A Wolf in LAMS Clothing: The Expansion of Off-Label Indications for Lumen-Apposing Metal Stents

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Abbreviations

LAMS	Lumen-apposing metal stents
PFC	Pancreatic fluid collections
EUS	Endoscopic ultrasound
WON	Walled-off necrosis
FDA	Food and drug administration
GATE	Gastric access temporary for endoscopy
EUS-GBD	EUS-guided gallbladder drainage
PCD	Percutaneous catheter drainage
EUS-GE	EUS-guided gastroenterostomy
L-GE	Laparoscopic gastroenterostomy
EPASS	EUS-guided balloon-occluded gastrojejunostomy bypass balloon
EUS-CDS	EUS-guided choledochoduodenostomy
MBDO	Malignant distal biliary obstruction
FCSEMS	Fully Covered self-expanding metal stents
DAE	Device-assisted enteroscopes
RYGB	Roux-en-Y gastric bypass surgery
ERCP	Endoscopic retrograde cholangiopancreatography

Lumen-apposing metal stents (LAMS) were initially designed to create a temporary communication between the lumen of the digestive tract and adjacent encapsulated pancreatic fluid collections (PFC). These stents, placed under guidance of endoscopic ultrasound (EUS), have improved the speed and efficacy of EUS-guided drainage of pancreatic fluid collections. Though there is ongoing debate regarding the superiority of LAMS over plastic stents, they appear to offer faster and probably superior clinical resolution of PFC, especially with solid necrotic debris, than do plastic stents

[1]. Owing to their large internal diameter, LAMS facilitate a free and repeated passage of endoscope into the walled-off necrosis (WON) cavity during direct endoscopic necrosectomy (DEN), especially those with > 40% solid debris, a procedure formerly time consuming and cumbersome when attempted using plastic stents. Despite these advantages, stent maldeployment and bleeding due to prolonged presence in situ are important concerns with LAMS, in particular since their short saddle length demands accurate deployment. Fabricated from the metallic alloy nitinol, their edges may erode the blood vessels in the cavity of WON during the resolution phase leading to hemorrhage due to the formation of pseudoaneurysms [2], mandating a prompt endoscopic reintervention to retrieve the LAMS within 4 weeks [3].

There are several LAMS available in the market with modifications of the design, guiding markers, anchoring force, cautery-enhanced delivery systems, and other enhancements. The first LAMS (AXIOS stent) was approved by the US Food and Drug administration (FDA) in the last quarter of 2013 specifically indicated for the drainage of pancreatic pseudocysts > 6 cm with $\geq 70\%$ fluid content. In 2015, the AXIOS stent with an electrocautery-enhanced delivery system was also approved for the same indication. Subsequent to these modifications, endoscopists started using LAMS for off-label indications, primarily to create an anastomosis between two natural lumens in the digestive and biliary tracts. In the ensuing years, interventional endoscopy involving LAMS was used to treat many complex conditions such as acute cholecystitis, distal malignant biliary obstruction, gastric outlet obstruction, and gastric access temporary for endoscopy (GATE) following bariatric gastric bypass surgery that hitherto had been treated surgically. Furthermore, due to its short saddle length, fully covered nature, and superior anchoring force, LAMS were also used to dilate refractory benign strictures in the gastrointestinal (GI) tract.

In this issue of *Digestive Diseases and Sciences*, Choi et al. [4], in their single-center retrospective series, compared the efficacy and safety of LAMS ($n = 303$) used for off-label indications vs. on-label indications, reporting that

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LAMS were used in > 60% cases for off-label indications. They found that LAMS, when used for off-label indications, had similar technical success (95.8% vs. 98.2%), clinical efficacy (83.2% vs. 89.4%) and adverse events (20.5% vs. 16.8%) as compared with their on-label use. They went to discuss the use of LAMS in several off-label indications.

One such off-label indication was EUS-guided gallbladder drainage (EUS-GBD), an increasingly attractive option in patients with acute cholecystitis carrying very high surgical risk [5]. In view of the lesser adverse events, reinterventions, unplanned readmissions, and recurrent cholecystitis, EUS-GBD is fast replacing percutaneous catheter drainage (PCD) of the GB. Similar to DEN, the endoscope is passed via LAMS into the GB, enabling the safe removal of gallstones, obtaining biopsies, and resecting polyps. These interventions, however, would be difficult following PCD of the GB [5]. Though cholecystectomy may be carried out safely following EUS-GBD, currently, EUS-GBD is primarily indicated in elderly individuals in whom surgery is considered to be very high risk.

Though EUS-GBD looks promising, there is insufficient data regarding: 1) cost-effectiveness given the need for higher reintervention and readmission in the competing PCD group and 2) long-term safety. The authors of the current study left LAMS for a median of 90 days, with the longest dwell time of up to 1800 days with a good safety record, avoiding reinterventions in 85.2% cases [4]. As this procedure involves puncturing a mobile GB through the gastric antrum or duodenum using an electrocautery-enhanced LAMS delivery system, a significant amount of experience in EUS-guided interventions is needed in order to perform EUS-GBD safely and effectively, currently limiting the procedure to high-volume centers.

EUS-guided gastroenterostomy (EUS-GE) is another off-label indication for malignant gastric outlet obstruction that in the past was often primarily treated with laparoscopic GE (L-GE). EUS-GE is not only cheaper and faster, but also facilitates early resumption of oral intake post-procedure with quicker recovery and a shorter hospital stay compared with L-GE [6]. Since the enterostomy created with EUS-GE is remote from the site of the malignancy, there is no tumor ingrowth, unlike the situation with enteral stents, conferring superiority of EUS-GE over endoscopically placed enteral stents. The use of large-bore (20 mm) LAMS is associated with an improved tolerance of a solid diet, similar to L-GE. The procedure is however technically challenging due to the presence of several anatomic factors such as a mobile proximal small bowel and a location farther (> 2 cm) from the stomach. Furthermore, the presence of ascites due to peritoneal carcinomatosis or other causes can collapse the bowel with resultant shape variability of the intestine [7]. Authors have reported procedure-related complications (n = 14) especially in the

initial 25 cases, likely attributable to operator inexperience [4]. LAMS were left for median of 120 days with the longest dwell time 660 days. Use of dedicated accessories such as a EUS-Guided Balloon-occluded Gastrojejunostomy Bypass (EPASS) balloon, nasobiliary catheter, or enteral feeding tube provides stable large-volume insufflation of the small bowel, improving technical feasibility and safety.

EUS-guided choledochoduodenostomy (EUS-CDS) using LAMS has a high (> 95%) technical and clinical success in patients with malignant distal biliary obstruction (MDBO) with biliary diameter > 17 mm [8]. LAMS used for thinner-caliber bile ducts are far more risky, with an increased probability of duodenal perforation, maldeployment, and biliary leak. Though LAMS of diameters 6 and 8 mm are usually preferred for EUS-CDS, they are not widely available. Compared with the long, cylindrical, fully covered self-expanding metal stents (FCSEMS), LAMS have shorter saddle length and wider flanges that may reduce the risk of stent migration and bile leak. The use of electrocautery-enhanced LAMS obviates the need for exchange of multiple accessories and tract dilatation, decreasing procedure length. Authors have reported recurrent jaundice in up to 20% of patients due to biliary food impaction, requiring prompt endoscopic clearance [4]. There is also a concern of recurrent obstruction as bile duct decompresses over the LAMS which is perpendicularly oriented after EUS-CDS [9]. Comparative studies have shown similar technical and clinical success between LAMS and FCSEMS used for EUS-CDS.

Reaching the excluded stomach and ampulla was formerly considered technically difficult when using device-assisted enteroscopes (DAE). Consequently, surgical/radiological options were frequently considered in patients after Roux-en-Y gastric bypass surgery (RYGB). Reconnecting the excluded stomach with the gastric pouch by creating a temporary fistula (GATE) using LAMS has enabled the success of many procedures such as pancreaticobiliary interventions using endoscopic retrograde cholangiopancreatography (ERCP) & EUS, mucosal inspection and related interventions in the excluded stomach. The authors of the current study performed same-session GATE in 53.8% and anchored the LAMS in up to 50% cases in order to prevent stent dislodgment. In the remaining cases, they had to wait a median of 30 days prior to performing a second-session GATE procedure, which has higher technical and clinical success than BAE-assisted interventions [10]. Since the major concern regarding this procedure is stent dislodgment during manipulation of the scope through the LAMS, that can cause free perforation, wider (20 mm) LAMS are preferred. LAMS are promptly removed in all patients after completion of the intended transgastric endoscopic procedure. In the current study authors reported that in majority (9/13), the fistula healed by secondary intent in the current study [4],

consistent with prior experience. In general, weight regain is not of a major concern following GATE procedure.

The authors of the current study noted that LAMS provide adequate clinical success in patients with refractory GI strictures (59.5%) [4]. Since LAMS, owing to its short length, are not suitable for long-segment strictures (> 1 cm), they are commonly used for short-segment, especially anastomotic strictures. Unlike fully covered metal stents (FCSEMS), LAMS offer superior lumen apposition with resultant uniform axial pressure distribution, thereby improving anchorage and reducing migration [11]; indeed, in the current study, a migration rate of 10.8% was reported, much lower than that with FCSEMS. Although fibrosis surrounding the stricture might reduce the clinical success rate, LAMS is still a viable option since LAMS are deployed across these refractory strictures over a guidewire under endoscopic and fluoroscopic guidance using therapeutic oblique viewing/forward view echoendoscope or gastroscope.

In conclusion, the use of LAMS has expanded horizons in the treatment of many challenging diseases in gastroenterology which were previously within the surgical/radiological domains. They are currently being used more frequently for off-label indications with equally good success and efficacy as those with on-label indications. Larger randomized studies comparing LAMS with existing techniques would improve understanding of therapeutic value. There is a need for stent and accessory modifications specifically designed and for these off-label indications intended to improve the safety and efficacy of LAMS for off-label indications as well.

Declarations

Conflict of interest None.

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