Role of EUS in drainage of peripancreatic fluid collections not amenable for endoscopic transmural drainage

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Background: Increasingly, peripancreatic fluid collections (PFCs) are managed endoscopically with conventional transmural drainage (CTD). The role of interventional EUS in drainage of PFCs requires further clarification, because the procedure is technically challenging, with limited availability.

Objective: Identify characteristics that determine the need for drainage of PFC by CTD versus EUS.

Patients: Consecutive patients with symptomatic PFCs (types: pseudocyst, abscess, and necrosis) referred for endoscopic drainage.

Study Design: Prospective study.

Setting: Tertiary-referral center.

Methods: After ERCP, transmural drainage was attempted by CTD. If unsuccessful, drainage by EUS was then attempted. Findings on contrast-enhanced CT and endoscopy were collected to identify characteristics that predict the need for CTD versus EUS drainage.

Main Outcome Measurements: Identify characteristics to determine whether CTD or EUS is best suited for drainage of a particular PFC. Technical outcomes and safety of both techniques were also compared.

Results: Of 53 patients with PFCs, CTD was technically successful in 30 (57%) and failed in 23 (43%). PFC regional location was the pancreatic head in 16, the body in 20, and the tail in 17; in these locations, CTD was successful in 13 (81%), 17 (85%), and 0, respectively. The causes of failed CTD were absence of luminal compression (LC) in 20, difficulty with scope positioning in 2, and bleeding with attempted drainage (portal hypertension) in 1. One PFC drained by CTD was later diagnosed as necrotic sarcoma. Of the 23 patients who failed CTD and underwent EUS, an alternate diagnosis of mucinous neoplasm was made in 2 patients, and EUS-guided drainage was successful in the other 21 patients (100%). Although CTD failed in all PFCs in the tail, all were successfully drained by EUS. In the pancreatic-head region, only those PFCs superior to pancreas and extending into porta hepatis (n = 3) required drainage by EUS. In the pancreatic body, only PFCs that developed bleeding from a transmural puncture or without definitive LC because of gastric mural edema (albumin < 1.5 mg/dL, n = 2) required EUS drainage. When compared with PFCs at other locations, those in the tail were best accessed by EUS ($P < .001$). Patients with luminal compression at CT were significantly more likely to undergo successful drainage by CTD (adjusted odds ratio [OR] 13.6; $P = .02$). When compared with CTD, EUS drainages were longer in duration (40 versus 75 minutes; $P < .001$), with similar rates of PFCs resolution (90% versus 95%). Although bleeding occurred in 1 patient in the CTD group, no complications were encountered in patients who underwent EUS-guided drainage. PFCs located at the tail of the pancreas were more likely to require drainage by EUS than CTD (adjusted OR 22.9, $P = .003$) when adjusted for the presence of luminal compression at CT, size of the PFC, serum albumin, and etiology of pancreatitis.

Limitations: Nonrandomized study.

Conclusions: Because a majority of PFCs can be drained by CTD in a shorter duration, with comparable outcomes, EUS-guided drainage should be reserved mainly for PFCs located at the pancreatic tail, because these are unlikely to cause luminal compression or are technically difficult to access. Also, all pseudocyst-type PFCs must be evaluated by EUS before any attempts at endoscopic drainage, because EUS identifies an alternate diagnosis in 5% of such patients. (Gastrointest Endosc 2007;66:1107-19.)

Abbreviations: CEA, carcinoembryonic antigen; CTD, conventional transmural drainage; DPEJ, direct percutaneous endoscopic jejunostomy; LC, luminal compression; OR, odds ratio; PFC, peripancreatic fluid collection.

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Endoscopic transmural drainage is a minimally invasive alternative to surgery for drainage of peripancreatic fluid collections (PFCs). Since the first reports by Sahel et al[1] and Cremer et al,[2] conventional transmural drainage (CTD) at endoscopy has become an established technique for the management of PFCs.[3-5] This procedure entails the creation of a fistulous tract between the PFCs and the

gastric lumen (cyst-gastrostomy) or the duodenal lumen (cyst-duodenostomy). After establishing access to the PFC, a nasocystic catheter or a stent is placed into the collection to facilitate drainage. The obvious limitation of this technique is its relatively "blind" approach. The risk of perforation is particularly high when endoscopically visible luminal compression (LC) is absent.[6-8] Another major complication is hemorrhage, which is encountered in approximately 6% of cases.[1,2,4,6-8] The ideal approach for PFC drainage would be to combine endoscopy with real-time visualization of the drainage procedure by using EUS. Several investigators described the use of EUS for guidance of transmural puncture and performing drainage.[9-13] By using this technique, puncture of PFC under direct sonographic visualization is possible in patients without LC and in those at high risk for bleeding, eg, those with portal hypertension.[13-15] This approach appears to improve both the safety of the procedure and the number of candidates amenable for PFC drainage.[13,14] However, EUS drainage of PFCs is technically challenging, time consuming, and requires expertise in advanced techniques.[16,17] Also, dedicated accessories for EUS drainage of PFCs are not uniformly available worldwide,[10,12] and the technology is still limited by its availability.[17-19] This prospective study was undertaken to identify characteristics that best predict the need for drainage of a PFC by CTD versus EUS. Also, the technical outcomes and the safety of both techniques were compared.

Capsule Summary

What is already known on this topic

- Ideal peripancreatic fluid collection (PFC) drainage would combine endoscopy with real-time visualization by using EUS.
- EUS-assisted drainage is technically challenging, time consuming, and requires expertise.

What this study adds to our knowledge

- Of 53 patients with PFC, conventional transmural drainage (CTD) failed in 23 (43%), who then underwent EUS, resulting in an alternate diagnosis of mucinous neoplasm in 2 patients and successful EUS-guided drainage in the other 21 patients.
- PFCs located at the tail of the pancreas were more likely to require drainage by EUS than CTD.

PATIENTS AND METHODS

Patients

Between July 2004 and June 2006, consecutive patients with a history of pancreatitis and symptomatic PFC were enrolled in this prospective study to identify characteristics that determine the need for transmural drainage of a PFC by using CTD versus EUS. Patients were excluded if CT findings were suggestive of pathology other than the PFC, if the PFC was less than 4 cm in size (even if measured at the time of EUS) or less than 6 weeks of age, if the PFC was located >1.5 cm from the EUS transducer, or if patients were less than 18 years of age. The study was approved by the institutional review board of the University of Alabama at Birmingham Medical Center. All patients provided written informed consent.

Protocol for PFC drainage

All patients underwent a contrast-enhanced CT at our institution before undergoing PFC drainage. However, contrast-enhanced CT performed within 1 week at an outside institution was considered acceptable if diagnostic in quality. All patients underwent ERCP while in the prone position; a therapeutic duodenoscope (TJF-160; Olympus America Corp, Melville, NY) was used. If a pancreatic leak was noted, every attempt was made to bridge the leak by transpapillary pancreatic stent placement. After ERCP, a search for an LC in the duodenum and the stomach was undertaken by using the duodenoscope. If no definitive LC was identified, then the duodenoscope was exchanged for a double-channel gastroscope (GIF 2T; Olympus), and a search for LC was attempted with the patient in the left lateral position. If LC was identified, then CTD was undertaken. In patients with LC, at least 5 attempts were made to puncture the gastric or the duodenal wall by using a needle-knife catheter to access the PFC. If all attempts failed or if bleeding was encountered or if no LC was identified at endoscopy, then the procedure was terminated and the patient underwent PFC drainage via EUS in the same endoscopic session (GF-UCT 140; Olympus).

Endoscopic findings were documented in detail: the site of LC, the site from where the PFC was accessed, EUS characteristics of the PFC, the reason for failure to drain by either modality (CTD versus EUS), and procedural complications. Intravenous ciprofloxacin (400 mg) was administered before the procedure and continued for 48 hours or until the time of discharge. Outpatients were prescribed twice-a-day oral ciprofloxacin (500 mg) to be started the night before the procedure and continued for 5 days after PFC drainage.

After PFC drainage, a radiologist trained in abdominal imaging and blinded to the procedural details reviewed preprocedure CT images and provided data on PFC location (head, body, tail, extension to other areas), size, type (pseudocyst, abscess, or necrosis), and presence or absence of LC.

Procedural technique

ERCP was routinely attempted before drainage of PFC in all patients. In patients with gallstone pancreatitis, biliary sphincterotomy was undertaken for extraction of common bile duct stones. A pancreatogram was attempted to define the communication between the duct and the PFC. In cases where the pancreatic duct was completely

disrupted and the proximal duct was accessible with a guidewire or in patients with a ductal stricture, a transpapillary bridging stent was placed by using a previously described technique.[20] ERCP was not undertaken in those patients in whom the extrinsic compression precluded scope passage to the second portion of the duodenum.

All CTDs were performed by using a triple-lumen needle knife (Microknife XL; Microvasive Endoscopy, Boston Scientific Corp, Natick, Mass) to create a cyst-enterostomy fistula. After access to the PFC, dilation of the fistula was performed by using an 8-mm biliary balloon dilator (Eliminator; CONMED Industries, Billerica, Mass). After dilation, in patients with pseudocysts, two 10F double-pigtail endoprostheses were placed (Fig. 1A-C). In patients with pancreatic abscess or necrosis, a 10F nasocystic catheter was placed in addition to the stents to facilitate periodic flushing. The catheters were flushed with 100 mL normal saline solution and aspirated vigorously every 4 hours. Patients were placed both in the right and left lateral decubitus positions at the time of flushing to ensure thorough evacuation of the PFC. Also, in patients with a pancreatic abscess or necrosis, a repeat CT study was obtained at 72 hours to assess response. If there was a decrease in size of the PFC, then the catheter was removed at the time of patient discharge from the hospital. If symptoms persisted without any decrease in size of the PFC on follow-up CT, repeat endotherapy was undertaken for dilation of the tract and placement of more stents.

All EUS-guided drainages were performed by using a 19-gauge needle (EUSN-19-T; Cook Endoscopy, Winston-Salem, NC) that was introduced into the PFC. Before puncture, the cyst morphology was evaluated by EUS, and color Doppler US was used to identify regional vessels. A 0.035-inch guidewire (X-wire; CONMED Industries, Billerica, Mass) was then introduced through the needle and coiled within the PFC under fluoroscopic guidance. The tract was sequentially dilated by first passing a 5F ERCP cannula and then a 10F ERCP inner guiding catheter over the guidewire. After this, dilation of the tract was performed by using an 8-mm biliary balloon dilator, and stent placement with or without nasocystic catheter placement was undertaken as described above (Fig. 2A-D). A needle knife was not used to puncture the PFC in any patient undergoing EUS-guided drainage.

All patients with pancreatic necrosis, pancreatic abscess, and pancreatic pseudocyst in the setting of smoldering pancreatitis[21] underwent placement of direct percutaneous endoscopic jejunostomy (DPEJ) feeding tubes by using a previously described technique[22] or underwent placement of percutaneous gastrojejunostomy feeding tube by interventional radiologists. The rationale was to provide symptomatic relief via strict pancreatic rest in these patients. All outpatients were admitted for overnight observation after PFC drainage.

All CTD and ERCP were undertaken by 2 pancreaticobiliary endoscopists (S.V., C.M.W.), each of whom perform

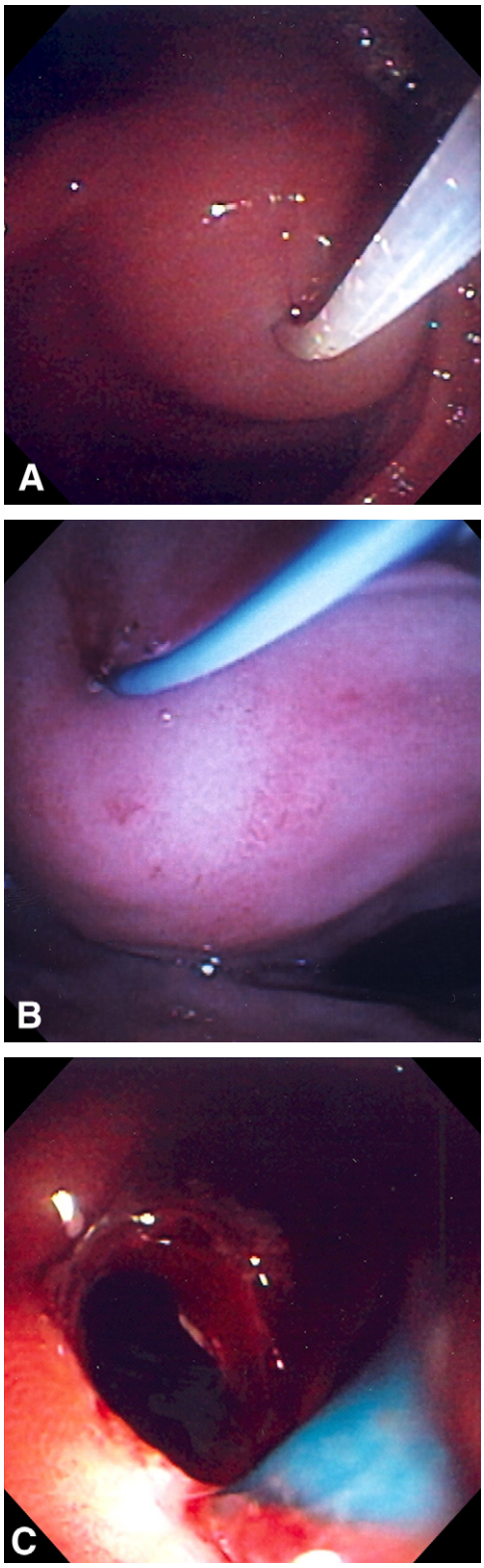

Figure 1. A, A PFC causing LC at the gastric antrum accessed by using a needle-knife catheter at CTD. **B,** The needle-knife catheter is exchanged for a 0.035-inch guidewire that is coiled within the PFC. **C,** Wide opening seen after dilation of the cyst-enterostomy tract by using an 8-mm through-the-scope biliary balloon dilator.

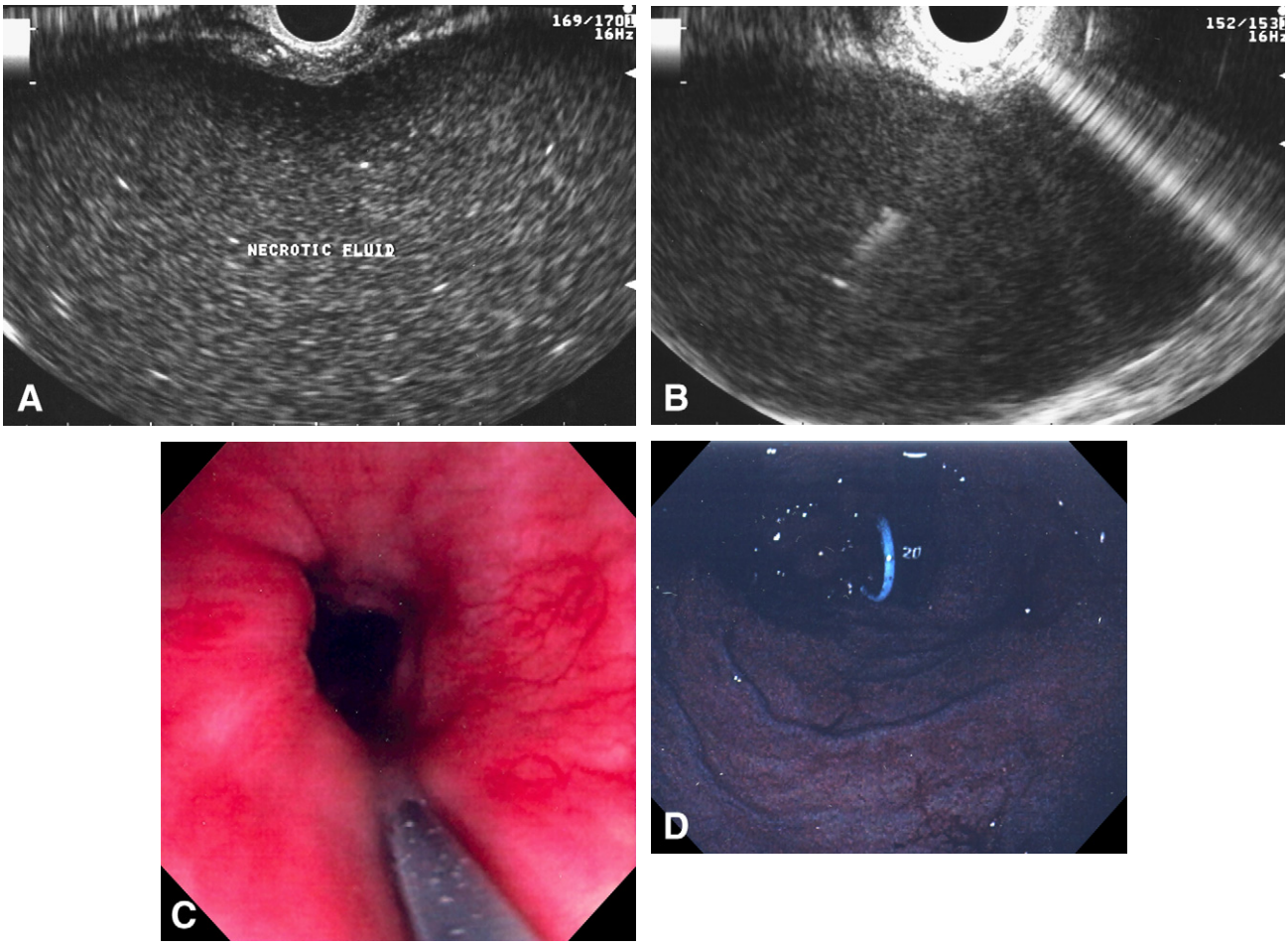

Figure 2. A, A PFC (105 × 88 mm) arising from the pancreatic tail as seen by using a linear echoendoscope. **B,** A PFC accessed under EUS guidance (via the gastric cardia) by using a 19-gauge FNA needle. **C,** After passage of a 0.035-inch guidewire, the cystenterostomy tract is dilated by using a 10F ERCP inner guiding catheter. **D,** After dilation of the cystenterostomy tract, a 10F double-pigtail plastic stent was deployed as seen on endoscopic retroflexion.

more than 400 ERCP procedures annually. All EUS-guided drainages were undertaken by 1 endosonographer (S.V.), who performs more than 450 EUS procedures annually; 25 EUS-guided drainages were undertaken by the endosonographer before the commencement of this study to achieve procedural expertise.

Definitions

PFC was categorized according to the Atlanta Classification,[23] based on CT imaging reviewed by a radiologist. Patients with a PFC localized near the head or the uncinate region of the pancreas was classified ''head.'' A PFC localized adjacent to the body of the pancreas or extending to the body-tail junction (from body of the pancreas) was classified ''body.'' A PFC localized to the tail of the pancreas or extending to the body-tail junction (from tail of the pancreas) was classified ''tail.''

Technical success was defined as the ability to access and drain a PFC by placement of transmural drain and/or stents. Treatment success was defined as complete resolution or a decrease in size of the PFC to $\leq$2 cm on CT in association with clinical resolution of symptoms. Treatment failure was defined as the persistence or worsening of symptoms in association with a PFC that had increased in size or that remained $>$2 cm in size on follow-up CT imaging performed at 6 weeks in all patients.

Bleeding was defined as any hemorrhagic event occurring at endoscopy that required endotherapy, blood product transfusion, or inpatient observation. Infection was defined as any septic event after the initial endoscopic drainage caused by contamination of the PFC, proven by new-onset fever, positive blood cultures, or by fluid cultures obtained at endoscopic revision. Perforation was diagnosed when pneumoperitoneum was evident on imaging studies in association with peritoneal signs. Stent migration was defined as the need to retrieve a stent from within the PFC or enteral lumen.

Follow-up

All patients were evaluated with contrast-enhanced CT and outpatient clinic visits at 6 to 8 weeks after PFC drainage. In patients with treatment success, the transpapillary

pancreatic stent, cyst-enterostomy stent, and the jejunostomy feeding tube were removed. Those with a partial decrease in size of PFC underwent replacement of transmural stents and were reevaluated after 1 month with repeat contrast-enhanced CT; if the PFC had resolved, then they were managed similarly to patients in whom treatment was successful. Those with treatment failure underwent repeat endotherapy or were referred for surgery. All patients were contacted at 6 months, by a telephone call, to obtain midterm follow-up. They were queried specifically with regard to pancreaticobiliary complaints, the need for subsequent hospitalization, CT, or other intervention.

Outcome measures

Characteristics that determine the need for drainage of a PFC by using CTD versus EUS were identified. Also, rates of technical and treatment success, complications, and reinterventions between procedural modalities were compared.

Statistical analysis

Continuous variables were reported by using means (and standard deviations) or medians (and interquartile range) with range. Means were compared by using the unpaired *t* test and medians by the Wilcoxon rank sum test (a nonparametric test for unpaired data). Categorical variables were reported by using frequencies (and percentages) compared by using the Fisher exact test. A definitive examination of factors was performed by multivariable logistic regression analysis, whereby the independent effect of each potential factor could be gauged over and above the contributions of each of the other factors. Each potential factor was evaluated by its odds ratio (OR) and the 95% CI for the OR. It is recognized that there was multiple testing of outcome data arising from individual patients; however, the definitive *P* values are those from the multivariable logistic regression analysis. Other statistical tests were taken as exploratory. Their uncorrected *P* values are presented for descriptive purposes. To calculate a priori sample size, we assumed that CTD would have 50% success in accessing a PFC, whereas EUS will have 95% success. With alpha = 0.05 (type I error) and 80% power, the sample size required to detect a statistically significant difference between procedures for accessing PFC was 18 for each group. A P value $<.05$ (2 tailed) was considered statistically significant. Analysis was conducted by using SAS statistical software (version 9.0; SAS Institute Inc, Cary, NC).

RESULTS

A total of 63 patients were recruited for participation in the study. Ten were excluded, because CTs performed at our institution revealed an alternate diagnosis in 2, and the PFC was less than 4 cm in 6 patients. Two other patients were excluded at the time of EUS, because the PFC size in the largest axis was less than 40 mm. A CT performed in both patients 5 days before EUS revealed a size (largest axis) of 60 mm and 55 mm, respectively.

The symptoms that indicated a requirement for drainage in the 53 patients were abdominal pain (n = 43), gastric outlet obstruction (n = 5), fever (n = 3), and biliary obstruction (n = 2). CTD was technically successful in 30 of 53 patients (57%). All patients who failed CTD (n = 23) underwent EUS. Patient demographics, clinical presentation, and laboratory data are shown in Table 1. Although there was no difference in the type of PFC drained by both modalities, the PFC drained by CTD was larger in size than those drained under EUS guidance ($P = .02$) (Table 2). The PFC location was the head of the pancreas in 16 patients, the body in 20, and the tail in 17. Drainage by CTD was successful in 13 (81%), 17 (85%), and 0, respectively. Of 23 patients who failed drainage by CTD and who underwent EUS, an alternate diagnosis of mucinous neoplasm was made in 2 patients, and EUS-guided drainage was successful in the other 21 patients (100%). When compared with PFC at other locations, those in the tail were best accessed by EUS ($P < .001$).

Head PFC

Thirteen of 16 PFCs (81%) arising from the pancreatic head had LC at endoscopy and were drained successfully by CTD. The mean size of the PFC (largest axis) in the 13 patients was 118.3 mm (range 70–186 mm). No LC was evident in 3 patients. At CT, the PFC was located superior to the pancreas and extended into the porta hepatis in these 3 patients, with a mean size of 129.3 mm (range 88-180 mm). All 3 PFCs at the porta hepatis were drained under EUS guidance via the gastroesophageal junction in 2 and via the gastric cardia in 1 (Fig. 3A-C) (Table 3).

Body PFC

Seventeen of 20 PFCs (85%) in the body of the pancreas were successfully drained by CTD. The mean size of the 17 PFCs (largest axis) was 114.6 mm (range 55-150 mm). Although LC was evident at endoscopy in 20 cases, only 17 could be drained successfully by CTD. Bleeding was encountered after transmural puncture in 1 patient, and the procedure was terminated (size 160 × 140 mm); this patient was found to have gastric varices at EUS and underwent successful drainage under EUS guidance via the gastric fundus. In the other 2 patients (PFC size 130 × 110 mm and 120 × 116 mm, respectively), the LC was indistinct because of mucosal edema. One patient with pancreatic necrosis had a serum albumin of 1.4 mg/dL (reference range 3.4–5.0 mg/dL), and the other with a pancreatic abscess had a serum albumin of 1.6 mg/dL. Despite 5 attempts at puncture, the PFC could not be accessed in either patient. Subsequently,

TABLE 1. Demographic characteristics, clinical presentation, and laboratory investigations of patients with PFC undergoing endotherapy

	Drainage modality			
Variables	**CTD, N (%) (N = 30)**	**EUS, N (%) (N = 23)**	***P****	**Total, N (%) (N = 53)**
Age (y)				
Mean (SD)	52.6 (12.2)	53.7 (16.8)	.79†	53.0 (14.2)
Median (IQR)	49.5 (41–63)	55 (39–71)		51 (41–64)
Range (min, max)	35–80	24–79		24–80
Sex			1.00‡	
Women	11 (36.7)	8 (34.8)		19 (35.8)
Men	19 (63.3)	15 (65.2)		34 (64.2)
Etiology			.01‡	
Idiopathic/SP surgery	5 (16.7)	12 (52.2)		17 (32.1)
Alcohol	13 (43.3)	5 (21.7)		18 (34.0)
Gall stones	8 (26.7)	5 (21.7)		13 (24.5)
Hypertriglyceridemia	4 (13.3)	1 (4.4)		5 (9.4)
Duration of episode (wk)				
Mean (SD)	11.3 (7.2)	12.5 (13.6)		11.8 (10.3)
Median (IQR)	8.5 (6–15)	9 (4–16)	.71§	9 (5–15)
Range (min, max)	4–32	3–68		3–68
WBC count (mm^3)				
Mean (SD)	12.4 (5.1)	11.5 (4.2)	.48†	12.0 (4.7)
Median (IQR)	12.6 (8.3–15.6)	11.9 (7.2–14.2)		12.4 (7.5–14.8)
Range (min, max)	3.8–26.7	4.9–21.8		3.8–26.7
Serum albumin (g/dL)				
Mean (SD)	2.9 (0.6)	2.7 (0.9)	.43†	2.8 (0.8)
Median (IQR)	2.9 (2.5–3.4)	2.6 (1.9–3.6)		2.9 (2.1–3.4)
Range (min, max)	1.8–3.8	1.2–4.2		1.2–4.2

SD, Standard deviation; *IQR*, interquartile range; *min*, minimum; *max*, maximum; *SP*, status-post; *WBC*, white blood cell.
*Two-tailed *P* value.
†Student unpaired *t* test.
‡Fisher exact test; *P* value calculated by comparing idiopathic/SP surgery vs other categories.
§Wilcoxon rank sum test.

both underwent drainage with EUS guidance via the greater curvature and the antrum, respectively.

Tail PFC

Of the 17 PFCs in the tail region, 13 were confined to the tail of the pancreas and 4 extended proximally up to the body-tail junction region. The mean PFC size was 92.4 mm (range 53-180 mm). Two of 4 patients in whom the PFC extended to the body-tail junction had LC at the fundus of the stomach; however, transmural puncture at CTD was unsuccessful, despite 5 attempts. In both patients, the endoscope could not be positioned appropriately, because the orientation was very oblique to the gastric lumen at the fundus. In 15 others, no LC was evident. Thus, CTD failed in all 17 patients. Fifteen PFCs were drained successfully under EUS guidance. The access site for EUS drainage in the 15 patients was either the gastric cardia (n = 8) or the fundus (n = 7). Two were not drained because an alternate diagnosis of mucinous neoplasm was established at EUS. In one, the aspirate was mucoid and carcinoembryonic antigen (CEA) level was greater than 480 ng/mL, consistent with a mucinous cystic neoplasm. This patient was not a surgical candidate and was managed conservatively. In another

TABLE 2. Characteristics of the PFCs

Variables	Drainage modality			
	CTD, N (%) (N = 30)	EUS, N (%) (N = 23)	P*	Total, N (%) (N = 53)
CT imaging			.78†	
Pseudocyst	20 (66.7)	14 (60.9)		34 (64.1)
Acute pancreatitis	10 (50.0)	12 (85.7)		22 (64.7)
Chronic pancreatitis	10 (50.0)	2 (14.3)		12 (35.3)
Necrosis	6 (20.0)	3 (13.0)		9 (17.0)
Abscess	4 (13.3)	6 (26.1)		10 (18.9)
Long axis (mm)				
Mean (SD)	120.6 (23.6)	99.5 (37.1)	.02‡	111.4 (31.7)
Median (IQR)	119 (110–138)	88 (70–130)		115 (88–133)
Range (min, max)	80–186	53–180		53–186
Short axis (mm)				
Mean (SD)	90.9 (19.2)	77.3 (24.8)	.04‡	85.0 (22.6)
Median (IQR)	92.5 (80–100)	68 (59–100)		84 (66–100)
Range (min, max)	48–132	42–120		42–132
PFC location			<.001†	
Head collection	13 (43.3)	3 (13.0)		16 (30.2)
Body collection	17 (56.7)	3 (13.0)		20 (37.7)
Tail collection	—	17 (73.9)		17 (32.1)
LC at CT				
Yes	29 (96.7)	7 (30.4)	<.001†	36 (67.9)
No	1 (3.3)	16 (69.6)		17 (32.1)

SD, Standard deviation; *IQR*, interquartile range; *min*, minimum; *max*, maximum.
*Two-tailed *P* value.
†Fisher exact test; categories "necrosis" and "abscess" combined to calculate *P* value.
‡Student unpaired *t* test.

patient, 2 cysts were seen in the tail of the pancreas and both were aspirated. Aspirate from the proximal cyst was clear, but wall thickening and a small mural nodule was seen within the cyst; the CEA level from the aspirate was 1598 ng/mL with an amylase of 41 U/L. The distal cyst had a clear aspirate as well; the CEA level was 14 ng/mL and amylase was 46,786 U/L. EUS-guided drainage was not attempted, given the cyst morphology in this patient. It was felt that the distal cyst resulted from a consequence of reactive pancreatitis induced by the proximal mucinous cyst neoplasm. This was confirmed at surgical histopathology.

Procedural data

Fourteen of 30 PFCs managed by CTD were drained via the duodenum; others were drained via the transgastric route. All PFCs drained by EUS were accessed via the transgastric or transesophageal route. There was no significant difference in outcomes between the transgastric, transduodenal, or transesophageal drainage routes. Only stents were placed for transmural drainage in 33 patients, and 18 underwent placement of both stents and nasocystic drainage catheters (Table 3). Before transmural drainage, a bridging stent was placed in the main pancreatic duct in 17 patients (31%), and a jejunostomy feeding tube was placed for enteral nutrition in 36 patients (65%). In 8 patients, ERCP was not undertaken, because the luminal compression caused by PFC precluded scope passage to the second portion of the duodenum. In others, pancreatic-stent placement was not undertaken as the local inflammation precluded identification of the ampulla (8) or because of the presence of complete distal pancreatic-duct disruption (20). Enteral nutrition was initiated for all patients with pancreatic abscess (10), necrosis (9),

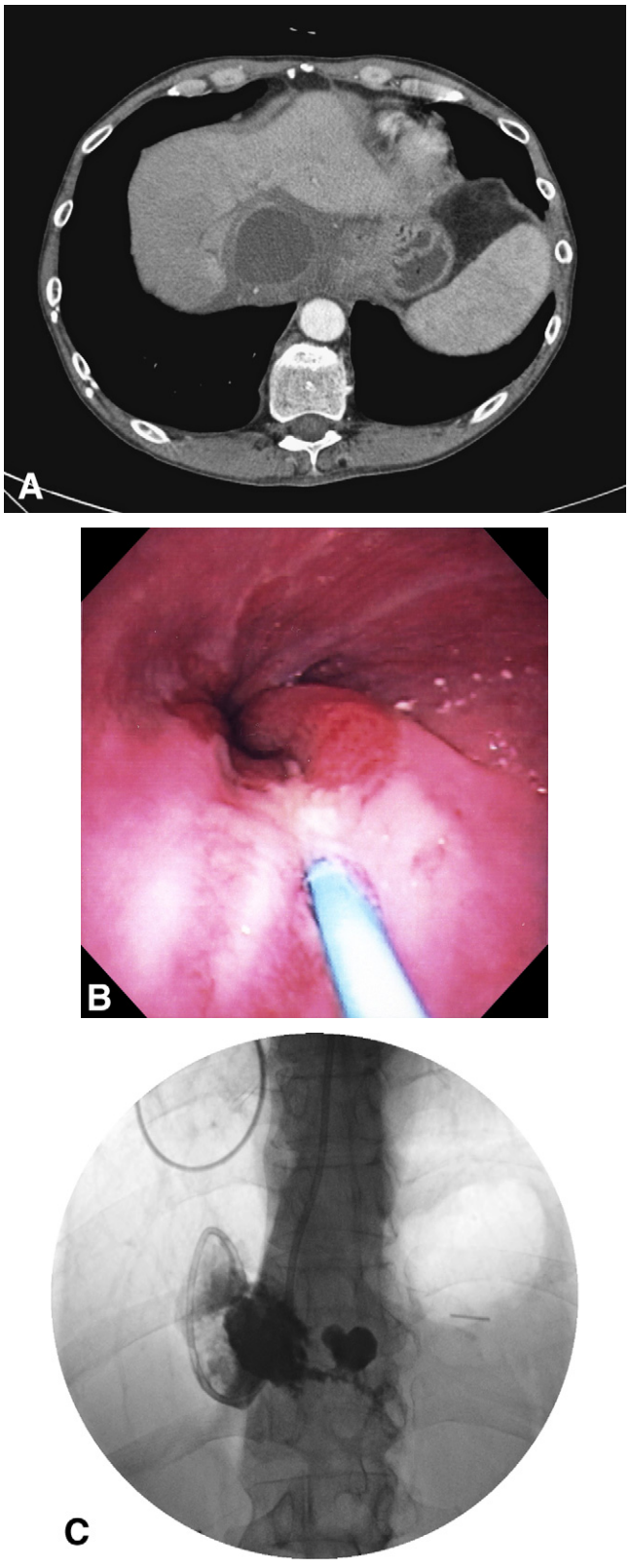

Figure 3. A, CT image, revealing a PFC extending superiorly from the porta hepatis. **B,** Placement of a nasocystic drainage catheter within the PFC under EUS guidance via the gastroesophageal junction. **C,** Injection of contrast through the drainage catheter reveals the PFC and its communication with the main pancreatic duct.

and smoldering pancreatitis (17). DPEJ was placed by endoscopists in 8 patients and by interventional radiologists in 28 others.

Treatment outcomes

There was no significant difference in outcomes between patients managed by CTD versus EUS. Treatment success was 90% in the CTD group versus 95% in the EUS group ($P = .63$) (Table 4). The median duration of hospitalization was 2 days for both the CTD and EUS groups, respectively ($P = .24$). Median procedural time for EUS-guided drainage (75 minutes, range 60-90 minutes) was significantly longer than that for CTD (40 minutes, range 38-50 minutes) ($P < .001$). Four patients required surgical intervention (3 in CTD and 1 in EUS group), because the PFC was persistent: necrosis (2), abscess (1), and necrotic sarcoma (1). In 1 patient with PFC drained by CTD, a diagnosis of necrotic sarcoma was made at surgical histopathology. This patient, at endoscopy, had a cloudy secretion on transmural puncture suggestive of an infected pseudocyst. This case was incorrectly diagnosed as a PFC based on preprocedural imaging studies. In 1 patient in the EUS group, the PFC diminished in size to 3 cm but with only partial relief of symptoms at 1-year follow-up. Tumor marker and chemistry studies from the PFC aspirate were suggestive of a pseudocyst. The patient declined any further interventions. At 6-month follow-up, all patients who had successful treatment outcomes were clinically well without any recurrence of symptoms.

Repeat interventions

Four patients in the CTD group underwent repeat endoscopy, with placement of more stents for ineffective drainage. Three patients had pancreatic necrosis or an abscess, and 1 had a pseudocyst. On repeat CT performed at 72 hours, there was no evidence of PFC resolution in 2 patients. Two other patients managed by CTD had only partial resolution of the PFC at 6 weeks, warranting repeat intervention. In 1 patient with pancreatic necrosis who had a 10F stent and a nasocystic catheter placed under EUS guidance, the catheter was inadvertently pulled. A repeat CT obtained at 72 hours revealed migration of the stent into the PFC; the stent was then successfully retrieved under EUS guidance (described below).

Complications

Bleeding was encountered at transmural puncture (CTD) in 1 patient with a PFC located in the body of the pancreas. This was managed by placement of hemoclips. He required blood transfusion, and the PFC was subsequently drained under EUS guidance. This patient had no prior history of coagulopathy or liver disease. Intervening vessels and gastric varices were noted both at EUS and CT. In 1 patient with pancreatic necrosis drained by EUS, migration of the transmural stent into the necrotic cavity

TABLE 3. Procedural details of patients undergoing drainage of PFC

Variables	Drainage modality			Total, N (%) (N = 53)
	CTD, N (%) (N = 30)	EUS, N (%) (N = 23)	P*	
Access site†			<.001‡‖	49
Bulb (transduodenal)	14	—		14
Transgastric				
Fundus	7	8		15
Cardia	—	9		9
Antrum	4	1		5
Greater curvature gastric	2	1		3
Lesser curvature	3	—		3
GE junction	—	2		2
Technical data†			.15‡	
Stent	22 (73.3)	11 (52.4)		33 (64.7)
Stent and drain	8 (26.7)	10 (47.6)		18 (35.3)
Complications			1.00‡	
None	29 (96.7)	23 (100)		52 (98.1)
Bleeding	1 (3.3)	—		1 (1.9)
Pancreatic stent			.04‡‖	
Yes	6 (20.0)	11 (47.8)		17 (32.1)
No	24 (80.0)	12 (52.2)		36 (67.9)
Jejunal feeding			.77‡	
Yes	21 (70.0)	15 (65.2)		36 (67.9)
No	9 (30.0)	8 (34.8)		17 (32.1)
Time for procedure (min)				
Mean (SD)	46.4 (16.5)	73.7 (26.6)		
Median (IQR)	40 (38–50)	75 (60–90)	<.001§‖	—
Range (min, max)	20–89	22–123		—
Hospital stay (d)				
Mean (SD)	3.2 (3.1)	2.6 (1.9)		2.9 (2.6)
Median (IQR)	2 (2–4)	2 (1–3)	.24§	2 (2–3)
Range (min, max)	1-18	1–8		1–18

GE, Gastroesophageal; *IQR*, interquartile range; *SD*, standard deviation; *min*, minimum; *max*, maximum.
*Two-tailed *P* value.
†Two mucinous neoplasms in the EUS group where drainage was not performed are excluded; the *P* value was calculated by comparing transduodenal vs transgastric access sites.
‡Fisher exact test.
§Wilcoxon rank sum test.
‖Statistically significant.

was noted at follow-up CT. The PFC was accessed via EUS, and the cyst-gastrostomy site was dilated to 45F by using a through-the-scope balloon. After dilation, the necrotic cavity was intubated by using a double-channel gastroscope, and the migrated stent was retrieved (Fig. 4A-C). Subsequently, the patient underwent 3 endoscopy sessions for extraction of more necrotic debris by using a foreign-body retrieval basket and a polypectomy snare. Two 10F stents and a nasocystic catheter were placed for drainage of the necrotic cavity. The patient recuperated

TABLE 4. Clinical outcomes of patients who underwent drainage of a PFC

Variables	Drainage modality			
	CTD, N (%) (N = 30)	EUS, N (%) (N = 23)	*P**	Total, N (%) (N = 53)
Surgery†			.63	
Yes	3 (10.0)	1 (4.8)		4 (7.8)
No	27 (90.0)	20 (95.2)		47 (92.2)
Symptoms on follow-up†			.63	
Persisted/ worse	3 (10.0)	1 (4.8)		4 (7.8)
Resolved	27 (90.0)	20 (95.2)		47 (92.2)
CT finding on follow-up†			.63	
Persisted	3 (10.0)	1 (4.8)		4 (7.8)
Resolved	27 (90.0)	20 (95.2)		47 (92.2)

*Two-tailed *P* value calculated by using the Fisher exact test.
†Two mucinous neoplasms in the EUS group are excluded.

well but had a persistent abscess on follow-up CT at 2 months that necessitated elective surgical drainage. No patient developed post-ERCP pancreatitis or superinfection.

Predictors for EUS-guided drainage

Adjusted ORs by using exact logistic regression are shown in Table 5. Factors of clinical or statistical significance were included in the model. The location of PFC and LC at CT remained significant when adjusted for size of PFC, serum albumin, and etiology of pancreatitis. PFCs located in tail region were significantly more likely to require drainage by EUS than CTD (even after adjusting for the other factors).

DISCUSSION

In this study, we demonstrated that, although most PFCs located in the pancreatic head or body can be drained by CTD, those at the tail of the pancreas are best drained under EUS guidance. Also, EUS provides an alternate diagnosis that impacts management decision in approximately 5% of PFCs that appear as pseudocyst by other imaging studies.

Before the era of CTD, endoscopic drainage of PFCs was possible only via the transpapillary route.[20,24-26] This, however, is possible only in the presence of a definitive communication between the pancreatic duct and a PFC. Although CTD can access PFCs that do not communicate with the pancreatic duct, because of the ability to perform drainage only in the presence of a definitive luminal compression, only 45% to 55% of all PFCs are amenable for CTD.[4-8] Similar to prior series, only 55% of all PFCs in the present study were amenable to CTD.

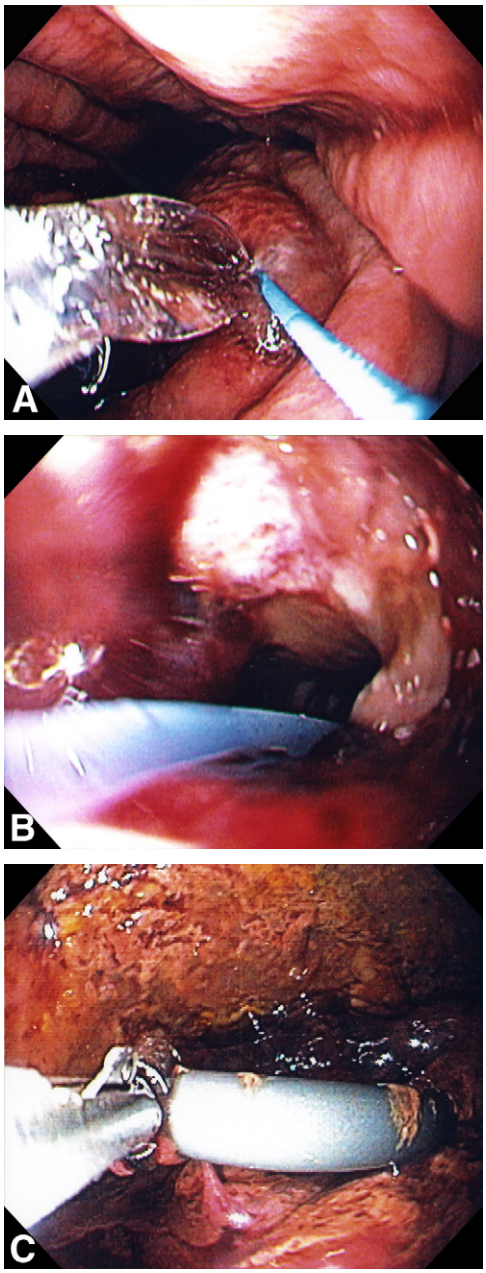

Figure 4. A, After accessing the PFC by using a 19-gauge needle and passage of a 0.035-inch guidewire, the cystenterostomy site is dilated by using a 45F through-the-scope balloon. **B,** Widely patent tract between the stomach and the PFC after dilation. **C,** The necrotic PFC cavity was intubated by using a therapeutic gastroscope, and the migrated stent was retrieved.

Given that CTD is effective only in patients with PFCs that cause LC, the overall technical success with the EUS-guided approach is clearly superior. Twelve studies that involved 145 patients reported a success rate of 95% for EUS-guided drainage of PFCs.[13,27] By using EUS, we were able to drain 100% of PFCs that were not amenable to CTD. Compared with other locations, PFC confined

TABLE 5. Adjusted ORs and 95% CIs for patients with PFC that require drainage under EUS guidance (vs conventional transmural drainage*)

Variable	Adjusted OR (95% CI)†	P
Location, tail vs head/body*	22.9 (2.6 to ∞)	.003
Size (mm)	1.03 (0.98–1.07)	.26
Albumin ≥3.5 vs <3.5*	0.8 (0.01–15.0)	
Compression on CT, no vs yes*	13.6 (1.4 to ∞)‡	.02

*Reference category.
†Calculated using multiple exact logistic regression; also adjusted for etiology ($P = 1.00$).
‡Median unbiased estimate calculated by using exact logistic regression.

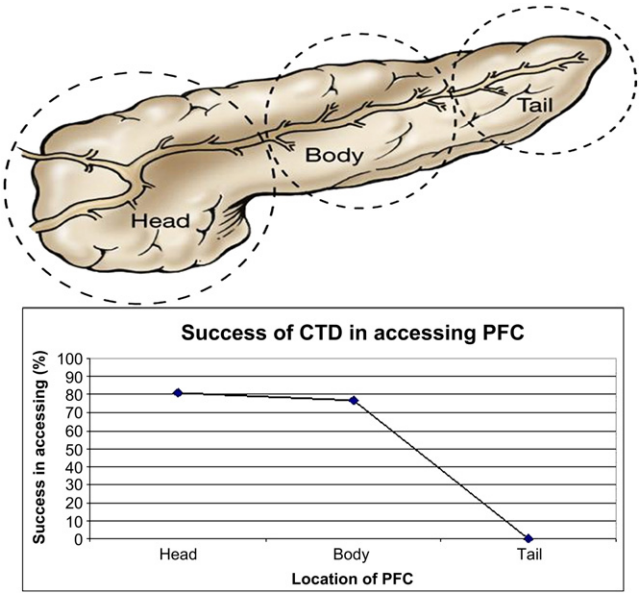

Figure 5. A PFC located at the tail region of the pancreas was more likely to fail drainage by conventional means than those located at other regions.

to the tail of the pancreas was best accessed under EUS guidance (Fig. 5). A PFC at this location tends to extend to the subphrenic, splenic, or pararenal space, or to the left upper quadrant. These areas typically do not extrinsically compress the GI tract and hence are difficult to access by CTD. Even if a PFC at this location causes LC, it is localized to the fundus or the cardia of the stomach; these are areas that are hard to access by CTD because of the difficulty in positioning the endoscope at these locations. However, at EUS, a PFC, irrespective of its location, can be well visualized at all times. Once access is established, a PFC can be drained successfully. However, unlike CTD, EUS-guided drainage involves the use of both fluoroscopy and sonography, and involves multiple steps, which make the procedure technically challenging and time consuming. There are no dedicated accessories for EUS-guided drainage of a PFC currently available in the United States. The development of such accessories may possibly shorten procedure time and make the procedure technically easier. Although none of the PFCs at the pancreatic tail were accessible for CTD in this study (maximum size 180 × 140 mm), it is possible that PFCs of a larger size or those that extend from the tail into other areas may cause LC and be amenable for CTD. Also, PFCs superior to the pancreas and extending into the porta hepatis or the gastrohepatic ligament did not cause LC and were amenable for drainage only under EUS guidance via the gastroesophageal junction or the gastric cardia. However, most localized PFCs arising from the head or the body of the pancreas cause LC of the stomach or the duodenum and are easily accessible to CTD provided the size is large (>5.5 cm in this study). In 2 patients with large PFC, CTD was unsuccessful in the setting of severe hypoalbuminemia. The gastric wall exhibited external compression, but this was nonfocal. It is possible that the gastric-wall layer was too thick from mucosal edema or an incorrect area was targeted for drainage.

Although there was a good correlation between CT and endoscopy for LC, this was not absolute in all patients (Table 2). Although CT demonstrated LC in 36 PFCs, only 29 were amenable for CTD. Of 19 PFCs without an LC on CT, 1 was amenable for CTD, because LC was evident at CTD. This discrepancy may be because of variation in positioning of the patient during CT versus endoscopy. Another explanation stems from a recent study that reported the pancreas, being a retroperitoneal organ, moves during respiration.[28]

Despite the inclusion of only those patients with bleeding at CTD or without a definitive LC, we did not encounter any procedural complications during EUS-guided drainage. Perforation has been reported as a complication during EUS-guided drainage of pancreatic pseudocysts by using the needle-knife technique.[11,13,15,29] It can sometimes be challenging to control the direction of the cut when using needle-knife catheters. This is particularly relevant when PFCs are accessed by EUS via atypical locations such as the cardia or the gastroesophageal junction. When deployed, the needle tends to point in a tangential angle, leading to an undesirable incision. A recent study attempted to overcome this limitation by using a bent needle knife, with modest success.[29] Also, unlike the FNA needle, the needle-knife catheter cannot be well visualized at EUS. In our experience, dilating the tract progressively by using over-the-wire ERCP catheters obviates the need for puncture when using a needle knife. Drainage was performed via the gastroesophageal junction in 2 patients with PFC at the porta hepatis. After the procedure, there was no clinical or radiologic evidence of pneumomediastinum in either patient. At 18 months, both were asymptomatic, without any evidence

of an esophagopancreatic fistula. The long-term consequence from exposure of the esophageal mucosa to pancreatic enzymes is unclear. Baron and Wiersema[15] reported on a patient with a pancreatic pseudocyst drained transesophageally under EUS guidance. After the procedure, this patient developed pneumomediastinum. A needle-knife catheter was used to puncture the PFC in that patient.

Although contrast-enhanced CT done earlier demonstrated a larger-size PFC, the PFC measured less than 4 cm at time of EUS in 2 patients who were ultimately excluded from this study. This spontaneous decrease in size of the PFC has been reported in 2 prior series.[30,31] More importantly, in 2 patients, EUS diagnosed mucinous cystic neoplasm that altered subsequent management plan. Also, 1 patient who underwent CTD was diagnosed later to have necrotic sarcoma that had metastasized to the pancreas. This patient presented initially with acute pancreatitis, and the pancreatic lesion was misdiagnosed as a pseudocyst. Fockens et al[30] reported a change in management in 9% of their patients with a pancreatic pseudocyst based on EUS findings. Patients at EUS were diagnosed to have cystic neoplasm of the pancreas, or the pseudocyst had resolved spontaneously, obviating the need for any drainage procedure. All cystic lesions of unclear etiology in the pancreas and those without a clinical history of pancreatitis are recommended for diagnostic evaluation before any attempt at drainage.[32,33] We recommend that all PFCs that are not completely typical by cross-sectional imaging, particularly of the pseudocyst type, irrespective of history of pancreatitis, should be assessed by EUS before drainage to definitively exclude a cystic neoplasm. Also, if the size of the PFC is borderline ($\leq$6 cm) and a CT had not been performed recently, then EUS can likely assess suitability for drainage as some pseudocysts may resolve spontaneously.

There are several limitations to this study. One, this was not a randomized trial. Subjecting only patients who failed CTD to EUS biased the study in favor of the CTD group. However, this study was designed specifically to identify those patients who fail drainage at CTD. This is important, because endoscopic drainage of PFCs has gained popularity over the last few years, and more endoscopists perform CTD than EUS-guided drainage.[3] Also, EUS is limited in availability, and interventional EUS requires a higher degree of technical expertise.[10,12,16] Two, transpapillary stent placement was technically successful in only 30% of patients in this study. The superiority of the combined approach (transpapillary and transmural) over transmural drainage alone remains unclear.[34] However, the number of patients who underwent transpapillary stent placement between groups was not significantly different and hence unlikely to influence outcomes. Three, the role of endoscopic management in pancreatic necrosis remains an area of debate.[33] Although none of our patients developed superinfection, the long-term outcome in patients with pancreatic necrosis was not favorable; 3 of 9 patients required surgery as definitive treatment. In only 1 patient did we intubate the necrotic cavity for removal of debris; in others, the PFC was flushed vigorously via nasocystic catheters every 4 hours. This treatment was probably suboptimal in this patient population. Removal of solid necrotic debris possibly is best achieved by endoscopic intubation of the necrotic cavity and removing the contents under direct vision by using various accessories, such as a snare or a basket.[35]

Although both CTD and EUS have been shown to be useful in drainage of PFCs, the specific role for each modality in drainage of PFCs has been unclear. In this study, we showed that a majority of PFCs can be drained by CTD in a shorter duration with comparable outcomes. EUS-guided drainage should be reserved only for PFC located at the pancreatic tail, because these are unlikely to cause LC or are technically difficult to access. Also, in 5% of pseudocyst-type PFCs, EUS establishes an alternate primary diagnosis. Therefore, all pseudocyst-type PFCs should be evaluated by EUS for confirmation of diagnosis before any attempts at endoscopic drainage.

DISCLOSURE

The authors do not have any disclosure to make.

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