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Lumen-apposing metal stents for drainage of pancreatic fluid collections: does timing of removal matter?

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Received 5 August 2021
Accepted 25 January 2022
Published Online First 25 February 2022

To cite: Nayar M, Leeds JS, UK & Ireland LAMS Colloborative,, *et al*. *Gut* 2022;**71**:850–853.

MESSAGE

Lumen-apposing metal stents (LAMS) are increasingly used for treatment of pancreatic fluid collections (PFC); some reports have recommended early removal due to an increased complication rate after 4–8 weeks. Analysing data from 18 UK and Ireland units retrospectively with a total of 1018 patients, initial bleeding was seen in only 1.1% of cases. During follow-up (n=952), there were 63 significant delayed complications such as bleeding (n=18) or buried stent (n=45). None of the factors analysed such as type (walled off necrosis vs pseudocyst) size of collection or timing of removal (4–8 weeks vs. >8 weeks) showed a correlation with delayed advse events (AE). These results provide further indirect evidence for leaving LAMS in situ beyond 4 weeks if required clinically.

IN MORE DETAIL

LAMS have become the treatment of choice for treatment of PFCs primarily related to ease of use and perceived advantage of a large lumen to facilitate drainage and direct endoscopic necrosectomy. Reported AE include bleeding, sepsis, and perforation and buried stent syndrome. Predictors of immediate and late AE are controversial. Stent indwelling time beyond 4 weeks has been reported as a predictor of delayed bleeding and buried stent syndrome and a consensus has formed to remove LAMS by 4 weeks. However, this recommendation is based primarily on data from one cohort in one centre[1 2] limiting the generalisability of the results.

A retrospective multicentre study involving 18 units from the UK & Ireland was performed with the aim of investigating the technical and clinical success of LAMS (Hot AXIOS Stent) for PFC and the incidence of immediate and delayed AE and their associated risk factors. Data on LAMS placed for drainage of PFC in adults (>18 years of age) between 2015 and 2019 were collected. As per UK and Irish republic guidance, ethical approval from an institutional review body was not required for this study. Institutional authorisation to hold a prospective patient database for use for quality improvement was obtained in each institution.

All procedures were performed by experienced endosonographers with a therapeutic echoendoscope. PFC were categorised in adherence to the revised Atlanta Criteria.[3] Under EUS guidance, the PFC was assessed and punctured from the stomach or duodenum. The exact technique of puncture and use of ancillary imaging or techniques including fluoroscopy, balloon dilatation, nasocystic drain and/or placement of plastic pigtail stent within the LAMS was at the endoscopists' discretion. Stent removal was not to a set protocol but in the latter part of the study period, influenced by early data indicating increased AE with longer LAMS indwelling time, there was a consensus to aim to remove the LAMS within 4–6 weeks if possible. Patient related, procedural and post procedural data were recorded on a standard proforma in each unit. Follow-up data were collected in real time on the electronic patient record and when patients came back for stent removal.

Data were anonymised prior to transmission for compiling into a central dataset for analysis. A number of cases in the present study were included in previous publications.[4 5]

The outcomes of the study were technical success (index attempt), immediate AE and significant delayed AE . Technical success was defined as the ability to deploy LAMS in the correct position to enable drainage of the PFC. Clinical success was

Key messages

What is already known on this topic

- With the increasing use of lumen-apposing metal stents (LAMS) for the treatment of pancreatic fluid collections (PFCs), there are reports of significant delayed events including buried stents and bleeding. The former could be related to the timing of removal of LAMS.

Why this study needed to be done

- The 4-week recommended interval for LAMS removal is based on data from a single centre thus limiting generalisability. Our study did not report increased rate of delayed events when the LAMS were removed beyond 4 weeks.

How this study might affect research, practice or policy

- Findings from the largest dataset in published literature adds to the existing knowledge on the use of LAMS for drainage of PFCs and its extended use in patients where clinically indicated. This will help promote further research in the treatment of PFCs.

Table 1 Patient demographic details, pancreatic fluid collections (PFC) aetiology, PFC characteristics and procedure details

Age (years)	**Median (IQR)**	**54 (43–64)**
Sex, n (%)	Female	420 (41.3)
	Male	598 (58.7)
Aetiology of pancreatitis, n (%)	Gallstones	488 (47.9)
	Alcohol	302 (29.7)
	Idiopathic	140 (13.7)
	Other	88 (8.6)
Type of collection, n (%)	WON	539 (52.9)
	PC	479 (47.0)
Size of collection (cm)	Median (IQR)	11 (9–14)
Percentage necrosis	<30%	597 (58.6)
	>30%	197 (19.4)
Procedure location, n (%)	Endoscopy unit	908 (89.2)
	Operating theatre	70 (6.9)
	Intensive care unit	40 (3.9)
Sedation	Conscious sedation	674 (66.2)
	General anaesthesia/Propofol	344 (33.8)
X-ray screening used, n (%)	No	762 (74.9)
	Yes	256 (25.1)
Stent size, n (%)	10 mm	128 (12.6)
	15 mm	848 (83.3)
	20 mm	42 (4.1)
Balloon dilatation of stent, n (%)	No	861 (84.6)
	Yes	157 (15.4)
Plastic stent, n (%)	No	826 (81.1)
	Yes	192 (18.9)
Nasocystic drain, n (%)	No	976 (95.9)
	Yes	42 (4.1)

defined as size of the PFC <2 cm on cross-sectional imaging or at the time of stent removal whichever came first.

Immediate AE were defined as occurring within 24 hours of the procedure and included maldeployment, stent dislodgement, internal and external migration, and bleeding as defined by ASGE lexicon.[6]

Significant delayed AE were defined as clinically significant bleeding occurring beyond 24 hours of LAMS placement and buried stent. A buried stent was defined as the finding of internal migration of LAMS or tissue overgrowth and failure to remove at the time of initial removal attempt.

Analyses were performed to examine factors associated with significant delayed AE. As data were compiled from a large number of centres, analyses were performed using multilevel statistical methods. Two-level models were used with patients nested within centres. Due to the binary nature of the outcome, the analyses were performed using multilevel logistic regression (Stata V.14). First, the separate association between each factor and AE was assessed in a series of univariable analyses. Subsequently, the joint association between variables was examined in a multivariable analysis. A backwards selection procedure was used to retain only the statistically significant variables. All clinically relevant variables were included as predictor variables.

A total of 1018 patients underwent EUS-guided drainage of PFC (WON 52.9%, PC 47.1%) with LAMS between October 2015 and January 2020. Table 1 details patient demographic details, PFC aetiology, PFC characteristics and procedure details.

Technical success was achieved in 97.1% (988/1018) patients. Immediate AE occurred in 3.8% (39/1018) patients (95% CI 2.7% to 5.2%) that included bleeding in 1.1% (11/1018) patients (95% CI 0.5% to 1.9%) of which two patients who had bleeding had balloon dilatation performed. Three cases of bleeding were categorised as severe. Stent maldeployment occurred in 2.2% (23/1018) patients (95% CI 1.4% to 3.4%) of which 13 were unspecified, 7 were within the cavity, 2 into colon and 1 within the stomach. In three patients, the reason for technical failure was not specified. One patient had a sedation-related adverse event.

Full follow-up information was available for 952 patients. Clinical success was recorded in 89.5% (852/952) (95% CI 87.4% to 91.4%). Total delayed AEs occurred in 17.5% (167/952) patients (95% CI 14.9% to 20.4%). Significant delayed AE occurred in 6.6% (63/952) (95% CI 5.1% to 8.4%) including buried stent in 4.7% (45/952) (95% CI 3.5% to 6.3%) and bleeding in 1.9% (18/952) (95% CI 1.1% to 3.0%).

The other 104 delayed AE included external migration in 70, internal migration in 25, blocked stent in 8 and gastrocolonic fistula in 1.

Median time to attempted LAMS removal was 7 weeks (IQR 5–12), 80.2% (687/856) (95% CI 77.4% to 82.9%) had a removal of LAMS >4 weeks after insertion. The most common clinical reasons for the late removal of LAMS was a combination of patients with WONs still undergoing endoscopic necrosectomy and/or delayed (>4 weeks) scheduled appointments for stent removal. The reason for late removal was not aetiology specific. Results of univariable analysis of factors associated with significant delayed AE are shown in table 2. On multilevel logistic regression, no variable was found to be associated with significant delayed AE.

COMMENT

LAMS with its unique single delivery design has the distinct advantage of ease of insertion in any facility (endoscopy unit, theatre or intensive care unit) without the use of ancillary equipment including guidewires and fluoroscopy for drainage of PFC. The present study represents the largest, multicentre cohort examining outcomes on the use of LAMS in patients with PFC. The study documented high technical (97.1%) and clinical (89.5%) success with immediate AE in 3.8% and significant delayed AE in 6.6%. The overall delayed AEs was 17.5%.

The technical success rate is in keeping with that previously reported[4 5 7] finding of a delayed bleeding rate of 1.9% is in keeping with previous studies.[8–12] In the present study, significant delayed AE were not associated with the interval between LAMS insertion and removal a number of previous studies have suggested a significant increase in bleeding risk when LAMS are left in situ for more than 4 weeks.[1 2] However, a recent literature review of bleeding events post LAMS placement identified 21 studies involving 1378 patients with a bleeding rate of 3.8% of which 46.2% occurred in the first week post LAMS placement.[12]

In contrast to our findings of no difference in AE between WOPN and PC and possible association of balloon dilatation with immediate AEs, a recent international multicentre study among 328 patients reported overall AE to be more likely in WOPN versus PC and cases with AEs were less likely to have undergone balloon dilatation of the tract.[5] The reasons underlying the differences in these studies are not easily identifiable; however, the present study was conducted in a much larger cohort across multiple centres. Whether there are differences in patient assessment or selection criteria for which patients undergo LAMS insertion cannot be assessed.

Table 2 Univariable analyses of factors associated with delayed bleeding and buried stent syndrome

Variable	Category	Adverse event n/N (%)	ORs (95% CI)	P value
Case per unit †	–	–	1.04 (0.98 to 1.11)	0.16
Age †	–	–	1.04 (0.88 to 1.24)	0.63
Sex	Female	21/391 (5.4%)	1	0.20
	Male	42/561 (7.5%)	1.43 (0.83 to 2.45)	
Aetiology	Gallstones	25/453 (5.5%)	1	0.56
	Alcohol	23/285 (8.1%)	1.50 (0.84 to 2.70)	
	Idiopathic	10/132 (7.6%)	1.40 (0.66 to 3.00)	
	Other	5/82 (6.1%)	1.11 (0.41 to 2.99)	
Sedation	Conscious	38/637 (6.0%)	1	0.25
	GA / Propofol	25/315 (7.9%)	1.36 (0.80 to 2.29)	
Type collection	WON	27/505 (5.4%)	1	0.10
	Pseudocyst	36/447 (8.1%)	1.55 (0.93 to 2.59)	
Cyst size *	–	–	1.21 (0.91 to 1.61)	0.19
Cyst size	≤10 cm	30/448 (6.7%)	1	0.93
(categorical)	>10 cm	33/504 (6.6%)	0.98 (0.58 to 1.63)	
Necrosis	<30%	40/564 (7.1%)	1	0.16
	>30%	8/190 (4.2%)	0.58 (0.26 to 1.25)	
Time to stent	≤4 weeks	11/169 (6.5%)	1	0.58
removal	4.1–8 weeks	17/324 (5.3%)	0.80 (0.37 to 1.75)	
attempt ‡	>8 weeks	26/363 (7.2%)	1.12 (0.53 to 2.34)	
Balloon dilation	No	57/807 (7.1%)	1	0.20
	Yes	6/145 (4.1%)	0.57 (0.24 to 1.34)	
Plastic stent	No	52/772 (6.7%)	1	0.76
	Yes	11/180 (6.1%)	0.90 (0.46 to 1.76)	
Nasocystic drain	No	60/912 (6.6%)	1	0.82
	Yes	3/40 (7.5%)	1.15 (0.34 to 3.84)	
Stent size	8–10 mm	8/122 (6.6%)	1	0.60
	15 mm	54/791 (6.8%)	1.04 (0.48 to 2.25)	
	20 mm	1/39 (2.6%)	0.38 (0.05 to 3.10)	
Number of	0	51/690 (7.4%)	1	0.13
necrosectomies	1	8/113 (7.1%)	0.95 (0.44 to 2.07)	
	2+	4/149 (2.7%)	0.35 (0.12 to 0.97)	

*OR given for a 5-unit increase in variable.
†OR given for a 10-unit increase in variable
‡Analysis performed for patients who had a stent removed only.

The most common delayed AE was found to be buried stents with an overall rate of 4.7% and this appears to be a commonly reported issue with LAMS. Management of a LAMS that is not immediately removable endoscopically or has become embedded in the intestinal wall can be challenging and resource intensive. Patients often require additional imaging prior to reattempting removal, additional endoscopic measures such as the 'stent-in-stent' technique or even surgery. Given the consequence of this AE, the ability to predict its occurrence would be valuable. However, no risk factors were identified in the present study and specifically, time from insertion to removal was not found to contribute to this AE. Delayed removal is sometimes necessary in patients with significant pancreatic necrosis with minimal clinical success at 4 weeks and these data support this approach. These findings from a real-life large dataset add to the existing literature on the use of LAMS for the drainage of PFCs and support the extended use LAMS in patients where clinically indicated.

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Contributors MN initiated the idea for the study, methodology, data collection and analysis and writing the manuscript and accepts full responsibility as guarantor. JSL and KO contributed to the methodology, analysis, data collection and writing of the manuscript. The UK & Ireland LAMS collaborative actively contributed to the data for patients in this study.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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