into the MTGT category.

Placement of a coaxial plastic double-pigtail stent within the LAMS to maintain stent patency and prevent LAMS-induced friction trauma, and the decision to place a permanent double-pigtail stent were left to the discretion of the performing endoscopist. In cases of persistent, infected, or worsening uncontrolled PFCs, a step-up approach was used. Image-guided percutaneous drainage was performed prior to surgical intervention. Rescue surgery was reserved only for emergent indications, including uncontrolled PFC, bleeding, or perforation.

Outcome definitions

Data on time until first follow-up CT imaging, resolution on cross-sectional imaging, duration of index stent(s), as well as time until final stent removal were collected. PFC resolution was defined as PFC size measuring less than 2 cm, whereas persistent PFC was defined as a fluid collection measuring 2 cm or larger. Technical success was defined by successful endoscopic placement of a transmural stent in the intended PFC. Clinical success was determined by symptom improvement and PFC imaging resolution or final stent removal. Clinical failure was defined as continued symptoms and/or persistent PFC after endoscopic intervention. Early endoscopic re-intervention, defined as within 4 weeks of the index drainage, was performed if there were symptoms suggestive of a persistent PFC or infection. PFC recurrence was defined as a fluid collection that developed in the same location after prior successful resolution. Long-term, or permanent, stents are stents intentionally placed without a plan for their scheduled removal following PFC resolution. All patients were followed until the last clinical encounter available in the electronic medical record.

Statistical analyses

Baseline demographics, clinical characteristics, endoscopic procedural details, and treatment outcomes were compared between the DPDS and non-DPDS cohorts. Given the sample size, normality was not assumed with continuous data variables. Therefore, descriptive statistics were computed as medians with interquartile range (IQR) or proportions with a 95 % confidence interval (CI), where applicable. The Wilcoxon's rank sum test and Fisher's exact test were used to compare continuous and categorical variables, respectively. A P value < 0.05 was regarded as statistically significant. The impact of DPDS on the outcomes was modeled using univariate logistic regression. The results are presented as an odds ratio (OR) with 95 %CI. Data management and computations were performed using STATA/IC, version 14.1 (Stata Corp., College Station, Texas, USA).

Results

Patient and pancreatic fluid collection characteristics

A total of 206 consecutive patients with PFCs underwent EUS-guided transmural drainage during the study period. In total, 65 patients were excluded, of whom 18 were excluded because of an equivocal DPD on imaging (▶ **Fig. 3**). Of the 141 patients

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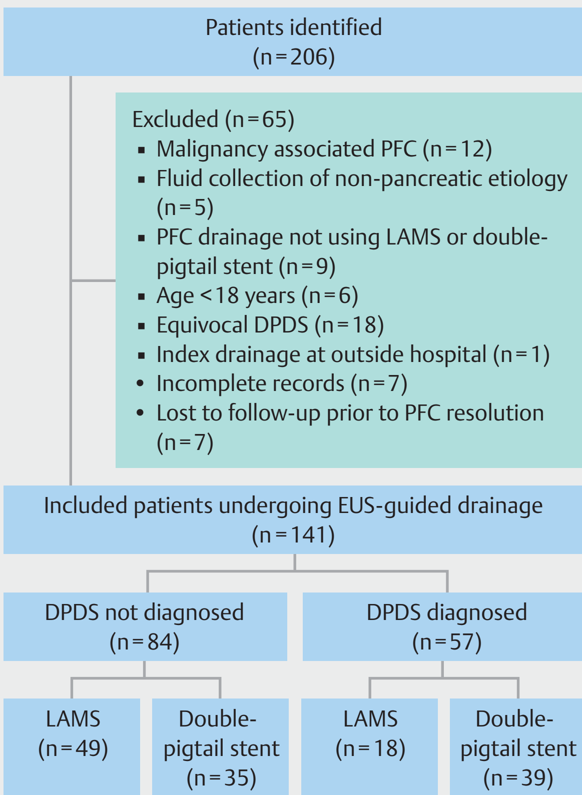

PFC, pancreatic fluid collection; LAMS, lumen-apposing metal stent; DPS, double pigtail stent; DPDS, disconnected pancreatic duct syndrome; OSH, outside hospital; EUS, endoscopic ultrasound

▶ **Fig. 3** Flowchart of the patients with pancreatic fluid collections (PFCs) who underwent endoscopic ultrasound (EUS)-guided drainage who were included in the study.
LAMS, lumen-apposing metal stent; DPDS, disconnected pancreatic duct syndrome.

included in the study, DPDS was diagnosed in 57 (40 %) and paracolic extension was seen in 28 (20 %) (▶ **Table 1**).

Patients with DPDS were found to have smaller fluid collections (median 82 mm [IQR 60 – 140 mm] vs. 120 mm [83 – 169 mm]; $P = 0.002$) and PFCs more often located in the body (25 % [95 %CI 14 % – 38 %] vs. 6 % [2 % – 13 %]; $P = 0.005$) compared with patients without DPDS. There was no difference in etiology of the PFCs, type or number of PFCs, or the presence of paracolic extension between the groups (▶ **Table 1**).

Procedural details

Double-pigtail stents (53 % [95 %CI 44 % – 61 %]) and a transgastric approach (54 % [95 %CI 45 % – 62 %]) were more frequently used in the index drainage procedures (▶ **Table 2**). A median of two index stents were placed, with a significantly longer duration of index stent placement in patients with DPDS than in those without (median 129 days [IQR 73 – 193 days] vs. 74 days [44 – 136 days]; $P = 0.006$). Patients with DPDS were more likely to have a plastic double-pigtail stent placed (OR 3.0 [95 % CI 1.5 – 6.2]; $P = 0.002$). In the overall cohort, 28 patients (20 %) were managed with permanent plastic double-pigtail stents, which were more likely to be placed in patients with DPDS (OR 6.4 [95 %CI 2.5 – 16.5]; $P < 0.001$).

There was no significant difference in choice of drainage route, number of index stents placed, total number of therapeutic endoscopic drainage procedures performed over a patient's treatment course, or the need for immediate necrosectomy in patients with DPDS vs. those without (▶ **Table 2**).

Treatment outcomes

Technical success was achieved in 100 % of patients, with clinical success achieved in 101 patients (72 % [95 %CI 63 % – 79 %]). The median time until final PFC resolution did not differ significantly between patients with and without DPDS (▶ **Table 2**).

There was no increased need for re-intervention: endoscopic necrosectomy (5 % [95 %CI 1 % – 15 %] vs. 16 % [9 % – 25 %]), additional endoscopic drainage (5 % [1 % – 15 %] vs. 4 % [1 % – 10 %]), subsequent percutaneous drainage (18 % [9 % – 30 %] vs. 13 % [7 % – 22 %]), or emergent surgery (4 % [0 % – 12 %] vs. 2 % [0 % – 8 %]) in patients with DPDS. In the entire cohort, four patients underwent emergent surgery for the following indications: uncontrolled PFC in the setting of a spontaneously out-migrated LAMS (n = 1), perforation following necrosectomy (n = 1), perforation during LAMS placement to tamponade bleeding at the site of a previously placed double-pigtail stent in a patient with DPDS (n = 1), and delayed bleeding secondary to LAMS erosion with resulting splenic artery pseudoaneurysm rupture in a patient with DPDS (n = 1). All four patients were initially drained via the transgastric route.

There were similar rates of procedural adverse events in patients with DPDS compared with those without: perforation/leak/puncture (5 % [95 %CI 1 % – 15 %] vs. 7 % [3 % – 15 %]), bleeding (2 % [0 % – 9 %] vs. 4 % [1 % – 10 %]), infection (2 % [0 % – 9 %] vs. 10 % [4 % – 18 %]), stent migration (4 % [0 % – 12 %] vs. 2 % [0 % – 8 %]), and gastric outlet obstruction (0 % [0 % – 6 %] vs. 2 % [0 % – 8 %]) (▶ **Table 2**).

Patients were followed for a median of 643 days [IQR 266 – 909 days] after the index drainage. DPDS was notably associated with increased rates of PFC recurrence (OR 8.0 [95 %CI 1.2 – 381.8]; $P = 0.04$) at a median of 194 days [IQR 122 – 491 days] (▶ **Table 3**). Of these six patients with recurrent PFC, five underwent successful repeat endoscopic drainage with a permanent double-pigtail stent (n = 3) or temporary LAMS (n = 2) with ultimate PFC resolution. One patient underwent percutaneous drainage followed by pancreaticoduodenectomy for intractable pain and a benign inflammatory pancreatic head mass with resultant CBD obstruction.

Twenty-eight patients were intended to have permanent transmural plastic double-pigtail stents placed, of which 23 (82 % [95 %CI 63 % – 94 %]) resulted in successful long-term PFC resolution. Long-term indwelling stents were left in place for a median of 555 days [IQR 116 – 899 days]. Two non-DPDS patients had recurrence of their PFCs despite well-positioned stents, with one undergoing subsequent percutaneous drainage. Three DPDS patients were considered failures of intended permanent plastic double-pigtail stent placement: one patient experienced stent obstruction secondary to an edematous duo-

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▶ **Table 1** Demographics of the 141 patients with pancreatic fluid collections (PFCs) who underwent endoscopic ultrasound-guided transmural drainage.

Factor	Level	DPDS (n = 57)		No DPDS (n = 84)		*P* value
		n (%)	95 %CI	n (%)	95 %CI	
Age, median (IQR), years		52 (41 – 62)		53 (42 – 65)		0.62
Sex	Male	39 (68 %)	5 % – 80 %	59 (70 %)	59 % – 80 %	0.85
Race	Caucasian	54 (95 %)	85 % – 99 %	78 (93 %)	85 % – 97 %	0.74
Etiology of PFC	Alcohol	10 (18 %)	9 % – 30 %	17 (20 %)	12 % – 30 %	0.64
	Gallstone	22 (39 %)	26 % – 52 %	26 (31 %)	21 % – 42 %	
	Other	25 (44 %)	31 % – 58 %	41 (49 %)	38 % – 60 %	
Type of PFC	Acute collection	1 (2 %)	0 % – 9 %	5 (6 %)	2 % – 13 %	0.24
	Pseudocyst	27 (47 %)	34 % – 61 %	30 (36 %)	26 % – 47 %	
	WON	29 (51 %)	37 % – 64 %	49 (58 %)	47 % – 69 %	
Location of largest PFC	Head	9 (16 %)	7 % – 28 %	21 (25 %)	16 % – 36 %	0.005
	Neck	5 (9 %)	3 % – 19 %	2 (2 %)	0 % – 8 %	
	Body	14 (25 %)	14 % – 38 %	5 (6 %)	2 % – 13 %	
	Tail	8 (14 %)	6 % – 26 %	21 (25 %)	16 % – 36 %	
	Multiple	21 (37 %)	24 % – 51 %	35 (42 %)	31 % – 53 %	
Multiple PFCs	One PFC	40 (70 %)	57 % – 82 %	48 (57 %)	46 % – 68 %	0.16
	Multiple PFC	17 (30 %)	18 % – 43 %	36 (43 %)	32 % – 54 %	
Size of largest PFC (long axis), median (IQR), mm		82 (60 – 140)		120 (83 – 169)		0.002
Paracolic extension		7 (13 %)	5 % – 24 %	21 (25 %)	16 % – 36 %	0.09

DPDS, disconnected pancreatic duct syndrome; CI, confidence interval; IQR, interquartile range; WON, walled-off necrosis.

denum requiring endoscopic replacement with shorter stents; the other two patients were noted to have recurrent PFCs due to spontaneous stent outmigration, one of which later resolved after replacement of the permanent stents.

Discussion

The management of PFCs varies widely and depends predominantly on fluid collection maturity and presence of solid necrosis. Our study shows that DPDS is associated with increased PFC recurrence. Although previous studies have suggested definitive endoscopic treatment of DPDS requires persistent drainage through prolonged or permanent stent placement or the establishment of a patent fistula, the optimal management of PFCs in the setting of DPDS remains unknown [16 – 19]. The treatment of DPDS has evolved over time, perhaps most significantly with the advent and increasing use of EUS-guided transmural drainage. In this study, DPDS was diagnosed in 40 % of patients with PFCs and was noted to be similar between patients with pseudocysts and those with WON. The incidence of DPDS in our study cohort is within the range previously reported in the literature at 16 % – 46 % of PFCs [3, 4,11]. There was no significant difference in clinical success between patients with and without DPDS, and DPDS was not observed to affect the median time until successful PFC resolution.

Our group previously investigated the use of large caliber SEMSs and LAMSs compared with double-pigtail stents in the endoscopic management of WON, but did not evaluate the impact of DPDS on clinical outcomes [20]. In this series, patients with DPDS were more likely to have plastic double-pigtail stents and permanent destination stents placed. The decision to intentionally leave double-pigtail stents in situ after confirmation of PFC resolution on imaging was left to the discretion of the performing endoscopist. Previous studies of patients with DPDS have shown decreased PFC recurrence with permanent stents, suggesting PFCs are more likely to recur after stent removal in those with DPDS [2, 14 – 16]. The PFC recurrence rate in DPDS patients noted in this series (9 %) is similar to the 6 % rate cited by others [11].

While permanent stents may migrate or become obstructed, resulting in fluid re-accumulation or infection, we did not find significantly increased incidences of these adverse events in patients with DPDS, as has been noted in prior studies [9, 18]. Given the potential for complications related to permanent indwelling stents, transduodenal drainage has been proposed as a viable alternative to long-term stenting, as this may

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▶ **Table 2** Procedural details and outcomes for the 141 endoscopic ultrasound-guided transmural drainage procedures.

Factor	Level	DPDS (n = 57)		No DPDS (n = 84)		*P* value
		n (%)	95 %CI	n (%)	95 %CI	
Technical success		57 (100 %)	94 % – 100 %	84 (100 %)	96 % – 100 %	0.40
Clinical success		42 (74 %)	60 % – 84 %	59 (70 %)	59 % – 80 %	0.71
Type of index stent	LAMS	18 (32 %)	20 % – 45 %	49 (58 %)	47 % – 69 %	0.002
	Double pigtail	39 (68 %)	55 % – 80 %	35 (42 %)	31 % – 53 %	
Coaxial double-pigtail placed with index LAMS		3 (17 %)	4 % – 41 %	11 (22 %)	12 % – 37 %	0.74
Index route of drainage	TG	27 (47 %)	34 % – 61 %	49 (58 %)	47 % – 69 %	0.18
	TD	22 (39 %)	26 % – 52 %	20 (24 %)	15 % – 34 %	
	TG + TD	8 (14 %)	6 % – 26 %	15 (18 %)	10 % – 28 %	
Placement of TD stent into 3 rd or 4th part of duodenum		10 (18 %)	9 % – 30 %	9 (11 %)	5 % – 19 %	0.32
Total number of stents placed during index session, median (IQR)		2 (2 – 2)		2 (1 – 3)		0.68
Permanent transmural stent placed		21 (37 %)	24 % – 51 %	7 (8 %)	3 % – 16 %	< 0.001
Percutaneous drain placement		10 (18 %)	9 % – 30 %	11 (13 %)	7 % – 22 %	0.48
Immediate necrosectomy		23 (40 %)	28 % – 54 %	39 (46 %)	35 % – 58 %	0.49
Re-intervention	Necrosectomy for infected collection	3 (5 %)	1 % – 15 %	13 (16 %)	9 % – 25 %	0.19
	Additional endoscopic drainage	3 (5 %)	1 % – 15 %	3 (4 %)	1 % – 10 %	
	Subsequent percutaneous IR drainage	10 (18 %)	9 % – 30 %	11 (13 %)	7 % – 22 %	
	Emergent surgery	2 (4 %)	0 % – 12 %	2 (2 %)	0 % – 8 %	
Procedural adverse events	Perforation/leak/puncture	3 (5 %)	1 % – 15 %	6 (7 %)	3 % – 15 %	0.66
	Bleeding	1 (2 %)	0 % – 9 %	3 (4 %)	1 % – 10 %	
	Infection	1 (2 %)	0 % – 9 %	8 (10 %)	4 % – 18 %	
	Stent migration	2 (4 %)	0 % – 12 %	2 (2 %)	0 % – 8 %	
	GOO	0 (0 %)	0 % – 6 %	2 (2 %)	0 % – 8 %	
Duration of index stent placement, median (IQR), days		129 (73 – 193)		74 (44 – 136)		0.006
Total number of therapeutic endoscopies, median (IQR)		2 (1 – 3)		2 (1 – 3)		0.68
Time until first follow-up CT, median (IQR), days		32 (11 – 60)		14 (5 – 42)		0.004
Time until final PFC resolution, median (IQR), days		70 (42 – 134)		67 (35 – 108)		0.21

DPDS, disconnected pancreatic duct syndrome; CI, confidence interval; LAMS, lumen-apposing metal stent; TG, transgastric; TD, transduodenal; IQR interquartile range; IR, interventional radiology; GOO, gastric outlet obstruction.

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▶ Table 3 Impact of disconnected pancreatic duct syndrome (DPDS) on endoscopic ultrasound-guided drainage of pancreatic fluid collections (PFCs).

Outcome	DPDS (n = 57)			
	n (%)	OR	95 %CI	*P* value
Clinical success	42 (74 %)	0.8	0.4 – 1.8	0.71
Re-intervention[1]	24 (42 %)	1.0	0.5 – 2.1	0.96
Percutaneous drainage	10 (18 %)	1.4	0.5 – 4.0	0.48
PFC recurrence	5 (9 %)	8.0	1.2 – 381.8	0.04
Procedural adverse events[2]	7 (12 %)	0.4	0.1 – 1.1	0.09
Overall mortality	2 (4 %)	0.5	0.1 – 2.8	0.47

OR, odds ratio; CI, confidence interval.
[1] Re-intervention includes the need for: endoscopic necrosectomy, additional endoscopic or percutaneous drainage, or emergent surgery.
[2] Procedural adverse events include: perforation/leak/puncture, bleeding, infection, stent migration, or gastric outlet obstruction.

result in chronic pancreaticoduodenal fistulas in the less vascularized duodenum [2, 15].

In a recent retrospective study investigating the impact of DPDS on the endoscopic treatment of PFCs, the authors demonstrated an increased need for endoscopic re-intervention, percutaneous drain placement, or surgery in patients with DPDS [11]. In our study, we observed that DPDS was not associated with an increased need for additional therapeutic endoscopic, percutaneous, or surgical intervention. One explanation is that our study only included EUS-guided drainage, which has been shown to have increased rates of technical or clinical success when compared to non-EUS guided transmural drainage [7, 21]. Another consideration is our use of only plastic double-pigtail stents and LAMSs to reflect current-day practice at our institution, whereas previous studies were performed prior to the development of LAMSs and used fully covered biliary or enteral SEMSs that were not designed for PFC drainage. The increased rates of re-intervention, whether endoscopic, percutaneous, or surgical, seen in previous studies may therefore reflect the heterogeneity inherent to the inclusion of conventional non-EUS-guided drainage and use of biliary or enteral SEMSs.

Our study is not without limitations. First are its intrinsic weaknesses as a retrospective single-center study at risk for selection bias. Second, while this is one of the largest studies investigating the impact of DPDS on the clinical resolution of PFCs, the overall sample size has limited statistical power, which may have limited our ability to detect small differences in outcomes, especially the need for subsequent percutaneous drainage or surgical intervention. Although follow-up imaging recommendations were standardized, there was an element of endoscopic variability in follow-up, as some patients underwent follow-up imaging and subsequent endoscopic procedures at their local hospital facility. While we excluded patients who did not undergo index drainage at our institution, patients who underwent subsequent follow-up at other facilities were not excluded as long as their medical records were available for review.

Another important limitation was that a variety of modalities, including MRCP, EUS, and CT, were used to diagnose DPDs. While these modalities may in theory overestimate the presence of a DPD owing to extrinsic compression of the main pancreatic duct from PFCs, mimicking the appearance of a DPD, EUS has been found to reliably diagnose DPDs when strict criteria are applied [22]. Similarly, MRCP has also been shown to accurately diagnose DPDs, with one study observing an accurate DPD exclusion rate of 93 % with MRCP [23], and another showing MRCP confirmation of DPDS in 91 % of ERCP-confirmed cases of DPDS [24].

The major strengths of our study are the exclusion of patients with an equivocal DPD and a merely disrupted pancreatic duct on imaging, our attempts to limit the heterogeneity seen in previous studies by including only patients who underwent EUS-guided transmural drainage with plastic double-pigtail stents or LAMSs, and our long-term follow-up period (median 21 months) that captures delayed adverse events and recurrent PFCs.

In conclusion, DPDS was frequently identified in patients with PFCs undergoing EUS-guided transmural drainage. DPDS was not associated with increased rates of clinical failure, need for endoscopic re-intervention, or need for step-up therapy. DPDS was associated with increased rates of symptomatic PFC recurrence after stent removal. Therefore, clinicians should carefully assess for the presence of DPDS when considering endoscopic therapy of PFCs.

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Competing interests

Dr. Abu Dayyeh is consultant for Metamodix, BFKW, DyaMx, Boston Scientific, USGI medical, and Endo-TAGSS. He received research support from Apollo Endosurgery, USGI, Spatz Medical, Boston Scientific, GI Dynamics, Cairn Diagnostics, Aspire Bariatrics, and Medtronic. He served as a speaker for Johnson and Johnson, Endogastric Solutions, and Olympus. Bret T Petersen: 3M: Stock Shareholder; Abbvie: Stock Shareholder; Boston Scientific: Grant/Research Support, Consulting; Exact Sciences: Stock Shareholder; GIE Medical: Consulting; Johnson & Johnson: Stock Shareholder; Medtronic: Stock Shareholder; Olympus America: Consulting. Andrew C Storm: Apollo Endosurgery: Consulting; Boston Scientific: Grant/Research Support; Endo-TAGSS: Grant/Research Support; Enterasense: Grant/Research Support; GI Dynamics: Consulting. Santhi S Vege: Uptodate: Royalties; vical: Consulting. Vinay Chandrasekhara – Consultant, Interpace Diagnostics. Shareholder, Nevakar Corporation. The other authors declare that they have no conflict of interest.

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References

[1] Banks PA, Bollen TL, Dervenis C et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013; 62: 102–111

[2] Nadkarni NA, Kotwal V, Sarr MG et al. Disconnected pancreatic duct syndrome: endoscopic stent or surgeon's knife? Pancreas 2015; 44: 16–22

[3] Lawrence C, Howell DA, Stefan AM et al. Disconnected pancreatic tail syndrome: potential for endoscopic therapy and results of long-term follow-up. Gastrointest Endosc 2008; 67: 673–679

[4] Nealon WH, Bhutani M, Riall TS et al. A unifying concept: pancreatic ductal anatomy both predicts and determines the major complications resulting from pancreatitis. J Am Coll Surg 2009; 208: 790–799; discussion 799-801

[5] Varadarajulu S, Lopes TL, Wilcox CM et al. EUS versus surgical cyst-gastrostomy for management of pancreatic pseudocysts. Gastrointest Endosc 2008; 68: 649–655

[6] Goyal J, Ramesh J. Endoscopic management of peripancreatic fluid collections. Frontline Gastroenterol 2015; 6: 199–207

[7] Varadarajulu S, Christein JD, Tamhane A et al. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc 2008; 68: 1102–1111

[8] Varadarajulu S, Noone TC, Tutuian R et al. Predictors of outcome in pancreatic duct disruption managed by endoscopic transpapillary stent placement. Gastrointest Endosc 2005; 61: 568–575

[9] Tellez-Avina FI, Casasola-Sanchez LE, Ramirez-Luna MA et al. Permanent indwelling transmural stents for endoscopic treatment of patients with disconnected pancreatic duct syndrome: long-term results. J Clin Gastroenterol 2018; 52: 85–90

[10] Yang D, Amin S, Gonzalez S et al. Transpapillary drainage has no added benefit on treatment outcomes in patients undergoing EUS-guided transmural drainage of pancreatic pseudocysts: a large multicenter study. Gastrointest Endosc 2016; 83: 720–729

[11] Bang JY, Wilcox CM, Navaneethan U et al. Impact of disconnected pancreatic duct syndrome on the endoscopic management of pancreatic fluid collections. Ann Surg 2018; 267: 561–568

[12] Mussetto A, Fugazza A, Fuccio L et al. Current uses and outcomes of lumen-apposing metal stents. Ann Gastroenterol 2018; 31: 535–540

[13] Han D, Inamdar S, Lee CW et al. Lumen apposing metal stents (LAMSs) for drainage of pancreatic and gallbladder collections: a meta-analysis. J Clin Gastroenterol 2018; 52: 835–844

[14] Shah RJ, Shah JN, Waxman I et al. Safety and efficacy of endoscopic ultrasound-guided drainage of pancreatic fluid collections with lumen-apposing covered self-expanding metal stents. Clin Gastroenterol Hepatol 2015; 13: 747–752

[15] Topazian M. Endoscopic ultrasound-guided drainage of pancreatic fluid collections (with video). Clin Endosc 2012; 45: 337–340

[16] Varadarajulu S, Wilcox CM. Endoscopic placement of permanent indwelling transmural stents in disconnected pancreatic duct syndrome: does benefit outweigh the risks? Gastrointest Endosc 2011; 74: 1408–1412

[17] Deviere J, Bueso H, Baize M et al. Complete disruption of the main pancreatic duct: endoscopic management. Gastrointest Endosc 1995; 42: 445–451

[18] Arvanitakis M, Delhaye M, Bali MA et al. Pancreatic-fluid collections: a randomized controlled trial regarding stent removal after endoscopic transmural drainage. Gastrointest Endosc 2007; 65: 609–619

[19] Rana SS, Bhasin DK, Sharma R et al. Factors determining recurrence of fluid collections following migration of intended long term transmural stents in patients with walled off pancreatic necrosis and disconnected pancreatic duct syndrome. Endosc Ultrasound 2015; 4: 208–212

[20] Abu Dayyeh BK, Mukewar S, Majumder S et al. Large-caliber metal stents versus plastic stents for the management of pancreatic walled-off necrosis. Gastrointest Endosc 2018; 87: 141–149

[21] Park DH, Lee SS, Moon SH et al. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: a prospective randomized trial. Endoscopy 2009; 41: 842–848

[22] Bang JY, Navaneethan U, Hasan MK et al. EUS correlates of disconnected pancreatic duct syndrome in walled-off necrosis. Endosc Int Open 2016; 4: E883–E889

[23] Kamal A, Singh VK, Akshintala VS et al. CT and MRI assessment of symptomatic organized pancreatic fluid collections and pancreatic duct disruption: an interreader variability study using the revised Atlanta classification 2012. Abdom Imaging 2015; 40: 1608–1616

[24] Drake LM, Anis M, Lawrence C. Accuracy of magnetic resonance cholangiopancreatography in identifying pancreatic duct disruption. J Clin Gastroenterol 2012; 46: 696–699

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