Review Article

Lumen-apposing metal stents in management of pancreatic fluid collections: The nobody's land of removal timing

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ABSTRACT Pancreatic fluid collections (PFCs) develop as a result of damage to the major or peripheral pancreatic ducts, complication due to acute or chronic pancreatitis, trauma or iatrogenic causes. PFCs include pancreatic pseudocysts (PPs) and walled-off necrosis (WON). PFCs usually resolve spontaneously and are asymptomatic, but if they persist, increase in dimension or became symptomatics, therapeutic intervention is required. Available therapeutic interventions include surgical, percutaneous, and endoscopic drainage. The endoscopic approach is nowadays considered the first line-treatment of PFCs due to various advantages when compared with surgical or percutaneous drainage: decreased morbidity, length of hospital stay, and reduced costs. In the last few years, the endoscopic ultrasound (EUS)-guided transmural drainage, initially with plastic stents, gained popularity. More recently, fully covered self-expanding lumen-apposing metal stents (LAMS) have been demonstrated to be both, safe and effective with high clinical and technical success, reducing the risk of perforation, peritoneal leakage, migration and facilitating the drainage of necrotic contents. In the last few years, several studies evaluating the safety and efficacy of LAMS and their differences with plastic stents have been performed, but literature on the removal timing of this device and associated complications is still limited. The aim of this review is to analyze studies reporting information about the retrieval timing of LAMS and the related adverse events.

Keywords: EUS, EUS-guided drainage, lumen apposing metal stent, pancreatic fluid collection, pancreatic pseudocyst, removal timing, walled-off necrosis

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INTRODUCTION

It is estimated that 5-15% of mild-moderate pancreatitis and 20% of necrotizing pancreatitis are complicated by the development of pancreatic fluid collections (PFCs): pseudocysts (PPs) or walled-off necrosis (WON), respectively.[1] The vast majority of acute PFCs resolve spontaneously and do not require any intervention. PFC drainage of mature collections with a definite wall is required when they rapidly increase in size, and/or become infected or symptomatic.[1] Percutaneous and surgical drainage were the main treatment modalities for symptomatic PFCs before the introduction of endoscopic transmural pancreatic drainage, first described in 1989,[2] with significant advantages in terms of morbidity and mortality.

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The endoscopic approach is now most commonly performed under endoscopic ultrasound (EUS)-guidance since it increases safety visualizing vessels in the drainage pathway and technical success, by including non-bulging PFCs and those located in the tail of the pancreas.[3] In the last couple of years, lumen-apposing metal stents (LAMS) have been preferred over plastic stents for management of PFCs and have shown several advantages over them. The bilateral double-walled anchoring flanges hold the gastric or duodenal wall in direct apposition to PFC on the newly formed anastomosis, thus preventing leakage and migration. The larger luminal diameter (10-15 mm) allows subsequent direct endoscopic debridement in case of WON, often required for effective control of infection. With the second-generation device, a further refinement of the stent delivery system has been developed. It incorporates an electrocautery tip, enabling a single device to be used, when previously multiple devices and steps were required.

Many systematic reviews and meta-analyses evaluating efficacy and safety of LAMS have been performed, but literature on the removal timing of this device is still scarce, with a lack of international consensus.

The recently published guidelines of the European Society of Gastrointestinal Endoscopy (ESGE)[3] on acute necrotizing pancreatitis recommend to retrieve LAMS within 4 weeks, but the level of evidence is low.

In order to improve the state of knowledge on this issue, we analyzed all eligible articles reporting timing and complications of LAMS removal.

METHODS

Study selection

We systematically analyzed Medline/Pubmed database in order to identify articles investigating LAMS placement for PFC drainage. The keywords used were: pancreatic fluid collection, pseudocyst, walled off necrosis, LAMS, Hot Axios, Axios, EUS guided drainage. The research resulted in identification of 45 publications; all the abstracts were initially screened for suitability. After exclusion of 27 studies, following the aforementioned criteria, a total of 18 publications were included in the review. Studies comparing different types of stents (self-expandable metal stents, plastic stents) and case reports were also included. There were no restrictions on the study dates and the last literature search was performed in October 2018.

Inclusion criteria

Studies reporting the timing of retrieval of LAMS placed for pancreatic fluid collection drainage in patients over the age of 18.

Exclusion criteria

Studies about LAMS not explicitly taking into consideration the removal timing, studies including only stents different than LAMS.

Outcome measures

These included efficacy of removal, complications such as the "buried stent syndrome", and immediate and delayed adverse events related to the stent retrieval.

Characteristics of included studies

Medline/Pubmed research resulted in the identification of 18 studies. After detailed examination of the full texts, 12 original studies, 2 case series, 2 case reports, 1 multi-institutional consensus and 1 evidence-based multidisciplinary guideline were considered eligible[1,3-19] for inclusion in our review. All articles cited in ESGE guidelines,[3] in relation to removal timing, were included.[4,5]

Not all the selected studies indicated in details the LAMS used. When reported, the most frequent ones were the Axios and Hot Axios stents. Axios stent TM (Boston Scientific, Natick MA, USA) is a through-the-scope, large-diameter, fully covered self-expanding metal stent (FCSEMS) with bilateral double-walled anchoring flanges specifically designed to create an anastomosis, holding the PFC wall in direct apposition to the stomach or duodenal wall. The "Hot" version of this device includes an electrocautery at the tip of the delivery catheter, allowing direct access to the PFC without the need for multiple steps. The stents are 10 mm in length and available in two different lumen diameters (10 mm and 15 mm). Very recently, a 20 mm diameter stent has become commercially available as well.

RESULTS

Description of included studies

18 studies were considered eligible. Of these, 12 were original articles, out of which 5 compared the efficacy of LAMS with other types of stents (plastic or double-flanged metal stents).[5-9] Among the original studies, 4 had a prospective[4,5,10,11] and 8 a retrospective design;[6-9,12-15] the other papers included a multi-institutional consensus on PFC drainage,[1] the 2018 ESGE guidelines on acute necrotizing pancreatitis,[3] 2 case reports[16,17] and 2 case series,[18,19] focusing on complications related to LAMS removal.

Patient and study characteristics

Patient characteristics, types of lesions and study details are summarized in Table 1.

Of the 12 original studies, 8 evaluated drainage of both PP and WON,[4,7,10-15] and 4 included only patients with WON.[5,6,8,9] The 2 case reports involved one patient with PP[17] and one with PFC (no further specification),[16] respectively, while the 2 case series included patients with PPs.[18,19]

Axios stent TM (Boston Scientific, MA, USA) was used in 7 of the original studies,[4,7,9-11,13,15] in 1 case series[18] and in 1 case report.[16] The other case series[19] and 3 of the 12 original studies[5,6,14] reported the use of the version with an incorporated electrocautery-enhanced delivery system, the Hot Axios. Both Axios and Hot Axios were used in 1 original study.[8] The type of LAMS was not described in 1 case report and in 1 original study.[12,17] ESGE guideline[3] refers to LAMS in general as well.

Outcome measures

Type of stent, removal timing and adverse events associated are summarized in Table 2.

Timing of LAMS removal

In a retrospective study by Bekkali *et al*.,[6] mean removal time was 9 weeks; at the time of publication of the study 2 LAMS were yet to be removed. In 6 studies[5,8,11,13,14,19] reported mean time of LAMS removal ranged between 8-12 weeks.

The removal timing was not precisely indicated in 3 studies.[7,9,12] The study by Lang *et al*.[7] reports stent removal at the discretion of the endoscopist, after resolution of the PFC was observed. Sahar *et al*.[9] wrote that "every LAMS has to be removed once placed" and reports the US FDA indications of stent dwell time approved for

Table 1: Type of lesions, patient characteristics (treated with LAMS) and study details

Author/Year	PCF Type	PFC size mm (range)	Male/tot patients (%)	Type of Study
Bekkali *et al*. 2017	WON	140 (110-170)	27/32 (84)	Original Article (retrospective)
Walter *et al*. 2014	45 WON/15 PP	90 (40-200)	38/62 (61)	Original Article (prospective)
Shah *et al*. 2015	WON	150 (90-230)	18/33 (54)	Original Article (prospective)
Lang *et al*. 2018	9 WON/10 PP	104 (67-155)	10/19 (53)	Original Article (retrospective)
Yoo *et al*. 2017	22 WON/3 PP	82 (60-170)	14/25 (56)	Original Article (retrospective)
Law *et al*. 2018	WON	9 (8-10)	32/46 (70)	Original Article (retrospective)
Adler *et al*. 2017	9 WON/4 PP	138 (60-159)	5/13 (38)	Original Article (retrospective)
Gornals *et al*. 2013	WON	90 (70-150)	7/9 (78)	Original Article (prospective)
Rinninella *et al*. 2015	52 WON/18 PP	100 (38-240)	22/70 (31)	Original Article (retrospective)
Siddiqui *et al*. 2016	68 WON/12 PP	118 (48-290)	48/80 (60)	Original Article (retrospective)
Bang *et al*. 2017	WON	> 60 mm	Not Indicated	Original Article (prospective)
Sahar *et al*. 2017	WON	153 (93-230)	17/25 (68)	Original Article (retrospective)
Fabbri *et al*. 2015	PFC	Not Indicated	1 (100)	Case Report
Zhu *et al*. 2018	PP	150 x 150	1 (100)	Case Report
Itoi *et al*. 2011	PP	98 (55-200)	12/15 (80)	Case Series
Seerden *et al*. 2016	PP	Not Indicated	2/2 (100)	Case Series
Arvanitakis *et al*. 2018	PFC	-	-	Guideline
Guo *et al*. 2017	PFC	-	-	Multi-institutional consensus

Table 2: Type of stent, removal timing and adverse events

Author/Year	Stent Type	Removal timing in weeks	Adverse Events (*n*)
Bekkali *et al*. 2017	Hot Axios	6-13	Buried Stent (1)
Walter *et al*. 2014	Axios	1-20	Tissue Ingrowht
Shah *et al*. 2015	Axios	3-9	None
Lang *et al*. 2018	Axios	At discretion of endoscopist after PFC resolution	None
Yoo *et al*. 2017	LAMS	At discretion of endoscopist after PFC resolution	None
Law *et al*. 2018	Axios and Hot Axios	4-12	None
Adler *et al*. 2017	Axios	4-16	None
Gornals *et al*. 2013	Axios	6-12	None
Rinninella *et al*. 2015	Hot Axios	4-16	Buried Stent (1)
Itoi *et al*. 2011	Axios	1-12	None
Siddiqui *et al*. 2016	Axios	4-16	None
Bang *et al*. 2017	Hot Axios	5-6	Buried Stent (2)
Sahar *et al*. 2017	Axios	Not indicated	None
Fabbri *et al*. 2015	Axios	4	Buried Stent (1)
Zhu *et al*. 2018	LAMS	20	Buried Stent (1)
Seerden *et al*. 2016	Hot Axios	12	Buried Stent (1)
Arvanitakis *et al*. 2018	LAMS	4	See Walter *et al*. and Bang *et al*
Guo *et al*. 2017	LAMS	3-12	Not Indicated

60 days. However, after these considerations, analyzing the adverse events, they reported the removal of a LAMS 73 days after release, due to the development of a large colonic fistula from erosion of the distal flange. It is unclear if they followed the FDA indications or they were guided by clinical/radiological findings. They also reported that LAMS were replaced with 2 double pigtail plastic stents in 67% of cases, in order to provide long-term drainage in disconnected pancreatic duct syndrome, not explaining the timing of the procedure. In the study by Yoo *et al.*,[12] stent removal was undertaken after complete decompression of the PFC without persistence of fluid component.

Adverse events and LAMS removal technique

Buried stent syndrome has been reported in 3 studies[5,6,14] and in 1 case report.[16] Fabbri *et al.*[16] encountered a complete buried stent recognizable by the presence of an orifice in the middle of a small bulge of gastric mucosa. They cannulated and dilated with a balloon and, after identification of the extremity embedded LAMS in the gastric wall, they removed it with a rat-tooth forceps, without adverse events. In the study by Bang *et al.*[5] 2 cases of buried stents were reported. In one, the stent was retrieved after transmural tract dilation using a large diameter biopsy forceps. In the other patient, stent retrieval resulted in massive hemorrhage requiring radiology-guided coil embolization. In the study by Bekkali *et al.*[6] (with a mean removal time of 9 weeks) one patient, lost to follow-up for 26 weeks, had a buried stent in the gastric wall. Further attempts at removal were postponed because of pregnancy.

Four studies[4,10,17,19] reported mucosal overgrowth. They were resolved endoscopically, without any further trouble in removing the stent.

Zhu *et al.*[17] found severe tissue adhesion after 5 months and removed LAMS wires one by one with forceps. In another case report,[19] the gastroscopy scheduled at three months showed tissue overgrowth at the gastric flange of the LAMS which made it impossible to remove with a rat-tooth forceps or snare. Forced argon plasma coagulation (APC), needle-knife incision, and dilation of the stent were necessary to remove it.

In the study by Yoo *et al.*,[12] all stents were successfully removed using a snare after PFC resolution without significant adverse events. There was a spontaneous extrusion of one LAMS into the enteral lumen after resolution of the WON.

We found no association between type/dimension of the PFC and removal complications or between removal timing and removal complications. Mucosal overgrowth or buried stent was not associated with longer indwell of the stent, since they appeared even after 4 weeks of placement.

DISCUSSION

Although we are well aware that the articles we evaluated are heterogeneous, we included all the papers reporting LAMS removal timing. This is because these stents are relatively new, their reported clinical experience is still scarce if compared to other types of stents, and the number of patients analyzed in this setting is still low.

The recently published ESGE guidelines[3] on acute necrotizing pancreatitis strongly recommended, in case of PFC drainage, a LAMS removal timing not exceeding 4 weeks. However, the cited studies on which the recommendation is based suffer of the same aforementioned limitations, hence the low quality of evidence. We decided to include this paper in order to underline the paucity of data in support of the statement.

In the study by Walter *et al.*,[4] the median time of removal in 47 patients was 32 days, in line with the suggested 4 weeks, but the differences in the group were huge: from 2-178 days; furthermore, the authors described a 23% of noted tissue growth in the stent, with uneventful removal, but with no specifications regarding the time of stent indwelling in the patient and the complication.

The largest study is the retrospective multi-centric analysis by Rinninella *et al.*,[14] which evaluated 93 patients with PFCs underwent drainage using the Hot Axios stent, with clinical resolution in 86 patients and successful stent removal in 83. In 2 patients with advanced malignant disease, the stent was left in place, while in one, lost at follow-up for more than 4 months, the stent was buried within the gastric wall due to overgrowth of the surrounding gastric mucosa. To avoid adverse events, the endoscopist decided to avoid stent removal.

Siddiqui *et al.*[15] performed a large multi-center, retrospective study on 82 patients with symptomatic PFC who underwent EUS-guided drainage by using the Axios stent. All stents were endoscopically successfully removed by using a snare or grasping forceps, after a median duration of 2 months (range 1-3 months), after PFC resolution. No significant clinical adverse events were described after stent retrieval.

In the study by Yoo *et al.*,[12] stent removal was performed after complete resolution of the PFC. Since the follow-up

period was 7-8 months, it remains a moot point whether the stent could be left *in situ* for such a long time?

We encountered the issue of the "buried stent" in a patient who underwent LAMS placement for a WON and then was lost at follow-up for 5 months. Although clinically silent and under monitoring, the stent is still in place after 2 failed attempts of removal. In this case, the stent was buried in the gastric mucosa, but with the help of a Needle Knife and using the APC device, we succeeded in completely freeing the proximal flange of the stent in the stomach. However, the distal flange remained buried in the retroperitoneal tissue. The policy of our center is to retrieve the LAMS within 4 weeks, as suggested by ESGE guidelines,[3] even though in at least 2 patients, with a radiological documented resolution of the WON at 3rd week, the 4-week scheduled removal was particularly complicated because of initial overgrowth of gastric mucosa on the proximal edge of the stent. A similar condition is described in the studies by Fabbri *et al.*[16] and Rinninella *et al.*[14]

Another case of "buried stent" is reported in the study by Bang *et al.*,[5] comparing PFC drainage with LAMS (12) vs plastic stents (9). In the LAMS group, stent retrieval was scheduled after 5 or 6 weeks post-index procedure, and was successfully performed in 10 patients. In the latter two, the LAMS were found buried under the gastric mucosa and removal was not free from adverse events. Although in this paper, data on timing makes the group of patients more homogeneous, the number is still too low to formulate any high-evidence recommendations.

The prospective analysis of Shah *et al.*[10] evaluated the outcomes of lumen-apposing, covered, self-expanding metal stent (LACSEMS) placement in 30 patients with PFCs. Except for 1 patient, with a second plastic drainage, among the remaining 29 patients, stents remained implanted for 31 days in 20 patients (+/- 9.9 days) and for 67 days in 9 patients (+/-10.8 days). Despite that mucosal overgrowth and hyper plastic tissue reaction were described in 2 cases, in all 29 patients, the stents were removed successfully.

CONCLUSION

The scarce available data tend to support the 4-week timing for LAMS removal, as recommended by ESGE guidelines.[3] Nevertheless, there is still a need for large prospective cohort studies, in order to prove a relationship between removal timing, outcome, and adverse events related to LAMS.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Guo J, Saftoiu A, Vilmann P, Fusaroli P, Giovannini M, Mishra G, *et al.* A multi-institutional consensus on how to perform endoscopic ultrasound-guided peri-pancreatic fluid collection drainage and endoscopic necrosectomy. Endosc Ultrasound 2017;6:285.
2. Kozarek RA, Patterson DJ, Ball TJ, Traverso LW. Endoscopic placement of pancreatic stents and drains in the management of pancreatitis. Ann Surg 1989;209:261-6.
3. Arvanitakis M, Dumonceau JM, Albert J, Badaoui A, Bali M, Barthet M, *et al.* Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. Endoscopy 2018;50:524-46.
4. Walter D, Will U, Sanchez-Yague A, Brenke D, Hampe J, Wollny H, *et al.* A novel lumen-apposing metal stent for endoscopic ultrasound-guided drainage of pancreatic fluid collections: A prospective cohort study. Endoscopy 2014;47:63-7.
5. 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;66:2054-6.
6. Bekkali N, Nayar M, Leeds J, Charnley R, Huggett M, Oppong K. A comparison of outcomes between a lumen-apposing metal stent with electrocautery-enhanced delivery system and a bi-flanged metal stent for drainage of walled-off pancreatic necrosis. Endosc Int Open 2017;5:E1189-96.
7. Lang GD, Fritz C, Bhat T, Das KK, Murad FM, Early DS, *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;87:150-7.
8. Law ST, De La SernaHiguera C, Gil Simón P, Pérez-MirandaCastillo M. Comparison of clinical efficacies and safeties of lumen-apposing metal stent and conventional-type metal stent-assisted EUS-guided pancreatic wall-off necrosis drainage: A real-life experience in a tertiary hospital. Surg Endosc 2018;32:2448-53.
9. Sahar N, Kozarek R, Kanji Z, Ross A, Gluck M, Larsen M, *et al.* Do lumen-apposing metal stents (LAMS) improve treatment outcomes of walled-off pancreatic necrosis over plastic stents using dual-modality drainage? Endosc Int Open 2017;5:E1052-9.
10. Shah RJ, Shah JN, Waxman I, Kowalski TE, Sanchez-Yague A, Nieto J, *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;13:747-52.
11. Gornals JB, De la Serna-Higuera C, Sánchez-Yague A, Loras C, Sánchez-Cantos AM, Pérez-Miranda M. Endosonography-guided drainage of pancreatic fluid collections with a novel lumen-apposing stent. Surg Endosc 2013;27:1428-34.
12. Yoo J, Yan L, Hasan R, Somalya S, Nieto J, Siddiqui A. Feasibility, safety, and outcomes of a single-step endoscopic ultrasonography-guided drainage of pancreatic fluid collections without fluoroscopy using a novel electrocautery-enhanced lumen-apposing, self-expanding metal stent. Endosc Ultrasound 2017;2:131.
13. Adler DG, Taylor LJ, Hasan R, Siddiqui AA. A retrospective study evaluating endoscopic ultrasound-guided drainage of pancreatic fluid collections using a novel lumen-apposing metal stent on an electrocautery enhanced delivery system. Endosc Ultrasound 2017;6:389.
14. Rinninella E, Rastislav K, Dollhopf M, Sanchez-Yague A, Will U, Tarantino I, *et al.* EUS-guided drainage of pancreatic fluid collections using a novel lumen-apposing metal stent on an electrocautery-enhanced

delivery system: A large retrospective study (with video). Gastrointest Endosc 2015;82:1039-46.
15. Siddiqui AA, Adler DG, Nieto J, Shah JN, Binmoeller KF, Kane S, *et al*. EUS-guided drainage of peripancreatic fluid collections and necrosis by using a novel lumen-apposing stent: A large retrospective, multicenter U.S. experience (with videos). Gastrointest Endosc 2016;83:699-707.
16. Fabbri C, Luigiano C, Marsico M, Cennamo V. A rare adverse event resulting from the use of a lumen-apposing metal stent for drainage of a pancreatic fluid collection: "The buried stent." Gastrointest Endosc 2015;82:585-7.
17. Zhu H, Dong Y, Xie P, Jin Z, Du Y. Cumbersome removal of a lumen-apposing metal stent in a case of refractory pancreatic pseudocyst. Gastrointest Endosc 2017;86:235-6.
18. Itoi T, Binmoeller KF, Shah J, Sofuni A, Itokawa F, Kurihara T, *et al*. Clinical evaluation of a novel lumen-apposing metal stent for endosonography-guided pancreatic pseudocyst and gallbladder drainage (with videos). Gastrointest Endosc 2012;75:870-6.
19. Seerden T, Vleggaar F. Endoscopic removal of buried lumen-apposing metal stents used for cystogastrostomy and cholecystogastrostomy. Endoscopy 2016;48:E179.