Journal of the Canadian Association of Gastroenterology, 2020, 3(1), 26–35
doi: 10.1093/jcag/gwy049
Original Article
Advance Access publication 12 September 2018

OXFORD

Original Article

The Evolution of EUS-Guided Transluminal Drainage for the Treatment of Pancreatic Fluid Collections: A Comparison of Clinical and Cost Outcomes with Double-Pigtail Plastic Stents, Conventional Metal Stents and Lumen-Apposing Metal Stents

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Abstract

Background: While most pancreatic fluid collections (PFCs) resolve spontaneously, endoscopic ultrasound-guided transluminal drainage (EUS-TD) may be necessary. EUS-TD has evolved from multiple double-pigtail plastic stents (DPPS) to fully covered self-expanding metal stents (FCSEMS) and lumen-apposing metal stents (LAMS). This study compares clinical attributes of DPPS, FCSEMS and LAMS.
Methods: This is a single-centre retrospective review of EUS-TD for PFCs. The primary outcome was clinical success. Secondary outcomes were technical success, procedure time, hospital length of stay (HLOS), number of endoscopies, need for necrosectomy, adverse events (AEs) and overall cost.
Results: Fifty-eight patients (37 male, average age 49 years) underwent a total of 60 EUS-TD procedures for PFCs (average size 11.2 cm with 29 pseudocysts and 29 walled-off necrosis). Ten patients (17%) underwent EUS-TD with DPPS and 48 patients (83%) with metal stents (32 FCSEMS, 16 LAMS). Overall technical and clinical success was 100% and 84%, respectively. Lumen-apposing metal stents had shorter procedure times (14.9 versus 63.6 DPPS, 39.1 min FCSEMS, $P < 0.001$), and no difference in AEs (3 of 16 versus 4 of 10 DPPS, 12 of 34 FCSEMS, ns). Double-pigtail plastic stents required more endoscopies (3.7 versus 2.3 LAMS, 2.3 FCSEMS, $P = 0.013$) and necrosectomies (4 of 10 [40%]) compared with 5 of 34 [15%] in the FCSEMS group and 3 of 16 [19%] in the LAMS group, respectively, $P = 0.001$) to achieve clinical resolution. The overall cost and HLOS was not significantly different between groups.
Conclusion: The use of LAMS for PFCs is not associated with any significant increase in cost despite technical (shorter procedure time) and clinical advantages (shorter indwell time, reduced need for necrosectomy and no increase in AEs).

Keywords: *Cyst drainage; Endoscopic ultrasound; Metal stent; Pancreatic fluid collections*

Pancreatic fluid collections (PFCs) develop most commonly as a result of severe acute pancreatitis. The revised Atlanta classification categorizes PFCs based on time elapsed from the episode of pancreatitis and the presence of necrosis (1). Although most PFCs resolve spontaneously, intervention for drainage may be necessary for infected walled-off necrosis (WON) or when a

Received: May 4, 2018; Accepted: September 3, 2018.

large pancreatic pseudocyst (PP) or WON causes compression of the gastroduodenal sweep or the biliary system, causing clinical symptoms such as abdominal pain, early satiety, gastric outlet obstruction or jaundice (2–5). There has been a paradigm shift from conventional treatment options of percutaneous drainage and open surgical drainage to less invasive modalities including endoscopic ultrasound-guided transluminal drainage (EUS-TD) and minimally invasive surgery, specifically video-assisted retroperitoneal dissection (VARD) (6–10). A randomized controlled trial (RCT) comparing EUS-TD to surgical cyst-gastrostomy found similar outcomes for successful treatment of pancreatic pseudocysts but with a shorter hospital stay and decreased overall cost (8). For infected WON, endoscopic transluminal necrosectomy (ETN) was associated with less morbidity and mortality than surgical debridement (7). However, because necrosectomy has an associated risk of complications (11–14), a step-up approach is gaining traction, with necrosectomy being reserved for those not responding to initial EUS-TD with or without irrigation (6, 7, 12, 15, 16). The results of the TENSION trial will provide more evidence on this (17). EUS-TD has evolved from multiple double-pigtail plastic stents (DPPS) to the use of metal stents as there is increasing literature reporting enhanced drainage and ease of necrosectomy, when needed, with metal stents (18–21). The recent trend in endoscopic ultrasound-guided transluminal drainage involves the use of a lumen-apposing metal stent (LAMS), with significant improvements in the ease of placement and ability to perform necrosectomy, although there have been concerns regarding buried stent and an increase in bleeding complications (22). In addition, because of a significantly higher upfront cost of the LAMS, there is a perceived overall increase in the cost of the procedure (23, 24).

This study examines the efficacy, safety and costs of EUS-TD for PFCs by comparing DPPS, fully covered self-expanding metal stents (FCSEMS) and LAMS.

METHODS

This is a retrospective review of EUS-TD of PFCs performed by 2 experienced endoscopists (CT and GS) at the University of Alberta Hospital, Edmonton, Alberta, from November 2010 to May 2018. Patients were included if they were more than 18 years of age and had an appropriate indication for drainage of a PFC. Indications for EUS-TD included abdominal pain, limitation of oral intake, symptoms of gastric or biliary obstruction, anorexia/weight loss, enlarging PFC or signs of infection of the PFC. Patients with coagulopathy (International Normalized Ratio > 1.5), thrombocytopenia (platelets < 50,000 mm^3), or active anticoagulation/antiplatelet medication were excluded. Patient demographic data including age, gender, cause of pancreatitis and size of PFC were collected. Efficacy was the primary outcome and was measured by clinical success (sustained resolution of the PFC at three months after stent removal). Secondary outcomes were technical success (successful procedure), time of procedure, hospital length of stay (HLOS) related to intervention, number of endoscopies from initial stent placement to three months after stent removal, number of times necrosectomy was performed, and adverse events (AEs) occurring up to 30 days after initial stent insertion.

Procedural Details

DPPS technique

All procedures were performed with a therapeutic linear echo-endoscope with a working channel of 4.2 mm (GF-UCT180, Olympus America, Centre Valley, PA, USA) under general anesthesia. Endosonographic interrogation of the PFC was done to assess for presence of necrotic material. Once an appropriate site was identified from the stomach or duodenum, cyst puncture was performed with a 19-gauge needle (Slimline Expect™, Boston Scientific Corporation, Marlborough, MA, USA). Fluid was aspirated and sent for analysis, including levels of amylase and carcino-embryonic antigen (CEA) and cytology and mucin staining. If the aspirate contained pus, the sample was also sent for microbiological assessment. The procedure was aborted if the aspirate revealed fresh blood.

If there were no contraindications to proceeding with EUS-TD, a 0.035-inch guidewire (Jagwire™, Boston Scientific Corporation, Marlborough, MA, USA) was introduced and coiled inside the cyst under fluoroscopic guidance. The needle was removed and a 10 French (Fr) cystotome (Cook Medical, Bloomington, IN, USA) advanced over the wire to create a fistula between the gastric/duodenal lumen and the cyst cavity. After the creation of this cyst-enterostomy (CE), a second 0.035-inch guidewire was advanced through the cystotome and coiled inside the cyst cavity. A balloon dilator (CRE™, Boston Scientific Corporation, Marlborough, MA, USA) was advanced over one of these wires into the cyst under endosonographic visualization. The echoendoscope was then distanced from contact with the mucosal surface, and dilation was performed endoscopically between 10 mm and 15 mm. The size of dilation was at the discretion of the endoscopist. Next, a 7 Fr DP plastic biliary stent was advanced over one of the wires, followed by a second 7 Fr or a 10 Fr DP stent over the other wire in sequence.

Follow-up procedures were performed for those patients with WON, with or without infection or for those patients with a pseudocyst exhibiting signs of secondary infection. Using a standard diagnostic video gastroscope (GIF180 and GIF190, Olympus America, Centre Valley, PA, USA), the CE tract was dilated with a balloon dilator to a size large enough to accommodate a diagnostic gastroscope. Once within the cavity, necrosectomy was performed using a variety of devices such as grasping forceps, snares or retrieval baskets. If irrigation was required to

flush the cavity or soften the necrotic material, a 7 Fr naso-cystic tube was placed within the cavity and flushed with normal saline for 72 hours. If there was evidence of infected necrosis, 100 to 150 mL of 3% hydrogen peroxide were irrigated within the cyst. The interval between endoscopic necrosectomy procedures was determined by the clinical progress of the patient and the discretion of the endoscopist.

FCSEMS technique

The procedural steps in this approach are similar to those for plastic stents up to the creation of the CE with a 10 Fr cystotome. After the cystotome was removed, the delivery system for a fully covered 10-mm wide, 4-cm long FCSEMS (Wallflex™, Boston Scientific Corporation, Marlborough, MA, USA) was then advanced over the single wire into the cyst under endosonographic guidance. At this stage, the echoendoscope was distanced from the mucosal surface to visualize the stent delivery system. Under fluoroscopic and endoscopic guidance, the stent was then fully deployed across the CE. The stent introduction system was then removed, and with the wire still in position within the deployed metal stent, a 7 Fr, 4-cm long DP plastic stent was placed across the metal stent. The purpose of this plastic stent was to anchor the metal stent and minimize migration before the complete resolution of the cyst. If there was evidence of infected WON, a 7 Fr naso-cystic tube was inserted into the cyst cavity and flushed with 150 to 200 ML of normal saline, followed by 100 to 150 ML of 3% hydrogen peroxide. Patients were admitted to the hospital postprocedure only if continuous irrigation via the naso-cystic tube was required. All other patients not requiring placement of a naso-cystic tube were discharged home and followed up in clinic. Patients underwent repeat abdominal imaging in four to six weeks after the EUS-TD and then followed up for stent removal if there was symptomatic and radiographic resolution of the cyst.

If a cystotome was not available, a needle-knife (Cook Medical, Bloomington, IN, USA) was used to create a fistulotomy, followed by a biliary balloon dilator (Hurricaine™, Boston Scientific Corporation, Marlborough, MA, USA) to dilate the tract to 4 mm before introducing the metal stent delivery system. The remainder of the procedure remains the same.

Alternatively, instead of using the straight FCSEMS with an anchoring DPPS within, a bi-flanged metal stent (Hanarostent™, MITech, South Korea) can be used in the same manner but without the need for a DP stent within. The rest of the procedure and follow up remains the same.

LAMS technique

The technique of placing a LAMS (Hot AXIOS™, Boston Scientific Corporation, Marlborough, MA, USA) is significantly different than the steps described for DPPS and FCSEMS. This particular LAMS comes available with an electrocautery-enhanced delivery system as a single device, which enabled the creation of the CE and placement of the stent without the need for accessory or device exchange. Because there was no need for guide-wire management, the entire procedure can be performed completely under endosonographic visualization in any regular endoscopy suite, thereby eliminating the need for a special fluoroscopy suite. We have performed all cases in a regular endoscopy room. The initial puncture was performed and access gained into the cyst. Then by sequentially unlocking and locking individual components of the delivery system, the intracystic flange of the stent was deployed first. This flange was then approximated against the cyst wall and followed by the release of the intraluminal end within the echoendoscope. At this point, by simultaneously pushing the stent outwards from the endoscope channel and moving the echoendoscope away from the mucosal surface, the stent was completely deployed. The placement of the stent was then verified endoscopically. We did not routinely dilate these stents with a balloon dilator and instead allowed the stent to expand on its own account over the next two to four days. We also did not perform necrosectomy at the same session as the initial deployment and would let the clinical/radiographic progress of the patient determine that need.

We performed a CT scan one week after the initial stent placement, and if there was symptomatic and radiographic resolution, the stent was removed within the following two weeks. However, if the clinical progress dictated, or if there was evidence of necrotic material on CT, early necrosectomy was performed as needed. We prefer the total indwell time of the LAMS to be less than three weeks to minimize the risk of a buried stent and stent-induced bleeding (22).

Regardless of the approach used, patients with suspected pancreatic duct (PD) disruption and leak on cross-sectional imaging underwent an attempt at concomitant endoscopic retrograde cholangio-pancreaticography (ERCP) with placement of a plastic PD stent.

Outcome Measures

1. *Primary outcome*
   (a) Clinical success: defined as symptomatic resolution of the PFC at three months after stent removal (or at three months after initial stent insertion if the intent is long-term indwell, such as with a disconnected duct syndrome)
2. *Secondary outcomes*
   (a) Technical success: defined as successful stent placement.
   (b) Time of procedure: calculated as time of esophageal intubation with echoendoscope to time of procedure completion and removal of the echoendoscope ('scope in/scope out' time)
   (c) Hospital length of stay: calculated as number of days spent in hospital when directly related to procedural intervention or subsequent admissions for AEs

(d) Number of endoscopies: counted from initial stent placement to any procedures within three months after stent removal
(e) Number of necrosectomy sessions
(f) Stent indwell time: counted from initial stent placement until removal
(g) AEs: defined as occurring within 30 days after initial stent insertion procedure

Cost Comparison

The total cost of each procedure (in Canadian Dollars) was calculated based on 2017 Alberta Health Services reimbursement codes (hospital and physician reimbursement, Table 1) for each EUS-TD (including anesthesia and radiology costs), all subsequent required procedures including interventions, and HLOS until stent removal or patient death.

Ethics

The institutional ethics review board of the University of Alberta Hospital approved the study.

STATISTICAL ANALYSIS

Data were analyzed using SPSS for Windows (Version 21; IBM, Armonk, NY). Frequencies are shown as mean with 95% confidence intervals. Variables between groups were compared using chi-square for categorical variables, while the student t-test was employed for continuous variables. Results were determined to be significant below an alpha value of 0.05.

RESULTS

Patient Characteristics

Between November 2010 and February 2018, 61 patients were referred for endoscopic drainage of PFCs. On an intention-to-treat basis, three patients did not undergo EUS-TD. Of these three patients, one patient had a bloody aspirate on initial needle puncture early on in our experience and did not undergo EUS-TD (currently, a bloody aspirate does not preclude EUS-TD unless there is objective evidence of active bleeding); and in the other two patients, necrotic debris was felt to be >80% of PFC volume, and for this reason, EUS-TD was not performed. Therefore, 58 patients underwent a total of 60 EUS-TD procedures for symptomatic PFCs (in two patients EUS-TD procedures were performed twice for separate PFCs). There were 37 males (64%), and the average age was 49 years (range 20 to 84 years). The most common cause of the PFC was acute pancreatitis in 53 of 58 patients (91%), and the most common etiology for acute pancreatitis was alcohol in 22 of 53 patients (42%), followed by idiopathic in 15 of 53 (28%), gallstones in 12 of 53 (22%), and other causes in 9 of 53 patients (8%) (post-ERCP in two, hypercalcemia in one, medication-induced in one, malignancy in two, postpancreatectomy collection in two and trauma in one patient).

Measuring the longest dimension on cross-sectional imaging, the average PFC size was 11.2 cm (range 3.6 to 23.8 cm). Based on type of PFC, 29 of 58 patients (50%) had a PP. Of these 29 patients, 28 (97%) were uncomplicated PPs, whereas one (3%) had an infected PP. Of the remaining patients, 16 of 58 patients (28%) had a sterile WON, and 13 of 58 patients (22%) had an infected WON. Endoscopic ultrasound-guided transluminal drainage was performed via a transgastric approach in 53 of 60 procedures (88%) and transduodenal approach in 7 of 60 (12%). Ten patients (17%) underwent drainage with DPPS. All these procedures were done before May 2015, after which a total of 48 of 58 patients (83%) underwent EUS-TD using metal stents (32 FCSEMS and 16 LAMS). Similar to the evolution of EUS-TD drainage from DPPS to metal stents, we saw a progressive change from straight conventional metal stents (e.g., Wallflex™) to bi-flanged conventional metal stents (e.g Hanarostent™) and finally to the LAMS (e.g., Hot Axios™). The baseline characteristics of patients and pancreatic fluid collections according to type of stent used for drainage are summarized in Table 2.

Three patients (5%) had concomitant ERCP and insertion of a transpapillary plastic pancreatic duct stent for documented pancreatic duct leaks. Ten patients (16%) underwent placement of a naso-cystic tube for infected WON at the time of EUS-TD with subsequent irrigation of the cavity for 48 to 72 hours.

Outcome Measures

The outcome measures are listed in Table 3. On an ITT basis, EUS-TD was successful in 58 of 61 patients (95%) that were referred for endoscopic management of PFCs. The procedure was technically successful in 58 of 58 patients (100%) when EUS-TD was attempted. The average procedure time was significantly shorter for LAMS compared with DPPS (14.9 [11.8,19.3] minutes versus 63.6 [46.3,85.9] minutes, $P < 0.001$) and FCSEMS (14.9 [11.8,19.3] minutes versus 39.1 [34.1,45.2] minutes, $P < 0.001$). While LAMS required significantly fewer endoscopic procedures compared with DPPS (2.3 [2.0,2.6] versus 3.7 [2.7,5.6], $P = 0.021$), the number of procedures did not differ between LAMS and FCSEMS (2.3 [2.0,2.6] versus 2.3 [1.9,2.7], $P = 0.788$). Neither the number of patients who required necrosectomy (4 of 10 [40%] DPPS, 5 of 34 [15%] FCSEMS, 3 of 16 [19%] LAMS) nor the average number of necrosectomy procedures performed (0.9 [0.2,1.7] DPPS, 0.24 [0.4,0.5] FCSEMS, 0.31 [0.1,0.5] LAMS) was significantly different among the stent groups. The average stent indwell time was significantly shorter for LAMS compared with DPPS (22.9 [17.7,27.2] days versus 212.5 [119.0,312.5] days, $P < 0.001$) and FCSEMS (22.9 [17.7,27.2] days versus 103.5 [75.0,136.0] days, $P = 0.001$).

Table 1. Costs associated with EUS-guided cyst-gastrostomy (all costs in $CDN based on 2017 Alberta Health Services reimbursement rates)

Diagnostic imaging component	
Radiology technician time, benefits, and clerical costs	55.56
Radiographic film (digital) and contrast	81.84
Fluoroscopy equipment service package (per case) ($25,000 per year/800 ERCPs)	31.25
Radiologist reimbursement fee	29.03
Gastroenterology Component	
Nursing salary and benefits (RN for procedure room and LPN for recovery room)	
RN	60.25
LPN	39.94
Medications (unit price)	
Midazolam (per mg)	1.25
Fentanyl (per 100 μg)	0.44
Diazemuls (per 5 mg)	1.15
Medical and surgical supplies (including gloves, IV tubing, O2 tubing etc.), scope disinfection and laundry	80.00
Endoscopy equipment service package (service contract with vendor per ERCP)	12.00
Lumen apposing metal stent	5000.00
Metal biliary fully covered (10 mm x 40 mm) stent	1500.00
19-gauge cyst access needle	235.00
10 French cystotome	395.00
10 French plastic biliary double-pigtail stent	195.00
7 French plastic biliary double-pigtail stent	195.00
Pushing catheter	60.00
Locking device for short-wire system	90.00
Stent extraction snare	11.00
Extraction basket	270.00
Balloon dilator	150.00
0.035-inch guide wire	100.00
Naso-biliary drain	218.00
Collection bag	15.00
Foreign body grasping forceps	185.00
Hydrogen peroxide 1 bottle (240 ml)	2.00
Gastroenterologist reimbursement fee	
EUS	205.19
Sphincterotomy	113.99
Gastroscopy	113.99
Balloon dilation	72.12
Stent insertion	113.99
Naso-biliary drain insertion	50.23
Anesthesia Component	
Anesthesia drugs	27.00
Anesthesia cost/case for GA (cost of gases, tubing, ECG leads etc.)	100.00
Anesthesia tech time and benefits ($50/hr)	50.00
Anesthesiologist reimbursement ($18.10 per 5 min)	217.20
Inpatient component	
Cost of medical ward/day	973.00
Cost of intensive care unit/day	3296.00

EUS, endoscopic ultrasound; CDN, Canadian; RN, registered nurse; LPN, licensed practising nurse; GA, general anesthesia

Table 2. Baseline patient demographics and characteristics of PFCs according to stent group

	DPPS	FCSEMS	LAMS
Patients (n)	10	32	16
Gender (M:F)	6:4	21:11	10:6
Age in years, (mean)	49	51	42
Etiology of PFC			
Acute pancreatitis (all causes)	10	29	14
Malignancy	-	2	-
Post-pancreatic resection	-	-	2
Trauma	-	1	-
Type of PFC			
PP	7	13	9
WON	2	9	5
Infected WON	1	10	2
Mean size of PFC, cm	11.5	11.3	10.9
Cost of stent(s) ($CAN)	390*	1695**	5000
Cost of initial EUS-TD ($CAN)	2814	3837	6020

PFCs, Pancreatic fluid collections; DPPS, Double-pigtail plastic stents; LAMS, Lumen-apposing metal stents; PP, Pancreatic pseudocyst; WON, Walled-off necrosis; *cost of 2 DPPS; **cost of 1 FCSEMS + 1 DPPS

Table 3. Procedure characteristics and outcome measures in 58 patients (60 stents)

	DPPS	FCSEMS	LAMS	*P-value*
Site of EUS-TD				
Trans-gastric	8	30	15	
Trans-duodenal	2	4	1	
Technical success (%)	100	100	100	
Mean procedure time, min [95%CI]	63.6 [46,86]	39.1 [34,45]	14.9 [12,19]	$P < 0.001$
Mean procedures per patient, n [95% CI]	3.7 [2.4,4.9]	2.3 [2.0,2.6]	2.3 [2.0,2.5]	$P = 0.013$
Patients requiring necrosectomy (n)	4	5	3	$P = 0.001$
Mean necrosectomy sessions, n [95% CI]	0.9 [0.1,2.0]	0.24 [0.03,0.5]	0.31 [0.1,0.6]	*ns*
Mean stent indwell, days [95% CI]	212.5 [119,313]	103.5 [75,136]	22.9 [18,27]	$P < 0.001$
Mean HLOS, days [95% CI]	8.9 [3.2,15.7]	10.5 [5.6,17.4]	4.9 [1.1,8.8]	*ns*
Adverse events, n (%)	4 (40)	12 (35)	3 (19)	*ns*
Mortality (n)	0	2	0	*ns*
Recurrence (n)	1	1	0	*ns*
Clinical success, n (%)	8 (80)	24 (75)	14 (88)	*ns*
Mean total cost in $CDN [95% CI]	15,782 [8106,26708]	14,243 [10000,19327]	10,929 [7983,14668]	*ns*

DPPS, Double-pigtail plastic stents; LAMS, Lumen-apposing metal stents; EUS-TD, endoscopic ultrasound-guided transmural drainage; SD, standard deviation; HLOS, Hospital length of stay

The mean overall follow-up time for LAMS was significantly shorter as these stents have only been recently available at our institution (4.5 [3.8,5.2] months versus 20.1 [16.7,23.5] months FCSEMS, $P < 0.001$ and 49.4 [38.4,60.5] months DPPS, $P < 0.001$). While HLOS was shortest among LAMS, this was not statistically significant. The lower number of days in hospital and lower number of overall endoscopic procedures are also reflected in our cost comparison.

The cost of individual stents and the overall cost of the initial EUS-TD procedure are listed in Table 2. The average overall cost for cyst resolution with EUS-TD using LAMS ($CDN 10,929 [7983,14668]) was not higher when compared with DPPS

($CDN 15,782 [8106,26708], $P = 0.254$) and FCSEMS ($CDN 14,243 [10000,19327], $P = 0.392$) as shown in Table 3.

The rate of AEs was similar for DPPS, FCSEMS and LAMS (4 of 10 [40%], 12 of 34 [35%] and 3 of 16 [19%], respectively). Two deaths occurred, both after FCSEMS EUS-TD. One patient died in the ICU within 24 hours of EUS-TD. This patient had an infected WON and was in the ICU with sepsis and severe thrombocytopenia on broad-spectrum antibiotics, vasopressors and continuous renal replacement therapy with a rising serum lactate level before the procedure. He was considered unsuitable for surgical intervention and, as a last resort, underwent EUS-TD. After the procedure, his lactate continued to rise, and he passed away within 24 hours. Cross-sectional imaging could not be performed to ascertain whether or not the EUS-TD had caused an AE responsible for mortality, although we suspect it was SIRS-related multi-organ failure. The second death was a 36-year-old male with alcohol-induced pancreatitis. He underwent EUS-TD (with a bi-flanged FCSEMS) for WON. Nine days following the procedure, he presented at the hospital with melena and syncope. His hemoglobin dropped from 96 g/L to 76 g/L. He underwent urgent gastroscopy showing a clot at the cyst-gastrostomy site. A CT angiogram was performed showing active bleeding from a splenic artery branch. Hepatobiliary surgery and interventional radiology were consulted immediately. Unfortunately, the patient developed massive hematemesis before radiologic intervention and became hemodynamically unstable. Resuscitation efforts were unsuccessful.

Follow-up data were available for 55 of 58 patients (95%). Three patients, two with FCSEMS and one with DPPS, were lost to follow-up. The overall clinical success of EUS-TD was 46 of 55 patients (84%). In subgroup analysis and on intention-to-treat basis, 8 of 10 patients (80%) with DPPS, 24 of 32 patients (75%) with FCSEMS and 14 of 16 patients (88%) with LAMS had clinical success. One DPPS patient had recurrence of the PP, and this was subsequently treated successfully with a FCSEMS. In the FCSEMS group, two patients died (as described previously), two patients had perforations and required surgery, one patient had recurrence of WON secondary to disconnected duct syndrome and underwent distal pancreatectomy and splenectomy, and one patient underwent surgery for failed endoscopic necrosectomy. One patient in the LAMS group had extension of the WON to both para-colic gutters and required surgical drainage even though the retro-gastric collection had effectively decompressed with LAMS placement. One patient in the LAMS group had recurrence of his PFC. This patient had a known pancreatic duct (PD) leak following distal pancreatectomy. He had undergone concurrent transpapillary PD stenting and EUS-TD with full resolution of his pseudocyst at three weeks but represented with symptoms and cross-sectional imaging confirming recurrence of the PFC one month post-LAMS removal. He subsequently underwent removal of his PD stent and EUS-TD with DPPS technique with intent for long-term indwell.

On subgroup analysis between PP and WON groups, no significant difference was found between LAMS, FCSEMS and DPPS with regards to our primary and secondary outcomes.

DISCUSSION

The treatment of pancreatic fluid collections has evolved from percutaneous and open surgical drainage to more minimally invasive approaches (6–10). In patients with WON, with or without infection, there is increasing evidence to support a step-up approach with the need for necrosectomy only in those that do not improve with adequate cyst drainage (25–29). The most important aspect in a step-up approach is the adequacy of drainage during the index EUS-TD procedure. There are published data on the reduced need for necrosectomy after the initial placement of a metal stent (28–30). The self-expanding nature of the metal stent maintains a patent fistulotomy site, thereby enhancing drainage. The latest advance in metal stents are LAMS, which have significant advantages allowing for a quick and safe deployment, wider diameter for improved drainage, access for necrosectomy, and decreased migration (31,32).

Our study describes the evolution of EUS-TD for all types of PFCs (PP, WON and IWON) using three different stent types (DPPS, FCSEMS and LAMS). Initially, DPPS were used for all PFCs. The change in practice occurred as there was improvement in the initial drainage procedure with metal stents. So currently, we preferentially use LAMS as the stent of choice for most PFCs and reserve the long-term indwell of DPPS to pancreatic fluid collections (without necrotic debris) that are refractory to transpapillary or transluminal drainage.

Our results show that although all three techniques had equivalent technical success, the use of LAMS is not associated with any significant increase in cost despite technical (shorter procedure time) and clinical (shorter indwell time, reduced need for necrosectomy and no apparent increase in AEs) advantages. In a similar study, Siddiqui et al. compared DPPS, FCSEMS and LAMS in their retrospective review of 313 patients (106 DPPS, 121 FCSEMS, 86 LAMS) (24). They only included patients with WON, and their overall technical and clinical success was 99% and 89%, respectively. There was a statistically significant difference among the stents used in their study, with DPPS having 81% resolution compared with 95% for FCSEMS and 90% for LAMS. These technical and clinical success rates are similar to ours.

One of the most significant differences we found in the evolution of stent usage is the procedure time. Fully covered self-expanding metal stents were placed in a significantly faster mean time than DPPS (39.1 minutes versus 63.6 ± 30 minutes), whereas LAMS took less than one-half the time compared with FCSEMS (14.9 minutes). Also, the LAMS delivery system is

much easier to use because it is almost completely under the control of the endoscopist avoiding the use of accessories such as wires and dilation balloons and the exchanges over a wire required for them. In two cases of FCSEMS, we experienced intraperitoneal perforations believed to be secondary to the placement of a guide-wire and naso-cystic drain. Furthermore, unlike DPPS and FCSEMS, LAMS do not require fluoroscopy. This makes the procedure safer for both patient and medical staff, saves cost, and allows for the procedure to be performed in any regular endoscopy room. We believe that the use of general anesthesia with airway protection is still beneficial to avoid the risk of aspiration after the cyst-gastrostomy is performed.

On average, patients with DPPS underwent twice as many endoscopies and more necrosectomy sessions compared with both the FCSEMS and LAMS groups. Similar results have also been described in literature (24, 33). On multivariant analysis, Ge et al. found DPPS to be associated with a higher rate of re-intervention when compared with LAMS (34). This is likely due to the smaller calibre of plastic stents and a higher tendency to occlude. Therefore, the initial and ongoing optimization of drainage appears to be the most important factor for a successful outcome. Even with LAMS, Sharaiha et al. found that the 15-mm-wide stent (Hot Axios 10 × 15 mm) had significantly better clinical success rates compared with the 10-mm-wide version (Hot Axios 10 × 10 mm) (35). We only used one 10-mm stent when we did not have a 15-mm stent available. It is our current practice to only use 15-mm LAMS for all PFCs.

While the overall HLOS was not significantly different between the three study groups, more patients in the LAMS group had day procedures performed, and 56% of patients did not require admission during the treatment phase. Published literature also supports this (36).

The mean stent indwell time was significantly different between all three categories of stents and, in our opinion, has evolved with the evolution of these stent types. The mean indwell time was longer for DPPS (213 days) compared with FCSEMS (104 days) and, in the case of two patients in our study, remain in situ indefinitely. This has been described in published literature as a reasonable approach especially in cases where PFC recurrence is considered to be high (37). The mean indwell time for LAMS was 23 days, significantly shorter even than for FCSEMS, but this was because of protocol design. The rationale for this originates from previous studies showing high rates of stent burial and stent-induced bleeding seen with LAMS when left in situ for six weeks or more (22, 24). This seems to be an inherent association because of the lumen-apposing design of LAMS. Bang et al. suggest that LAMS preferably be followed up and removed within three weeks of insertion (22). This formed the basis for our LAMS protocol, which requires a CT scan one week after insertion to determine if the fluid collection has resolved. If symptomatic and radiographic resolution is confirmed, the stent is removed within the following two weeks. If there is concern of persistent necrotic debris on CT scanning, early necrosectomy is performed with removal of the LAMS within three weeks of insertion. In our protocol, no patient experienced stent burial or stent-induced bleeding during the period of LAMS indwell.

Overall, LAMS was associated with fewer AEs than both DPPS and conventional metal stents. These results are similar to those described in published literature (37, 38). We believe that this may possibly be from avoidance of wires and balloon dilators, accessories usually associated with complications. Furthermore, the larger diameter of the LAMS allows better drainage with lower risk of stent occlusion, which avoids the risk of infection. There were no migrations or buried stents in the LAMS group, whereas external stent migration into the lumen occurred with four FCSEMS (12%) and one DPPS (10%).

While LAMS appear to be proving very effective and safe for the EUS-TD of PFCs, the perception is that the significant upfront cost may limit the generalizability of their use. However, our cost comparison of actual expenses incurred showed no significant difference between the three stent types in terms of overall costs of care. Bekkali et al. compared FCSEMS to LAMS and also did not find the overall costs to be statistically different (€17,189 versus €18,221, $P = 0.98$) (36). Ang et al. compared procedure-related costs of DPPS and FCSEMS and concluded that there was no overall cost difference. However, on subgroup analysis of PPs and WONs, it was cheaper to drain noninfected PPs with DPPS versus FCSEMS (33). Mukai et al. also retrospectively compared bi-flanged metal stents with DPPS (39). Their cost analysis revealed no statistical difference. While they did note that DPPS was cheaper overall, when re-intervention was required for complicated WON, the cost of DPPS was greater than with bi-flanged metal stents (39).

It is quite clear that LAMS appear to be more cost-effective for WON and IWON, but recent data support the use of DPPS for noninfected PPs. Although MRI is superior than CT in identifying necrotic debris (40–42), we do not have timely access to MRI but have daily availability of EUS at our centre. However, we recognize that in very large PFCs, EUS may not be able to identify necrotic debris because of limitations in the range of endosonographic visualization. As a matter of institutional protocol, therefore, we now use metal stents (preferably LAMS) for all inflammatory PFCs and reserve DPPS for those that recur (such as with the disconnected duct syndrome) or those that are noninflammatory in etiology (such as after pancreatic resection, trauma or malignancy). Our cost comparison also supports this practice. As shown in Table 2, our cohort had a significant proportion of PPs (70% in DPPS, 41% in FCSEMS and 56% in the LAMS group) and, despite the higher upfront cost, LAMS are not more expensive than DPPS and FCSEMS and have associated clinical benefits.

There certainly are limitations to our study. This is a retrospective review, and as such, selection and treatment bias can be introduced. Although, our patient demographics and PFC fluid characteristics did not differ significantly among the three study groups. The main limiting factor is that over time there was increasing clinical experience with the procedure so that use of LAMS was associated with performance after the most expertise had been gained (i.e., the most optimal conditions for success). Only one type of LAMS (Hot AXIOS) is available at our institution, and as such, our findings cannot be generalized to other types of LAMS at this time. As LAMS have only recently been available, the mean overall follow-up time for this patient group was shortest, and this limits our ability to predict long-term clinical resolution of PFC post-EUS-TD. Furthermore, the number of patients studied is relatively small.

In conclusion, our results show that DPPS, FCSEMS and LAMS are safe and effective for EUS-TD of PFCs with similar rates of technical success and clinical outcomes. LAMS are superior to both DPPS and FCSEMS because they decrease initial procedure time, avoid fluoroscopy and the use of other endoscopic accessories, have shorter stent indwell time, and lower the rate of AEs. While the initial cost is a concern for many centres, thereby limiting the use of LAMS, we did not find a significant difference in overall costs between the groups. We therefore suggest that LAMS are safe and effective and may be the preferred method of EUS-TD. Adequately sized, randomized, controlled trials are needed to validate these recommendations and assess the generalizability of these results.

ACKNOWLEDGEMENTS

This study was presented as a poster at the Canadian Digestive Disease Week, February 25–29, 2016, Montreal, Quebec, Canada.

Conflicts of Interest

GS is a consultant for Boston Scientific Corporation and has received honoraria for speaking and proctoring engagements. However, no funding was received for the purposes of this study. VF, SK, SS, CT and PDS have no conflict to disclose relevant to this study.

Author Contributions

VF collected and analyzed data, cowrote and edited the manuscript. SK cowrote and reviewed the manuscript. SS analyzed data and reviewed the manuscript. CT reviewed and edited the manuscript. PDS reviewed and edited the manuscript. GS cowrote and edited the manuscript and is the article guarantor.

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