Transpapillary drainage has no added benefit on treatment outcomes in patients undergoing EUS-guided transmural drainage of pancreatic pseudocysts: a large multicenter study


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ABSTRACT

Background and Aims: The need for transpapillary drainage (TP) in patients undergoing transmural drainage (TM) of pancreatic fluid collections (PFC) remains unclear. The aims of this study were to compare treatment outcomes between patients with pancreatic pseudocysts undergoing TM versus combined (TM and TP) drainage (CD) and to identify predictors of symptomatic and radiologic resolution. Methods: Retrospective review of 375 consecutive patients with PFC who underwent endoscopic ultrasound (EUS)-guided TM from 2008 to 2014 at 15 academic centers in the United States. Main outcome measures included TM and CD technical success, treatment outcomes (symptomatic and radiologic resolution) at follow-up, and predictors of treatment outcomes on logistic regression. Results: A total of 375 patients underwent EUS-guided TM drainage of a PFC, of which 174 were pseudocysts. TM alone was performed in 95 (55%) and CD in 79 (45%) pseudocysts. Technical success: TM 92(97%) versus CD 35(44%) (P=0.0001). There was no difference in adverse events between the TM (15%) and CD (14%) cohorts (P=0.23). Median long-term (LT) follow-up after transmural stent removal was 324 days (interquartile range, 72-493 days) for TM and 201 days (interquartile range: 150-493 days) (P=0.37). There was no difference in LT symptomatic resolution (TM: 69% vs CD: 62%, P=0.61) or LT radiologic resolution (TM: 71% vs CD: 67%, P=0.79). TP attempt was negatively associated with LT radiologic resolution of pseudocyst (OR, 0.11; 95% CI, 0.02-0.8; P=0.03). Conclusions: TP has no benefit on treatment outcomes in patients undergoing EUS-guided TM of pancreatic pseudocysts and negatively impacts long-term resolution of PFC.
INTRODUCTION

Pancreatic fluid collections (PFCs) due to pancreatic duct (PD) disruption can develop as a consequence of acute or chronic pancreatitis, pancreatic surgery, and trauma [1-3]. Pancreatic pseudocysts are a type of PFC characterized by a well-encapsulated fluid collection with minimal to no necrotic debris. Although pseudocysts develop in up to 20% of cases of acute pancreatitis, most of these resolve spontaneously [4]. Treatment is warranted in the setting of persistent symptoms or adverse events. Symptoms, including abdominal pain, early satiety, jaundice, or weight loss, are often due to luminal (gastric or duodenal) and/or biliary obstruction. Pseudocyst superinfection can lead to abscess formation and thus represents an absolute indication for drainage [5].

Endoscopic transmural drainage (TM) has become the first-line therapy for symptomatic pancreatic pseudocysts given its similar efficacy, shorter recovery times, fewer adverse events and improved cost-effectiveness when compared with surgical cystogastrostomy [6]. This technique involves the creation of a communication between the pseudocyst and the gastroduodenal lumen (cystogastrostomy or cystoduodenostomy), allowing the internal drainage and collapse of the pseudocyst [7]. With technical advances in endoscopy, conventional endoscopic drainage has largely been replaced with endoscopic ultrasound (EUS)-guided TM drainage, as the latter is associated with higher technical success and fewer adverse event rates, especially in the absence of a visible endoscopic bulge [8,9].

The role of transpapillary drainage (TP) in patients with pancreatic pseudocysts undergoing TM remains unclear. Theoretically, TP through the placement of a PD endoprosthesis across the site of a leak/disruption may facilitate healing by bypassing the defect and allowing direct flow of the pancreatic secretions into the duodenum. However, the current
data on combined transmural and transpapillary drainage (CD) is scarce and inconsistent. Hookey and colleagues performed endoscopic drainage of PFC in 116 patients and reported no significant difference in clinical success rates between patients who underwent TM alone (90.6%) in comparison with those who underwent CD (82.9%). Furthermore, a higher recurrence rate was observed in patients with PFC drained by a combined approach (26.8%) versus TM only (8.3%; \( p = 0.015 \)) [10]. On the contrary, in a separate retrospective study of PFC drainage, Trevino et al reported that patients who underwent a combined approach (TM and TP with bridging PD stent) were more likely to have treatment success than patients who did not undergo PD stenting during TM drainage (97.5% vs 80%; adjusted risk ratio [RR] =1.14; 95% confidence interval [CI], 1.01-1.29; \( p = 0.036 \)) [11].

The primary aim of this multicenter, retrospective study was to compare treatment outcomes in patients with pancreatic pseudocysts who underwent EUS-guided TM alone versus CD. A secondary objective was to identify factors associated with successful clinical outcomes in the endoscopic management of pseudocysts.

**METHODS**

This multi-center retrospective study included all consecutive patients \( \geq 18 \) years old who underwent attempted EUS-guided PFC drainage at 15 academic tertiary referral centers in the United States between January 2008 and September 2014. Patients were identified through prospectively maintained endoscopic databases and chart review. All data were extracted and compiled into a central database. Informed procedural consents were obtained from all patients. This study was approved by the institutional review board for human research at each of the participating institutions. All endoscopic procedures were performed according to the ASGE
practice guideline recommendations on antibiotic prophylaxis and management of antithrombotic agents and coagulopathy [12, 13].

Data collection was separated into 3 categories: baseline, procedural, and postprocedural data. Baseline data of interest included patient demographics, etiology of pancreatitis, presence of chronic pancreatitis, characteristics of PFC, and findings on index imaging before drainage. Procedure-related data included technical aspects for both TM and TP drainage. Relevant EUS-guided TM data included method of cystoenterostomy tract creation, route of drainage, placement of nasocystic drain, and type and number of transmural stent(s) used. Endoscopic retrograde pancreatography (ERP) data included findings on pancreatogram and type of ERP intervention performed when applicable. All procedure-related adverse events were reviewed. Postprocedure data included duration of follow-up, need for additional intervention(s), and treatment outcomes.

Definitions

PFCs were classified as per the revised Atlanta classification as acute peripancreatic fluid collection (APFC), pseudocysts, acute necrotic collection (ANC) or walled-off necrosis (WON) [14]. Adverse events were assessed based on previously established criteria by the American Society of Gastrointestinal Endoscopy (ASGE) [15]. Patients were divided into 2 groups: TM alone versus CD. Patients in the TM group underwent EUS-guided TM only whereas those in the CD group underwent ERP with attempted TP in addition to TM (Figure 1). TM technical success was defined as successful placement of a minimum of one transmural stent during PFC drainage. TP technical success was defined as completion of the intended diagnostic and/or therapeutic ERP. CD technical success constituted both TM and TP technical success. Symptom resolution was defined as the complete absence of any symptoms, including pain, gastric outlet obstruction,
biliary obstruction, and/or infection. Radiologic resolution was defined as the complete resolution of the pseudocyst on repeat imaging at the time of follow-up.

**Main Outcome Measures**

The primary aim of the study was to compare symptomatic and radiologic resolution of patients with pancreatic pseudocysts who underwent TM alone versus CD. A secondary aim was to identify potential clinical predictors of symptom, radiologic resolution of PFC and/or adverse events after endoscopic drainage.

**Follow-Up**

Treatment outcome measures were evaluated at both short-term (ST) and long-term (LT) follow-up. ST follow-up was defined as an interval of ≥2 weeks after transmural stent placement but before stent removal. LT follow-up was defined as a period ≥2 weeks after transmural stent removal.

**Statistical Analysis**

Descriptive statistics were calculated for all demographic, imaging, and clinical variables and were reported as mean ± standard deviation (SD), median with interquartile ranges (IQR), and/or as a proportion. Univariate analysis was performed by using the chi-square test and the Fisher exact test for categorical variables and the t test for continuous variables when indicated. Multivariate analysis was performed by using logistic regression to assess factors associated with symptom resolution, radiologic resolution of pseudocysts, and adverse events. The variables included in the logistic regression model were chosen based on statistical significance (cut-off P value of 0.2) on univariate analysis. All statistical analysis was performed with the SPSS
software v22 (IBM, SPSS Statistics, Armonk, NY). A $P$ value less than 0.05 was considered statistically significant.

**RESULTS**

**Patient Characteristics and Pancreatic Pseudocysts**

A total of 375 patients underwent EUS-guided transmural PFC drainage during the study period. Of these patients, 215 (mean age 52.7; 66.8% male) underwent TM whereas 161 (mean age 51.4; 64% male) had CD. A total of 289 patients were initially diagnosed with pseudocysts based on the timing of the PFC in relationship to the onset of acute pancreatitis and on index cross-sectional imaging characteristics. An additional 115 patients were excluded given the presence of solid debris seen at the time of EUS. The final analysis included 174 patients with pseudocysts, of which 95 and 79 underwent TM and CD drainage; respectively.

Baseline characteristics of patients with pseudocysts are summarized in table 1. There was no significant difference in patient age, gender, etiology of pancreatitis, or presence of chronic pancreatitis in patients who underwent TM versus CD. The median size of the pseudocysts was similar in patients who underwent TM drainage (9.0 cm; IQR, 7.3-12.3 cm) and CD (9.5 cm; IQR, 7.1-12.2 cm) ($p=0.17$). Overall, abdominal pain was the most common indication for pseudocyst drainage in both groups (90.5% in TM vs 86.1% in CD; $p=0.47$). Other indications included gastric outlet obstruction, biliary obstruction, and/or infection (Table 1). PD leak/disruption on index imaging was more commonly reported in patients who underwent CD (14/79; 17.7%) versus TM drainage (6/95; 6.3%) ($p=0.03$).

**Technical parameters and Outcomes**

*EUS-guided transmural drainage*
The procedural technique of EUS-guided transmural drainage for patients who underwent TM versus CD drainage is summarized in Table 2. In both groups, a 19-gauge EUS needle was used for access and fistula creation via a transgastric or transduodenal approach in nearly all cases. There was no significant difference in the type of transmural stent(s) used for pseudocyst drainage between the 2 groups. The most common TM drainage intervention was placement of a median of two 10F (51.9% in TM vs 65.2% in CD; \( p=0.13 \)) or two 7F stents (26% in TM vs 22.7% in CD; \( p=0.19 \)). Overall, transmural stent(s) remained in place for a median of 96 and 95 days in the TM and CD drainage group, respectively (\( p=0.25 \)). A nasocystic drain was placed in 5 (5.3%) patients who underwent TM and none in those who had CD (\( p=0.06 \)).

**ERP-guided transpapillary drainage**

Seventy nine patients with pseudocysts in the CD group underwent attempted ERP-guided TP (Figure 2). TP was performed during the same TM session in 31 cases. The median time interval between TM and TP in the remaining cases was 0 days (range; 0-34 days). Reasons for failed pancreatogram (\( n = 13 \)) included inability to reach/identify the papilla (15.4%) or unsuccessful PD cannulation (61.4%). In those with a successful pancreatogram (\( n = 66; 83.5\% \)), PD leak/disruption was reported in 47 (71.2%) patients. Other findings included PD stricture (31.8%) and pancreaticolithiasis (10.8%). A normal pancreatogram was only seen in 6 (9%) patients (Figure 2). A PD stent was placed in 50 (83.3%) patients, of which 47 (94%) were performed in the setting of a PD leak/disruption. Most PD stents inserted were either 7F (24/50; 48%) or 5F (23/50; 46%) in diameter. Overall, the PD stent was reported to traverse the defect in 17/47 (36.2%) of the cases (Figure 2). Other interventions performed during ERP included sphincterotomy (65%), sphincteroplasty (23.3%), and/or stone extraction (6.7%). Overall, stents remained in place for a median of 53 days (IQR: 32-88 days).
Outcomes

Technical success rate for EUS-guided transmural drainage was 96.8% (92/95) in TM and 98.7% (78/79) in CD (p=0.63) (Figure 3). Reasons for failure in the 3 patients from the TM group included inability to dilate the fistulous tract in 1, hypoxemia with termination of the procedure in 1, and failure to advance the stent in 1 patient. TM drainage was unsuccessful in 1 patient who underwent CD due to stent migration after deployment resulting in perforation. The migrated stent was removed followed by endoscopic closure of the gastric defect.

TP was attempted in 79 patients, of which a successful pancreatogram was achieved in 66 patients (Figure 3). The intended diagnostic and/or therapeutic intervention was completed in 36 patients (PD endoprosthesis failed to traverse a PD leak or disruption in 30 patients). Thus, the technical success rate for TP was 46% (36/79). Because CD technical success was defined as both TM and TP technical success, CD technical success was 44% (35/79). Overall, technical success rate of TM (96.8%) was significantly higher than for CD (44%) (p<0.0001).

Procedural Adverse Events

Overall, adverse event rates were not significantly different between patients who underwent TM (14.7%) versus CD (13.9%) (p=1.0). Procedural adverse events for pseudocyst drainage are summarized in Table 3. Bleeding was managed with endoscopic hemostasis and blood transfusion (n = 4) or coil embolization by interventional radiology (n = 3). One patient in the CD group required urgent laparotomy due to perforation during ERP. Two cases of perforation during TM stent placement did not require any specific intervention whereas endoscopic removal of a migrated TM stent and gastric defect closure was performed in one patient who underwent CD. Two patients developed mild post-ERP pancreatitis, requiring only
intravenous fluids and symptomatic control. Pseudocyst drainage complicated by infection were managed by repeat endoscopic drainage with upsizing of TM stent(s) and nasocystic drain placement (n = 3) or CT-guided percutaneous drain placement (n = 2). One patient who underwent TM died from cardiopulmonary arrest after aspiration.

**Treatment Outcomes and Follow-up**

The median ST follow-up was 52 (IQR, 36-86) days for TM and 54 (IQR, 38-71) days for CD (p=0.41). Complete symptomatic resolution at ST follow-up was reported in 42 (72.4%) patients who underwent TM drainage and 47 (67.1%) patients who had CD (odds ratio [OR], 1.28; 95% CI, 0.60-2.75; p=0.41) (Figure 4). Radiologic resolution of PFC at ST follow-up was also not significantly different after TM (48/72; 66.7%) or CD (41/68; 60.3%) (OR, 1.32; 95% CI, 0.67-2.63; p=0.48).

The median LT follow-up was 324 (IQR: 72-493) days for TM and 201 (150-438) days for CD (p=0.37). Similarly, there was no difference in symptomatic resolution (69% in TM vs 61.5% in CD) (OR, 1.39; 95% CI, 0.50-3.84; p=0.61) or radiologic resolution of PFC (71% in TM vs 66.7% in CD) (OR, 1.22; 95% CI, 0.43-3.46; p=0.79) between the 2 cohorts on LT follow-up (Figure 4). A subgroup analysis comparing patients with pseudocysts who underwent TM (n = 95) versus those who had a technically successful CD (n = 35) also failed to demonstrated any difference in symptom or radiologic resolution rates at ST and LT follow-up (data not shown). In aggregate, 32 (18.4%) and 104 (59.8%) patients were lost to ST and LT follow-up, respectively.

**Predictors of treatment outcomes and adverse events**
Univariate and multivariate logistic regression was performed to identify predictors of adverse events, symptomatic and radiologic resolution on ST and LT follow-up. The factors included were age, gender, etiology of pancreatitis (other vs ETOH), chronic pancreatitis (yes vs no), indication for PFC drainage (present vs absent), type of pre-drainage index cross-sectional imaging (other vs CT), size of PFC, location of PFC (body/tail vs head), PD leak/disruption (yes vs no), and TP attempted (yes vs no).

On multivariate analysis, TP attempted was the only clinical variable negatively associated with LT radiologic resolution of PFC (OR, 0.11; 95% CI, 0.02-0.8; \( p = 0.03 \)) even after adjusting for other statistically significant variables (Table 4). Logistic regression showed absence of statistically significant predictors of ST symptomatic/radiologic resolution, LT symptomatic resolution, or adverse events (data not shown).

**DISCUSSION**

Endoscopic transmural drainage has largely replaced surgery as the first-line therapy for the management of pancreatic pseudocysts due its comparable clinical efficacy, shorter post-procedural recovery time, lower costs and adverse event rates [6]. Published data on the role of concomitant transpapillary drainage (TP) in patients undergoing transmural drainage (TM) of pancreatic pseudocysts is limited and conflicting. In our current multicenter study, there was no difference in treatment outcomes or adverse event rates in patients who underwent EUS-guided TM alone compared with those undergoing a combined transmural and transpapillary approach (CD).

A prior single center retrospective study suggested that placement of a bridging PD stent across the ductal disruption favorably impacts treatment outcomes in patients undergoing TM of
Patients who underwent PD stenting were significantly more likely to have treatment success than those who did not have a PD endoprosthesis (97.5% vs 80%; adjusted RR, 1.14; 95% CI, 1.01-1.29; p=0.036). However, in a subsequent larger study by the same authors of 211 patients undergoing PFC drainage, only type of PFC was a predictor of clinical outcomes [14]. Treatment success was more likely for patients with pseudocysts or abscess than necrosis (adjusted OR, 7.6; 95% CI, 2.9-20.1; p<0.0001). On the contrary, PD stent in patients undergoing TM of PFC was not found to be a predictor of treatment success (adjusted OR, 1.70; 95% CI, 0.56-5.14; p=0.34). The findings of the latter study are congruent with our results and those previously reported in the literature. Hookey and colleagues [10] evaluated clinical outcomes in 116 patients who underwent endoscopic drainage of PFC. In their study, there was no significant difference in the rate of clinical success between patients who underwent EUS-guided TM (90.6%) compared with CD (82.9%). Indeed, there was actually a higher recurrence rate with a combined approach (26.8%) compared with TM alone (8.3%) (p=0.015). The authors stipulated that the addition of TP may potentially hinder the patency and maturation of the cyst-enterostomy fistula and thus limit the resolution of the PFCs [10]. This explanation may account for the negative association between attempting TP in patients who underwent CD and LT radiologic resolution in our study (OR, 0.11; 95% CI, 0.02-0.8; p=0.03).

In this study, EUS-guided TM was technically successful in over 96.8% of the patients with pseudocysts. This high technical success rate is comparable and in agreement to those previously reported [8-10, 14, 16-23]. On the contrary, the technical success of TP in patients who underwent CD was significantly lower (46%). Placement of a bridging stent across the PD disruption for TP has been correlated with improved treatment outcomes [24, 25]. In this study, 47 (71.2%) patients had a PD disruption/leak on pancreatogram; however, the PD stent bridged
the disruption/leak in only 17 (36%) of the patients; thereby, contributing to the overall low technical success rate of TP. The low technical success associated with placing a stent across the PD disruption/leak has been previously documented. In 2 separate studies, successful placement of a bridging PD stent across a disruption/leak was reported in the range of 40.2% for pseudocysts to as low as 17.5% for WON [11,16]. Cited reasons for failure include complete ductal disruption, inability to complete the ERP due to luminal obstruction, surgically altered anatomy, and/or failed PD cannulation [10, 11, 26]. Furthermore, as shown in a subgroup analysis in this study, even when a PD stent is successfully placed across the leak/disruption in patients who undergo CD, there was no difference in treatment outcomes when compared with patients who underwent TM alone. Thus, although there is a paucity of studies that have directly evaluated PD disruption and healing after TM alone, the positive clinical outcomes associated with PFC resolution and low recurrence rates would suggest this to be an effective treatment modality in most patients with PD disruption, including those with a disconnected pancreatic duct syndrome [27,28]. Altogether, the low technical success rate of TP, the well-recognized potential adverse events associated with ERP, and the absence of definitive improved treatment outcomes with a combined drainage approach, suggests that TP has no benefit in patients with pseudocysts undergoing endoscopic TM.

This study has several strengths. This is the largest multicenter experience on EUS-guided TM of pseudocysts reported to date. Second, patients with pseudocysts were identified based on established criteria and by the omission of patients with solid debris within the fluid collection on EUS [1]. Third, instead of using post-drainage PFC size as the only surrogate marker for treatment success, the main outcomes in this study were defined as the complete resolution of symptoms and radiographic findings on follow-up, presumably clinically more
relevant endpoints. Last, not only was treatment efficacy assessed immediately after endoscopic drainage, but long-term treatment effect was estimated by evaluating clinical outcomes after transmural stent removal (median 259 days; IQR: 113-429 days). This is a key point as ultimate therapeutic outcomes should be assessed once the prostheses are removed, thus signaling the true completion of therapy.

There are also limitations to this study. The study design was retrospective with its inherent limitations. Although baseline characteristics were similar between the 2 cohorts, PD leak/disruption on index imaging was more commonly seen in patients who underwent CD versus TM drainage. However, this difference between the 2 groups may be clinically insignificant as PD leak/disruption was not found to be a predictor of treatment outcomes in this study. Nonetheless, given the retrospective nature of this study, it remains unclear whether the association of CD with worse treatment outcomes when compared with TM alone was due to failure of TP or whether the need for TP in this cohort was a surrogate of more refractory disease. Future trials including patients with PD leak/disruption randomized to TM versus CD are needed to further define the significance of PD leak/disruption and mode of endoscopic drainage. Second, although the decision to proceed with TP was per the endoscopist’s discretion and in some cases performed routinely in the management of pseudocysts; other potential reasons were not captured in this study. Furthermore, in aggregate, the rates of symptom and radiologic resolution (60.3%-72.4%) of pseudocysts after endoscopic drainage in this study appear to be lower than those reported in the literature, which range from 75% to 100% [18-26]. This discrepancy in outcomes can be in part accounted by the heterogeneous criteria used in defining treatment success, varied procedural techniques used, diverse patient populations and timing of the interventions among the prior studies, as well as our own use of very stringent
criteria for ST and LT follow-up and definitions of success. Overall, the results of this large multicenter study may be more generalizable than from those reported in prior single center studies. Another limitation to our study is that most cases of TM involved the use of plastic stents whereas there has been a recent shift toward the use of metal stents, including the lumen-apposing type [22]. In spite of this difference, there are no prospective comparative studies to date showing differences between metal and plastic stents for pseudocyst drainage. Another major limitation is that a significant portion of patients were lost to follow-up and thus the potential for selection bias. Most of the participating institutions in this study are tertiary referral centers and thus a large proportion of patients included in this study were lost to follow-up upon completion of the intervention. Last, although this represents the largest multicenter series on EUS-guided pseudocyst drainage, small sample size on subgroup analysis could have precluded the detection of any meaningful differences in outcomes. Hence, the lack of statistically significant difference may not necessarily exclude the possibility of clinically relevant differences.

In summary, this study demonstrated that TP may have no added benefit on treatment outcomes in patients undergoing EUS-guided TM of pancreatic pseudocysts. TP was technically unsuccessful in more than half of the patients who underwent CD and was negatively associated with pseudocyst resolution on follow-up. However, the lack of a statistically significant difference in outcomes between TM and CD does not immediately exclude potential clinically significant differences. As such, future larger, randomized controlled trials evaluating the role of bridging PD stent placement in patients with PD disruption/leak undergoing transmural pancreatic pseudocyst drainage are needed to corroborate these findings.
REFERENCES


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Table 1. Patient characteristics of patients with pseudocysts undergoing endoscopic drainage

<table>
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<th>TM (n=95)</th>
<th>CD (n=79)</th>
<th>P value</th>
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<tr>
<td>Age, mean (SD), years</td>
<td>52.7 (15.7)</td>
<td>50.9 (14.6)</td>
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<td>Males; n(%)</td>
<td>65 (68.4)</td>
<td>49 (62)</td>
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<td>Etiology of Pancreatitis</td>
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<td>Alcohol; n(%)</td>
<td>29 (30.5)</td>
<td>32 (40.5)</td>
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<td>Gallstones; n(%)</td>
<td>22 (23.2)</td>
<td>17 (21.5)</td>
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<td>Idiopathic; n(%)</td>
<td>24 (25.3)</td>
<td>19 (24.1)</td>
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<td>Other; n(%)</td>
<td>19 (21)</td>
<td>11 (13.9)</td>
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<td>Presence of underlying chronic pancreatitis, n(%)</td>
<td>47 (49.5)</td>
<td>32 (40.5)</td>
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<tr>
<td>Size of drained PFC (cm); median (IQR)</td>
<td>9.0 (7.3-12.3)</td>
<td>9.5 (7.1-12.2)</td>
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<td>PFC location</td>
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<tr>
<td>Head; n(%)</td>
<td>22 (23.2)</td>
<td>22 (27.8)</td>
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<td>Body; n(%)</td>
<td>57 (60)</td>
<td>48 (60.8)</td>
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<td>Tail; n(%)</td>
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<td>Pain; n(%)</td>
<td>86 (90.5)</td>
<td>68 (86.1)</td>
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<td>Gastric outlet obstruction; n(%)</td>
<td>19 (20)</td>
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<td>Infection; n(%)</td>
<td>8 (8.4)</td>
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Table 2. EUS-guided transmural drainage technique

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<td><strong>Type of EUS needle</strong></td>
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<td>19-gauge; n(%)</td>
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<td>Trans-gastric; n(%)</td>
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<td>Trans-duodenal; n(%)</td>
<td>6 (6.3)</td>
<td>5 (6.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Unspecified; n(%)</td>
<td>5 (5.3)</td>
<td>4 (5)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Dilation of transmural tract</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical dilation (Balloon/Bougie); n(%)</td>
<td>75 (78.9)</td>
<td>64 (81)</td>
<td>0.85</td>
</tr>
<tr>
<td>Electrocautery (needle knife/cystotome); n(%)</td>
<td>20 (21.1)</td>
<td>15 (19)</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Type of transmural stent(s)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plastic; n(%)</td>
<td>77 (81.1)</td>
<td>63 (79.7)</td>
<td>0.69</td>
</tr>
<tr>
<td>Metal; n(%)</td>
<td>11 (11.6)</td>
<td>16 (20.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Lumen-apposing metal stent; n(%)</td>
<td>3 (3.2)</td>
<td>0 (0)</td>
<td>0.25</td>
</tr>
<tr>
<td>Unspecified; n(%)</td>
<td>4 (4.1)</td>
<td>0 (0)</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Duration of transmural stent(s); median (IQR) days</strong></td>
<td>96 (52-123)</td>
<td>95 (49-158)</td>
<td>0.25</td>
</tr>
<tr>
<td>Nasocystic drain; n(%)</td>
<td>5 (5.3)</td>
<td>0 (0)</td>
<td>0.06</td>
</tr>
</tbody>
</table>
Table 3. Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>TM drainage</th>
<th>CD drainage</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>5 (5.3)</td>
<td>2 (2.5)</td>
<td>0.46</td>
</tr>
<tr>
<td>Perforation</td>
<td>2 (2.1)</td>
<td>3 (3.8)</td>
<td>0.66</td>
</tr>
<tr>
<td>Infection</td>
<td>4 (4.2)</td>
<td>2 (2.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>Post-ERCP pancreatitis</td>
<td>NA</td>
<td>2 (2.5)</td>
<td></td>
</tr>
<tr>
<td>Cardiopulmonary</td>
<td>1 (1.1)</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Death</td>
<td>1 (1.1)</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.1)</td>
<td>2 (2.5)</td>
<td>0.59</td>
</tr>
<tr>
<td>Overall</td>
<td>14/95 (14.7)</td>
<td>11/79 (13.9)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Table 4. Clinical predictors of long-term (LT) radiologic resolution of PFC

<table>
<thead>
<tr>
<th>Clinical Variable</th>
<th>Univariate analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.03 (0.99-1.08)</td>
<td>1.04 (0.99-1.10)</td>
</tr>
<tr>
<td>Sex (male vs female)</td>
<td>0.31 (0.06-1.59)</td>
<td>0.31 (0.05-2.18)</td>
</tr>
<tr>
<td>Etiology of pancreatitis (other vs ETOH)</td>
<td>0.33 (0.07-1.53)</td>
<td>0.19 (0.03-1.16)</td>
</tr>
<tr>
<td>Gallstone</td>
<td>2.75 (0.45-16.9)</td>
<td>2.05 (0.26-16.4)</td>
</tr>
<tr>
<td>Chronic pancreatitis (yes vs no)</td>
<td>1.88 (0.48-6.9)</td>
<td></td>
</tr>
<tr>
<td>Indication for PF drainage (present vs absent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>0.43 (0.05-3.84)</td>
<td></td>
</tr>
<tr>
<td>Gastric outlet obstruction</td>
<td>1.34 (0.14-12.7)</td>
<td></td>
</tr>
<tr>
<td>Biliary obstruction</td>
<td>0.5 (0.04-6.02)</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>0.9 (0.16-5.0)</td>
<td></td>
</tr>
<tr>
<td>Type of Index Imaging (other vs CT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRCP</td>
<td>0.86 (0.15-4.92)</td>
<td></td>
</tr>
<tr>
<td>Size of PFC</td>
<td>1.00 (0.99-1.02)</td>
<td></td>
</tr>
<tr>
<td>Location of PFC (Body/tail vs Head)</td>
<td>0.77 (0.14-4.2)</td>
<td></td>
</tr>
<tr>
<td>PD leak/disruption (yes vs no)</td>
<td>1.97 (0.22-17.8)</td>
<td></td>
</tr>
<tr>
<td>TP attempted (yes vs no)</td>
<td>0.22 (0.04-1.11)</td>
<td>0.11 (0.02-0.8)</td>
</tr>
</tbody>
</table>

OR (95% CI)                  P value  OR (95% CI)                  P value

0.12                        0.14                0.06
0.16                        0.14                0.07
0.06                        0.07                0.50
0.37                        
0.45                        
0.80                        
0.59                        
0.90                        
0.86                        
0.43                        
0.76                        
0.54                        
0.03
Figure 1. Endoscopic view of transmural drainage alone via the stomach (1A) and of a combined transpapillary and transmural approach (1B).

Figure 2. Flow diagram of patients who underwent endoscopic retrograde pancreatography (ERP) in addition to EUS-guided transmural pancreatic pseudocyst drainage. PD=pancreatic duct.

Figure 3. Technical success of transmural (TM), transpapillary (TP) and combined (CD) drainage.

Figure 4. Treatment outcomes (symptomatic and radiologic resolution) and follow-up. TM=transmural drainage; CD=combined drainage; IQR=interquartile range.
ERP Attempted (n=79)

Successful Pancreatogram (n=66)

Findings on Pancreatogram n(%) 
- Normal: 6 (9)
- PD leak/disruption: 47 (71.2)
- PD stricture: 21 (31.8)
- PD stones: 7 (10.8)

Failed Pancreatogram (n=13)

Failed PD cannulation (n=8; 61.4%)
Unable to reach/identify papilla (n=2; 15.4%)
Unspecified (n=3; 23.2%)

Type of ERP intervention n(%) 
- PD sphincterotomy: 39 (65)
- PD stent: 50 (83.3)
- PD sphincteroplasty: 14 (23.3)
- Stone extraction: 4 (6.7)

PD stent traversed PD leak/disruption (n=17; 36.2%)
95 pseudocysts
TM

79 pseudocysts
CD

Median Short-Term Follow-Up
52 (IQR 36-86) days

Symptomatic
Resolution
42.58 (72.4\%)

Radiologic Resolution
48.72 (66.7\%)

Symptomatic
Resolution
47.70 (67.1\%)

Radiologic Resolution
41.68 (60.3\%)

Median Long-Term Follow-Up
324 (IQR 224-493) days

Symptomatic
Resolution
20.29 (69\%)

Radiologic Resolution
22.31 (71\%)

Symptomatic
Resolution
24.39 (61.5\%)

Radiologic Resolution
24.36 (66.7\%)
Acronyms

Transpapillary drainage = TP
Transmural drainage = TM
Pancreatic fluid collections = PFC
Combined drainage = CD
Endoscopic ultrasound = EUS
Short-term follow-up = ST follow-up
Long-term follow-up = LT follow-up
IQR = interquartile range
Pancreatic duct = PD
Endoscopic retrograde pancreatography = ERP
Acute peripancreatic fluid collection = APFC
Acute necrotic collection = ANC
Walled-off necrosis = WON
American Society of Gastrointestinal Endoscopy = ASGE
Standard deviation = SD
Alcohol = ETOH