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Equivalent efficacy and safety of plastic stents and lumen-apposing metal stents in the treatment of peripancreatic fluid collections: a prospective cohort study

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Abstract

Background Endoscopic ultrasound (EUS)-guided transmural drainage using double pigtail plastic stents (DPPS) has been routine for the treatment of peripancreatic fluid collections (PFC). Lumen-apposing metal stents (LAMS) have since their introduction been the preferred choice; however, their superiority has not been proven. The aim of this study was to compare the efficacy and safety of DPPS and LAMS.

Methods This was a single-center, prospective study that included consecutive patients undergoing EUS-guided drainage between January 2010 and December 2020. The primary endpoints were technical success, clinical success and adverse event rate, while the secondary endpoints included symptomatic relief, length of hospital stay, and need for adjunct drainage. A subgroup analysis of walled-off necrosis (WON) was performed.

Results A total of 89 patients (median age 56 years) underwent EUS-guided transmural drainage (DPPS: n=53; LAMS: n=36) because of a pseudocyst (n=37) or a WON (n=52). Both DPPS and LAMS had a 100% technical success rate and a comparable adverse event rate (4% vs. 6%, P=0.24). An equivalent efficacy was recorded for the drainage of PFC comparing DPPS and LAMS, and no significant statistical difference was recorded in clinical success (DPPS 60% vs. LAMS 61%, P=0.94) or the need for reintervention (DPPS 11% vs. LAMS 13%, P=0.72).

Conclusions In this large, prospective study of EUS-guided drainage of peripancreatic fluid collections, LAMS and DPPS showed equivalent safety, technical success, clinical success and hospital stay. Both techniques were associated with a comparable need for complementary necrosectomy.

Keywords Pancreatic pseudocyst, stents, endoscopic ultrasonography self-expandable metallic stents, drainage

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Introduction

Peripancreatic fluid collections (PFCs) may develop from acute or chronic pancreatitis. According to the revised Atlanta classification [1], these are divided into 4 subtypes: acute peripancreatic fluid collections, acute necrotic collections, pseudocysts, and walled-off necroses (WON). These collections are differentiated based on duration (less than or greater than 4 weeks from onset of acute pancreatitis), and presence or absence of necrosis. Most PFCs have spontaneous resolution; however, drainage is needed when they cause symptoms—e.g., persistent abdominal pain, infection or gastroduodenal obstruction [2]. The management of PFCs has evolved from a percutaneous or open surgical approach to minimally invasive endoscopic ultrasound (EUS)-guided drainage. The traditional procedure is the placement of double pigtail plastic stents (DPPS). The introduction of lumen-apposing metal stents (LAMS) has revolutionized the management of PFCs, because of their much shorter procedure time and, in addition, a larger lumen diameter, which in theory reduces the risk of

occlusion compared with DPPS and facilitates easy access for necrosectomy.

Most studies comparing DPPS and LAMS are retrospective [3-5]. The 2 existing randomized trials [6,7] analyzing the drainage of WON showed no superiority of LAMS compared to DPPS regarding clinical efficacy, need for necrosectomy, hospital stay or adverse event rate. Hence, the superiority of LAMS in the drainage of PFCs has yet not been established; nevertheless, most centers have completely abandoned the plastic stents. The aim of this study was to evaluate the clinical safety and efficacy of LAMS and DPPS in a larger population and clinical setting.

Patients and methods

Sahlgrenska University Hospital (SUH) is the tertiary referral center for both EUS and pancreatic surgery in the western region of Sweden (population: 2.1 million). Interventional EUS has been performed since 2006. Within the catchment area, patients suffering from all types of severe pancreatic disease are referred to SUH for assessment and advanced care.

Study setting

All patients aged >18 years with PFCs referred to the endoscopy unit of SUH during the period from January 2010 to December 2020 for assessment with EUS were eligible for study inclusion. The PFCs were verified by cross-sectional imaging (computed tomography [CT] and/or magnetic resonance imaging) and were classified as pseudocysts or WON, according to the revised 2012 Atlanta classification of pancreatitis [1]. Etiologies of PFC were recorded (Table 1) and data were extracted from a prospectively maintained database.

To limit the influence of percutaneous techniques on the study findings, we excluded patients with preexisting transabdominal drainage catheters prior to the index EUS-intervention. In cases where the EUS assessment showed spontaneous resolution of the cyst, the patient was excluded (Fig. 1).

The study was approved by the Regional Ethical Review Board of Gothenburg (Dnr: 573-09) and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008). Written informed consent was obtained from all the patients included. The study was registered at ClinicalTrials.gov (NCT02845258).

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Table 1 Baseline characteristics and procedure related data

Characteristics	DPPS (n=53)	LAMS (n=36)
Patient characteristics		
Patient age, median (range)	54 (27-82)	60 (21-91)
Sex (male: female)	31:22	24:12
PFC characteristics		
Etiology of PFCs n (%)		
Alcohol-induced pancreatitis	17 (32%)	10 (28%)
Gallstone pancreatitis	16 (30%)	11 (30%)
Drug-induced pancreatitis	3 (6%)	0 (0%)
Idiopathic pancreatitis	6 (11%)	5 (14%)
Hyperlipidemia-induced pancreatitis	3 (6%)	1 (3%)
Chronic pancreatitis	7 (13%)	6 (17%)
Post ERCP pancreatitis	1 (2%)	3 (8%)
Location of PFC n (%)		
Caput pancreatis	14 (26%)	9 (25%)
Corpus pancreatis	22 (42%)	20 (56%)
Cauda pancreatis	17 (32%)	7 (19%)
Type of PFC n (%)		
Pseudocyst	22 (42%)	15 (41%)
WON	31 (58%)	21 (59%)
Size of fluid collection (cm)		
Long axis median (IQR, Range)	12 (7, 3-23)	10 (7, 2-30)
Short axis median (IQR, Range)	8 (5, 3-20)	9 (6, 3-20)

PFC, pancreatic fluid collection; ERCP, endoscopic retrograde cholangiopancreatography; WON, walled-off necrosis; IQR, interquartile range

Data collection

Previous and current medical records of all included patients were thoroughly screened at the time of EUS, and relevant data were recorded (demographics, disease-specific and procedure-related data). Data during follow up and patient outcome after EUS were extracted from the medical files at 30 days and at 3 months post-EUS. The duration of the procedure was not recorded, since all available studies and clinical experience show a significantly shorter procedural time for drainage using LAMS compared to DPPS [6,7].

Selection of therapeutic approach

At the start of the introduction of LAMS (2016) both LAMS and DPPS were used. However, because of the shorter procedural time, and hence less use of general anesthesia, LAMS progressively became the stent of choice. The study was set in a real-life clinical setting where the management of every single PFC patient is individualized, which in turn leads to a personalized approach when it comes to the choice of stents.

Procedural technique

In all procedures, a therapeutic echoendoscope (working channel 3.8 mm, EG-3870UTK, Pentax, Tokyo, Japan) and a modern ultrasound processor (HI VISION Ascendus, Hitachi),

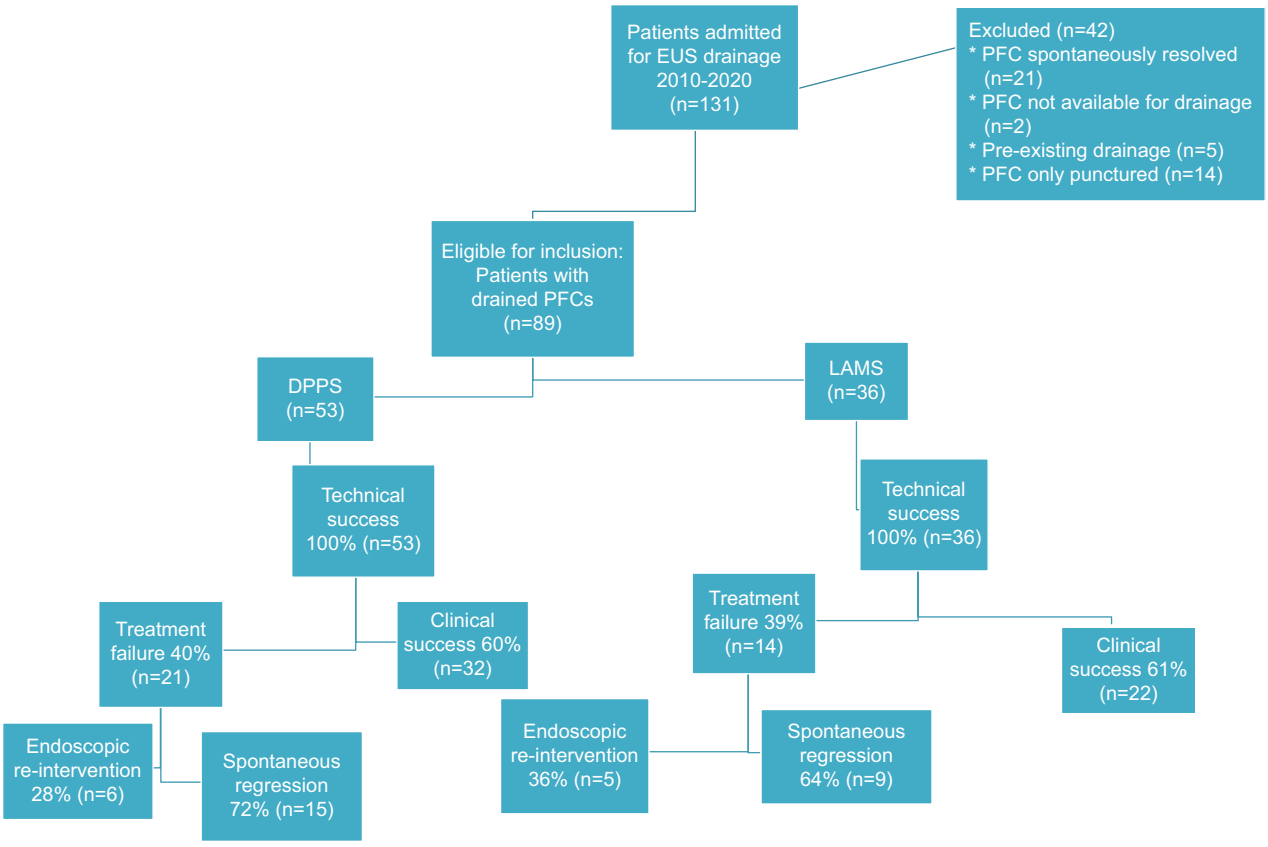

Figure 1 Flow diagram of patient enrolment and overall clinical outcomes
PFC, pancreatic fluid collection; EUS, endoscopic ultrasound; DPPS, double pigtail plastic stent; LAMS, lumen-apposing metal stent

were used. In general, patients were examined under general anesthesia while they underwent EUS-guided drainage with DPPS, and under continuous sedation (midazolam; alfentanil) when undergoing EUS-guided drainage with LAMS.

In all procedures, the echoendoscope was introduced, the PFC was visualized by ultrasound, and the best possible access route without interfering vessels was identified. Before drainage and by means of ultrasound, the endosonographer confirmed that the estimated point of access was at a sufficient distance distal from the gastroesophageal junction, and that the stomach wall and the wall of the PFC were properly adherent. The LAMS were removed within 3 months. In general, the DPPS were removed after 18 months, given the nature of this treatment. The 2 methods were, however, compared at a 3-month follow up, when the effect of the treatment is thought to be final.

EUS-guided drainage with LAMS

For the PFC access 100 W pure cut was applied before the stent was deployed. The LAMS used in this study was Hotaxios™ (Boston Scientific®). During 2016-2018 a 15-mm diameter Hotaxios stent was used, while from 2018 on the 20-mm Hotaxios stent was used.

EUS-guided drainage with non-cautery access and the use of DPPS

A 19-G access needle (EchoTip®, Cook Medical®) was used to access the PFC. Then, a 0.035×260-cm Super Stiff guidewire (Boston Scientific®) was placed through the needle into the PFC, and finally the obtained transgastric lumen was dilated by the needle sheath. The needle was retracted while the guidewire was left in the PFC. Further dilatation of the lumen was achieved via the use of a CRE™ balloon dilatation catheter, usually 15-18 mm (Boston Scientific®), with <15 mm defined as minor dilatation and 15-18 mm defined as major dilatation. A second guidewire was then introduced. Finally, 2 DPPS (Cook Medical®, 7 Fr, 7 cm) were released.

Primary endpoint

The primary endpoint in this study was clinical success rate, defined as a complete resolution of the PFC on CT with the initial stent and within 1 month. Treatment failure, i.e., no clinical success, was recorded when the initial stent was insufficient in achieving complete PFC resolution. Definitions of all endpoints are presented in Appendix A. A need for further endoscopic reintervention within 3 months, resulting in either additional stenting or a change

of stent treatment, was defined as need for reintervention. Intervention-free survival was defined as a complete resolution of PFC with the initial stent and/or spontaneous resolution of PFC within 3 months, without the need for endoscopic reintervention.

However, endoscopic inspection of the PFC or regular endoscopic necrosectomy, which are essential parts of the treatment of WONs, was not defined as a treatment failure. Instead, these interventions were analyzed as secondary endpoints. Scheduled stent extraction was not regarded as a reintervention.

Secondary endpoints

Secondary endpoints studied were technical success rate, adverse event rate, symptomatic relief, hospital stay, duration of antibiotic treatment, adjunct drainage, necrosectomy and nasocystic drainage. Adverse events were defined as complications related to the EUS-procedure within 30 days [8]. A subgroup analysis was performed in patients with WON, and for comparing LAMS of large (20 mm) and moderate (15 mm) diameter. A further exploratory subgroup analysis was the effect of the diameter of the tract dilatation in DPPS on adverse events.

Statistical analysis

During the pre-LAMS era of the study timeframe (years 2010-2015), only the DPPS technique was applied. A sample size calculation was performed in 2015 (statistical power: 80%, alpha error: 0.05) with the aim of detecting a 25% difference in the clinical success rate of DPPS and LAMS (non-paired proportions, 2-sided), and based on data from other groups [9,10]. The calculation returned a value of n=36 EUS-guided LAMS-procedures required. A 2-tailed $P<0.05$ was regarded as statistically significant for all analyses. All the statistical calculations and tests were performed using IBM SPSS Statistics V.25.0. Descriptive continuous data were represented as median and range, while descriptive categorical data were represented as frequencies. The categorical primary outcome variable was analyzed using a chi-square test. Secondary variables with a binary outcome were analyzed either using a chi-square test or Fisher's exact test, as appropriate. To analyze the non-normally distributed and continuous secondary variables the Mann-Whitney test or the independent 2-samples' *t*-test was used. Intervention-free survival was analyzed using the Kaplan-Meier log-rank test.

Results

Baseline characteristics

Baseline characteristics and procedure related data are presented in Table 1. A total of 89 patients (DPPS n=53; LAMS n=36) with PFCs underwent EUS-guided drainage between 2010 and 2020, when study enrolment ended. The patients' median age was 57 (range: 21-92) years. The PFCs were localized in all parts of the pancreas. The etiology of the PFCs was predominantly pancreatitis due to alcohol (30%) or biliary pancreatitis (30%) (Table 1). Based on the Atlanta classification, 37 patients had a pseudocyst (42%) and 52 had a WON (58%). In both groups the majority of PFC's consisted of a single cyst. In only 2 patients, the stent was placed via the transduodenal route. Regarding anesthesia, 68% of the LAMS patients were drained under conscious sedation, compared with 32% of patients treated with DPPS (DPPS n=10; LAMS n=41).

Primary endpoint

Clinical success

Comparable efficacy was recorded for the drainage of PFC with DPPS and LAMS (Table 2). No significant statistical difference was observed in the resolution of the PFC (DPPS 60% vs. LAMS 61%, P=0.94) or the need for further endoscopic reintervention (DPPS 11% vs. LAMS 13%, P=0.72).

Treatment failure requiring reintervention was similar (LAMS 39% vs. DPPS 40%, P=0.72). The intervention-free survival was comparable in both the PFC study population and in the WON subgroup, as demonstrated by the Kaplan-Meier curve (Fig. 2).

Secondary endpoints

Technical success

Technical success was achieved in all 89 (DPPS: n=53/53; LAMS n=36/36) patients, since all the cysts eligible for drainage could be drained as planned (Fig. 1).

Adverse event rates

The frequency of adverse events was low (DPPS 2/53, 4 % vs. LAMS 2/36, 6 %, P=0.69). Two of the patients were being treated for a pseudocyst and 2 for a WON. There was no procedure-related mortality in any group. Minor intraprocedural hemorrhage was observed in 5 patients of the DPPS group during tract dilatation.

Severe adverse events

Bleeding

Two patients suffered a major bleeding. A 69-year-old man being treated for a WON had hematemesis the same day after DPPS insertion. Eventually, he became hemodynamically unstable. The patient was stabilized on medical treatment and 4 units of erythrocyte transfusion. The most severe adverse event occurred in a 63-year-old male patient with a pseudocyst after

Table 2 Outcome of treatment for all PFC

Outcome	DPPS (n=53)	LAMS (n=36)	P-value
PRIMARY endpoints			
Technical success n (%)	53 (100%)	36 (100%)	>0.99
Clinical success			
PFC complete resolution on CT, n (%)	32 (60%)	22 (61%)	0.94
Treatment failure, n (%)	21 (40%)	14 (39%)	0.94
Need for reintervention, n (%)	6 (11%)	5 (13%)	0.72
Overall adverse events n (%)	2 (4%)	2 (6%)	0.24
Major bleeding, n	1	1	0.78
Pneumoperitoneal leakage, n	1	1	0.78
Need for emergency surgery, n	1	1	0.78
SECONDARY endpoints			
Symptomatic relief: reduced pain, n (%)	29 (55%)	24 (67%)	0.38
Hospital stay (days), median (IQR, range)	13 (10, 2-86)	12 (20, 2-90)	0.65
Hospital readmission or still in hospital, n (%)	24 (45%)	16 (44%)	0.94
Adjunctive percutaneous drainage, n (%)	6 (11%)	4 (11%)	0.97

PFC, pancreatic fluid collection; DPPS, double pigtail plastic stent; LAMS, lumen-apposing metal stent; IQR, interquartile range

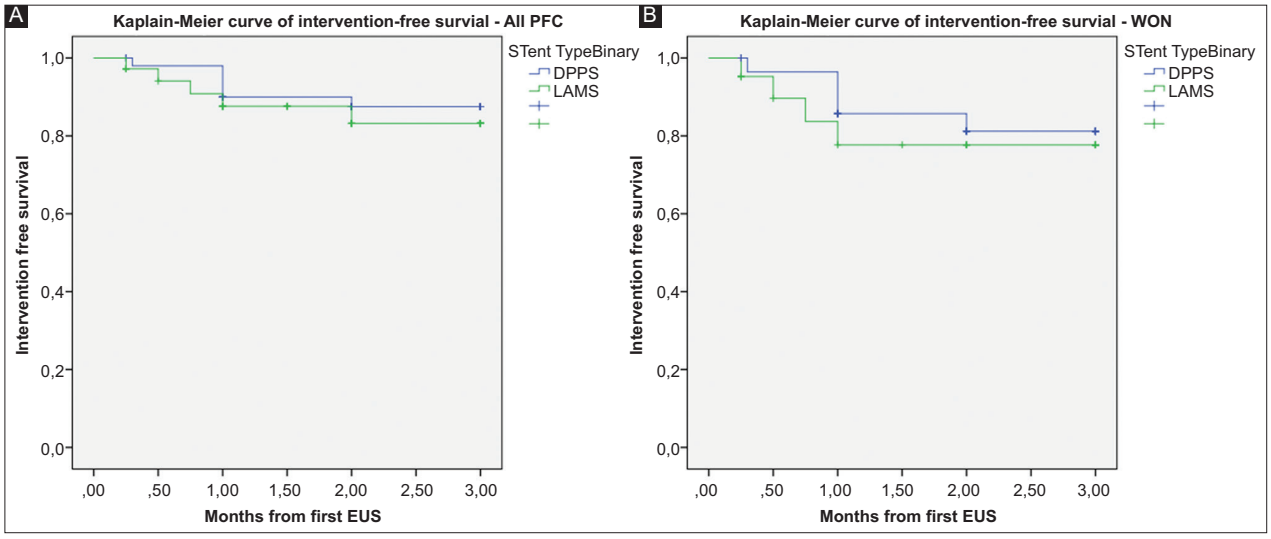

Figure 2 Kaplan-Meier curve for intervention-free survival: (A) all PFC, (B) WON. In both groups, patients had similar intervention-free survival within the first 3 months regardless of stent used for drainage

PFC, pancreatic fluid collection; WON, walled-off necrosis; DPPS, double pigtail plastic stent; LAMS, lumen-apposing metal stent; EUS, endoscopic ultrasound

biliary pancreatitis. Six days post-EUS, the patient developed a massive hemorrhage and became hemodynamically unstable. The patient was still in the hospital and was immediately transferred to the operating room, where the bleeding was managed surgically (Table 2). The cause of bleeding was a perforation of the splenic artery caused by the LAMS.

Perforation

In the DPPS group, a 51-year-old male patient suffered from post-EUS perforation of the stomach. This complication was discovered 1 day after the EUS-procedure and it was caused by a migrated pigtail stent. The perforation was managed surgically with explorative laparotomy, suturing of the perforation and drainage (Table 2). In the LAMS group, a 68-year-old male patient with a pseudocyst due to alcohol-induced pancreatitis developed a pneumoperitoneum after stent insertion. He suffered from pain and infection, both successfully managed conservatively (Table 2).

Symptomatic relief

No significant statistical difference was recorded in symptomatic relief between the 2 groups (DPPS 55% vs. LAMS 67%, P=0.38).

Hospital stay and need for readmission

In the analysis of all PFCs, there was no statistically significant difference in the median length of hospital stay (13 vs.

12 days, P=0.65) or in the number of patients rehospitalized after treatment (45% DPPS vs. 44% LAMS, P=0.96). In the WON subgroup, the hospital stay was numerically equal (14 vs. 14 days, P=0.68). In the DPSS group, 51% of the patients were still in hospital or were rehospitalized within the first 30 days, compared to 52% in the LAMS group.

Duration of antibiotic treatment

Patients treated with LAMS required a numerically longer period of treatment with antibiotics (median number of days n=14 vs. n=7, P=0.13).

Adjunct drainage

Comparing DPPS vs. LAMS, there was no difference in the need for adjunct percutaneous drainage, either in the entire PFC group (11% vs. 11%, P=0.97) or in the WON subgroup (13% vs. 19%, P=0.34).

The number of patients needing endoscopic necrosectomy in WON

The number of patients undergoing endoscopic necrosectomy after the insertion of a stent was numerically higher in the LAMS group (3% DPPS vs. LAMS 33%, P=0.13) (Table 3).

The need for adjunct nasocystic drainage as additional therapy in WON

There was no difference in the need for nasocystic drainage (38% DPPS vs. LAMS 33%, P=0.69). Independent variables with potential effect on the outcome of the stent used were studied in an exploratory subgroup analysis.

Tract dilatation and number of pigtail stents used

In 27 cases the tract used for insertion of the pigtail stent was dilated using a balloon smaller than 15 mm, while in 26 cases the tract was dilated at a minimum of 15 mm and no more than 18 mm. In a subgroup analysis of balloon dilatation <15 mm and ≥15 mm, there was no significant difference in rate of bleeding (11% vs. 8%, P=0.67) or overall adverse events (12% vs. 15%, P=0.72). Nor was there a difference in the need for repeated endoscopy (74% vs. 73%, P=0.93) due to treatment failure. A large majority of the patients (n=46, 87%) received 2 DPPS (the remaining 7 patients received 1, 3 or 4 stents). There was no statistically significant difference in the number of stents placed and the need for reintervention (P=0.75).

Size of LAMS

Comparing the 15-mm LAMS with the 20-mm LAMS, we recorded no statistically significant difference in clinical success (11/21 vs. 11/15, P=0.20) or adverse events (2/21 vs. 0/15, P=0.22) (Table 4).

Discussion

In this large prospective study comparing DPPS and LAMS in the EUS-guided drainage of peripancreatic fluid collections, we did not record any significant difference in the outcome regarding technical or clinical success, nor in any of our secondary endpoints. Both methods seem to be equally safe, with a low rate of adverse events. The results were similar in both the entire group of patients and in the WON subgroup. The 2 largest prospective studies [7,11] on this subject, including 59 and 60 patients, concluded that, even though LAMS appear to be safe and efficient, they were not significantly superior to DPPS. A recent meta-analysis also showed that deployment of DPPS

Table 3 Outcome of treatment for WON

WON subgroup	DPPS (n=31)	LAMS (n=21)	P-value
PRIMARY endpoints			
Clinical success			
PFC complete resolution on CT, *n* (%)	17 (55%)	13 (62%)	0.61
Treatment failure, *n* (%)	14 (45%)	8 (38%)	0.61
Need for repeat intervention, *n* (%)	5 (16%)	4 (19%)	0.78
SECONDARY endpoints			
Technical Success, *n* (%)	31 (100%)	21 (100%)	>0.99
Symptomatic relief: reduced pain, *n* (%)	15 (48%)	14 (67%)	0.57
Hospital stay (days), *median (IQR, range)*	14 (9, 2-86)	14 (25, 2-90)	0.68
Hospital readmission or still in hospital, *n* (%)	16 (51%)	11 (52%)	0.96
Duration of antibiotic treatment, days median *(IQR, range)*	7 (12, 0-99)	14 (25, 0-94)	0.13
Endoscopic necrosectomy *n* (%)	1 (3%)	7 (33%)	0.13
Adjunct percutaneous drainage *n* (%)	4 (13%)	4 (19%)	0.54
Simultaneous nasocystic drainage *n* (%)	12 (38%)	7 (33%)	0.69

WON, walled-off necrosis; DPPS, double pigtail plastic stent; LAMS, lumen-apposing metal stent; PFC, pancreatic fluid collection; CT, computed tomography; IQR, interquartile range

Table 4 Outcome of treatment in subgroup analysis of LAMS

LAMS subgroup	LAMS 15 mm (n=21)	LAMS 20 mm (n=15)	P-value
PRIMARY endpoints			
Clinical success (within 3 months)			
PFC complete resolution on CT, n (%)	11 (52%)	11 (73%)	0.20
Treatment failure, n (%)	10 (48%)	4 (27%)	0.20
Need for reintervention, n (%)	4 (19%)	1 (7%)	0.29
SECONDARY endpoints			
Technical success, n (%)	31 (100%)	15 (100%)	>0.99
Overall adverse events, n (%)	2 (9%)	0	0.22
Symptomatic relief: reduced pain, n (%)	11 (65%)	13 (87%)	0.17
Hospital stay (days), median (IQR, range)	12 (20, 2-90)	11 (8, 4-52)	0.97
Hospital readmission or still in hospital, n (%)	11 (52%)	5 (33%)	0.25
Adjunct percutaneous drainage, n (%)	0	4 (26%)	0.02

LAMS, lumen-apposing metal stent; PFC, pancreatic fluid collection; CT, computed tomography; IQR, interquartile range

across LAMS for drainage of PFCs has no significant impact on clinical success and complications, including stent migration and occlusion, bleeding, infection or perforation [12].

The technical success was 100% regardless of the stent used, which is in line with other studies [4]. Both types of stents performed comparably well in the resolution of the PFC and in their need for endoscopic reintervention.

A large retrospective, multicenter study that compared the efficacy of LAMS and plastic stent for drainage of WON showed lower clinical success and a higher number of reinterventions in the DPPS group [13]. This finding could be explained by the technically more demanding insertion of DPPS. However, 2 recent retrospective studies [7,14] observed no difference in clinical outcomes.

Comparing DPSS and LAMS, there was no difference in either the rate or the severity of adverse events. Overall, the rate of adverse events was low (4%). At our center, a non-cautery dilatation technique for access to PFCs is applied when DPPS are used. Five cases of intraprocedural minor hemorrhage were observed in the DPPS group. However, these minor bleedings resulted in no clinical consequence for the patients, since they could be managed immediately. Other studies have not shown any significant difference in feasibility between a cautery and a non-cautery access technique [15]. Our results further support that the non-cautery access technique is a safe and efficient method. The use of conscious sedation, as administered in our center during the current study, is supported by several others [16]. The low adverse event rate recorded implies that conscious sedation is adequate for a safe EUS-guided drainage procedure of PFCs, regardless of the type of stent used.

Once a PFC is successfully drained with a LAMS, the stent may come in direct contact with adjacent structures, such as blood vessels, causing bleeding. For this reason, the LAMS is extracted within 3 months, whereas the plastic stents were left for at least 18 months, which has been our clinical practice since the start of this treatment. A higher rate of procedure-related bleeding in LAMS was shown by Lang *et al* [3], although this was not observed in our study. However, the 1 bleeding that occurred in our study in the LAMS groups was severe and required acute life-saving surgery. A study by Brimhall *et al* found a higher risk of pseudoaneurysm bleeding associated with LAMS. In view of the severity of these bleedings, the clinician should potentially be more active in the use of cross-sectional imaging in cases where a vessel is seen adjacent to the LAMS [17]. In cases with vessels adjacent to the WON, DPPS should be considered for drainage.

No patient in our study cohort died within 90 days post-EUS, which is a low number compared to the mortality rates of around 3% in trials with a similar-sized study population [4,6,7]. One factor influencing this finding could be the university hospital study setting. In our center, patients are observed in a dedicated upper gastric surgical ward with an interventional radiology unit and an emergency operating room close by in case of life-threatening complications.

Approximately only half of the study population (DPPS 55% vs. LAMS 45%, P=0.3) suffered from pain prior to treatment. The percentage of patients who experienced pain relief was higher in the LAMS group compared with DPPS, but the difference did not reach statistical significance. However, this has not been well studied in the available literature, and a blinded randomized setting would be more optimal to answer this question.

In line with the results from the 2 randomized studies on this subject [6,7], there was no statistically significant difference in our study in the median days spent in hospital (DPPS 9 days vs. LAMS 25 days, P=0.13) by patients with a WON. In comparison, the patients in the randomized Danish study [6] stayed a median of 43 and 58 days, respectively. In another comparison, the patients treated for WON in the American study [7] had a median stay of only 12 and 6 days in hospital for DPPS and LAMS, respectively. Probably, this discrepancy in numbers better reflects a difference between the 3 study centers rather than the WON disease itself or the method of drainage. Possibly, the LAMS is preferred in more difficult cases of necrotizing pancreatitis, explaining the subsequent longer hospital stay for these patients. A selection bias of this sort could explain the difference in our study. A randomized, multicenter study with a standardized treatment protocol is warranted to elucidate what type of drainage stent results in the shortest hospital stay.

A unique aspect of the current study is that we analyzed the need for additional percutaneous drainage in PFCs already

drained with either DPPS or LAMS. Our results show that the use of LAMS does not affect the need for percutaneous or nasocystic drainage.

The number of patients undergoing endoscopic necrosectomy was non-significantly but numerically higher in the LAMS group (P=0.13). This is most likely explained by a selection bias, explained by the fact that LAMS is the preferred stent used in WON patients [18]. In theory, the wider diameter of the LAMS is meant to facilitate more rapid resolution of the necrotic contents and to enable easier access for further endoscopic necrosectomy. Hence, in parity with other centers [6], clinicians in our study had a lower threshold to refer patients with LAMS to a necrosectomy compared with patients with DPPS.

As an exploratory endpoint we examined the clinical success and rate of adverse events in the DPPS group based upon the diameter of the tract of access acquired by balloon dilatation. The optimal size of tract dilatation when introducing a plastic stent has not been studied previously. As described above, we recorded no difference in rate of bleeding or perforation comparing minor and major dilatation. These results indicate that it is safe and feasible to create a wider tract for drainage. In theory, a larger lumen will facilitate better drainage, but surprisingly, the size of tract dilatation did not correlate with the clinical success or need for repeat endoscopic procedures. However, our study suggests that is safe to use a large balloon (15-18 mm) for tract dilatation. Such management enables the easy insertion of 2 or more plastic stents.

The results for the 2 sizes of LAMS were comparable, and even though the results might be in favor of the 20-mm LAMS, a significant superiority compared with the 15-mm LAMS could not be proven. Similarly, a multicenter study by Parsa *et al*, including 102 WON patients [19], showed no significant effect of LAMS size on clinical outcome or adverse events. Taking place in a single center with 2 experienced endoscopist treating the patients was a strength of this study, since it provided consistency for the 2 study groups and associated technical difficulties.

We believe that our approach gives a fairer comparison, since the 2 endoscopists were already trained in successful drainage with plastic stents when the LAMS was introduced. The sample size of this study was large (89 patients), and the study was powered to 80% with 36 patients in the LAMS group, making it to date the largest prospective study on this subject.

However, the study also had some limitations. First, it was not a randomized trial and patient selection bias towards treatment of WON with LAMS based on its theoretical advantage is evident. Furthermore, all technical components of the EUS-procedures were left to the endoscopist to decide, which is a selection bias and limitation of the study. The 10-year study timeframe might be a disadvantage for the DPPS group, since the endoscopists gain more experience over time. The study compared outcomes between the 2 modalities in 2 different eras, and this might have had an impact on the results, since the overall treatment of patients with PFC gradually improves. This was a single-center study undertaken at a tertiary referral center, and all procedures were performed by expert endoscopists, which may raise the concern of the generalizability of the trial results. However, the single-center design strengthens the impact of the results, because the treatment and follow-up protocol were standardized. Another potential limitation is that we only evaluated a single design of LAMS, Hotaxios™ (Boston Scientific®).

With comparable clinical results, LAMS is nevertheless a more expensive method. Our group calculated the cost of LAMS (Appendix B) at around €2000, compared with €630 for DPPS (2 double pigtail stents). Cost comparative studies support the cost-effectiveness of DPPS [20]. However, when considering the technical advantages of LAMS, primarily a shorter procedure time, many studies argue that it is just as cost-effective [21]. However, the general comparability in clinical efficacy and the evident difference in material cost makes DPPS a good alternative for low-income countries.

In conclusion, our study shows that the use of DPPS and LAMS in EUS-guided drainage of PFCs, with or without the development of WON, is comparably efficient with respect to safety and patient outcomes. Although a large-diameter LAMS was expected to facilitate the drainage of necrotic material, the use of a 20-mm LAMS did not result in significantly higher cyst resolution or lower need for reintervention, compared to a 15-mm LAMS. Nor did a large 15-18-mm dilatation of the access tract improve the outcome, compared to a moderate <15 mm dilatation, in DPPS drainage. This large prospective study adds new knowledge on the tract dilatation approach, on the need for repeated endoscopy, and on the non-cautery technique itself. Since no study so far has proven the superiority of LAMS, except for its shorter procedure time compared to DPPS, perhaps its use should be tailored to the patient.

Summary Box

What is already known:

- Lumen apposing metal stents (LAMS) and double pigtail plastic stents (DPPS) show equivalent safety, technical success, and clinical success in the treatment of pancreatic fluid collections (PFCs)
- Both methods (LAMS and DPPS) have a similarly low rate of adverse events
- LAMS is clinically the preferred stent in patients with walled-off necrosis requiring repeated endoscopic necrosectomies

What the new findings are:

- The non-cautery access technique for DPPS deployment seems safe and efficient
- The size of tract dilatation does not seem to be correlated with clinical success, rate of adverse events or need for repeat endoscopic procedures
- The choice of drainage (LAMS and DPPS) does not seem to affect the need for percutaneous or nasocystic drainage

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