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Efficacy and safety of endoscopic drainage of peripancreatic fluid collections: a retrospective multicenter European study

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Abstract

Background Endoscopic ultrasound (EUS)-guided transmural drainage allows treatment of symptomatic peripancreatic fluid collections (PFCs), with lumen-apposing metal stents (LAMS) and double pigtail plastic stents (DPPS) being the 2 most frequently used modalities.

Methods Consecutive patients undergoing PFC drainage in 10 European centers were retrospectively retrieved. Technical success (successful deployment), clinical success (satisfactory drainage), rate and type of early adverse events, drainage duration and complications on stent removal were evaluated.

Results A total of 128 patients—92 men (71.9%), age 57.2±11.9 years—underwent drainage, with pancreatic pseudocyst (PC) and walled-off necrosis (WON) in 92 (71.9%) and 36 (28.1%) patients, respectively. LAMS were used in 80 (62.5%) patients and DPPS in 48 (37.5%). Technical success was achieved in 124 (96.9%) of the cases, with no difference regarding either the type of stent (P>0.99) or PFC type (P=0.07). Clinical success was achieved in 119 (93%); PC had a better response than WON (91/92 vs. 28/36, P<0.001), but the type of stent did not affect the clinical success rate (P=0.29). Twenty patients (15.6%) had at least one early complication, with bleeding being the most common (n=7/20, 35%). No difference was detected in complication rate per type of stent (P=0.61) or per PFC type (P=0.1). Drainage duration was significantly longer with DPPS compared to LAMS: 88 (70-112) vs. 35 (29-55.3) days, P<0.001.

Conclusions EUS-guided drainage of PFCs achieves high percentages of technical and clinical success. Drainage using LAMS is of shorter duration, but the complication rate is similar between the 2 modalities.

Keywords Peripancreatic fluid collection, drainage, stent, endoscopic ultrasound

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Conflict of Interest: None

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Introduction

Pancreatitis represents one of the most common gastrointestinal disorders and the most common pancreatic disease. One of the most severe complications of pancreatitis is the development of a peripancreatic fluid collection (PFC) [1]. If this becomes symptomatic or infected, interventional therapy is deemed necessary [2]. Endoscopic therapy was introduced, initially using plastic stents, and has gradually become the method of choice, as it combines safety and cost-effectiveness [3,4]. Plastic stents, usually double plastic pigtail stents (DPPS) even today, remain the type most commonly used. However, as their use has a high migration risk and they are also prone to occlusion due to their small caliber, the placement of

multiple stents, necessitating repeated access to the PFC and reinterventions, is often required [5,6]. The metal stents used for PFC drainage were initially fully or partially covered, but more recently their design has evolved: lumen-apposing metal stents (LAMS) were introduced, whose shape minimizes the risk of migration. LAMS are made with wide flanges on both ends, providing anchoring within the PFC and an even distribution of pressure on the luminal walls [7]. However, after the initial enthusiasm over the advantages of LAMS, an increasing number of reports also highlighted various limitations and adverse events associated with their use [8,9]. Thus, in this study from 10 European tertiary centers, we sought to evaluate the efficacy and safety of endoscopic ultrasound (EUS)-guided drainage of PFCs and to compare the technical and clinical outcomes and adverse events of drainage with LAMS and DPPS.

Materials and methods

Study design and participating centers

This international, multicenter, retrospective cohort study involved 10 European tertiary hospitals across 4 European countries: Athens, Greece (5 centers); Milan/Foggia/Verona, Italy; and Zagreb, Croatia and Budapest, Hungary. The study data are presented according to the Strengthening the Reporting of OBservational Studies in Epidemiology (STROBE) statement (Supplementary Table 1) [10].

Inclusion and exclusion criteria

Consecutive patients who underwent EUS-guided drainage of a PFC, a pancreatic pseudocyst or walled-off necrosis (WON), classified according to the revised Atlanta criteria [1], with either a LAMS or DPPS between June 2016 and December 2019 were considered eligible for inclusion. These patients had been diagnosed with a symptomatic PFC, based on a clinical evaluation of symptoms and findings from cross-sectional imaging of the abdomen with ultrasound, computed tomography, magnetic resonance imaging, or EUS. Exclusion criteria comprised: age <18 years; diagnosis of a cystic neoplasm; known diagnosis of pancreatic malignancy; and cases where follow up was not available. All patients provided written informed consent prior to the procedure. Patients were identified from a prospectively maintained database across each center, with all data being extracted and finally compiled into a main database. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

PFC drainage procedure

Patients received nil by mouth for 6 h prior the procedure. Prophylactic antibiotics were given at the discretion (type and dosage) of the endoscopist and as per institutional protocol. All procedures were performed by experienced interventional endoscopists (each having completed ≥100 EUS-guided transmural drainages) and under monitored anesthesia, with sedation consisting of incremental doses of propofol, on demand and per typical institutional practices. The echoendoscopes that were used were either Olympus (GF-UCT140-AL5 or GF-UCT180 + EU-ME2 Premier Plus, EVIS EUS, Olympus Optical Co. – Europa, Hamburg, Germany) or Pentax (FG-36UA or EG-3870UTK, connected with Hitachi Avius, PENTAX Europe GmbH, Hamburg, Germany). Punctures were conducted in a standardized manner, as previously described [11], while the final decision on which type of stent (LAMS, DPPS) was made based on each endoscopist's assessment.

PFC drainage with LAMS

Upon establishment of the vessel-free tract (Fig. 1A-C), following confirmation that the distance between the EUS probe and the PFC was ≤1 cm, the LAMS (HOT AXIOS, Boston Scientific Corporation, Marlborough, MA, USA) was applied by the "free hand technique"; the stent was inserted into the PFC with cautery assistance, followed by deployment of the distal and the proximal flange under EUS or endoscopic vision, thus completing stent placement (Fig. 1D-F). All LAMS that were used in this study were HOT AXIOS.

PFC drainage with DPPS

The PFC was directly punctured using a 10-Fr Cystotome (Cystotome TM, Cook Medical, Winston Salem, NC, USA; or the Cysto-Gastro-Set RU, ENDO-FLEX GmbH, Voerde, Niederrhein, Nordrhein-Westfalen, Germany) under ultrasound and fluoroscopic guidance. One or 2 guidewires

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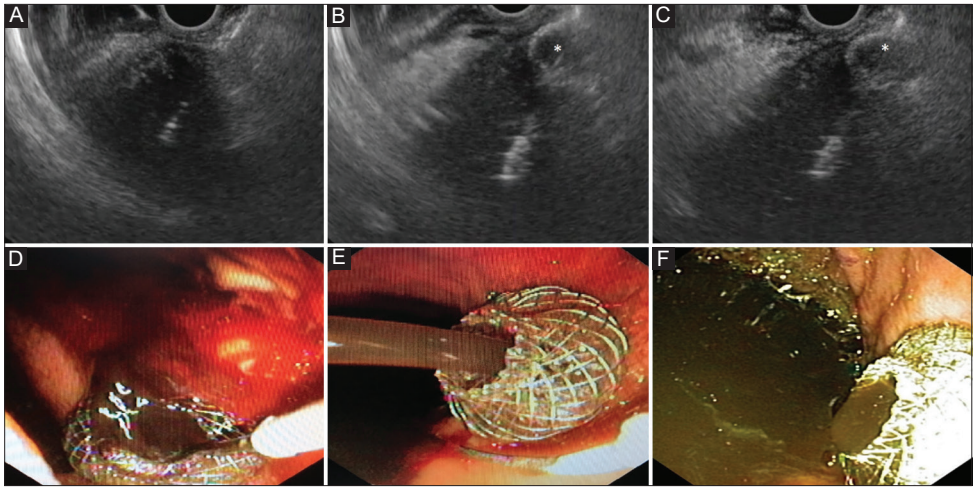

Figure 1 (A) Endosonographic view of the catheter of the lumen-apposing metal stent (LAMS) advancing in a peripancreatic fluid collection; (B and C, white asterisk) deployment of the distal flange of the LAMS; (D) endoscopic view of the deployment of the distal flange of the LAMS; (E and F) gradual emptying of the collection within the gastric lumen

were then pushed into the cavity through the cystotome and pneumatic dilation of the fistula was performed using a 6- or 8-mm balloon (MaxForce, Boston Scientific) and 1 or 2 DPPS (3 cm length, 7 or 10 Fr diameter) deployed into the PFC. DPPS were removed when clinical success of drainage was achieved, as defined below.

Study definitions

Technical success was considered as the successful deployment of the LAMS or at least one DPPS between the gastrointestinal tract and the PFC (i.e., the ability to place a stent in the intended target PFC). For the purposes of this study, only the cases where deployment was achieved in a single attempt were included in the analysis. Clinical success was considered as the successful drainage of the PFC, defined as a decrease in the size of the PFC to ≤3 cm on cross-sectional imaging, with resolution of symptoms at 6-month follow up (i.e., ability to drain the PFC) [9,12]. Early adverse events (AEs) with severity graded as per the American Society for Gastrointestinal Endoscopy (ASGE) lexicon [13], included AEs occurring within 30 days following the procedure.

Study endpoints

The primary endpoint was to assess the rates of technical and clinical success, as well as the early AEs related to all the procedures involved in the endoscopic drainage of PFCs. Secondary endpoints comprised: (i) comparison regarding technical success, clinical success, time needed to drain the PFC, rate of early AEs, complication rate upon stent removal and ease of stent placement (using a visual scale 1-10, with 1=extremely difficult and 10=extremely easy) between the LAMS and DPPS treatment groups; and (ii) comparison regarding technical success, clinical success, rate of early AEs and complication rate upon stent removal between the LAMS and DPPS treatment groups, in the setting of the 2 types of PFC (pancreatic pseudocyst/WON).

Statistical analysis

Continuous variables are reported as mean ± standard deviation (SD), or median and range, where appropriate. Categorical variables are presented as proportions and 95% confidence intervals (CIs). A P-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 25 (IBM, Chicago, Illinois, USA).

Results

Patient demographics and procedure characteristics

During the study period, 159 patients were initially assessed for eligibility, but only 128 of them (mean age 57.2±11.9 years, 71.9% male] met the inclusion criteria and were included in the analysis; these patients comprised 80 patients treated with a LAMS and 48 treated with a DPPS (Fig. 2). Patients' baseline and procedural characteristics are summarized in Table 1. Ninety-two patients had a pseudocyst (71.9%) and 36 a WON (28.1%), with the majority of the lesions being located in the body of the pancreas (n=56/128, 43.8%) and transgastric (n=117/128, 91.4%) being the predominant approach. Among the 80 patients treated with LAMS, a stent with a diameter of 15 mm was most frequently used (n=61/80, 76.2%), while among the 48 patients treated with DPPS, stents of 3 cm length (35.2%) and 7 Fr diameter (54.9%) were mainly used.

Primary endpoint

The overall technical success was 96.9% (n=124/128; 95%CI 93.9-99.9), while clinical success was achieved in 93.0% (n=119/128; 95%CI 88.5-97.4) of the patients. A total of 20 early AEs were observed, resulting in an AE rate of 15.6% (95%CI 9.3-21.9). Overall, there were 4 cases (n=4/128) of initial stent deployment failure; LAMS were used in 3 and DPPS in 1 patient. Regarding LAMS, there was one case of failure to deploy within the cyst, one failure associated with diathermy malfunction and one due to bleeding. The single case of DPPS failure was due to bleeding.

Secondary endpoints

Technical success was achieved in 96.3% (n=77/80; 95%CI 92.1-100) of patients in the LAMS group, compared to 97.9% (n=47/48; 95%CI 93.9-100) in the DPPS group (P>0.99, Fig. 3). Clinical success did not differ significantly between the LAMS and DPSS groups: 76/80 (95.0%, 95%CI 90.2-99.8) vs. 43/48 (89.6%, 95%CI 80.9-98.2); P=0.29] Drainage time was significantly shorter in the LAMS group (88 vs. 35 days; P<0.001). No significant differences between the 2 groups regarding ease of placement, as rated by endoscopists (6.7 vs. 6.7; P=0.96). The rate of early AEs was similar between the 2 groups: 14/80 (17.5%, 95%CI 9.2-25.8) vs. 6/48 (15.2%, 95%CI 3.1-21.9); P=0.61 (Table 2). Of the severe AEs among LAMS patients, bleeding was the most common (n=6), with 4 of them eventually requiring angiographic embolization to be controlled. Finally, 2 cases of perforation occurred in each group. In each perforation case, with either LAMS or DPPS, the stent was immediately retracted and the perforation site was closed with endoscopic clips. The same procedure was repeated with a second cystoenterostomy created successfully at a different location, using LAMS in 2 cases and DPPS in the other 2. It should be noted that the majority of AEs were effectively managed conservatively, requiring no further surgical intervention. The complication rate at stent removal was significantly higher in the LAMS group: 10/80 (13.5%, 95%CI 5.3-19.7) vs. 0/48 (0%, 95%CI 0-0); P=0.03. Tissue overgrowth was the most prevalent complication (n=5/10, 50%), but none of these cases required re-stenting. The mean and median times until LAMS removal were 61.8 and 35 days, respectively.

Technical success was similar for patients undergoing pseudocyst drainage with either a LAMS or DPPS: 51/52 (98.0%, 95%CI 89.7-99.9) vs. 40/40 (100%, 95%CI 91.1-100); P>0.99 (Table 3). The finding was consistent for clinical success and rate of early AEs: 52/52 (100%, 95%CI 97.1-100) vs. 39/40 (97.5%, 95%CI 86.8-99.9), P=0.435; and 7/52 (13.4%, 95%CI 5.6-25.8) vs. 4/40 (10.0%, 95%CI 27.9-23.7); P=0.750, respectively. Contrariwise, the rate of complications at stent removal was significantly higher in the LAMS group: 8/52 (15.4%, 95%CI

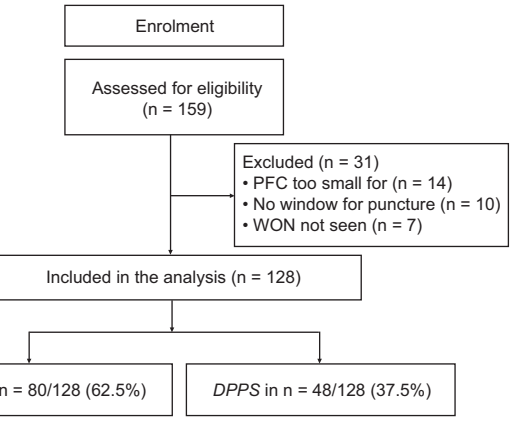

Figure 2 Study flowchart
PFC, peripancreatic fluid collection; WON, walled-off necrosis; LAMS, lumen-apposing metal stents; DPPS, double pigtail plastic stents

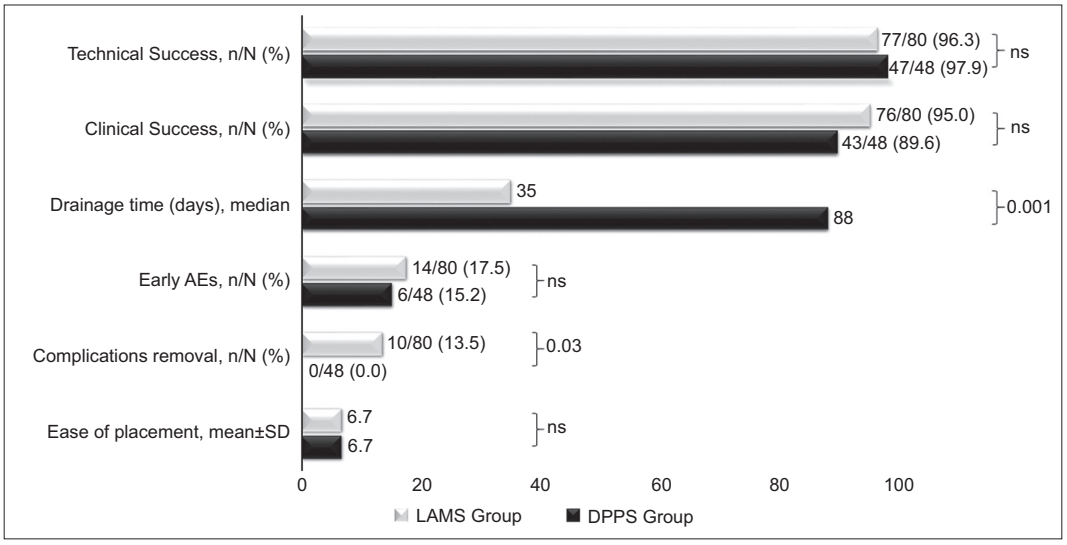

Figure 3 Comparison of clinical outcomes between the LAMS and DPPS groups
LAMS, lumen-apposing metal stents; DPPS, double pigtail plastic stents; AEs, adverse events; SD, standard deviation; ns, not significant

Table 1 Patients' baseline and procedural characteristics

Characteristics of patients and collections			
Sex, n (%)	Overall (n=128)	Pseudocyst (n=92)	WON (n=36)
Male	92 (71.9)	69 (75.0)	23 (63.9)
Female	36 (28.1)	23 (25.0)	13 (36.1)
Age (years), mean±standard deviation	57.2±11.9	56.2±12.7	60.4±11.3
		Pseudocyst	WON
Type of PFC, n (%)		92 (71.9)	36 (28.1)
PFC location, n (%)	Overall	Pseudocyst	WON
Head	15 (11.7)	13 (14.1)	2 (5.6)
Isthmus	9 (7.0)	5 (5.5)	4 (11.2)
Body	56 (43.8)	40 (43.5)	16 (44.4)
Tail	48 (37.5)	34 (36.9)	14 (38.8)
PFC size (cm), mean±standard deviation	11.8±4.7	11.8±4.7	11.8±4.7
Contributing centers, n (%)	Overall	Pseudocyst	WON
Greece, Athens	36 (28.2)	20 (21.8)	16 (44.4)
Italy, Milan	43 (33.6)	31 (33.6)	12 (33.3)
Croatia, Zagreb	19 (14.8)	17 (18.5)	2 (5.6)
Italy, Foggia/Verona	26 (20.3)	24 (26.1)	2 (5.6)
Hungary, Budapest	4 (3.1)	0 (0)	4 (11.1)
Technical characteristics of transmural drainage			
Drainage access, n (%)	Overall	LAMS	DPPS
Transgastric	117 (91.4)	71 (88.8)	46 (95.6)
Transduodenal	11 (8.6)	9 (11.2)	2 (4.4)
Type of stent, n (%)	Overall	Pseudocyst	WON
AXIOS	80 (62.5)	52 (56.5)	28 (77.7)
Double pigtail	48 (37.5)	40 (43.5)	8 (22.3)
LAMS length (mm), n (%)	Overall	Pseudocyst	WON
10	80 (100)	52 (56.5)	28 (77.7)
LAMS diameter (mm), n (%)	Overall	Pseudocyst	WON
10	19 (23.8)	13 (25.0)	6 (21.4)
15	61 (76.2)	39 (75.0)	22 (78.6)
Number of DPPS, n (%)	Overall	Pseudocyst	WON
1	26 (54.1)	26 (65.0)	0 (0)
2	21 (43.8)	14 (35.0)	7 (87.5)
3	1 (0.8)	0 (0)	1 (12.5)
DPPS length (cm), n (%)	Overall	Pseudocyst	WON
3	25 (35.2)	21 (38.8)	4 (25.0)
4	10 (14.1)	4 (7.1)	6 (37.5)
5	2 (2.8)	2 (3.4)	0 (0)
6	17 (23.9)	15 (27.2)	2 (12.5)
7	10 (14.1)	8 (14.3)	2 (12.5)
8	7 (9.9)	5 (9.2)	2 (12.5)
DPPS size (Fr), n (%)	Overall	Pseudocyst	WON
7	39 (54.9)	27 (50.0)	12 (54.5)
9	3 (4.2)	3 (5.5)	0 (43.8)
10	29 (40.9)	0 (0)	5 (22.8)

WON, walled-off necrosis; LAMS, lumen-apposing metal stent; DPPS, double pigtail plastic stent

6.8-28.1) vs. 0/40 (0%, 95%CI 0-0); P=0.045. Neither sex nor type of drainage approach (transgastric vs. transduodenal) were found to have any impact on drainage outcomes (Supplementary Table 2).

As far as drainage outcomes among patients with WON is concerned, technical success was similar between LAMS and DPPS: 26/28 (92.8%, 95%CI 76.5-99.1) vs. 7/8 (87.5%, 95%CI 47.3-99.7); P=0.541 (Table 3). Clinical success and rate of early AEs did not differ significantly between the LAMS and DPSS groups: 24/28 (85.7%, 95%CI 67.3-95.9) vs. 4/8 (50.0%, 95%CI 15.7-84.3), P=0.05; and 7/28 (25.0%, 95%CI 10.7-44.9) vs. 2/8 (25.0%, 95%CI 31.9-65.1), P>0.99, respectively]. The rate of complications at stent removal was also similar between the 2 groups: 2/28 (7.1%, 95%CI 8.8-23.5) vs. 0/8 (0%, 95%CI 0-0); P>0.99.

Discussion

During the past 2 decades, EUS-guided transmural drainage has revolutionized the approach to symptomatic PFCs, allowing the achievement of technical success rates that exceed 90% and clinical success rates that range between 75% and 90% by performing a minimally invasive procedure [14,15]. Moreover, the advent of LAMS promised to overcome the fundamental caveats of DPPS [3]. Nevertheless, compelling evidence favoring the use of LAMS instead of DPPS in resolving PFCs is so far lacking in the published literature. Hence, current European Society of Gastrointestinal Endoscopy guidelines advocate the implementation of either plastic stents or LAMS for endoscopic transmural drainage [16]. However, one should bear in mind that this is only a weak recommendation based on moderate quality evidence, since data on the efficacy of LAMS remain scant.

Analysis of our primary endpoint showed high rates of technical and clinical success (96.9% and 93%, respectively), along with favorable results and an excellent patient safety profile. Endoscopic transmural PFC drainage can be a challenging procedure [3]. Although early data demonstrated that biliary DPPS can be effectively applied to treat symptomatic PFCs [17], studies that followed revealed the disadvantages associated with their small lumen diameter, the need for multiple stents to allow adequate drainage, occlusion and subsequent infection, significantly worse performance in the case of WON, stent-related AEs (up to 18%) and technical difficulty in the placement of multiple DPPS [5]. In light of these observations, we saw the advent of LAMS, whose bi-flared flanges enable firm tissue apposition, decreasing

Table 2 Early adverse events and their management, overall and per group

Parameter	Overall	LAMS group, n=14	DPPS group, n=6	P-value	Pseudocyst n=11	WON n=9	P-value
Adverse event, n (%)				0.157			0.485
Bleeding	7 (35)	6 (42.9)	1 (16.7)		5 (45.6)	2 (22.2)	
Perforation	4 (20)	2 (14.3)	2 (33.3)		2 (18.4)	2 (22.2)	
Migration	3 (15)	2 (14.3)	1 (16.7)		1 (9.0)	2 (22.2)	
Obstruction/fever	4 (20)	4 (28.6)	0 (0)		1 (9.0)	3 (33.4)	
Pain	1 (5)	0 (0)	1 (16.7)		1 (9.0)	0 (0)	
Other (transient pylorus obstruction)	1 (5)	0 (0)	1 (16.7)		1 (9.0)	0 (0)	
Adverse event management, n (%)				0.354			0.642
Conservative*	13 (65)	8 (57.1)	5 (83.3)		8 (72.7)	5 (55.5)	
Additional treatment**	7 (35)	6 (42.9)	1 (16.7)		3 (27.3)	4 (44.5)	

*Medications (proton pump inhibitors, antibiotics, and analgesics), surveillance; **stent repositioning or replacement, angiographic embolization (4 cases of not self-resolved bleeding, all of them with LAMS)

LAMS, lumen-apposing metal stents; DPPS, double pigtail plastic stents; WON, walled-off necrosis

Table 3 Clinical endpoints per peripancreatic fluid collection and stent type

Pancreatic pseudocyst, n=92					
Endpoints	LAMS group (n=52)		DPPS group (n=40)		P-value
	N (%)	95%CI	N (%)	95%CI	
Technical success, n (%)	51 (98.0)	89.7-99.9	40 (100)	91.1-100.0	> 0.99
Clinical success, n (%)	52 (100)	97.1-100.0	39 (97.5)	86.8-99.9	0.435
Early AEs, n (%)	7 (13.4)	5.6-25.8	4 (10.0)	27.9-23.7	0.750
Complications at removal, n (%)	8 (15.4)	6.8-28.1	0 (0)	0-0	0.045
Walled-off necrosis, n=36					
Endpoints	LAMS group (n=28)		DPPS group (n=8)		P-value
	N (%)	95%CI	N (%)	95%CI	
Technical success, n (%)	26 (92.8)	76.5-99.1	7 (87.5)	47.3-99.7	0.541
Clinical success, n (%)	24 (85.7)	67.3-95.9	4 (50.0)	15.7-84.3	0.054
Early AEs, n (%)	7 (25.0)	10.7-44.9	2 (25.0)	31.9-65.1	> 0.99
Complications at removal, n (%)	2 (7.1)	8.8-23.5	0 (0)	0-0	> 0.99

AEs, adverse events; LAMS, lumen-apposing metal stent; DPPS, double pigtail plastic stent; CI, confidence interval

migration risk, while their wide-caliber lumen allows the performance of endoscopic necrosectomy as well as improved drainage [3]. Beyond their theoretical advantages, the efficacy of these devices was indeed corroborated, as data that followed showed a technical success of 95% and clinical success rates of 85-90%, with minimal risk of migration (5%) [7,18,19].

Our study also demonstrated that EUS-guided drainage with LAMS for the management of PFCs resulted in technical and clinical success rates similar to those of DPPS, according to most of the available data. Although LAMS have been increasingly used for endoscopic drainage of PFCs, large prospective studies comparing them to DPPS in terms of clinical or technical success remain limited, leaving the choice of stent dependent upon several factors—endoscopist's discretion, local availability, reimbursement policy, etc.—rather than strong evidence-based findings that actually favor one type of stent over the other [16]. In the only randomized controlled trial available to date, no significant difference in treatment outcomes was found between LAMS and plastic stents [20]. This issue has been also at the focal point of several meta-analyses, with the latest and largest reporting no significant difference between LAMS and DPPS in terms of technical success or AEs. Although LAMS use resulted in higher clinical success, less recurrence and fewer additional interventions, one should also pay attention to the fact that in studies of WON LAMS was associated with more perforations [15]. However, a second read between the lines calls for careful interpretation even of these results. More specifically, the majority of individual studies enrolled had a retrospective design, including different types of metal stents or assessing the efficacy of LAMS or DPPS separately, thus raising concerns about biases and heterogeneity [14]. Forthcoming adequately powered, randomized controlled studies should systematically document factors (lesion type, location, endoscopist's expertise level), that could allow for identification of heterogeneity in the treatment effect and ultimately settle this dispute.

A point that deserves attention is the fact that LAMS deployment resulted in a higher AE rate compared to DPPS, similar to the incidence reported in the most recent and largest meta-analyses on this topic [14,21]. Moreover, we identified bleeding once again as the most worrisome AE-related to LAMS in the setting of PFC drainage, finding that individual studies as well as meta-analyses confirm that it occurs at a significantly higher rate compared to DPPS (19% vs. 1%; P=0.003) [14,21,22]. A plausible explanation for this notion is that the radial force exerted by the LAMS on the walls of the cyst may contribute to hemostasis, but bleeding risk remains, as collapse of the cavity after drainage may lead to erosion of the posterior wall of the cavity by the stent. Other large registry-based studies did not support this notion [9,22,23], but this may be attributed to the inclusion exclusively of WON, or to a mixture of PFCs and variability in the endoscopist's expertise level, combined with differences in the definition and interpretation of AEs.

LAMS seem to outperform their counterparts in the management of WON, since it is difficult for the solid encapsulated necrotic material to drain spontaneously, requiring additional procedures, i.e., endoscopic necrosectomy in 60% [3,24]. When, however, the drainage of a pancreatic pseudocyst comes into question, literature data are sparse [25]. To make things even more confusing, published studies usually group WON and pancreatic pseudocysts together during their analysis, despite the different outcomes following endoscopic intervention. In this regard, the current study displayed similar performance between DPPS and LAMS groups regarding procedural outcomes of WON and pseudocyst drainage, with only the rate of complications upon removal being higher in the LAMS group.

As far as implications in everyday clinical practice are considered, the nature of the PFC itself might eventually hold the pivotal role in guiding appropriate stent selection for each occasion. Thus, LAMS apparently represent the optimal modality for WON drainage; on the other hand, multiple indwelling DDPS placement should be preferred for the initial management of patients with pancreatic pseudocysts, since this strategy is not only efficient and safe in the long term, as was shown recently [26], but also cost-effective [4]. Nevertheless, there is much work still in progress [27], as factors such as clinical status, pancreatic duct integrity, patient compliance and endoscopist's expertise level represent "gray" areas whose potential impact on the efficacy of each method remains unknown.

The strengths of this study include its multicenter design, accurately simulating everyday real-world clinical practice and contributing significantly to the generalizability of our findings. The large number of patients enrolled, the application of strict diagnostic criteria and the use of standardized definitions for AEs are also among the study's assets.

There are also limitations related to our study that merit attention, with the cardinal one attributable to its retrospective design. In this sense, one might repudiate the novelty and quality of the evidence presented, given its relation to previous publications on this topic; however, the current study, by reporting on the accumulated experience of a considerably large cohort of patients from 10 tertiary hospitals across 4 European countries, enriches the literature by providing not only real-world data throughout a continent, but also clinically rich insights into real-world evidence that plays an increasing role in healthcare decisions. Real-world evidence can be generated by different study designs, not only randomized controlled trials, but also large sample observational studies that can accurately replicate everyday clinical practice. In this regard, the current iteration *per se* constitutes a kind of novelty that may expand our knowledge to support decision-making, improving safety and effectiveness, and ultimately patient-related outcomes. Second, it should be highlighted that only a single design of commercially available LAMS was included in this analysis; thus, is not possible to generalize to other LAMS. Third, the stent management algorithm and follow-up protocol were neither uniform nor standardized across centers, so variability among physicians and clinical settings might have resulted in heterogeneity. Another limitation is that the decision on which type of stent (LAMS, DPPS) to be used was based on each physician's assessment. Finally, we did not undertake an official cost-effectiveness analysis and we did not report on late AEs, nor on the number of necrosectomy sessions, their efficacy and the PFC recurrence rate after stent removal.

To conclude, the findings of this study suggest that EUS-guided drainage of PFCs is associated with high percentages of technical and clinical success, regardless of the stent used (LAMS or DPPS). Notably, early AEs were similar between the 2 types of drainage, but tended to occur more frequently when LAMS were used. While further prospective randomized trials are needed to enhance our knowledge about PFC treatment and to identify factors that determine clinical success, while minimizing the risk of AEs, the use of DPPS in cases of pseudocyst drainage and the use of LAMS in cases of WON, necessitating further step-up approaches, seems a reasonable approach.

Summary Box

What is already known:

- Lumen-apposing metal stents (LAMS) and double pigtail plastic stents (DPPS) are the 2 modalities used most frequently for endoscopic ultrasound-guided transmural drainage of symptomatic peripancreatic fluid collections (PFCs)
- Strong evidence favoring the use of LAMS instead of DPPS in resolving PFCs is lacking so far

What the new findings are:

- DPPS and LAMS achieved equal rates in terms of technical and clinical success when used for the drainage of symptomatic mature PFCs
- LAMS implementation resulted in a significantly shorter drainage time

References

1. Banks PA, Bollen TL, Dervenis C, et al; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102-111.
2. Andalib I, Dawod E, Kahaleh M. Modern management of pancreatic fluid collections. *J Clin Gastroenterol* 2018;**52**:97-104.
3. Giovannini M. Endoscopic ultrasound-guided drainage of pancreatic fluid collections. *Gastrointest Endosc Clin N Am* 2018;**28**:157-169.
4. Chen YI, Khashab MA, Adam V, et al. Plastic stents are more cost-effective than lumen-apposing metal stents in management of pancreatic pseudocysts. *Endosc Int Open* 2018;**6**:E780-E788.
5. Varadarajulu S, Bang JY, Phadnis MA, Christein JD, Wilcox CM. Endoscopic transmural drainage of peripancreatic fluid collections: outcomes and predictors of treatment success in 211 consecutive patients. *J Gastrointest Surg* 2011;**15**:2080-2088.
6. Tyberg A, Karia K, Gabr M, et al. Management of pancreatic fluid collections: A comprehensive review of the literature. *World J Gastroenterol* 2016;**22**:2256-2270.
7. Shah RJ, Shah JN, Waxman I, et al. Safety and efficacy of endoscopic ultrasound-guided drainage of pancreatic fluid collections with lumen-apposing covered self-expanding metal stents. *Clin Gastroenterol Hepatol* 2015;**13**:747-752.
8. Bang JY, Hasan M, Navaneethan U, Hawes R, Varadarajulu S. Lumen-apposing metal stents (LAMS) for pancreatic fluid collection (PFC) drainage: may not be business as usual. *Gut* 2017;**66**:2054-2056.
9. Yang J, Chen YI, Friedland S, et al. Lumen-apposing stents versus plastic stents in the management of pancreatic pseudocysts: a large, comparative, international, multicenter study. *Endoscopy* 2019;**51**:1035-1043.
10. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;**61**:344-349.
11. Möller K, Papanikolaou IS, Toermer T, et al. EUS-guided FNA of solid pancreatic masses: high yield of 2 passes with combined histologic-cytologic analysis. *Gastrointest Endosc* 2009;**70**:60-69.
12. Bang JY, Hawes R, Bartolucci A, Varadarajulu S. Efficacy of metal and plastic stents for transmural drainage of pancreatic fluid collections: a systematic review. *Dig Endosc* 2015;**27**:486-498.
13. Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. *Gastrointest Endosc* 2010;**71**:446-454.
14. Guzmán-Calderón E, Chacaltana A, Díaz R, Li B, Martinez-Moreno B, Aparicio JR. Head-to-head comparison between endoscopic ultrasound guided lumen apposing metal stent and plastic stents for the treatment of pancreatic fluid collections: A systematic review and meta-analysis. *J Hepatobiliary Pancreat Sci* 2022;**29**:198-211.
15. Lyu Y, Li T, Wang B, Cheng Y, Chen L, Zhao S. Comparison between lumen-apposing metal stents and plastic stents in endoscopic ultrasound-guided drainage of pancreatic fluid collection: a meta-analysis and systematic review. *Pancreas* 2021;**50**:571-578.
16. Arvanitakis M, Dumonceau JM, Albert J, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. *Endoscopy* 2018;**50**:524-546.
17. Bang JY, Wilcox CM, Trevino JM, et al. Relationship between stent characteristics and treatment outcomes in endoscopic transmural drainage of uncomplicated pancreatic pseudocysts. *Surg Endosc* 2014;**28**:2877-2883.
18. Talreja JP, Shami VM, Ku J, Morris TD, Ellen K, Kahaleh M. Transenteric drainage of pancreatic-fluid collections with fully covered self-expanding metallic stents (with video). *Gastrointest Endosc* 2008;**68**:1199-1203.
19. Lee BU, Song TJ, Lee SS, et al. Newly designed, fully covered metal stents for endoscopic ultrasound (EUS)-guided transmural drainage of peripancreatic fluid collections: a prospective randomized study. *Endoscopy* 2014;**46**:1078-1084.
20. Bang JY, Navaneethan U, Hasan MK, Sutton B, Hawes R, Varadarajulu S. Non-superiority of lumen-apposing metal stents over plastic stents for drainage of walled-off necrosis in a randomised trial. *Gut* 2019;**68**:1200-1209.
21. Zhou X, Lin H, Su X, et al. Metal versus plastic stents for pancreatic fluid collection drainage: a systematic review and meta-analysis. *J Clin Gastroenterol* 2021;**55**:652-660.
22. Lang GD, Fritz C, Bhat T, et al. EUS-guided drainage of peripancreatic fluid collections with lumen-apposing metal stents and plastic double-pigtail stents: comparison of efficacy and adverse event rates. *Gastrointest Endosc* 2018;**87**:150-157.
23. Fugazza A, Sethi A, Trindade AJ, et al. International multicenter comprehensive analysis of adverse events associated with lumen-apposing metal stent placement for pancreatic fluid collection drainage. *Gastrointest Endosc* 2020;**91**:574-583.
24. van Brunschot S, van Grinsven J, van Santvoort HC, et al; Dutch

Pancreatitis Study Group. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. *Lancet* 2018;**391**:51-58.
25. Sharaiha RZ, Tyberg A, Khashab MA, et al. Endoscopic therapy with lumen-apposing metal stents is safe and effective for patients with pancreatic walled-off necrosis. *Clin Gastroenterol Hepatol* 2016;**14**:1797-1803.
26. Gkolfakis P, Bourguignon A, Arvanitakis M, et al. Indwelling double-pigtail plastic stents for treating disconnected pancreatic duct syndrome-associated peripancreatic fluid collections: long-term safety and efficacy. *Endoscopy* 2021;**53**:1141-1149.
27. Gornals JB, Perez-Miranda M, Vazquez-Sequeiros E, et al; Spanish Working Group on Pancreatic Collection Therapy. Multicenter study of plastic vs. self-expanding metal stents in endoscopic ultrasound-guided drainage of walled-off pancreatic necrosis - PROMETHEUS: a randomized controlled trial protocol. *Trials* 2019;**20**:791.

Supplementary material

Supplementary Table 1 STROBE Statement - Checklist

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3
		Introduction	
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
		Methods	
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow up	7-8
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	11
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	11
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	11
		(b) Describe any methods used to examine subgroups and interactions	11
		(c) Explain how missing data were addressed	11
		(d) If applicable, explain how loss to follow-up was addressed	11
		(e) Describe any sensitivity analyses	11
		Results	
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	12
		(b) Give reasons for non-participation at each stage	12
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarize follow-up time (e.g., average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12
		(b) Report category boundaries when continuous variables were categorized	12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	13,14

(Contd...)

Supplementary Table 1 *(Continued)*

	Item No	Recommendation	Page No
		Discussion	
Key results	18	Summarize key results with reference to study objectives	15,16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalizability	21	Discuss the generalizability (external validity) of the study results	17
		Other information	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	2

*Give information separately for exposed and unexposed groups

Supplementary Table 2 Clinical endpoints per gender and drainage access type

Endpoints	Male (n=92)		Female (n=36)		P-value
	N, (%)	95%CI	N, (%)	95%CI	
Technical Success, n (%)	89 (96.7)	90.7-99.3	35 (97.2)	85.4-99.9	0.686
Clinical Success, n (%)	89 (96.7)	90.7-99.3	30 (83.3)	67.2-93.6	0.150
Early AEs, n (%)	15 (16.3)	9.4-25.4	5 (13.9)	4.6-29.5	0.484
Complications at removal, n (%)	8 (8.7)	3.8-16.4	2 (5.5)	6.8-18.6	0.133
Trans-gastric approach, n=117					
	LAMS Group (n=71)		DPPS Group (n=46)		P-value
	N, (%)	95%CI	N, (%)	95%CI	
Technical Success, n (%)	68 (95.6)	88.1-99.1	45 (97.8)	88.4-99.5	0.486
Clinical Success, n (%)	68 (95.6)	88.1-99.1	41 (89.1)	76.4-96.4	0.155
Early AEs, n (%)	12 (16.9)	9.1-27.7	6 (13.0)	4.9-26.3	0.612
Complications at removal, n (%)	9 (12.7)	5.9-22.7	0 (0.0)	0-0	> 0.99
Trans-duodenal approach, n=11					
	LAMS Group (n=9)		DPPS Group (n=2)		P-value
	N, (%)	95%CI	N, (%)	95%CI	
Technical Success, n (%)	9 (100.0)	66.3-100.0	2 (100.0)	15.8-100.0	0.621
Clinical Success, n (%)	8 (88.9)	51.7-99.7	2 (100.0)	15.8-100.0	0.818
Early AEs, n (%)	2 (22.2)	2.8-60.1	0 (0.0)	0-0	0.655
Complications at removal, n (%)	1 (11.1)	2.8-48.2	0 (0.0)	0-0	> 0.99

LAMS, lumen-apposing metal stents; DPPS, double pigtail plastic stents; AEs, adverse events; CI, confidence interval