Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos)

Shyam Varadarajulu, MD, John D. Christein, MD, Ashutosh Tamhane, MD, MSPH, Ernesto R. Drelichman, MD, C. Mel Wilcox, MD, MSPH

Birmingham, Alabama, USA

Background: Although prior studies evaluated the role of EUS and EGD for drainage of pancreatic pseudocysts, there are no randomized trials that compared the technical outcomes between both modalities.

Objective: To compare the rate of technical success between EUS and EGD for transmural drainage of pancreatic pseudocysts.

Study design: A prospective randomized trial.

Setting: A tertiary-referral center.

Patients: Those with a history of pancreatitis and symptomatic pancreatic pseudocysts that measured greater than 4 cm in size who were referred for endoscopic transmural drainage. Patients with pancreatic abscess or necrosis were excluded.

Main Outcome Measurements: Technical success was defined as the ability to access and drain a pseudocyst by placement of transmural stents. Complications were assessed at 24 hours and at day 30. Treatment success was defined as the complete resolution or decrease in size of the pseudocyst to $\leq$2 cm on CT in association with clinical resolution of symptoms at 6 weeks of follow-up.

Results: Thirty patients were randomized to undergo pseudocyst drainage by EUS (n = 15) or EGD (n = 15) over a 6-month period. Of the 15 patients randomized to EUS, drainage was not undertaken in one, because an alternative diagnosis of biliary cystadenoma was established at EUS and was excluded (after randomization) from analysis. The mean age of the patients was 47 years; 62% were men (18/29). Except for their sex, there was no difference in patient or clinical characteristics between the 2 cohorts. Although all the patients (n = 14) randomized to an EUS underwent successful drainage (100%), the procedure was technically successful in only 5 of 15 patients (33%) randomized to an EGD ($P < .001$). All 10 patients who failed drainage by EGD underwent successful drainage of the pseudocyst on a crossover to EUS. There was no significant difference in the rates of treatment success between EUS and EGD after stenting, either by intention-to-treat (ITT) analysis (100% vs 87%; $P = .48$) or as-treated analysis (95.8% vs 80%; $P = .32$). Major procedure-related bleeding was encountered in 2 patients in whom drainage by EGD was attempted; one resulted in death and the other necessitated a blood transfusion. No significant difference was observed between EUS and EGD with regard to complications either by ITT (0% vs 13%; $P = .48$) or as-treated analyses (4% vs 20%; $P = .32$). Technical success was significantly greater for EUS than EGD, even after adjusting for luminal compression and sex (adjusted exact odds ratio 39.4; $P = .001$).

Limitation: Short duration of follow-up.

Conclusions: When available, EUS should be considered as the first-line treatment modality for endoscopic drainage of pancreatic pseudocysts given its high technical success rate. (Gastrointest Endosc 2008;68:1102-11.)

Endoscopic transmural drainage is a minimally invasive alternative to surgery for drainage of peripancreatic fluid collections (PFC). Since the first reports by Sahel et al[1] and Cremer et al,[2] transmural drainage by EGD has become an established technique for management of PFCs.[3-5] This procedure entails the creation of a fistulous tract between the PFC and the gastric lumen (cyst-gastrostomy) or duodenal lumen (cyst-duodenostomy), followed by placement of a nasocystic catheter or a stent to facilitate drainage. The obvious limitation of this technique is its relatively ''blind'' approach. The risk of perforation is particularly high when luminal compression is not visible at endoscopy.[6-8] Another major complication

Abbreviations: DPEJ, direct percutaneous endoscopic jejunostomy; ITT, intention-to-treat; OR, odds ratio; PFC, peripancreatic fluid collection; UAB, University of Alabama at Birmingham.

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is hemorrhage after puncture of a PFC and is encountered in approximately 6% of cases.[1,2,4,6-8] The use of EUS has been more recently reported for guidance of transmural puncture and for performing drainage of a PFC.[9-13] By using this technique, puncture of a PFC under direct sonographic visualization is possible in patients without luminal compression and in those patients at high risk for bleeding, eg, those with portal hypertension.[13-15] This approach may improve both the safety of the procedure and the number of candidates amenable for PFC drainage.[13,14] However, there are no randomized trials that compared the technical outcomes between EUS and EGD for drainage of a PFC. This randomized study was designed to compare the rate of technical success between EUS and EGD for transmural drainage of pancreatic pseudocysts.

Capsule Summary

What is already known on this topic

- Endoscopic transmural drainage of peripancreatic fluid collections may be associated with bleeding and perforation in up to 10% of patients.

What this study adds to our knowledge

- In 30 patients randomized to undergo pseudocyst drainage by EGD or the EUS-guided approach, all patients who had an EUS underwent successful drainage.
- EGD was technically successful in only 33%; all who failed underwent successful drainage on crossover to EUS.

PATIENTS AND METHODS

Patients

Between May to October 2007, consecutive patients with a history of pancreatitis and symptomatic pseudocysts referred to the University of Alabama at Birmingham (UAB) Medical Center were randomized to undergo transmural drainage under EUS guidance or by EGD. Patients were excluded if CT findings were suggestive of pathology other than a pseudocyst, if a pseudocyst was ≤ 4 cm in size, or if patients younger than 18 years of age. Patients with pancreatic abscess or necrosis by CT were excluded from the study. Patients enrolled in this trial were not included in any database analysis previously reported from our center. The study was approved by the institutional review board of the UAB Medical Center. All patients provided written voluntary informed consent for participation in the study.

Methods

All the patients underwent a contrast-enhanced CT at our institution before undergoing pseudocyst drainage. ERCP was routinely attempted with the patient in the prone position and by using a therapeutic duodenoscope (TJF-160; Olympus America Corp, Melville, NY) before drainage of the pseudocyst in all the patients. In patients with gallstone pancreatitis, a biliary sphincterotomy was undertaken for extraction of common bile duct stones. A pancreatogram was attempted to define communication between the duct and the pseudocyst. 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.[16] ERCP was not undertaken in those patients in whom the extrinsic compression precluded duodenoscope passage to the second portion of the duodenum. Intravenous ciprofloxacin (400 mg) was administered before the procedure and continued for 48 hours or until the time of patient discharge. Outpatients were prescribed twice-a-day oral ciprofloxacin (500 mg) to be started the night before the procedure and continued for 2 days after pseudocyst drainage.

After ERCP, an endoscopy nurse opened a sealed envelope that contained computer-generated randomization assignments. Patients were randomized to undergo pseudocyst drainage by EGD or under EUS guidance. If treatment was unsuccessful by either modality, then drainage was attempted by a crossover of the patient to the alternate treatment wing. Procedural details were documented prospectively: presence or absence of luminal compression, morphology of the pseudocyst on EUS, reason for failure to drain by EGD or EUS, procedural duration, and procedure-related complications if encountered. Also, characteristics of the pseudocyst, such as its size and location on CT, were documented.

Procedural technique

In patients randomized for drainage by EGD after ERCP, a search for a luminal compression in the duodenum and stomach was undertaken by using the duodenoscope. If no definitive luminal compression was identified, then the duodenoscope was exchanged for a double-channel gastroscope (GIF 2T; Olympus), and a search for luminal compression was attempted with the patient in the left lateral position. If a luminal compression was identified, then at least 5 attempts were made to puncture the gastric or duodenal wall by using a needle-knife catheter (Microknife XL; Microvasive Endoscopy, Boston Scientific Corp, Natick, Mass) to access the pseudocyst. If all attempts failed or if bleeding was encountered or if no luminal compression was identified at EGD, then the patient was crossed over to the EUS group, and drainage was attempted by using an echoendoscope (GF-UCT 140; Olympus). All drainages by EGD were performed by using a triple-lumen needle-knife (Microknife XL; Microvasive) to create a cyst-enterostomy fistula. After access to the pseudocyst, a 0.035-inch guidewire (X-wire; CONMED Corporation,

Billerica, Mass) was coiled within the pseudocyst and dilation of the fistula was performed by using an 8-mm biliary balloon dilator (CRE balloon; Microvasive) under fluoroscopic guidance. After dilation, two 10F double-pigtail endoprostheses were placed (Video 1, available online at www.giejournal.org). A sample of the aspirate was routinely sent for Gram stain and culture in all the patients.

All EUS-guided drainages were performed by using a 19-gauge needle (EUSN-19-T; Cook Endoscopy, Winston-Salem, NC), which was introduced into the pseudocyst by using an echoendoscope (GF-UCT 140; Olympus). Before a puncture, the cyst morphology was evaluated by an EUS, and color Doppler US was used to identify regional vessels. A 0.035-inch guidewire (X-wire; CONMED) was then introduced through the needle and coiled within the pseudocyst under fluoroscopic guidance. The tract was sequentially dilated by first passing a 5F ERCP cannula, a 10F ERCP inner guiding catheter (OASIS system; Cook), and an 8-mm biliary balloon dilator; stenting was then undertaken (two 7F double-pigtail endoprostheses), as described above. A needle-knife was not used to puncture the pseudocyst in any patient undergoing EUS-guided drainage (Video 2, available online at www.giejournal.org).

Other treatment

All patients with a pancreatic pseudocyst in the setting of smoldering pancreatitis[17] underwent placement of a direct percutaneous endoscopic jejunostomy (DPEJ) feeding tube by using a previously described technique,[18] or they underwent placement of a 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 pseudocyst drainage.

All EGDs and ERCPs were undertaken by 2 therapeutic endoscopists (S.V., C.M.W), each of whom perform more than 400 ERCP procedures annually. Both endoscopists have an individual life-time experience of performing more than 100 pseudocyst drainages by using EGD. All EUS-guided drainages were undertaken by one endosonographer (S.V.), who performs more than 600 EUS procedures annually. The endosonographer has a life-time experience of performing 110 EUS-guided drainage procedures that include PFC, right upper-quadrant fluid collections, and pelvic abscesses.

Definitions

A pseudocyst was categorized according to the Atlanta classification,[19] and its location in the pancreas was classified according to a previously defined method.[20] Technical success was defined as the ability to access and drain a pseudocyst by placement of transmural stents. Treatment success was defined as complete resolution, or a decrease in size, of the pseudocyst to $\leq$2 cm on CT in association with clinical resolution of symptoms at 6-week follow-up.

Complications were classified as major and minor. All perforations were classified as major and was diagnosed when pneumoperitoneum was evident on imaging studies in association with peritoneal signs. All infections were classified as major and was defined as any septic event after the initial endoscopic drainage caused by contamination of the pseudocyst, proven by new-onset fever, positive blood cultures, or by fluid cultures obtained at endoscopic revision. Major bleeding was defined as any hemorrhagic event that required endotherapy, blood product transfusion, or inpatient observation, or that was revealed by the presence of dry blood within the pseudocyst or GI lumen at autopsy. Minor bleeding was defined as self-limited bleeding that occurred during transmural drainage of the pseudocyst that resolved by itself without the need for any intervention during endoscopy. Stent migration was classified as a minor complication and was defined as the need to retrieve a stent from within the pseudocyst or the enteral lumen. Procedural duration was defined as the time between endoscopic intubation and withdrawal of the echoendoscope or gastroscope after completion of requisite therapy. Time for an ERCP was not taken into consideration when calculating procedural duration for pseudocyst drainages.

Follow-up

All the patients were evaluated with contrast-enhanced CT and an outpatient clinic visit at 6 weeks after pseudocyst drainage. In patients with treatment success, the transpapillary pancreatic stent, cyst-enterostomy stent, and jejunostomy feeding tube were removed. Those with a partial decrease in size of the pseudocyst underwent replacement of transmural stents and were reevaluated after 1 month with another contrast-enhanced CT; if the pseudocyst had resolved, then they were managed in a similar manner to patients in whom treatment was successful. Those with treatment failure underwent surgery.

Outcome measurements

The main outcome measurement was the rate of technical success between EGD and EUS for performing pancreatic pseudocyst drainages. The secondary outcome measurements were treatment success between EUS and EGD after successful transmural stenting and the rates of procedure-related complications between both the modalities.

Statistical analysis

The sample size was calculated based on technical success, because this was the primary objective of the study, and prior studies[13,20] did not compare this objective in a randomized fashion. To calculate a priori sample size, alpha was set to 0.05 (2-tailed) and power was 80%, with unmatched design (independent proportions), and 1:1 ratio for both arms (EUS vs EGD). Based upon a previous

study,[20] technical success for EUS was 100% and, for EGD, was 55%. The required sample size to detect a significant difference was 26 (13 in each group).

In the intention-to-treat (ITT) analysis, the study groups were compared in terms of the procedure they were randomly allocated to, irrespective of the technical success and/or failure of the procedure to preserve randomization. In the as-treated analysis, a subject was grouped according to the procedure that was successful in draining the pseudocyst. Thus, for example, a subject initially randomized to the EGD arm but later crossed over (because of the failure of EGD) to the EUS arm, which, in turn, was successful in draining the pseudocyst, was grouped in the EUS arm for as-treated analysis but was grouped in the EGD arm for ITT analysis. For technical success, the ITT and as-treated analyses were the same, because the decision of a crossover was dependent on this outcome. For complications and treatment success, both ITT and as-treated analyses were reported.

Statistical analysis was performed by using SAS software, version 9.1 (SAS Institute Inc, Cary, NC). For normally distributed variables, means were compared by using the unpaired *t* test. For variables with skewed distributions, the Wilcoxon rank sum test for unpaired data was used, and medians were reported. Proportions were compared by using the Fisher exact test, and its extension was used for more than dichotomous categories. All the *P* values reported are 2-tailed. An association between technical success and various factors was examined by using crude and adjusted odds ratios (OR) with corresponding 95% CIs. Adjusted ORs were calculated by using the logistic regression method. Factors were included in the logistic model based upon their clinical and/or statistical significance. In situations in which the logistic regression model suffered from ''quasi-complete'' separation, exact logistic regression models were used to generate median unbiased estimates of the ORs with corresponding 95% CIs.[21] In the case of ''complete'' separation, models were fit without the variable or variables in question. The resulting *P* values and adjusted ORs from the multivariable logistic regression analysis only assessed the roles of variables independently associated with technical success, after adjusting for contributions of the other variables in the exact model. It is recognized that several statistical tests were performed on outcome data arising from individual patients. Therefore, the *P* values stated are their nominal values, uncorrected for multiple testing. However, it was noted that a correction for multiple testing, such as the method of Bonferroni, would not have removed the statistical significance of the variables in the logistic model.

RESULTS

Of 42 patients who were screened for participation in the study, 12 were excluded because CT revealed pancreatic abscess or necrosis in 8 patients, the pseudocyst was <4 cm in 3, and a cyst neoplasm was suspected in one patient (Fig. 1). Thirty patients were randomized to undergo pseudocyst drainage by EGD (n = 15) or EUS (n = 15). Of the 15 patients randomized to EUS, drainage was not undertaken in one, because an alternative diagnosis of biliary cystadenoma was established at EUS and was excluded (after randomization) from analysis. This patient was initially seen with persistent abdominal pain and was diagnosed by CT to have a pancreatic pseudocyst in the setting of chronic pancreatitis. At EUS, small septations rather than debris were seen within the cyst and FNA did not reveal any inflammatory cells. The patient underwent surgery and was diagnosed to have a biliary cystadenoma.

Thus, for analysis, 29 patients were included, with 14 in the EUS arm and 15 in the EGD arm (ITT analysis). The mean age of the patients was 47 years; 62% (18/29) were men. For the variables (except hospital stay), shown in Table 1, the ITT and as-treated analyses were the same as variables that existed and/or collected before the point of the crossover. Except for sex, there were no significant differences in patient or clinical characteristics between both cohorts (Table 1). There were no significant differences in pseudocyst size, location, or the presence or absence of luminal compression between both cohorts (Table 1).

Although all the patients (n = 14) randomized to EUS underwent successful drainage (100% [95% CI, 76.8%-100%]), the procedure was technically successful in only 5 of 15 (33.3% [95% CI, 11.8%-61.6%]) randomized to EGD ($P < .001$) (Fig. 1). Reasons for technical failure in 10 patients randomized to EGD were as follows: the absence of luminal compression in 9 and active bleeding after attempted puncture of the pseudocyst in one patient. All 10 patients who failed drainage by EGD underwent successful drainage of the pseudocyst on crossover to EUS. Thus, for as-treated analysis, 24 subjects were grouped into the EUS arm and 5 in the EGD arm (Fig. 1).

As per ITT analysis, treatment was successful (radiologic resolution of a pseudocyst in association with symptom relief) in all the 14 patients (100% [95% CI, 76.8%-100%]) randomized to EUS and in 13 patients randomized to EGD (86.7% [95% CI, 59.5%-98.3%]) (Fig. 1). Based on as-treated analysis, treatment was successful in 23 patients managed by EUS (95.8% [95% CI, 78.9%-99.9%]) and in 4 patients treated by EGD (80.0% [95% CI, 28.4%-99.5%]). There was no significant difference in rates of treatment success between EUS and EGD after stenting, either by ITT ($P = .48$) or as-treated analyses ($P = .32$). Although treatment was successful in all 14 patients randomized to EUS-guided drainage, one of the 10 patients who crossed over to the EUS group eventually required surgery, because he continued to have persistent abdominal pain after transmural drainage. A follow-up CT revealed

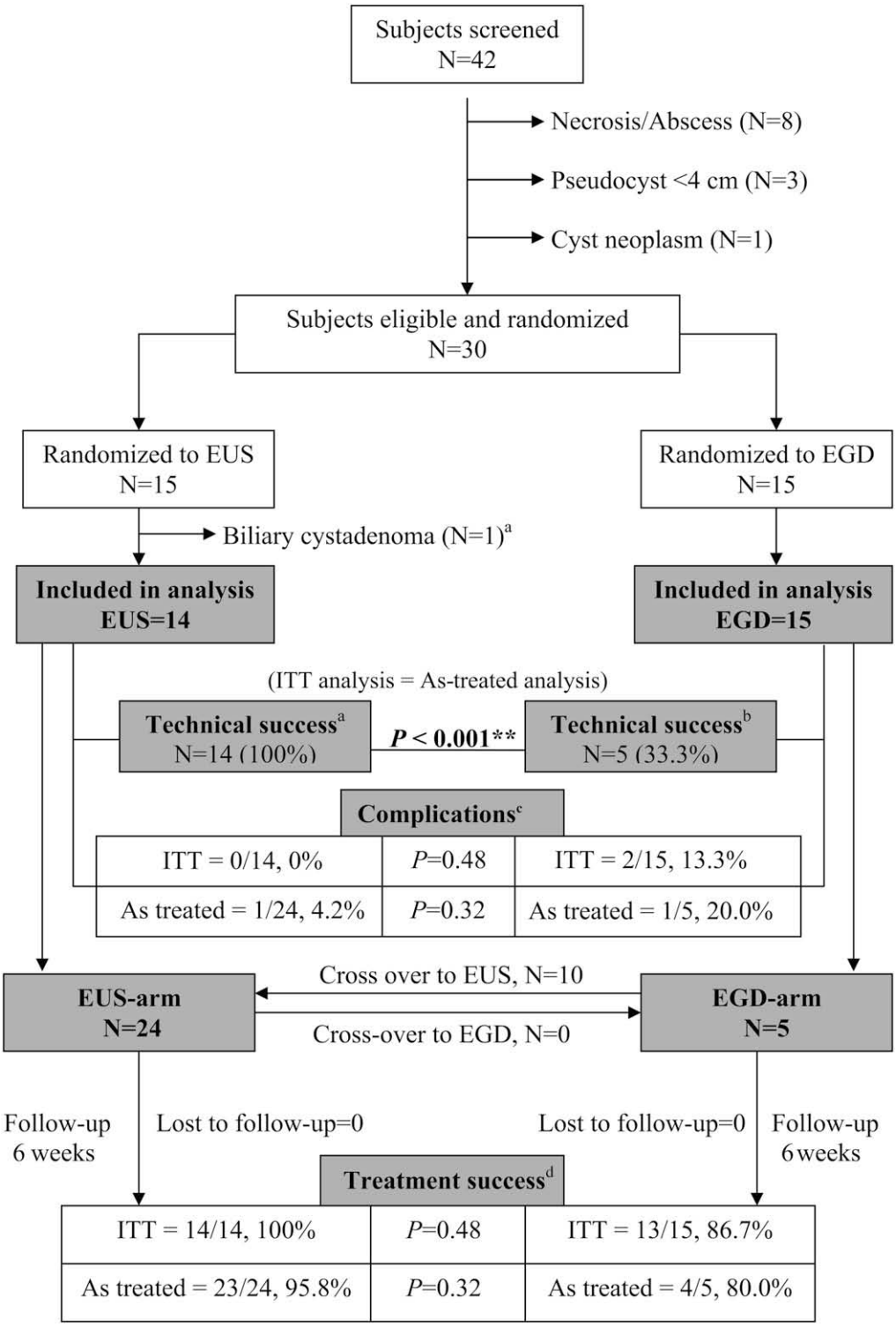

Figure 1. Flow diagram of the study subjects randomized to under pseudocyst drainage. *ITT,* Intention-to-treat analysis, ie, as originally randomized.
[a]Drainage was not undertaken, because a diagnosis of biliary cystadenoma was established at EUS; the subject was ineligible to be included in the study and, therefore, was excluded (after randomization) from analysis.
[b]Technical success was defined as the ability to access and drain a pseudocyst by placement of transmural stents.
[c]One subject with EGD-related bleeding had technical failure, and the other patient, with a technically successful EGD, died 4 hours after the procedure.
[d]Treatment success was defined as the complete resolution or decrease in size of the pseudocyst to ≤ 2 cm on a CT in association with clinical resolution of symptoms at 6-week follow-up.
**Statistically significant.

TABLE 1. Comparison of subject characteristics, laboratory findings, and other clinical parameters at initial presentation between patients randomized to an EUS and an EGD*

Variable	EUS, no. (%) (N = 14)	EGD, no. (%) (N = 15)	P†	Total, no. (%) (N = 29)
Age (y)				
Mean (SD)	42.8 (14.6)	51.1 (8.2)	.07‡	47.1 (12.3)
Range (min, max)	19-66	38-65		19-66
Men	5 (35.7)	13 (86.7)	.01§‖	18 (62.1)
Indication				
Abdominal pain	13 (92.9)	12 (80.0)	.60§	25 (86.2)
Gastric outlet obstruction	–	–		–
Both	1 (7.1)	3 (20.0)		4 (13.8)
Etiology				
Alcohol	3	7	.07¶	10
Idiopathic	4	5		9
Gall stones	1	3		4
After surgery	3	–		3
Other	3	–		3
White cell count (mm^3)				
Median	6.9	9.1	.55#	7.8
Percentile (5th-95th)	6.1-19.7	4.6-24.2		5.8-19.7
Albumin (g/dL)				
Mean (SD)	2.6 (0.7)	2.8 (0.9)	.57‡	2.7 (0.8)
Range (min, max)	1.2-3.7	1.3-4.6		1.2-4.6
Location**			.27§	
Head	–	5		5
Body	5	4		9
Tail	9	6		15
Long axis (mm)				
Median	65	70	.63#	70
Percentile (5th-95th)	50-120	42-130		50-120
Luminal compression	4 (28.6)	6 (40.0)	.70§	10 (34.5)
Duration of procedure (min)				
Median	19.5	28.0	.09#	–
Percentile (5th-95th)	14-55	18-110		–
Hospital stay(d)††				
Median	2	1	.21#	2
Percentile (5th-95th)	1-9	1-8		1-8

min, Minimum; *max,* maximum.
*Except for the hospital stay, analysis either by the ITT method or the as-treated method would yield the same results, because the variables were collected and/or existed before the point of a crossover to the other arm; the ITT results of hospital stay are presented in footnote ††.
†Two-tailed *P* value.
‡Student *t* test for unpaired data.
§Fisher exact test.
‖Statistically significant.
¶Extension of the Fisher exact test for situations with more than dichotomous categories.
#Wilcoxon rank sum test for unpaired data.
**Head and body lesions combined to calculate *P* value.
††One of the patients with EGD technical success died within 4 hours of the procedure and is excluded; by using as-treated analysis (24 EUS, 4 EGD), median hospital stay for EUS vs EGD did not differ significantly (2 vs 1; $P = .17$).

no change in size of the pseudocyst at 72 hours in this patient. Treatment was a failure in one of the 5 patients who underwent drainage by EGD, because she died 4 hours after the procedure because of massive hemorrhage within the pseudocyst. Three of 10 patients who crossed over to the EUS cohort because of a lack of a luminal compression at EGD underwent transduodenal drainage compared with 2 patients who underwent transduodenal drainage at EGD. All these 5 patients who underwent transduodenal drainage by both modalities had successful technical and clinical outcomes. All the patients in both cohorts underwent a follow-up CT and clinic visit at 6 weeks, with the exception of one patient who underwent follow-up at 10 weeks.

Major procedure-related bleeding was encountered in 2 patients in whom drainage by EGD was attempted. One patient for whom an EGD was technically successful died 4 hours after the procedure. An autopsy revealed the cause of death to be massive hemorrhage within the pseudocyst, and small varices were noted in the gastric wall at the site where the transmural stents were deployed. These varices were not visible at an endoscopy, and only self-limited minimal bleeding was encountered at the time of pseudocyst drainage in this patient. The other patient in whom EGD technically failed (crossed over to an EUS) developed active bleeding at an attempted puncture of the pseudocyst. This was controlled by injection of 8 mL of 1:10,000 epinephrine at the site of transmural puncture by using the needle-knife catheter, and the bleeding ceased in 3 minutes. This patient subsequently underwent successful cyst-gastrostomy under EUS guidance. An intervening vessel was noted at EUS (Fig. 2A and B), and the patient required 2 units of blood transfusion and was discharged home after overnight observation. As per ITT analysis, none of the patients randomized to EUS encountered any complication (0% [95% CI, 0.0%-23.2%]), whereas 2 patients randomized to an EGD developed complications (13.3% [95% CI, 1.7%-40.5%]) (Fig. 1). Based on as-treated analysis, one of the patients treated with EUS encountered complications (4.2% [95% CI, 0.1%-21.1%]), and one of the patients treated with EGD encountered complications (20.0% [95% CI, 0.5%-71.6%]). These differences between EUS and EGD with regard to complications were not significant either by ITT ($P = .48$) or as-treated analyses ($P = .32$). No other procedural complications were encountered. One patient with large gastric varices was randomized to the EUS cohort and underwent successful drainage of the pseudocyst (Fig. 3A and B).

A pancreatogram was performed in 20 patients, and a bridging stent was successfully deployed in 13. A pancreatogram was unsuccessful (n = 10) because of the presence of an altered anatomy in 4, failed cannulation in 3, and duodenal compression in 3 patients. Among patients in whom a pancreatogram was obtained, placement of a bridging stent was unsuccessful in 7 cases because of complete disruption of the main pancreatic duct at the head region. Enteral nutrition was initiated in 7 patients, with smoldering pancreatitis by means of DPEJ in 1 patient and percutaneous gastrojejunostomy feeding-tube placement in 6 patients. There was no significant difference in rates of pancreatic stenting or enteral nutrition between patients randomized to EUS versus EGD-guided drainages (data not shown). There was no significant difference in the median duration of hospital stay after pseudocyst drainage by EUS versus EGD (2 vs 1 day, $P = .21$) (Table 1). Also, there was no significant difference in median procedural duration between patients who underwent EUS versus EGD-guided drainages (19.5 vs 28 minutes, $P = .09$).

Whether technical success remained greater for EUS than EGD, even after adjusting for confounding factors, was examined by multivariable analysis (Table 2). Factors with clinical or statistical significance included in the logistic models are shown in Table 2. A model with all the variables (from Table 2) suffered ''complete separation.'' A model with only significant ($P \leq .05$) factors (procedure, sex, and luminal compression) had quasi-complete separation of data points. Exact logistic regression for this model (Table 2) showed that EUS had significantly greater technical success than EGD (adjusted OR 39.4; $P = .001$) when adjusted for sex and luminal compression. The addition (model not shown) of either or both pseudocyst ''size'' and ''location'' to the above model (procedure, sex, and luminal compression) produced either complete or quasi-complete separation of data points; the exact logistic regression was also degenerate. Therefore, these variables could not be included in the model.

DISCUSSION

In this randomized trial, the technical success rate of EUS was found to be significantly higher than EGD for transmural drainage of pancreatic pseudocysts. Although not statistically significant, EUS demonstrated a superior safety profile when compared with EGD.

The technical superiority of EUS over EGD for PFC drainage was previously demonstrated in 2 reports.[13,20] Although prospective, both studies were conducted in a nonrandomized fashion. In the first study, by Kahaleh et al,[13] which included 99 patients, drainage by EGD was undertaken when luminal compression was present and EUS-guided drainage was undertaken in the absence of luminal compression. Forty-six of 99 patients (46%) required drainage under EUS guidance because of the lack of luminal compression. In the second study by our group, which included 53 patients, EGD was first attempted in all the patients, followed by EUS if EGD was unsuccessful.[20] EGD failed in 43% of patients, who subsequently required drainage under EUS guidance. In both

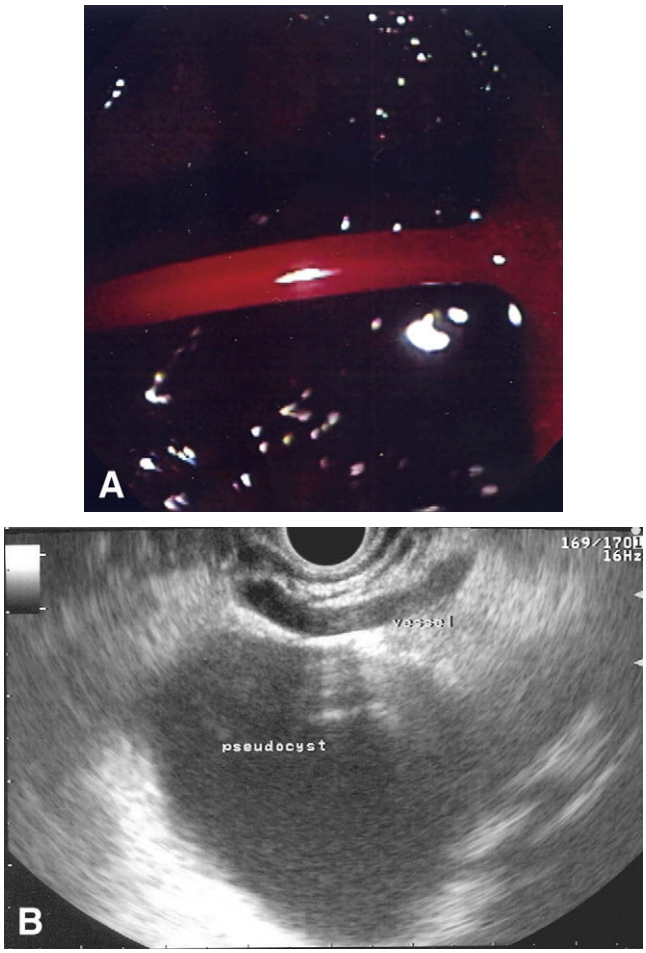

Figure 2. A, Bleeding after attempted puncture of the pseudocyst by EGD. **B,** EUS revealed intervening vasculature.

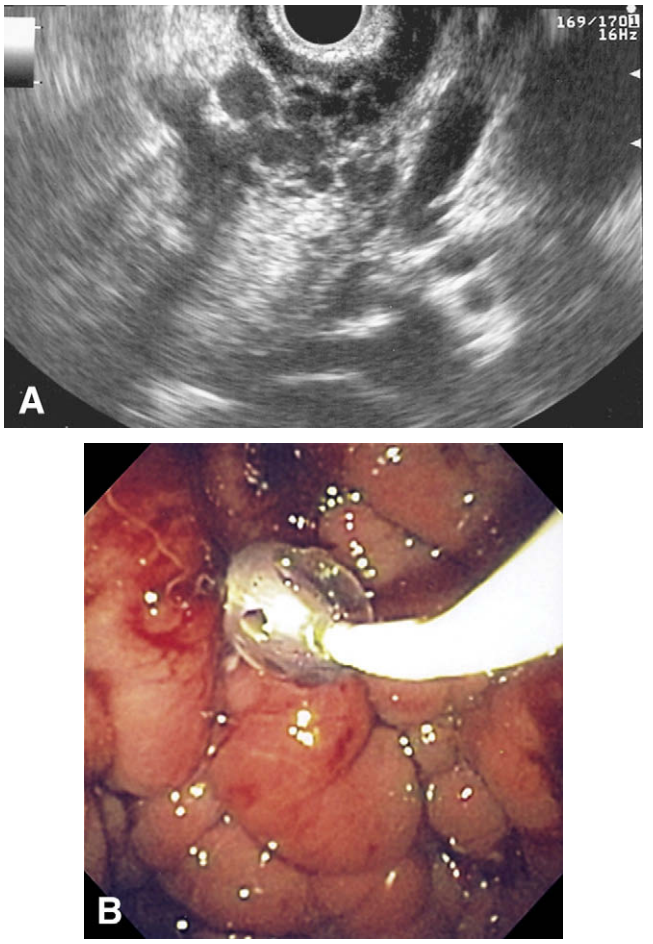

Figure 3. A, Transgastric EUS-guided drainage of a pancreatic pseudocyst in a patient with gastric varices as noted by EUS. **B,** Subsequently drained under EUS guidance.

studies,[13,20] there was no statistical difference in rates of treatment success or complications between both treatment modalities. In the present study, only 33% of patients randomized to undergo EGD underwent successful pseudocyst drainage, whereas all the patients randomized to undergo EUS underwent successful transmural drainage. Failure to establish drainage by EGD was primarily because of the lack of luminal compression in a majority of the patients. The greater technical success rate for EUS is by virtue of its ability to visualize and access extramural lesions. In patients with a well-defined luminal compression, drainage by EGD is likely to be successful in most cases. As in prior studies,[13,20] after transmural drainage, there was no significant difference in rates of pseudocyst resolution between patients randomized to EGD or EUS. In the 2 prospective studies[13,20] that compared treatment outcomes after pseudocyst drainage by EGD versus EUS, the rates of treatment success were 90% versus 95% and 93% versus 94%, respectively. Also, there was no significant difference in rates of complications between EGD versus EUS, 18% versus 19% and 3% versus 0%, respectively.[13,20]

In this study, one of the 15 patients randomized to EUS was diagnosed to have an alternative diagnosis before transmural drainage. In a prior report, 5% of patients with pancreatic pseudocysts referred for endoscopic drainage were diagnosed, by using EUS, to have a mucinous neoplasm.[20] Fockens et al[22] reported a change in management in 9% of their patients with pancreatic pseudocyst based on EUS findings. Patients at EUS were diagnosed to have cystic neoplasm of the pancreas or the pseudocyst had resolved spontaneously, which obviated the need for any drainage procedure.[22]

Bleeding and perforation are the 2 major complications encountered in 2% to 10% of patients undergoing endoscopic drainage of pancreatic pseudocysts.[4,6-8,23] Prior studies that compared the rates of complications between EGD-guided and EUS-guided drainage have not shown a statistical difference because of the small sample size in the enrolled series.[13,20] Although there was no statistical difference in this study, clinically significant complications were encountered in 2 of 15 patients randomized to undergo drainage by EGD. Although one patient died

TABLE 2. Multivariable analysis examining the association between the type of procedure and technical success (yes vs no‡) adjusting for confounding factors

Variable	Crude OR (95% CI)	P*	Adjusted OR (95% CI)†	P*
Procedure: EUS vs EGD‡	30.6 (4.0 to ∞)§	<.001‖	39.4 (4.0 to ∞)§	.001‖
Women vs men‡	10.0 (1.1-95.2)	.045‖	0.2 (0.01 to ∞)§	1.00
Luminal compression: yes vs no‡	8.1 (0.9-77.1)	.07	20.7 (2.1 to ∞)§	.007‖
Long axis (mm)	1.03 (0.99-1.07)	.13	–	–
Location				
Head vs tail‡	2.7 (0.2-30.1)	.43	–	–
Body vs tail‡	1.3 (0.2-7.5)	.74	–	–
Albumin (g/dL)	0.6 (0.2-1.6)	.30	–	–
Age (y)	0.95 (0.9-1.0)	.16	–	–

*P values reported are 2-tailed.
†Adjusted ORs were calculated by the exact logistic regression method.
‡Referent category.
§Median unbiased estimate calculated by exact logistic regression because of quasi-complete separation of data points.
‖Statistically significant.

from massive bleeding, the other patient only required a blood transfusion. Bleeding in both patients was because of the presence of gastric collaterals or intervening vasculature that was not visible at endoscopy. There were no procedure-related complications in any patient who underwent EUS-guided drainage. EUS enables the identification of collateral vasculature and thereby provides a safe window for transmural puncture of the pseudocyst. Even in patients with large gastric varices, EUS permits the identification of an appropriate site for performing safe transmural drainage (Fig. 3A and B). If intracystic hemorrhage is encountered at transmural puncture, this can be appreciated at EUS as a hyperechoic area that gradually expands within the cyst lumen and can be managed appropriately.[24]

There are several limitations to this study. One, we compared outcomes between EUS and EGD only for those patients with pancreatic pseudocysts. Hence, the role of these modalities for the management of patients with pancreatic abscess or necrosis was not evaluated. Two, the rate of technical success for EGD in this study was only 33%, which is less than the 54% to 57% success rates reported in other series.[13,20] One contributing factor could be that the median size of the pseudocyst (in the longest axis) in the present study was comparatively smaller than that reported in one[20] of the prior reports (70 mm vs 115 mm) and, therefore, the pseudocysts were less likely to induce luminal compression. However, the median size was certainly well above the cutoff specified for inclusion criteria in this study. The other contributing factor could be the experience level and familiarity of the endoscopists with either technique for performing pseudocyst drainage. This is unlikely to be the case, because both endoscopists in this study had adequate technical proficiency for drainage of pancreatic pseudocysts when using EGD. Furthermore, the blinding of an investigator to the technique to which the patient was randomized is neither feasible nor practical, and, therefore, it is difficult to exclude the possibility of bias completely. Three, there was a difference in the caliber of stents placed between the EUS and EGD cohorts in this study. It has been our experience that 10F stents are more difficult to deploy when using the GF-UCT 140 linear echoendoscope, because the biopsy channel is only 3.7 mm, whereas 7F stents can be easily deployed. This is particularly relevant when performing transmural drainage via the duodenum where the echoendoscope is acutely angulated in position. However, the biopsy channel is 4.2 mm in the TJF-160 duodenoscope, and there is no difficulty in placing 10F stents. Although it is technically possible to place 10F stents via the echoendoscope, the procedural duration is longer given the difficulty encountered while placing them. In a prior study reported by our group,[20] in which we deployed 10F stents when using the echoendoscope, the procedural duration for EUS-guided drainage of PFC was longer compared with only 20 minutes in the present study. Four, this study was not powered to detect a statistically significant difference in rates of complications between both cohorts. Post hoc analysis showed that a sample size of at least 112 (56 in each group) or 146 (73 in each group) would have been required (alpha 0.05 and power 80%) to detect a statistically significant difference between the 2 cohorts for ITT (0% vs 13.3%) and as-treated analysis (4.2% vs 20.0%), respectively. However, we believe that the differences observed in this study with regard to

complications are clinically significant. Other studies showed a difference in rates of complications of only 1% to 3% between EUS and EGD.[13,20] Five, the duration of follow-up of patients after pancreatic pseudocyst drainages was short and hence the long-term clinical outcomes were not evaluated. At a mean follow-up of 142 days (range 116-254 days), there was no clinical recurrence of the pseudocyst in any patient. Although this was not the primary objective of this study, a long-term follow-up is required for definitive evaluation of a durable response to therapy and for assessing complication risks. In conclusion, when available, EUS should be considered as the first-line treatment modality for endoscopic drainage of pancreatic pseudocysts given its high technical success rate.

DISCLOSURE

The authors report that there are no disclosures relevant to this publication.

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Current affiliations: Division of Gastroenterology-Hepatology (S.V., A.T., C.M.W.), Department of Surgery (J.D.C., E.R.D.), University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, USA.

Reprint requests: Shyam Varadarajulu, MD, Division of Gastroenterology-Hepatology, University of Alabama at Birmingham Medical Ctr, 410 LHRB, 1530 3rd Ave S Birmingham, AL 35294.