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Title:
Drainage of pancreatic fluid collections using a lumen-apposing metal stent with an electrocautery-enhanced delivery system

Date:
2021-12-01

Citation:
Khan, S., Chandran, S., Chin, J., Karim, S., Mangira, D., Nasr, M., Ermerak, G., Trinh, A., Kia, C. Y. H., Mules, T., Zad, M., Ang, T. L., Johns, E., Tee, D., Kaul, A., Ratanachu-Ek, T., Jirathan-Opas, J., Fisher, L., Cameron, R. ,... Devereaux, B. (2021). Drainage of pancreatic fluid collections using a lumen-apposing metal stent with an electrocautery-enhanced delivery system. Journal of Gastroenterology and Hepatology Australia, 36 (12), pp.3395-3401. https://doi.org/10.1111/jgh.15658.

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Drainage of pancreatic fluid collections using a lumen-apposing metal stent with an electrocautery-enhanced delivery system

ABSTRACT

Background and Aim

Our aim was to evaluate the efficacy and safety of a lumen-apposing metal stent with an electrocautery-enhanced delivery system (EDS-LAMS) for EUS-guided drainage of pancreatic fluid collections (PFCs) in regular clinical practice.

Methods

A retrospective and subsequent prospective analysis was undertaken of all patients who underwent EUS-guided drainage of their PFCs using the EDS-LAMS at 17 tertiary therapeutic endoscopy centers.

Results

208 cases of EDS-LAMS deployment were attempted in 202 patients (mean age 52.9 yr) at time of evaluation. 97 patients had pancreatic pseudocysts (PP), 75 walled-off pancreatic necrosis (WOPN), 10 acute peripancreatic fluid collections (APFC), 6 acute necrotic collections (ANC) and 14 post-operative collections (POC). Procedural technical success was achieved in 202/208 cases (97.1%). Maldeployment occurred in 7/208 cases (3.4%). Clinical success was achieved in 142/160 (88.8%) patients (PP 90%, WOPN 85.2%, APFC 100%, ANC 75%, POC 100%). Delayed adverse events included stent migration in 15/202 (7.4%), stent occlusion and infection in 16/202 (7.9%), major bleeding in 4/202 (2%) and buried EDS-LAMS in 2/202 (1%). PFC recurrence occurred in 13/142 (9.2%) patients. 9/202 (4.5%) required surgical or radiological intervention for PFC management after EDS-LAMS insertion.

Conclusions

This large international multi-center study evaluating the EDS-LAMS for drainage of PFCs in routine clinical practice suggests that the EDS-LAMS are safe and effective for drainage of all types of PFCs; however, further endoscopic therapy is often required for WOPN. Major bleeding was a rare complication in our cohort.

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jgh.15658

KEYWORDS

Endoscopic ultrasound; pancreatitis; pancreatic fluid collections; lumen-apposing metal stents

INTRODUCTION

Pancreatic fluid collections (PFCs) develop as a complication of acute or chronic pancreatitis, abdominal trauma or surgical complications [1-4]. They can be broadly categorized as acute peripancreatic fluid collections (APFC), acute necrotic collections (ANC), pancreatic pseudocysts (PP) and walled-off pancreatic necrosis (WOPN) based on characteristics such as presence/absence of an organized inflammatory wall or necrotic material within the collection, as well as time to development from the pancreatic injury [1]. Postoperative collections (POC) are PFCs that develop as a result of a pancreatic duct leak following pancreatectomy or pancreaticoduodenectomy, and can lead to increased mortality and hospital length of stay [5].

Currently, drainage options for symptomatic PFCs include surgical, percutaneous or endoscopic techniques [2,3,6,7]. Surgical drainage, while effective, is invasive and associated with high rates of morbidity and mortality [2,3,8-10]. Percutaneous drainage with an external drain is associated with a significant risk of fistula formation, higher rates of re-intervention and longer hospital length of stay [3,11]. Endoscopic ultrasound (EUS) allows both excellent assessment of PFCs and surrounding vasculature, as well as direct access for transmural drainage. EUS-guided transmural drainage of PFCs is associated with superior success rate, morbidity, mortality and hospital length of stay [10,12,13]. EUS-guided drainage has therefore become the preferred method for PFC drainage at most centers [13].

The options for EUS-guided drainage include the placement of plastic double pigtail stents (DPS), fully-covered self-expanding metal stents (FCSEMS) and more recently, lumen-apposing fully-covered self-expanding metal stents (LAMS). Advantages of LAMS include a larger diameter, shorter length, bilateral lumen-apposing flanges to prevent migration and easy

access into the PFC cavity for direct endoscopic necrosectomy (DEN) [13]. A novel EDS-LAMS (Hot AXIOS; Boston Scientific, Marlborough, MA, USA) has the added advantage of an electrocautery enhanced delivery system that allows passage of the catheter and LAMS into the PFC with a single EUS-guided puncture, without the need for tract dilatation, guidewire exchanges or the use of fluoroscopy. Recent retrospective studies from the USA and Europe have shown high technical and clinical success rates, with reported adverse event rates ranging between 5 – 14% [14-18]. However, recent small studies have questioned LAMS' superiority over DPS, and raised concerns over higher adverse event rates including major bleeding and buried LAMS [19,20]. Additionally, the novel EDS-LAMS may be associated with higher device costs impacting its overall cost effectiveness [20].

The aim of this large, international, multi-centre study was to evaluate the efficacy and safety of the EDS-LAMS for EUS-guided drainage of symptomatic PFCs in clinical practice.

METHODS

A multi-center retrospective then prospective study was conducted at 17 tertiary therapeutic endoscopy centres (Australia 11, New Zealand 3, Thailand 2, Singapore 1). A standardized data spreadsheet capturing patient demographics, PFC characteristics, procedural details, clinical outcomes and adverse events was distributed to all participating centers for data collection from local databases and patient records. The study received ethics approval from our institutional review board (Austin Health Human Research Ethics Committee) and site-specific authorizations from the other relevant institutional review boards. The study concept and design were investigator initiated and no financial support was received. Data collection was performed in accordance with the provisions of the Declaration of Helsinki.

All consecutive patients who underwent attempted EUS-guided drainage of their PFC with the EDS-LAMS from the time of its introduction in each of the participating centres were included in the study. Data were collected prospectively upon commencement of the study, while data on all consecutive cases prior to this date were collected retrospectively. The commencement date of prospective data collection and therefore the proportion of prospective cases varied

between centres. If a second EDS-LAMS was inserted for PFC non-resolution or recurrence, only the initial EDS-LAMS was included for data analysis. The EDS-LAMS evaluated in this study is a saddle-shaped, nitinol, braided, lumen-apposing metal stent fully covered with a silicon membrane. The stent has bilateral wider flanges designed to anchor the stomach or duodenal wall in direct apposition to the PFC wall and is delivered on an electrocautery-enhanced delivery catheter that allows direct puncture into the PFC. The EDS-LAMS used in this study included the 8mm, 10mm and 15mm lumen diameter stents. The choice of stent diameter was at the discretion of the treating physician.

Procedural Techniques

Indications for drainage and procedural decisions were at the discretion of the treating clinician. PFC drainage was performed using a therapeutic linear echoendoscope. EUS imaging was used to determine the optimal puncture site of the PFC (transgastric or transduodenal) and the EDS-LAMS was then deployed as per the manufacturer's instructions. The use of fluoroscopy and/or the insertion of a guidewire into the cyst cavity was at the discretion of the treating clinician depending on the clinical circumstances. Decisions regarding anesthesia, use of peri-procedural antibiotics, placement of coaxial DPS or nasocystic tubes at index endoscopy, post-procedural management and requirement for direct endoscopic necrosectomy (DEN), and timing of stent removal were determined by individual site or treating clinician preference.

Outcome Measures and Definitions

The PFCs were classified as PP, WOPN, APFC or ANC based on either cross-sectional imaging or EUS findings, as per the Revised Atlanta Classification [1]. Post-operative pancreatic collections (POC) were also included in our study. Infection status of PFC was determined by the treating clinician based on a combination or clinical, biochemical, imaging and/or microbiological assessment. The primary outcome of this study was to evaluate the clinical success rate of EDS-LAMS for the drainage of PFCs, defined as the resolution of PFC at the time of endoscopic LAMS removal without the requirement for ongoing transmural PFC drainage with DPS or another LAMS. Cases where the PFC had resolved but long-term DPS were left in-situ due to disrupted pancreatic duct syndrome were defined as clinical success.

Cases that required either surgical or radiological intervention for management of their PFC following LAMS insertion were not included as clinical success. Patients who did not have their LAMS removed endoscopically were excluded from clinical success analysis, as we felt that the efficacy of the LAMS could not be clearly determined in these circumstances. Secondary endpoints included, procedural technical success, PFC recurrence rates, number of additional endoscopic sessions required for DEN, the requirement for non-endoscopic therapy for management of PFC following LAMS insertion, early adverse events, delayed adverse events and adverse events associated with stent removal. Procedural technical success was defined as successful deployment of the LAMS resulting in drainage of PFC contents into the stomach/duodenal lumen. PFC recurrence was defined as re-formation of PFC requiring further endoscopic management following initial resolution and LAMS removal. Early adverse events were defined as either immediate procedure-related adverse events or adverse events occurring within the first 24-hours of LAMS insertion.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

RESULTS

Patients and Demographics

Between 1st August, 2016 and 30th April, 2019 we identified 202 patients who underwent attempted EUS-guided drainage of their PFCs using the EDS- LAMS following its introduction at 17 centres. The data set includes a retrospective analysis of consecutive patients followed by prospective patient recruitment after ethics approval at individual sites. The date of EDS-LAMS introduction and ethics approval allowing prospective data collection varied at each site. Overall the proportion of retrospective and prospective cases was 77%:23%. The mean age of our patient cohort was 52.9 years (SD 15.8) (Male: 57.9%, Female: 42.1%). The etiology of the PFCs were predominantly gallstone pancreatitis (41.1%), alcohol-induced pancreatitis (26.2%), unexplained acute pancreatitis (12.4%) and post-operative (6.9%). PFCs were sterile

in 53.5% of patients and infected in 46.5%. A higher proportion of APFCs (8/10, 80%), ANCs (5/6, 83.3%) and WOPN (53/75 70.7%) were infected collections compared to pseudocysts (22/97, 22.7%). The mean size of the PFC was 10.6 cms (SD 4.8) in maximal diameter. Patient demographics and PFC characteristics by PFC classification are detailed in Table 1.

Technical Success

A total of 202 EDS-LAMS were successfully deployed from 208 attempts at EDS-LAMS insertion, with an overall technical success rate of 97.1%. The mean procedural time was 36 minutes (SD 22). There were 7 cases of initial maldeployment, none of which occurred into the PFC side. In 1/7 case the maldeployed stent was able to be re-positioned successfully and was therefore not counted as a technical failure. In 5/6 cases of technical failure, a second stent was immediately placed into the same PFC, and in 1/5 of these cases a third stent was then placed into a different PFC at the index endoscopy. In the remaining 1/6 case of technical failure the procedure was abandoned without any further attempts.

Procedural Details

41 patients (20.1%) received either a coaxial DPS (23 patients, 11.4%), a nasocystic tube (13 patients, 6.4%) or both (5 patients, 2.5%) during the same procedure as EDS-LAMS insertion. A total of 73 patients (36.1%) required at least one additional endoscopic procedure for DEN. Overall, an additional 150 sessions of DEN were required across the cohort. This was highest in the WOPN group, where 45 patients (60%) required a total of 111 extra sessions for DEN. The remaining 39 extra sessions for DEN were performed in patients with PP (n= 17: 20 sessions), APFC (n=4: 7 sessions), ANC (n=3: 6 sessions) and POC (n=4: 6 sessions). Complete procedural details are summarized in Table 2.

Clinical Success

Of the 202 EDS-LAMS placed successfully, 160 were removed endoscopically at the time of evaluation of the study data (79.2%). Overall, clinical success was achieved in 142/160 cases (88.8%). The clinical success rate was highest for POCs (11/11, 100%) and APFCs (4/4, 100%), followed by PPs (72/80, 90%), WOPN (52/61, 85.2%), and ANCs (3/4, 75%).

Endoscopic LAMS removal was successful in 160/160 cases (100%). The mean LAMS in-dwelling time was 50.7 days (range 1-281). Reasons for absence of endoscopic removal in the 42 cases include: death with LAMS in-situ (12/42), stent migration (15/42), LAMS yet to be removed at conclusion of data collection (5/42), LAMS intentionally left in-situ indefinitely (1/42), surgical removal (5/42) and lost to follow-up (4/42). PFC recurrence after initial clinical success occurred in 13/142 cases (9.2%). The mean follow-up duration was 15.2 weeks (SD 14.4). Following EDS-LAMS insertion, surgical intervention for PFC management was required in 7/202 (3.5%) patients and radiological intervention in 2/202 (1%) patients. Patients with residual PFC at endoscopic LAMS removal were managed with DPS (12/18, 66%), another LAMS (2/18, 11.1%), surgically (2/18, 11.1%) or conservatively (2/18, 11.1%). A detailed breakdown of clinical outcomes by PFC classification is summarized in Table 2, and by individual site in Supplementary Table.

Early Adverse Events

Procedure-related adverse events included 2 cases (0.9%) of minor bleeding that did not require further endoscopic intervention and 3 cases (1.4%) of immediate post-procedural fever treated successfully with antibiotics.

Delayed Adverse Events

LAMS occlusion and resultant infection necessitating further endoscopic intervention occurred in 16/202 cases (7.9%). The rate of stent occlusion and infection was higher in the WOPN group (11/75 cases, 14.7%) than the PP group (2/97 cases, 2.1%). Overall, there were 15 cases of stent migration into the gastrointestinal lumen (7.4%). In 3 cases stent migration occurred during DEN, and the remainder of cases occurred spontaneously. There were no cases of stent migration into the PFC cavity. Delayed major bleeding as a direct result of the LAMS occurred in 4/202 cases (2%). All 4 cases were due to splenic artery hemorrhage requiring emergency laparotomy in 2 cases, embolization by interventional radiology in 1 case, and resulting in cardiac arrest and subsequent death in the remaining 1 case. Other delayed adverse events included minor bleeding not requiring further intervention in 2/202 cases (1%), PFC leak with peritoneal contamination due to immature WOPN wall in 1/202 case (0.5%), sepsis unrelated

to LAMS occlusion in 4/202 cases (2%) and a cerebrovascular accident in 1/202 case (0.5%). Overall, death with LAMS in-situ occurred in 12/202 cases (5.9%); however, there was only 1 case of death directly attributed to the LAMS. There were no significant adverse events related to transduodenal position of the LAMS.

Adverse Events associated with LAMS Removal

Of the 160 cases where the LAMS was removed endoscopically, there were 3/160 cases of self-limited minor bleeding associated with stent removal that did not require further intervention (1.9%). There were 2/160 cases of buried LAMS (1%). In 1 of these cases (LAMS in-dwelling time 75 days) the LAMS was successfully removed endoscopically following exposure of the LAMS with argon plasma coagulation. The other case resulted in a contained retroperitoneal perforation that resolved with conservative management (LAMS in-dwelling time 30 days). Complete adverse events are summarized in Table 3.

DISCUSSION

This international multi-center study presents data on a large cohort of patients who received the novel EDS-LAMS for drainage of their PFCs. Our findings demonstrate high technical success, overall high clinical success and relatively low adverse events despite long LAMS in-dwelling times. Only a few other studies have specifically evaluated the EDS-LAMS for PFC drainage, but these have shown technical success rates of 98.9 – 100% [15,18,20]. The overall technical success rate in our cohort was 97.1%. Importantly, this data set includes a substantial number of cases early in the experience of many users as data was collected from the point of introduction of this new device at each center. We felt that placement of the EDS-LAMS was relatively straightforward in the majority of cases despite the initial early-user learning curve. Furthermore, the traditional EUS-guided methods of transmural drainage requiring needle access to the PFC, guidewire placement, tract dilatation and multiple guidewire exchanges are often time consuming. The overall mean procedure time for EDS-LAMS placement in our cohort was 36.2 minutes but with a wide range of times between centers (5 – 128 min). Interestingly, 3 of the centers had mean procedure times of less than 20 minutes, suggesting that these LAMS can be inserted time efficiently if required. Additionally, due to its lack of

ancillary equipment requirements and shorter procedure times without the necessity of fluoroscopy, the EDS-LAMS may be feasible to insert in an expanding set of circumstances including unstable patients with high anesthetic risk, or in less familiar environments such as intensive care units.

Our overall clinical success rate was 88.8% with a 90% clinical success rate in the PP group and 85.2% in the WOPN group. Despite small numbers, both the POC and APFC groups had clinical success in 100% of patients. Moreover, only 9 patients (4.5%) required surgical or radiological intervention for management of their PFC following EDS-LAMS insertion. This is comparable to the success rates of the smaller European, United Kingdom and USA cohorts, that have reported clinical success rates of 91-100% for PP and 81-94% for WOPN [14,16,17,18,20,21]. Our clinical success rate was high considering these are, multinational data that reflect a wide range of unit protocols, endoscopist preferences and experience. However, if the cases of LAMS migration (despite PFC resolution), surgically removed LAMS (including those cases where surgery was an adjunct to EUS drainage) and death attributed to LAMS are defined as failure of intended therapy, then the overall rate of clinical failure rises from 18/160 (11.2%) to 39/181 (21.5%). Therefore, it is important to note that adverse events resulting in earlier than desired LAMS dislodgement/removal contribute considerably to clinical failure.

The most common delayed adverse event in our cohort was LAMS occlusion and infection requiring unplanned intervention, which occurred in 7.9% of patients. As expected, this was statistically more likely in the WOPN group compared to the PP group (14.7% vs 2.1%, p = <0.01). We feel that LAMS occlusion by necrosum and subsequent infection within the PFC cavity is more a reflection of the underlying disease process rather than stent malfunction. Moreover, the presence of the LAMS was beneficial in the treatment of stent occlusion as it provides a wide lumen through which DEN can be performed with relative ease. Interestingly, individual sites that routinely placed coaxial DPS or a nasocystic tube for necrotic collections had a lower rate of stent occlusion and infection (2/75, 2.7%) than sites where this was not routine practice (14/147, 9.5%), although this did not reach statistical significance (p = 0.06). A recent retrospective study comparing LAMS alone vs LAMS plus coaxial DPS placement

showed a significantly lower rate of global adverse events in the LAMS plus coaxial DPS group [22]. For WOPN and ANCs, we propose this strategy of routinely placing coaxial DPS immediately following LAMS insertion to reduce the risk of occlusion and requirement for unplanned DEN. This strategy likely reduces the risk of stent occlusion itself due to the freely mobile plastic stent dislodging necrosum before settling within the LAMS lumen and possibly further reducing the risk of infection by providing ongoing drainage even if the LAMS lumen is occluded by necrosum. Excluding stent occlusion, delayed adverse events related directly to the LAMS occurred in 22 of 202 patients (10.9%). Stent migration rate in our cohort was 7.4% with no difference between the PP and WOPN groups. Moreover, only 3 of the 15 cases of migration occurred during DEN, supporting the notion that DEN through the LAMS is safe, effective and relatively straightforward.

Two recent studies have raised concerns about high rates of major bleeding associated with LAMS use for PFC management [19,20]. Bang et al reported major gastrointestinal bleeding in 3/31 patients (9.7%) and 1 case of major bleeding during endoscopic LAMS removal. A retrospective study by Lang et al reported LAMS-associated bleeding in 4/19 (21%) patients, although details regarding severity and subsequent management are unknown [19]. In our large cohort, we observed a much lower major bleeding rate of 2% (4 patients). There were also no cases of major bleeding associated with endoscopic stent removal. However, it is important to note that the major bleeding cases in our cohort were serious adverse events resulting in significant morbidity and death in one case.

Bang et al also reported 2/31 cases (6.5%) of buried LAMS within the gastric mucosa at the time of endoscopic removal at 5- and 6-weeks post-insertion [20]. We observed only 2 cases (1%) of buried LAMS at the time of endoscopic removal. Furthermore, the mean LAMS in-dwelling time in our cohort was more than 7 weeks (50.7 days) with a maximum in-dwelling time of 281 days. Thus, our low rate of major bleeding and buried LAMS is particularly important. We feel that further investigation is required to elucidate safe timelines for removal, particularly in patients with slower resolution of their PFC.

It is also important to note that while clinical success for the management of PFCs with LAMS is high, it's superiority over plastic stents remains unclear [19,20,23,24]. The EDS-LAMS is not yet routinely available in many regions of the world and the higher device cost remains a limiting factor in many units. However, it is also important to acknowledge that device cost makes up only a proportion of overall cost for the care of these complex patients, and there appears to be no difference in overall treatment costs when comparing LAMS vs DPS for the management of PFCs [20]. We therefore recommend the development of consensus guidelines based on device availability, cost and user experience.

Our study has several inherent limitations in its retrospective nature. There was considerable variation in follow-up which may underestimate long term adverse events and subsequent PFC outcomes. Another potential limitation was the variability in endoscopist experience and technique, as well as in procedural practices and clinical preferences between the participating sites. Our cohort also consisted of a heterogenous group of patients with many different etiologies and clinical course. However, these are limitations that exist across the medical literature, particularly in multi-center retrospective studies.

The strengths of this study include multi-center recruitment across 17 centers from 4 countries, including a number of non-expert centers. We believe this adds considerable generalizability to our results and presents real-world translatable data. In addition, a large proportion of our data was collected prospectively (91/202, 45%), therefore potentially limiting bias. Another strength is that the number of patients recruited is one of the largest cohorts to date reporting on the use of the EDS-LAMS for drainage of PFCs. Finally, our study is unique in that we included data and individually assessed the role of the EDS-LAMS for EUS-guided drainage of PFCs in routine clinical practice. Our experience suggests that the EDS-LAMS is effective for drainage of all types of PFCs, but can be associated with significant stent occlusion requiring further endoscopic intervention in WOPN. High technical success rates and short procedural times are clear advantages of the novel EDS-LAMS, and the previously reported complications of major bleeding and buried LAMS were rare in our cohort. Further randomized

trials and consensus guidelines are required to clarify best-practice and cost-effectiveness in the endoscopic management of PFCs.

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ABBREVIATIONS

LAMS, lumen-apposing metal stent; PFC, pancreatic fluid collection; EUS, endoscopic ultrasound; PP, pancreatic pseudocyst; WOPN, walled-off pancreatic necrosis; APFC, acute peripancreatic fluid collection; ANC, acute necrotic collection; POC, post-operative collection; FCSEMS, fully-covered self-expanding metal stent; DEN, direct endoscopic necrosectomy; DPS, double pigtail stent; SD, standard deviation

TABLE 1: Patient demographics and PFC characteristics

	All PFCs, n = 202	PP, n = 97	WOPN, n = 75	APFC, n = 10	ANC, n = 6	POC, n = 14
Age, years (SD) †	52.86 (15.83)	51.79 (15.78)	53.83 (16.06)	47.5 (17.96)	56.17 (11.93)	57.36 (39 – 76)
Sex, no. (%)						
Male	117 (57.9)	63 (64.9)	40 (53.3)	7 (70)	3 (50)	4 (28.6)
Female	85 (42.1)	34 (35.1)	35 (46.7)	3 (30)	3 (50)	10 (71.4)
PFC etiology, no. (%)						
Alcohol	53 (26.2)	33 (34)	16 (21.3)	4 (40)	0 (0)	0 (0)

Gallstone	83 (41.1)	36 (37.1)	42 (56)	2 (20)	3 (50)	0 (0)
Idiopathic	25 (12.4)	14 (14.4)	8 (10.7)	1 (10)	2 (33.3)	0 (0)
Autoimmune	1 (0.5)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Post-ERCP	4 (2)	1 (1)	2 (2.7)	0 (0)	1 (16.7)	0 (0)
Trauma	8 (4)	5 (5.2)	2 (2.7)	1 (10)	0 (0)	0 (0)
Drug related	3 (1.5)	2 (2.1)	1 (1.3)	0 (0)	0 (0)	0 (0)
Hypertriglyceridaemia	3 (1.5)	1 (1)	2 (2.7)	0 (0)	0 (0)	0 (0)
Post-operative	14 (6.9)	0 (0)	0 (0)	0 (0)	0 (0)	14 (100)
Other	8 (4)	4 (4.1)	2 (2.7)	2 (20)	0 (0)	0 (0)
PFC infection status, no. (%)						
Infected	94 (46.5)	22 (22.7)	53 (70.7)	8 (80)	5 (83.3)	6 (42.9)
Sterile	108 (53.5)	75 (77.3)	22 (29.3)	2 (20)	1 (16.7)	8 (57.1)
Maximal PFC diameter, cms (SD) *	10.63 (4.81)	10.53 (5.03)	10.96 (4.43)	10.2 (4.17)	12.95 (5.95)	8.93 (4.93)

† Variables are presented as mean values with standard deviation in brackets
PFC, pancreatic fluid collection; PP, pancreatic pseudocyst; WOPN, walled-off pancreatic necrosis; APFC, acute peripancreatic fluid collections; ANC, acute necrotic collection; POC, post-operative collection; ERCP, endoscopic retrograde cholangiopancreatography

TABLE 2: Procedural details and clinical outcomes

	All PFCs	PP	WOPN	APFC	ANC	POC
Procedural technical success, no. (%)	202/208 (97.1)	97/99 (98)	75/79 (95)	10/10 (100)	6/6 (100)	14/14 (100)
Procedural time, minutes (SD) †	36.24 (21.89)	36.69 (20.78)	32.38 (22.66)	60.2 (21.19)	45 (21.21)	31.5 (10.9)
Site of LAMS placement, no. (%)						
Gastric	192/202 (95)	91/97 (93.8)	72/75 (96)	10/10 (100)	5/6 (83.3)	14/14 (100)
Duodenal	10/202 (5)	6/97 (96.2)	3/75 (4)	0/10 (0)	1/6 (16.7)	0/14 (0)
LAMS lumen size, no. (%)						
15mm	154/202 (76.2)	68/97 (70.1)	65/75 (86.7)	9/10 (90)	5/6 (83.3)	7/14 (50)
10mm	47/202 (23.3)	28/97 (28.9)	10/75 (13.3)	1/10 (10)	1/6 (16.7)	7/14 (50)
8mm	1/202 (0.5)	1/97 (1)	0/75 (0)	0/10 (0)	0/6 (0)	0/14 (0)
ERCP + transpapillary stent, no. (%)	6/202 (3)	1/97 (1)	3/75 (4)	0/10 (0)	0/6 (0)	2/14 (14.3)
Stent through LAMS ‡, no. (%)						

Double pigtail	23/202 (11.4)	11/97 (11.3)	7/75 (9.3)	2/10 (20)	0/6 (0)	3/14 (21.4)
Nasocystic	13/202 (6.4)	2/97 (2.1)	7/75 (9.3)	4/10 (40)	0/6 (0)	0/14 (0)
Both	5/202 (2.5)	0/97 (0)	4/75 (5.3)	1/10 (10)	0/6 (0)	0/14 (0)
Patients requiring extra endoscopic sessions §, no. (%)	73/202 (36.1)	17/97 (17.5)	45/75 (60)	4/10 (40)	3/6 (50)	4/14 (28.6)
Number of extra endoscopic sessions § (%)						
1	35/202 (17.3)	14/97 (14.4)	17/75 (22.7)	1/10 (10)	1/6 (16.7)	2/14 (14.3)
2	21/202 (10.4)	3/97 (3.1)	12/75 (16)	3/10 (30)	1/6 (16.7)	2/14 (14.3)
3	7/202 (3.2)	0/97 (0)	6/75 (12)	0/10 (0)	1/6 (16.7)	0/14 (0)
> 3 [total no. of sessions]	10/202 (5) [52]	0/97 (0)	10/75 (13.3) [52]	0/10 (0)	0/6 (0)	0/14 (0)
Total number of extra endoscopic sessions	150	20	111	7	6	6
Mean no. of extra endoscopic sessions	0.74	0.21	1.48	0.7	1	0.43
Mean no. of extra endoscopic sessions in patients requiring at least 1 extra session	2.05	1.18	2.47	1.75	2	1.5
Requirement for non-endoscopic therapy for PFC management, no. (%)						
Surgical	7/202 (3.5)	2/97 (2.1)	2/75 (2.7)	2/10 (20)	0/6 (0)	1/14 (7.1)
Radiological	2/202 (1)	0/97 (0)	1/75 (1.3)	1/10 (10)	0/6 (0)	0/14 (0)
Successful LAMS removal if attempted endoscopically ¶, no. (%)	160/160 (100)	80/80 (100)	61/61 (100)	4/4 (100)	4/4 (100)	11/11 (100)
LAMS in-dwelling time, days (SD) †	50.65 (40.43)	54.55 (45.15)	46.32 (35.59)	37.5 (10.81)	56.5 (28.45)	37.83 (36.48)
Clinical Success ᵗ, no. (%)	142/160 (88.8)	72/80 (90)	52/61 (85.2)	4/4 (100)	3/4 (75)	11/11 (100)
Sustained PFC resolution, no. (%)	129/142 (90.8)	63/72 (87.5)	50/52 (96.2)	3/4 (75)	3/3 (100)	10/11 (90.9)
PFC recurrence, no. (%)	13/142 (9.2)	9/72 (12.5)	2/52 (3.8)	1/4 (25)	0/3 (0)	1/11 (9.1)
Follow-up duration, weeks (SD) †	15.24 (16.04)	15.25 (17.27)	15.25 (15.17)	7 (3)	12.8 (12.54)	12.58 (12.1)

† Variables are presented as mean values with standard deviation in brackets

‡ Only includes stents placed through LAMS during the same endoscopy as initial LAMS placement; does not include stents inserted later following direct endoscopic necrosectomy

§ Extra endoscopic sessions (usually for direct endoscopic necrosectomy) excluding LAMS insertion and removal sessions

¶ Excludes cases of LAMS migration, LAMS removed surgically, death prior to LAMS removal, LAMS left in-situ indefinitely, LAMS not yet removed and lost to follow-up with LAMS in situ

ᵗ Resolution of PFC at time of endoscopic LAMS removal without requirement for ongoing transmural drainage; patients who did not have LAMS removed were excluded

PFC, pancreatic fluid collection; PP, pancreatic pseudocyst; WOPN, walled-off pancreatic necrosis; APFC, acute peripancreatic fluid collections; ANC, acute necrotic collection; POC, post-operative collection; ERCP, endoscopic retrograde cholangiopancreatography; LAMS, lumen-apposing metal stent; DEN, direct endoscopic necrosectomy

TABLE 3: Adverse events

	All PFCs	PP	WOPN	APFC	ANC	POC
Procedural adverse events, no. (%)						
Maldeployment	7/208 (3.4)	2/99 (2)	5/79 (6.3)	0/10 (0)	0/6 (0)	0/14 (0)
Minor bleeding	2/208 (0.9)	0/99 (0)	1/79 (1.3)	1/10 (10)	0/6 (0)	0/14 (0)
Major bleeding	0/208 (0)	0/99 (0)	0/79 (0)	0/10 (0)	0/6 (0)	0/14 (0)
Fevers	3/208 (1.4)	1/99 (1)	1/79 (1.3)	0/10 (0)	0/6 (0)	1/14 (0)
Delayed adverse events, no. (%)						
Stent migration	15/202 (7.4)	8/97 (8.2)	6/75 (8)	0/10 (0)	0/6 (0)	1/14 (7.1)
Stent occlusion and infection †	16/202 (7.9)	2/97 (2.1)	11/75 (14.7)	3/10 (30)	0/6 (0)	0/14 (0)
Major bleeding †	4/202 (2)	2/97 (2.1)	1/75 (1.3)	0/10 (0)	0/6 (0)	1/14 (0)
Minor bleeding	2/202 (1)	1/97 (1)	1/75 (1.3)	0/10 (0)	0/6 (0)	0/14 (0)
Peritoneal contamination	1/202 (0.5)	0/97 (0)	1/75 (1.3)	0/10 (0)	0/6 (0)	0/14 (0)
Sepsis unrelated to stent occlusion	4/202 (2)	2/97 (2.1)	1/75 (1.3)	0/10 (0)	1/6 (16.7)	0/14 (0)
Stroke	1/202 (0.5)	0/97 (0)	1/75 (1.3)	0/10 (0)	0/6 (0)	0/14 (0)
Death attributed directly to LAMS	1/202 (0.5)	0/97 (0)	1/75 (1.3)	0/10 (0)	0/6 (0)	0/14 (0)
Death with LAMS in situ, no. (%)	12/202 (5.9)	4/97 (4.1)	5/75 (6.7)	2/10 (20)	1/6 (16.7)	0/14 (0)
Stent removal adverse events, no. (%)						
Minor bleeding	3/160 (1.9)	2/80 (2.5)	1/61 (1.6)	0/4 (0)	0/4 (0)	0/11 (0)
Major bleeding	0/160 (0)	0/80 (0)	0/61 (0)	0/4 (0)	0/4 (0)	0/11 (0)
Buried LAMS	2/160 (1)	2/80 (2.5)	0/61 (0)	0/4 (0)	0/4 (0)	0/11 (0)

† Requiring endoscopic, surgical or radiological intervention

PFC, pancreatic fluid collection; PP, pancreatic pseudocyst; WOPN, walled-off pancreatic necrosis; APFC, acute peripancreatic fluid collections; ANC, acute necrotic collection; POC, post-operative collection; ERCP, endoscopic retrograde cholangiopancreatography; LAMS, lumen-apposing metal stent;

SUPPLEMENTARY TABLE: Site by site analysis

	Site A	Site B	Site C	Site D	Site E	Site F	Site G	Site H	Site J	Site K	Site L	Site M	Site N	Site O	Site P	Site Q
No. of patients	7	9	18	10	8	18	10	18	6	20	4	16	33	9	8	8
No. of LAMS used	7	9	18	11	8	21	10	19	6	20	4	16	33	10	8	8
PFC Classification†																
PP	4/7 (57.1)	1/9 (11.1)	13/18 (72.2)	6/10 (60)	3/8 (37.5)	6/18 (33.3)	4/10 (40)	8/18 (44.4)	5/6 (83.3)	13/20 (65)	2/4 (50)	7/16 (43.8)	14/33 (42.4)	5/9 (55.6)	1/8 (12.5)	5/8 (62.5)
WOPN	2/7 (28.6)	8/9 (88.9)	3/18 (16.7)	3/10 (30)	4/8 (50)	10/18 (55.6)	3/10 (30)	9/18 (50)	0/6 (0)	5/20 (25)	0/4 (0)	5/16 (31.3)	11/33 (33.3)	3/9 (33.3)	6/8 (75)	3/8 (37.5)
APFC	0/7 (0)	0/9 (0)	0/18 (0)	0/10 (0)	0/8 (0)	0/18 (0)	0/10 (0)	0/18 (0)	0/6 (0)	0/20 (0)	1/4 (25)	1/16 (6.3)	8/33 (24.2)	0/9 (0)	0/8 (0)	0/8 (0)
ANC	1/7 (14.3)	0/9 (0)	2/18 (11.1)	1/10 (10)	0/8 (0)	0/18 (0)	0/10 (0)	0/18 (0)	1/6 (16.7)	0/20 (0)	0/4 (0)	0/16 (0)	0/33 (0)	1/9 (11.1)	0/8 (0)	0/8 (0)
POC	0/7 (0)	0/9 (0)	0/18 (0)	0/10 (0)	1/8 (12.5)	2/18 (11.1)	3/10 (30)	1/18 (5.6)	0/6 (0)	2/20 (10)	1/4 (25)	3/16 (18.8)	0/33 (0)	0/9 (0)	1/8 (12.5)	0/8 (0)
Technical success†	6/7 (85.7)	9/9 (100)	18/18 (100)	11/11 (100)	8/8 (100)	19/21 (90.5)	10/10 (100)	18/19 (94.7)	5/6 (83.3)	20/20 (100)	4/4 (100)	16/16 (100)	33/33 (100)	9/10 (90)	8/8 (100)	8/8 (100)
Plastic stent placed through LAMS at insertion †	4/6 (66.7)	4/9 (44.4)	0/18 (0)	2/11 (18.2)	0/8 (0)	0/19 (0)	0/10 (0)	0/18 (0)	0/5 (0)	0/20 (0)	0/4 (0)	16/16 (100)	15/33 (45.5)	0/9 (0)	0/8 (0)	0/8 (0)

Requirement for non-endoscopic therapy for PFC management †	0/7 (0)	0/9 (0)	0/18 (0)	1/10 (10)	0/8 (0)	1/18 (55.6)	0/10 (0)	1/18 (5.6)	0/6 (0)	2/20 (10)	0/4 (0)	0/16 (0)	3/33 (9.1)	1/9 (11.1)	0/8 (0)	0/8 (0)
Endoscopic LAMS removal †	4/6 (66.7)	8/9 (88.9)	15/18 (83.3)	9/11 (81.8)	7/8 (87.5)	13/19 (68.4)	9/10 (90)	15/18 (83.3)	4/5 (80)	15/20 (75)	4/4 (100)	13/16 (81.3)	22/33 (66.7)	7/9 (77.8)	7/8 (87.5)	8/8 (100)
LAMS in-dwelling time, days	83.25	24	48.29	49.9	40.38	44.6	79	41.6	100.25	55.22	25.75	42.85	54.17	94.22	24.14	25.5
Clinical success †	4/4 (100)	8/8 (100)	15/15 (100)	9/9 (100)	7/7 (100)	12/13 (92.3)	8/9 (88.9)	11/15 (73.3)	4/4 (100)	13/15 (86.7)	4/4 (100)	13/13 (100)	19/22 (86.4)	5/7 (55.6)	7/7 (100)	3/8 (37.5)
PFC recurrence †	0/4 (0)	0/8 (0)	0/15 (0)	0/9 (0)	1/7 (14.3)	1/12 (8.3)	0/8 (0)	1/11 (9.1)	1/4 (25)	4/13 (30.8)	2/4 (50)	0/13 (0)	1/19 (5.3)	0/5 (0)	0/7 (0)	2/3 (66.7)
Follow-up duration, weeks	9.33	13.67	10.42	18.8	7.75	8.27	26.11	16.53	12.5	20.27	12.5	5.19	15.41	42.89	32.43	44.25
Adverse events †																
Maldeployment	1/7 (14.3)	1/9 (11.1)	0/18 (0)	0/11 (0)	0/8 (0)	2/21 (9.5)	0/10 (0)	1/19 (5.3)	1/6 (16.7)	0/20 (0)	0/4 (0)	0/16 (0)	0/33 (0)	1/10 (10)	0/8 (0)	0/8 (0)
Migration	2/6 (33.3)	0/9 (0)	2/18 (11.1)	2/11 (18.2)	1/8 (12.5)	2/19 (10.5)	0/10 (0)	0/18 (0)	0/5 (0)	3/20 (15)	0/4 (0)	0/16	2/33 (6.1)	1/9 (11.1)	0/8 (0)	0/8 (0)
Occlusion	0/6 (0)	0/9 (0)	0/18 (0)	0/11 (0)	2/8 (25)	3/19 (15.8)	0/10 (0)	3/18 (16.7)	1/5 (20)	1/20 (5)	1/4 (25)	0/16 (0)	2/33 (6.1)	1/9 (11.1)	0/8 (0)	2/8 (25)
Major bleeding	0/6 (0)	0/9 (0)	1/18 (5.6	0/11 (0)	0/8 (0)	1/19 (5.3)	0/10 (0)	1/18 (5.6)	0/5 (0)	0/20 (0)	0/4 (0)	1/16 (6.3)	0/33 (0)	0/9 (0)	0/8 (0)	0/8 (0)

Death with LAMS in situ †	1/6 (16.7)	0/9 (0)	0/18 (0)	0/11 (0)	0/8 (0)	1/19 (5.3)	0/10 (0)	0/18 (0)	0/5 (0)	0/20 (0)	0/4 (0)	1/16 (6.3)	5/33 (15.2)	0/9 (0)	1/8 (12.5)	0/8 (0)

† Variable presented as number of patients, with percentage in brackets
PFC, pancreatic fluid collection; PP, pancreatic pseudocyst; WOPN, walled-off pancreatic necrosis; APFC, acute peripancreatic fluid collections; ANC, acute necrotic collection; POC, post-operative collection; LAMS, lumen-apposing metal stent;