

International, multicenter retrospective trial comparing the efficacy and safety of bi-flanged versus lumen-apposing metal stents for endoscopic drainage of walled-off pancreatic necrosis

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Abstract

Background To compare fully covered bi-flanged metal stents (BFMS) and lumen-apposing metal stents (LAMS) for endoscopic ultrasound (EUS)-guided drainage/debridement of pancreatic walled-off necrosis (WON).

Methods Patients with WON managed by EUS-guided therapy were divided into those who underwent: 1) drainage using BFMS; and 2) drainage using LAMS and scheduled direct endoscopic necrosectomy (DEN). Clinical success (resolution of the WON), technical success (successful stent placement), and adverse events (AEs) were evaluated.

Results 387 patients underwent WON endoscopic drainage, 205 using BFMS and 182 using LAMS. The clinical success in the BFMS or LAMS groups were similar (197 [96.1%] vs. 174 [95.6%]; $P=0.81$). Median number of procedures required for WON resolution was significantly lower in BFMS compared to LAMS (2 vs. 3, $P<0.001$). Technical success for stent placement was similar in BFMS and LAMS groups (203 [99%] vs. 180 [99%], $P=0.90$). Procedure-related AEs were similar in the BFMS and LAMS groups (19 [9.3%] vs. 20 [10.9%], $P=0.61$). Stent dysfunction with occluding debris was higher in the BFMS group compared to LAMS group (21 [10.2%] vs. 11 [5.9%], $P=0.04$). The migration rate was higher in the BFMS group than in the LAMS group (15 [7.3%] vs. 3 [1.6%]; $P<0.001$). DEN was required in 23 [11.2%] patients in the BFMS group after lack of WON resolution by conservative means.

Conclusion BFMS with a “step-up approach” and LAMS with scheduled DEN are both safe and effective for EUS-guided drainage/debridement of WON.

Keywords Pancreatic walled off necrosis, acute pancreatitis, bi-flanged metal stents, lumen-apposing metal stents, endosonography

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Introduction

Endoscopic ultrasonography (EUS)-guided drainage via transmural stents is increasingly considered first-line therapy in the management of symptomatic pancreatic fluid collections (PFCs) [1,2]. In the context of walled off necrosis (WON), a mature encapsulated collection of pancreatic necrosis that contains both liquid and solid components, transmural drainage alone may be

inadequate and endoscopic necrosectomy may be required [3-6]. Transmural direct endoscopic necrosectomy (DEN) after stent placement involves drainage and endoscopic debridement of the WON through the gastric or duodenal wall. Several studies have demonstrated that this approach is superior to surgical necrosectomy and percutaneous catheter drainage, with superior outcomes, fewer adverse events and lower healthcare costs [7,8].

Historically the placement of multiple double pigtail plastic stents (DPTs) has been the mainstay of therapy for endoscopic management of WON with regard to access and drainage. However, their use is limited by their small caliber lumen, cumbersome delivery system and consequent loss of patency, requiring the need for multiple stent placement and revisions [9-11]. Furthermore, in cases where DEN is necessary, balloon dilation of the tract is required to allow passage of endoscope into the collection for each necrosectomy session [12].

Two novel fully covered self-expanding metal stents have been designed specifically for the treatment of PFCs: the lumen-apposing metal stent (LAMS) (AXIOS™ Stent; Boston Scientific Corporation, Marlborough, MA), with both proximal and distal anchor flanges, and the bi-flanged metal stent (BFMS) (NAGI stent; Taewoong Medical Co., Ltd., Goyang, Korea). Both LAMS and BFMS have high reported rates of technical (89-100%) and treatment success (93-100%) in the management of symptomatic PFCs [13-19].

The aim of our study was to evaluate the efficacy and safety of fully covered self-expanding BFMS and LAMS for EUS-guided drainage/debridement of pancreatic WON.

Patients and methods

Patients

The endoscopy databases at 5 tertiary centers were queried for all patients who had undergone EUS-guided drainage/

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Conflict of Interest: Ali Siddiqui: Consultant Boston Scientific, Medtronic, AbbVie; Jose Nieto: Consultant Boston Scientific, Medtronic; Janak Shah: Consultant Boston Scientific, Medtronic; Kenneth F. Binmoeller: Consultant Boston Scientific, Developer of the AXIOS stent with Xlumena; Thomas Kowalski: Consultant Boston Scientific, Medtronic, Cook Medical; David Loren: Consultant Boston Scientific, Medtronic, Cook Medical; Douglas G. Adler: Consultant Boston Scientific, Medtronic, Merit; Reem Z. Sharaiha: Consultant Boston Scientific, Apollo; Michel Kahaleh: Consultant Boston Scientific; Nageshwar D. Reddy; Developed the Nagi stent with Taewoong Endoscopy

debridement of a pancreatic WON between November 2009 and December 2015. Only patients with a 6-month or greater follow up were included in the study.

We included patients who had a pancreatic WON, demonstrated by computed tomography (CT) or magnetic resonance imaging, with the following symptoms: 1) refractory abdominal pain; 2) gastric outlet or biliary obstruction; 3) ongoing systemic illness, anorexia, and weight loss; 4) rapidly enlarging WONs; and/or 5) infected WONs. A pancreatic WON was defined as a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis that had developed a well-defined inflammatory wall (as per the Revised Atlanta Classification) [4].

Patients at the Asian Institute of Gastroenterology underwent therapy with BFMS. Patients at Thomas Jefferson University, University of Utah, New York Presbyterian Hospital, Borland-Groover Clinic, and California Pacific Medical Center underwent therapy with LAMS.

We excluded patients who had pancreatic pseudocysts, neoplastic cystic lesions, coagulopathy (international normalized ratio >1.5) and thrombocytopenia (platelets <50,000 /mm³), or imaging showing that the WON wall was not in close contiguity (>2 cm) to the EUS probe.

Procedure and technique

Initial endoscopic drainage of the WON cavity

All patients underwent endoscopy using a linear array echoendoscope under monitored anesthesia care or general anesthesia. Patients were administered broad-spectrum antibiotics before and after the procedure. The echoendoscope was used to examine the site of the WON. EUS imaging under Doppler flow guidance was used to assess local vasculature and determine the cyst puncture site (either trans-gastric or trans-duodenal). A 19-G needle was used to perform the primary puncture into the WON cyst cavity. The contents were then aspirated to confirm the location and the aspirate was sent for microbiology. A 0.025" or 0.035" guidewire was inserted through the needle and then coiled into the PFC. The needle was then withdrawn, leaving the guidewire in the cyst. A fistulous tract was created using a needle knife or a 6 French cystotome (Endoflex GmbH, Dusseldorf, Germany) followed by a 4 mm or 6 mm controlled radial expansion wire-guided balloon dilation. Stent delivery catheters for either the LAMS or BFMS were then placed over a guidewire and advanced into the WON. The distal flange was deployed under EUS guidance so that it was positioned against the WON wall. Deployment of the proximal flange was then performed under endoscopic guidance. The selection of stent diameter was at the discretion of the endoscopist. In patients with LAMS, the deployed stent lumen was then dilated up to the diameter of the stent with a controlled radial expansion balloon to allow for optimal stent luminal expansion.

Patient follow up after procedure

All patients were observed after the procedure with an overnight hospital admission. Broad spectrum intravenous antibiotics with

the ability to penetrate pancreatic necrosis (e.g., carbapenems, quinolones, metronidazole) were continued for 2-3 days, after which the route was changed to oral. In patients with persistent or new onset symptoms, a non-contrast CT scan was carried out to assess the response to treatment and exclude any procedure-related adverse events. Endoscopic reintervention was performed on patients who had refractory abdominal pain, persistent fevers, nausea/vomiting, or those with ongoing systemic inflammatory response syndrome even after initial stent placement.

Patients in the LAMS group who remained symptomatic without clinical improvement after 72 h underwent DEN. The necrotic cavity was entered transmurally via an endoscope at regular intervals until complete resolution of the necrotic cavity was confirmed endoscopically and/or by cross-sectional imaging. Irrigation of the WON cavity with 3% hydrogen peroxide during DEN was performed at the endoscopist's discretion.

Patients in the BFMS group were treated using a "step-up approach". As the first step in this approach, any occluding debris was cleared using endoscopic devices (de-clogging) using snare or forceps if there was no clinical improvement in the patient 72-96 h after initial BFMS placement. In patients who did not improve with de-clogging of the stent, the second step was to place an 8.5-Fr nasocystic tube (NCT) within the lumen of the WON and perform irrigation with saline and 3% hydrogen peroxide (each session of irrigation was done at 8 hourly intervals using 20 mL of 3% H₂O₂, followed 10 min later by 100 mL saline). Those without improvement then underwent the third step treatment, i.e., DEN. Subsequent sessions of DEN were dependent on the patients' symptoms.

All patients underwent imaging with a contrast-enhanced abdominal CT or transabdominal ultrasound at 4-8 weeks after initial stent placement, followed by an outpatient clinic visit. The stent was removed if complete WON decompression was achieved, i.e., the WON had completely resolved without leaving any residual fluid component. Patients were then followed at regular intervals for at least 6 months in an ambulatory setting after stent removal and repeat imaging was performed if there was any clinical suspicion of WON recurrence.

Outcome measures

The primary outcome of this study was to evaluate the clinical success rate of the LAMS and BFMS for therapy of WON at 6-month follow up, defined as: i) complete radiological resolution of WON; ii) no need for further treatment of the WON with percutaneous or surgical drainage; and iii) resolution of clinical symptoms. Secondary outcomes evaluated were technical success (ability to access and drain a WON by placement of transmural stents), adverse events (AEs), stent migration, stent dysfunction after placement, the number of endoscopic reinterventions required, and WON recurrence rates after stent removal.

Procedure-related AEs were defined as those that occurred within 7 days of the procedure. Major bleeding was defined as

hemodynamic instability and/or bleeding in which endoscopic intervention was unsuccessful in obtaining hemostasis and which required embolization or surgical intervention. Minor bleeding was defined as bleeding that was controlled with endoscopic intervention. Procedure-related death was defined as death within 48 h of the procedure, or resulting from events directly related to the procedure. Information on all patients who died was collected. Long-term AEs (endoscopic reintervention because of stent dysfunction due to occluding debris and stent migration) were defined as AEs that occurred 7 or more days after the index stent placement procedure.

Stent migration was divided into 2 types: clinically insignificant and clinically significant. Clinically insignificant migration was defined as spontaneous external migration of a stent after complete resolution of WON. Clinically significant migration was defined as stent migration that occurred before the WON had resolved, and could be either internal or external, as follows: internal migration was migration of the stent inside the WON cavity with persistent WON, whereas external migration was migration of the stent into the lumen with persistent WON.

Statistical analysis

This was a retrospective cohort study. We divided the subjects into 2 groups according to the type of stent used to drain the WON: 1) LAMS and 2) BFMS. Outcomes between the groups were compared using Student's *t*-test for continuous variables and the chi-square test for categorical variables. Generalized linear modeling (GLM) was performed on categorical and continuous variables in order to assess the impact of the stent type. All initial GLMs were univariate, with stent type as the only predictor. A multivariate GLM was also run in order to assess the impact of stent type in the presence of age, sex, WON size and short-term AEs as indicators of the odds of successful WON resolution. The Akaike information criterion was used to determine the most appropriate link function in the GLMs for each outcome. Statistical significance was determined *a priori* as $P \leq 0.05$.

Results

Baseline characteristics

We evaluated 387 patients with symptomatic pancreatic WONS in whom EUS-guided drainage using either LAMS or BFMS was performed. The median age of the patients was 43 (range 11-87) years and 27% were female. The overall etiologies of the patients' pancreatitis were gallstones (36.9%), alcohol (39.5%), idiopathic (17.3%), and other causes (6.72%). The WON were located in the head (8.3%) or body and tail (90.9%). The median size of the WON was 100 (range, 30-260) mm. The patients and the WON characteristics of the 2 groups are

Table 1 Patient demographics and pancreatic fluid collection characteristics

Characteristics	All patients N = 387	BFMS N=205	LAMS N=182	P-value
Sex				
Female	103	24 (11.7%)	79 (43.4%)	<0.0001
Male	284	181 (88.3%)	103 (56.6%)	
Mean age (years)	43.6	34.8	53.4	<0.001
Race				
White	143	0 (0%)	143 (78.6%)	<0.0001
Black	14	0 (0%)	14 (7.7%)	
Hispanic	15	0 (0%)	15 (8.2%)	
Other	215	205 (100%)	10 (5.5%)	
Pancreatitis etiology				
Gallstone	143	55 (26.8%)	88 (48.4%)	<0.0001
Alcohol	151	91 (44.4%)	60 (33%)	
Idiopathic	67	52 (25.4%)	15 (8.2%)	
Trauma	0	0 (0%)	0 (0%)	
Autoimmune	2	0 (0%)	2 (1.1%)	
High triglycerides	17	3 (1.5%)	14 (7.7%)	
Drug related	7	4 (2%)	3 (1.6%)	
Mean WON long axis measurement (mm)	112.9	108.7	117.7	0.0598
Site of WON				
Pancreatic head	32	24 (11.7%)	8 (4.4%)	0.0105
Pancreatic body/tail	352	181 (88.3%)	171 (95.6%)	
Stent characteristics				
Stent characteristics (diameter × length)		29 (14×10mm) 27 (14×20mm) 106 (16×10mm) 32 (16×20mm) 11 (14×30mm)	59 (10×10mm) 122 (15×10mm) 1 (20×10mm)	

*Statistically significant

BFMS, fully covered bi-flanged metal stent; LAMS, lumen-apposing metal stent; WON, pancreatic walled-off necrosis

Table 2 Procedural characteristics and adverse events

Characteristics	BFMS N=205	LAMS N=182	P-value
Site of cyst- enterostomy			
Stomach	205 (100%)	119 (65.4%)	<0.0001
Duodenal bulb	0 (0%)	63 (34.6%)	
Procedural technical success (%)	99	98.9	0.9048
Procedure-related adverse events			
None	186 (90.7%)	162 (89%)	0.61
Clinically significant bleeding	2 (1%)	5 (2.7%)	
Suprainfection	15 (7.3%)	12 (6.6%)	
Perforation	2 (1%)	3 (1.6%)	

BFMS, fully covered bi-flanged metal stent; LAMS, lumen-apposing metal stent

summarized in Table 1. As compared to the LAMS group, patients in the BFMS group were significantly younger, mostly male, all Asian in ethnicity—due to the location of the center where BFMS was utilized—and had alcohol as the predominant etiology of pancreatitis.

Procedure characteristics of initial EUS-guided WON drainage procedure

A total of 182 patients underwent WON cavity drainage using LAMS and 205 had drainage using BFMS (Table 2).

Table 3 Results of endoscopic ultrasound-guided drainage/debridement for WON

Characteristics	BFMS N=205	LAMS N=182	P-value
Mean number of endoscopic sessions for WON resolution	1.54	2.71	<0.001
Total number of endoscopic sessions after stent placement			
1	156 (76.1%)	38 (20.9%)	<0.0001
2	10 (4.9%)	64 (35.1%)	
≥3	39 (19%)	80 (44%)	
Success rate for endoscopic drainage of WON (%)	96.1%	95.6%	0.8078
Recurrence of WON after endoscopic stent removal (%)	2.4%	0%	0.25

BFMS, fully covered bi-flanged metal stent; LAMS, lumen-apposing metal stent; WON, pancreatic walled-off necrosis

Trans-gastric drainage was performed in 324 patients (83.7%), while 63 patients (16.27%) had trans-duodenal drainage.

Clinical success

At 6-month follow up, overall clinical success with successful eradication of the WON was achieved in 95.6% patients with LAMS and 96.1% of patients with BFMS (P=0.80). Patients whose symptoms did not resolve with endoscopic therapy required additional interventions in the form of percutaneous or surgical drainage (Table 3). On multivariate analysis, the type of stent, age, sex and WON size did not predict the success of WON resolution (Table 4).

The median number of procedures required for WON resolution after initial stent placement was significantly lower with BFMS stents (2, range 2-5) compared to LAMS (3, range 2-8) (P<0.001). Approximately 44% of patients with LAMS stents required 3 or more endoscopic sessions for DEN following stent placement in comparison to only 16.3% of patients with BFMS stents.

The LAMS were successfully removed once complete resolution of the WON had been confirmed by CT scan after a mean time of 26 (range 17-72) days. The BFMS were successfully removed after confirmation of complete resolution of WON by CT scan after a mean time of 37 days (range 14-87) days.

In the BFMS group, 162 (72%) patients underwent stent removal after 4-8 weeks, 15 (7%) patients had spontaneous migration of the BFMS into the gastric lumen due to complete resolution of the pancreatic WON, and 21 (10%) reported for late removal of the BFMS for logistical reasons.

Technical success

There was no statistically significant difference in the overall technical success (ability to access and drain a WON by placement of transmural stents) between the LAMS and BFMS groups (98.9% vs. 99%, respectively, P=0.9048; Table 2). There was maldeployment of the LAMS in 2 patients.

Of the 2 patients with technical failure in the BFMS group, the first patient had a large WON with an entry point close to the gastroesophageal junction, posing a technical challenge to stent deployment, while the second patient had an internally

Table 4 Multivariate analysis evaluating predictors of success for WON resolution

Predictors of Success	Odds ratio (95%CI)	P-value
Stent type		
LAMS	Ref	0.6795
BFMS	1.31 (0.37-4.64)	
Age	1.00 (0.96-1.04)	0.9764
Sex	0.59 (0.15-2.30)	0.4451
WON size (mm)	1.00 (0.99-1.01)	0.5605
Procedural adverse events	1.13 (0.31-4.15)	0.8494

*Statistically significant

BFMS, fully covered bi-flanged metal stent; LAMS, lumen-apposing metal stent; WON, pancreatic walled-off necrosis; CI, confidence interval

migrated BFMS as the result of an obscured endoscopic view during deployment.

In the patients where LAMS were successfully deployed, the diameters of the stents were: 10 mm (n=7) and 15 mm (n=173). In the BFMS group, the stent diameters were: 12 mm (n=3), 14 mm (n=98), and 16 mm (n=104).

Patients with stent maldeployment were referred for drainage of their WON by either surgical or interventional radiology management.

Procedure-related AEs (within 7 days of index procedure)

In the LAMS group, procedure-related AEs occurred in 20 (10.9%) patients. Five patients had major bleeding requiring abdominal angiography. Three patients developed perforation during the cyst-enterostomy requiring surgical closure. Suprainfection requiring intravenous antibiotics occurred in 12 patients.

In the BFMS group, procedure-related AEs occurred in 19 (9.3%) patients. Two patients had major bleeding, with one requiring abdominal angiography and one needing surgery. Two patients developed perforation during the cyst-enterostomy requiring surgical closure. Suprainfection requiring intravenous antibiotics occurred in 15 patients.

Patients in the BFMS group had a similar rate of procedure-related AEs compared to the LAMS group (9.3% vs. 10.9%,

P=0.61). On multivariate logistic regression analysis, there was no statistically significant difference between the stents as regards the risk of procedural AEs (odds ratio 1.13, P=0.84), even after adjustment for sex, age and cyst size. These results are summarized in Table 2.

Long-term AEs (7 or more days after index endoscopy)

Long-term AEs (endoscopic reintervention because of stent dysfunction due to occluding debris and stent migration) were significantly more frequent in the BFMS group at 17.6% (36/205 patients) compared to the LAMS group at 7.7% (14/182 patients; P=0.0039).

Stent dysfunction

Stent dysfunction with occluding debris was significantly more common in the BFMS group compared to the LAMS group (10.2 % and 5.9%, respectively, P=0.04).

Endoscopic reintervention

Endoscopic reintervention via DEN was performed in 151/182 (82.9%) patients treated with a LAMS. Thirty-eight patients had one session, 64 had 2 sessions, and 49 had 3 or more sessions in order to achieve WON resolution. Hydrogen peroxide-assisted necrosectomy was performed in 37 of these patients.

In the BFMS group, reintervention was required in 49 (23.9%) patients who had persistent symptoms after initial stent placement. Stent dysfunction with occluding debris was noted in 21 patients; 10 patients improved with de-clogging while 11 patients required NCT placement with irrigation, because of the presence of visible debris within the WON. Another 28 patients went directly to the second step of NCT placement, when infected debris within WON was noted without stent dysfunction. In total 39 patients required NCT irrigation, which was maintained for 3-7 days. After clinical improvement, a relook WON inspection was done and those patients who had healthy granulation tissue (observed in 10) with no significant debris had the NCT removed. Six patients with adherent mild debris required placement of a plastic stent within the BFMS. Another 23 patients (11.2%) who did not improve with NCT and lavage required DEN.

Stent migration

The overall migration rate (significant and insignificant) was higher in the patients with BFMS (n=15) compared to those with LAMS (n=3) (7.3% vs. 1.6%; P=0.0008). However, there was no difference between the BFMS and LAMS groups in the clinically significant migration (2.4% vs. 1.6%, respectively; P=0.73). Stent migrations in the LAMS group occurred spontaneously and the stent passed without incident. All clinically significant migrations in the BFMS group occurred during DEN. Of these, 2 patients had internal migration into the WON and the BFMS

stents were repositioned using grasping forceps. The other 3 patients had external migration and the stent was repositioned successfully into the WON using grasping forceps.

Patient follow up

Symptomatic PFC recurrence after stent removal occurred in no patients in the LAMS group compared to 5 patients in the BFMS group (P=0.25). All of these patients had a disconnected pancreatic duct and were treated successfully by EUS-guided drainage using plastic stents.

Discussion

EUS-guided drainage/debridement of WON using transmural stents is now the preferred modality for the treatment of pancreatic WON, because of its lower complication rates, and significantly lower morbidity and mortality when compared to surgery [5-7,20-22]. DPTs have historically been the first-line endoscopic accessory used in the endoscopic management of PFCs, including WON. There are, however, several inherent disadvantages to the use of DPTs in the management of WON, including their small diameter (7-10 Fr), high rates of stent occlusion and migration, and the need for multiple stent placements to obtain adequate drainage and debridement [9-11,23].

Limitations in the conventional accessories used to manage WON have led to the invention of specialized metal stents for PFC drainage. The "saddle-shaped" lumen-apposing fully covered metal stent (AXIOS™) and the bi-flanged metal stent (NAGI™) are custom-made for debridement of PFCs and have been demonstrated to have a high success rate for the drainage/debridement of WON [15,17,18,24]. Several studies to date have demonstrated the LAMS and BFMS to be safe and effective, with high rates of technical (89-100%) and clinical success (77-100%) [13-15,17,19,25-28]. A unique feature of these stents is that their unique design, with a large inner diameter, allows direct endoscopic debridement of WONs after stent deployment by passage of the standard endoscope through the stent lumen without stent removal; the anchoring flanges prevent stent dislodgement during the debridement. The LAMS is presently FDA approved in the United States for drainage of PFCs, while the BFMS stent is currently not available for use in the United States.

In a multicenter retrospective study, Siddiqui *et al* reported a technical success rate of 97.5% and 88% clinical success in WON drainage using LAMS [28]. Two cases of technical failure were due to stent maldeployment in the pancreatic pseudocyst group. Sharaiha *et al*, in a retrospective analysis of 124 patients with WON, achieved a clinical success rate of 86% of patients using the LAMS [17].

Equally high rates of clinic and technical success have been noted with the use of the BFMS in the management of PFCs, including WON. In a retrospective case series, Yamaoto *et al* reported on the use of the BFMS in the treatment of PFCs in

9 patients (5 patients with pseudocysts and 4 patients with WON). Technical success was 100% and clinical success was achieved in 77.8%. Drainage of pancreatic pseudocysts was achieved in all patients, while complete remission of infection was noted in 2/4 patients (50%) of patients with WON. There was 1 episode of internal stent migration thought to be due to complete resolution of the cyst. No stent-related complications were noted [27]. Chandran *et al* evaluated the role of BFMS in 47 patients with PFCs and reported a technical success rate of 98.1% and 76.6% clinical success (36/47 patients). The lower clinical success rate was attributed to a large subgroup of patients with WON, infected WON and infected pseudocyst. Notably, 34 of 36 patients (94.4%) with successful resolution of PFCs showed a sustained response for more than 6 months [14].

In the present study we found similarly excellent technical success rates in patients with LAMS and BFMS (98.9% vs. 99%, $P=0.9$). Technical failure was noted in 2 patients in both the LAMS and BFMS groups. Clinical success for WON drainage was not significantly different in the LAMS and BFMS groups (95.6% vs. 96.1%, $P=0.8078$). During long-term follow up, 8 patients in each group required additional therapy in the form of surgical debridement or percutaneous catheter drainage because of failure of endotherapy.

DEN was performed in 151 patients in the LAMS cohort (82.9%) compared to 23 patients in the BFMS cohort (11.2% of total treated with BFMS). Patients in the LAMS group underwent a great number of DEN, since the management protocol in all these centers scheduled aggressive DEN until resolution of the WON. This was different from the management protocol in the BFMS cohort, where a step-up approach was adopted; DEN in these patients was only performed if other adjunctive interventions with de-clogging, nasocystic catheters and hydrogen peroxide were not successful [21,29].

The median number of procedures required for WON resolution after initial stent placement was significantly higher with LAMS compared to BFMS. The larger internal diameter of the BFMS may have been more effective for spontaneous WON drainage. Furthermore, DEN carried out through the wider BFMS may have been more effective for debris evacuation, obviating the need for additional endoscopic sessions. As noted above, the increased number of procedures required in the LAMS group may simply be a reflection of the protocol followed in these centers, where the endoscopists believed in scheduled aggressive DEN.

The most frequent AEs associated with endoscopic drainage and DEN in patients with WON are bleeding, perforation or post-procedure infection [30]. Despite the unique anchoring design, intended to ensure firm anchorage, there have been reports of stent migration and dislodgement reported with both the LAMS and BFMS [25,26]. Rinninella and Shah each reported one case of stent migration with LAMS [26,31]. Ang *et al* observed a high stent migration rate (6.3%) with BFMS; they postulated that the high risk of migration with BFMS may be due to a lack of lumen apposition and excessive length. Similarly, in our study, stent migration was higher in the BFMS cohort, although in the majority of cases it was not clinically significant. Spontaneous migration in the LAMS was not associated with AEs. All migrations in the BFMS happened during DEN.

Our study showed that patients in the BFMS group had a significantly higher rate of stent occlusion with debris compared to the LAMS group. This difference may reflect an inherent disadvantage with the step-up approach used in the BFMS cohort, as compared to DENs after a planned interval in the LAMS cohort (during which any debris partially occluding the stent would have been removed). Our study shows similar results to those of Bekkali *et al* [35], where LAMS were superior to BFMS in terms of procedure time, with comparable AEs and success.

In our study, external stent migration was noted in 3/182 (1.65%) patients in the LAMS group and 5/205 (2.4%) patients with BFMS stents. This incidence is consistent with other studies. Bapaye *et al* recently reported a migration rate of 2.7% in patients with BFMS. In the present study, procedural AEs were similar in the LAMS group (20/182; 11%) and the BFMS group (19/205; 9.3%). Previous studies have reported similar complications with the use of BFMS [16, 24,32,33]. Significant bleeding was higher in the LAMS cohort as compared to the BFMS group. While bleeding at the time of stent deployment or within the following week is difficult to explain, since all these procedures were done under EUS Doppler guidance, this could be related to stent erosion into a vessel as the WON cavity wall collapses, or a pseudoaneurysm in the cavity wall.

Our study has several strengths. Thus far the majority of available literature on the use of the specialized BFMS, customized for management of PFCs, have been single-arm non-comparative case series reporting efficacy for all PFCs, including pseudocyst and WON, in small groups of patients. Our study is the only one to date that has performed a comparison, evaluating the efficacy and safety of lumen-apposing LAMS and BFMS in patients with WON.

The present study does have a number of limitations. It was retrospective in nature, with its inherent limitations including variable follow up of patients, quality of cross-sectional imaging at different centers and variability in the technique of the endoscopist. In addition, the BFMS were used in one center in India, while the LAMS were used in centers in the USA; hence the patients studied had different demographic characteristics. As the subjects in each cohort were not from the same representative sample, there was significant heterogeneity between the 2 groups. We also did not have data on the percentage of solid debris in the WON cavity, which could potentially influence procedural success.

The optimal stent for endoscopic drainage of WON remains unsettled. Several authors have argued that, based on the current literature, there are insufficient data to support the routine use of one stent type over another [34]. With the advent of new stents such as the LAMS and BFMS, customized for PFC drainage, there may be a trend toward using these stents especially in the management of WON when necrosectomy is required. In this study we have demonstrated that endoscopic therapy of WON using either LAMS with scheduled DEN and BFMS using a step-up approach is safe and equally effective in terms of overall treatment efficacy. Further randomized controlled studies are needed to confirm these results and investigate the long-term results, cost-effectiveness and complication rates of these stents.

Summary Box

What is already known:

- Fully covered bi-flanged metal stents (BFMS) and lumen-apposing metal stents (LAMS) have both been shown in individual clinical trials to be safe and effective for endoscopic ultrasound-guided drainage of pancreatic walled-off necrosis

What the new findings are:

- In this unique retrospective clinical study that directly compared the clinical outcomes and adverse events of the BFMS and LAMS, the clinical success and adverse events in the BFMS and LAMS groups were similar
- Stent migration rate for BFMS was significantly higher compared to LAMS

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