Safety and Efficacy of Endoscopic Ultrasound-Guided Drainage of Pancreatic Fluid Collections With Lumen-Apposing Covered Self-Expanding Metal Stents

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BACKGROUND & AIMS: Plastic stents, placed via endoscopy to drain pancreatic fluid collections (PFCs), require repeat access. Covered metal stents are larger in diameter and can be inserted in a single step, but can migrate. We evaluated the safety and efficacy of a lumen-appro sing, covered, self-expanding metal stent (LACSEMS) for PFC drainage.

METHODS: We performed a prospective study of the outcomes of stent placement in 33 patients (18 men; age, 53 ± 14 y; 28 with chronic pancreatitis) with symptomatic pancreatic pseudocysts and walled-off necrosis (≥6 cm with ≥70% fluid content). Subjects were enrolled at 7 tertiary care centers (6 in the United States and 1 in Europe) from October 2011 through August 2013. Cystenterostomies were created based on endoscopist preference. Safety outcomes included infection, bleeding, perforation, tissue injury, and stent migration. Efficacy end points included LACSEMS placement, patency, and removal, as well as 50% or more reduction in PFCs.

RESULTS: The mean size of the patients’ PFCs was 9 ± 3.3 cm. LACSEMSs were placed successfully via endoscopic ultrasound guidance in 30 patients (91%); the remaining 3 patients received 2 double-pigtail stents. One subject could not be evaluated because of a pseudoaneurysm. In the patients receiving LACSEMSs, PFCs resolved in 27 of 29 (93%). Overall, PFCs resolved in 30 of 33 patients (91%). Endoscopic debridement through the LACSEMS was conducted in 11 subjects. Complications (15%) included abdominal pain (n = 3), spontaneous stent migration, back pain (n = 1), access-site infection, and stent dislodgement (n = 1).

CONCLUSIONS: LACSEMSs were placed successfully in 91% of subjects with PFCs. Overall, 93% had PFC resolution. Advantages of LACSEMSs over other stents include single-step deployment and the ability to perform endoscopic debridement with minimal stent migration. Clinicaltrials.gov: NCT01419769.

Keywords: Pseudocyst Drainage; EUS; Axios; Clinical Trial.

Pancreatic fluid collections (PFCs) include acute peripancreatic fluid collections, pancreatic pseudocysts, acute necrotic collections, and walled-off pancreatic necrosis (WON) that are encapsulated collections with necrosis after 4 weeks. Pancreatic pseudocysts (PPs) can result from pancreatic inflammation resulting from pancreatitis, trauma, or pancreatic ductal obstruction.1,2 The incidence of pseudocysts in acute pancreatitis is 5% to 16% and 20% to 40% in chronic pancreatitis. Symptomatic PFCs may be treated surgically, percutaneously, or endoscopically.3–5 Surgery is associated with higher rates of morbidity (7%–37%) and mortality (6%)6 whereas the external catheter in

Abbreviations used in this paper: EUS, endoscopic ultrasound; LACSEMS, lumen-apposing, covered, self-expanding metal stent; PFC, pancreatic fluid collections; PP, pancreatic pseudocyst; WON, walled-off necrosis.
percutaneous treatment increases the risk of infection or the formation of a pancreaticocutaneous fistula.7–9

With more recent technical advances and experience, endoscopic drainage now is widely accepted and has replaced surgery as the first-line therapy for pseudocyst drainage owing to its less invasive nature, shorter recovery times, lower cost, and lower complication rates.9

The median rates of endoscopic PFC drainage for technical success, PFC resolution, complications, and recurrence associated with transmural pseudocyst drainage were 93.8%, 87.5%, 16.9%, and 7.5%, respectively.10–21 Under endoscopic ultrasound guidance, the clinical success rate for pancreatic fluid collection drainage was 89.14%, with a complication rate of 10.7% (range, 0.26–3.3%).19

The endoscopic transmural drainage procedure involves the following 3 main steps: (1) accessing the pseudocyst by creating a tract, (2) tract dilation, and (3) placing a drainage device. Plastic pigtail stents of varying sizes (7F–10F) and covered self-expanding metal stents are used as the drainage device.22–25 Although the pigtail feature of the plastic stents prevents migration, their narrow lumen may cause premature occlusion requiring frequent stent exchanges or placement of additional stents.25 Fully covered, self-expanding biliary metal stents offer a larger-diameter lumen for a more efficient and shorter duration of drainage and longer patency.10,13 However, they are tubular and may migrate,3 resulting in inefficient drainage, content leakage, retrieval and replacement of migrated stent, and possible mucosal injury.22

Recently, a study conducted by Itoi et al27 reported the use of a novel “barbell-shaped,” lumen-apposing, covered, self-expanding metal stent (LACSEMS). The device allows endoscopic ultrasound (EUS)-guided, transmural endoscopic drainage of pancreatic pseudocysts into the upper gastrointestinal tract through its large lumen and its ability to appose the PFC wall to the stomach or duodenal wall. The LACSEMS were placed successfully in 15 patients, with no pseudocyst recurrence during the 11.4-month median follow-up period and only 1 stent migration.22

Gornals et al26 compared 9 PFC patients with LACSEMS with 10 previously consecutively recruited PFC patients with plastic stents and reported similar technical (88.8%) and clinical (100%) success rates. However, the plastic stent group reported a higher number of stents (n = 15) and a higher median procedure time (42.8 ± 3.1 min), 2 migrations, 2 recurrences, and 2 complications.

The aim of this multicenter, single-arm study was to evaluate the safety and efficacy of the LACSEMS for the transmural drainage of symptomatic PPs and WON.

Methods

The study was a prospective, multicenter, nonblinded, single-arm study conducted from October 2011 to August 2013 at 7 tertiary care centers. The trial was performed under an Investigation Device Exemption seeking Food and Drug Administration clearance.

The primary end point was achievement of PFC resolution, defined as reduction in PFC size to 50% or less than initial size, after 30 or 60 days after LACSEMS placement.

Device Description

The LACSEMS (Axios; Xlumena, Mountain View, CA) consists of a barbell-shaped, flexible, fully covered, self-expanding nitinol stent housed within a catheter-based delivery system. The stents are available in 2 sizes (lumen diameter x length): 10 × 10 mm and 15 × 10 mm. The 10-mm saddle length is designed to appose the stomach or duodenum to the PFC wall.

The stent was intended for temporary implantation (up to 60 days) and was removed upon confirmation of PFC resolution.

Operator Training

Advanced endoscopists with experience in therapeutic endoscopy and endosonography underwent a training session consisting of didactic review and performance of the procedure on an animal model. A LACSEMS placement under EUS guidance and removal was performed.

Patient Screening and Intervention

Adults (age, 18–75 y) with symptomatic PPs or WON meeting all of the following criteria were included: 6 cm or greater diameter (based on the computed tomography scan or transabdominal ultrasound), adherence to bowel wall, and 70% or more fluid content. Cystic neoplasms and immature pseudocysts were excluded.

Subjects were enrolled in the trial within 30 days of screening. Radiographic evaluation (abdominal computed tomography, transabdominal ultrasound, or magnetic resonance imaging) was conducted within 30 days of intervention to characterize the PFC size, fluid content, and relationship to the bowel wall. Radiographic evaluation was conducted 30 days after stent placement and repeated at 60 days after the procedure only if the PFC was unresolved at 30 days.

Intervention. The procedure was performed under monitored or general anesthesia using a therapeutic linear array echoendoscope (Olympus Medical, Tokyo, Japan). Endoscopic ultrasound was performed to locate the PFC, measure and confirm the size, assess the fluid content, and evaluate bowel wall adherence.

An access tract was created (Figure 1A) using conventional endoscopic tools as per the endoscopist’s preference (eg, a fine-needle aspiration needle, needle knife, or cystotome) followed by placement of a
0.035-inch guidewire. The needle was removed, and the tract was dilated using either a dilating bougie (6F–10F Soehendra dilator; Cook Medical) or a dilating balloon (4- or 6-mm Hurricane; Boston Scientific, Natick, MA).

The selection of a 10-mm or 15-mm stent diameter was based on the contents of the PFC and the presence of solid debris identified on EUS. A 15-mm diameter was preferred for PFCs containing solids or necrotic material, allowing for subsequent debridement, irrigation, and cystoscopy. The LACSEMS was inserted over a guidewire, and the distal stent flange was deployed. After the stent’s distal flange position against the inner pseudocyst wall was verified via EUS, the proximal flange was deployed within either the stomach or the duodenum under endoscopic visualization (Figure 1B). Visualization of drainage through the stent was considered successful placement (Figure 1C and D). After deployment, balloon dilation (up to 10 mm) through the stent was performed per the endoscopist’s preference.

Necrosectomy sessions for walled-off necrosis were performed at the discretion of the endoscopist, typically every 2 days until complete clearance of the necrosis.

PFC resolution was assessed at 30 or 60 days. If resolved, a snare large enough to fit over the proximal flange of the LACSEMS was placed and then tightened until the stent lumen (saddle) collapsed, enabling removal of the stent during endoscopy.

Antibiotic therapy was initiated preoperatively, after the placement procedure patients were required to receive ciprofloxacin 500 mg orally twice daily (or acceptable alternative antibiotic therapy) until 1 week after stent removal.

Inspection of flow, tissue changes, and endoscopic documentation were obtained at the time of stent placement and removal. A follow-up office visit was conducted 7 days after stent removal. Endoscopy was performed at 7 days only if ulceration was noted at the site of stent removal during the stent removal visit.

Nonserious and serious adverse events were monitored for up to 6 months after stent removal and were determined either to be related or unrelated to stent implantation and/or the endoscopic procedure.

Analyses

A review of published endoscopic transmural PFC drainage data within the past 5 years was performed to discern the specific complication rates (0% to up to 44.4%) and technical/clinical success rates (80%–100%) to calculate a sample size of 30 subjects based on safety and effectiveness rates. Thirty-three subjects were enrolled to account for drop-out and loss to follow-up evaluation.

Effectiveness end points included the following: stent lumen patency at 30 days and/or 60 days, stent removability at 30 days and/or 60 days, technical success, and PFC resolution. The safety end point was defined as freedom from major complications through the 1-week duration after stent removal study period.

The end points were analyzed for both the intent-to-treat and per-protocol populations.

PFC resolution was defined as at least a 50% decrease in PP size, based on radiographic analysis at 30 days and/or 60 days. Technical success was defined as placement of the LACSEMS and removal of the LACSEMS using a standard endoscopic snare.

The primary end points were evaluated through 1 week after stent removal; overall safety was captured as adverse events and continued until study termination.

Evaluations were performed at baseline, the 30-day and/or 60-day visits, 1 week after stent removal, and at 3 and/or 6 months after stent removal.

All authors had access to the study data and reviewed and approved the final manuscript.

Results

Demographics

From October 2011 to August 2013, there were 33 patients (18 men; age, 53 ± 14 y) enrolled. Etiologies included the following: pancreatitis of unknown etiology, 45% (n = 15); gallstone pancreatitis, 18% (n = 6); alcohol-induced pancreatitis, 18% (n = 6); postsurgical pancreatitis, 12% (n = 4); and other indications, 6% (n = 2) (Table 1). Gallstone disease and alcohol abuse were present in 20% of subjects. Two subjects had
Efficacy Data

LACSEMSs were placed successfully in 30 of 33 (91%) patients with no intraoperative complications (Table 2). The remaining 3 patients received double-pigtail stents. LACSEMS placed included 18 of the 10 × 10 mm size and 12 of the 15 × 10 mm size. Stent patency was confirmed with drainage visualized for all stents placed. Unsuccessful LACSEMS deployment in 3 subjects was caused by stent malposition (n = 2) and delivery handle malfunction (n = 1). The procedure time was 64 ± 38 minutes. The total fluoroscopy time was 4.5 ± 3.4 minutes (n = 21). The mean length of hospital stay was 6.6 ± 13.6 days (n = 29). Eleven of 29 subjects were discharged the same day.

One subject was not evaluable because of a pseudoaneurysm and had plastic stents and a nasocystic tube placed in an additional puncture site, alongside the LACSEMS to drain blood clots. The LACSEMS was removed after 79 days without any further complications.

For the rest of the 29 LACSEMS patients, stents remained implanted for 31 days in 20 patients (±9.9 d) and for 67 days in 9 patients (±10.8 d). Lumen patency was 93% (27 of 29) at stent removal. Three subjects had debris, resulting in partial occlusion at 30 days or earlier after placement.

Eleven WON subjects underwent a total of 22 direct endoscopic debridement sessions through the indwelling LACSEMS and PFC resolution was achieved in 10 subjects. Seven of the 22 debridement procedures were performed when the subject showed septic symptoms such as fever (n = 3), abdominal pain (n = 4), or infection (n = 2).

The LACSEMS removal success rate was 96.7% (29 of 30). Tissue changes after stent removal included mild hyperplastic tissue reaction (n = 8), minor self-limiting bleeding (n = 2), mucosal overgrowth (n = 1), and granulation tissue (n = 1). In all cases, LACSEMS removal proceeded with no clinical sequelae.

During subsequent endoscopies, 3 subjects had plastic stents placed through the LACSEMS for the following reasons: treatment of a collapsed pseudocyst wall onto the distal end of the LACSEMS before complete drainage, treatment of LACSEMS dislodgment after debridement, and treatment of partially occluded LACSEMS caused by necrosis.

PFC resolution. Overall, PFC resolution was achieved in 30 of 33 (91%) subjects. Per-protocol PFC resolution was achieved in 27 of 29 (93%) subjects who received LACSEMSs, including subjects who had plastic stents placed or alongside the LACSEMS. Ten of 29 LACSEMS subjects had repeat endoscopic interventions.

Two of the 3 subjects who received plastic stents only achieved PFC resolution.

The mean PFC size was 9 ± 3.3 cm. The PFC size decreased significantly (6.7 cm; 95% confidence interval, 4.3–9.1 cm) from the time of LACSEMS placement to 30 days after placement.
5.6–7.8; P < .0001) from baseline (10 ± 4 cm) to 30 days after stent placement (3.4 ± 3.9 cm). For 10 subjects, the PP size was 1.9 ± 1.6 cm at 60 days.

**Safety Data**

One LACSEMS subject was not evaluable because of a pseudoaneurysm. One subject required stent removal at 21 days owing to partial debris occlusion. One subject with severe necrotizing pancreatitis had their LACSEMS dislodged inadvertently during debridement performed at 18 days. This patient had both percutaneous and subsequently surgical debridement, and is clinically well 30 months after enrollment. One subject experienced spontaneous stent migration at 43 days as a result of unknown causes.

Complications were noted in 5 (15.2%) patients and included access-site infection (n = 1), stent migration/dislodgement (n = 1), back pain (n = 1), fever with prolonged hospitalization (n = 1), and abdominal pain requiring endoscopy (n = 1).

**Discussion**

Endoscopic drainage of pancreatic pseudocyst is now the preferred option at many tertiary centers. A randomized controlled trial by Varadarajulu et al. comparing endoscopic with surgical cystogastrostomy showed that endoscopic treatment was associated with shorter hospital stays, better physical and mental health of patients, and lower cost.

Compared with conventional transmural drainage, EUS-guided drainage is beneficial in defining the characteristics of a PFC, especially if nonbulging, identifying intervening vasculature and ruling out malignancies. A meta-analysis conducted by Panamonta et al. compared EUS-guided drainage with conventional transmural drainage and experienced a higher technical success rate for EUS-guided drainage compared with conventional transmural drainage.

Conventionally, multiple plastic stents typically are placed to drain PFCs. However, the migration rates, the smaller diameter, and the need for repeat guidewire access through the enterostomy for multiple stent placements, has necessitated alternative options such as placing metal stents to permit efficient drainage. Talreja et al. published a study on the efficacy of using fully covered metal stents with fins to drain PFCs.

The study by Penn et al. placed double-pigtail plastic stents through off-label, biliary, fully covered, self-expanding, biliary metal stents to anchor the metal stents and reduce migration and allow for drainage along the length of the plastic stents.

Because of the barbell shape of the LACSEMS, the placement of plastic stents through the LACSEMS would not be required because the large diameter ensures apposition and a reduced risk of migration. In addition, luer-locking the delivery system to the echoendoscope working channel ensured single-step deployment. Antilhon et al. and recently Mangiavillano et al. reported that single-step, EUS-guided drainage of PFC is more successful than a 2-step technique.

We showed a technical success rate of 91% and a PFC resolution rate of 93%. Stent patency was 93% at the time of removal. Sixty-nine percent of the LACSEMS patients achieved PFC resolution at 30 days. The 3 unsuccessful LACSEMS placements may have been related to limited operator experience at the study onset and 1 device malfunction. Gornals et al. reported one unsuccessful attempt (n = 9) and Itoi et al. reported none (n = 20). It is likely that technical success will increase with additional experience and use.

Itoi et al. also evaluated the LACSEMS for gallbladder drainage (n = 5), with immediate resolution of acute cholecystitis after stent implantation. Turner et al. successfully used the LACSEMS for gallstone removal and cholecystoduodenal drainage in a patient with cholecystitis and unresectable cholangiocarcinoma.

A distinct advantage of the anchoring design and large lumen diameter of this device is the ability to perform direct endoscopic necrosectomy through the stent using a standard 9.2-mm gastroscope while maintaining stent integrity, especially if the 15-mm diameter stent is used. In this study, we performed 22 debridement sessions in 11 WON patients. The large diameter enables endoscope advancement into the PFC for debris removal while the flanges keep the stent in place.

Although our study was a large, multicenter, prospective assessment of the LACSEMS, it only evaluated a single cohort with no control arm.

In conclusion, our study showed that the LACSEMS is safe and efficient for PFC drainage. Advantages of LACSEMS compared with other stents include single-step deployment and the ability to perform direct endoscopic debridement with minimal stent migration. Whether the safety and efficacy of LACSEMS is superior to conventional double-pigtail plastic stents for pseudocyst drainage would require a prospective, randomized, controlled trial.

**Uncited References**

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**References**


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