

Endoscopic ultrasound-guided drainage with lumen-apposing metal stents: a good safety profile also in the long term?

Lumen-apposing metal stents (LAMS) have been specifically developed for the endoscopic drainage of pancreatic fluid collections (PFCs) and walled-off necrosis (WON). These two-flanged dedicated devices with a large inner diameter and a short body allow to connect the gastrointestinal lumen with other walled compartments or adjacent lumens. The indications for LAMS placement are expanding by taking advantage of the stent shape. These stents can be used in any scenario that would benefit from creating an anastomosis, such as endoscopic ultrasound (EUS)-guided choledochoduodenostomy, endoscopic gallbladder drainage, gastrojejunostomy for the management of gastric outlet obstruction, and fistula creation in patients with altered anatomy (1). Benign strictures (2) and surgical complications of bariatric surgery (3) also pertain to the spectrum of recently described LAMS applications.

EUS-guided drainage of PFC/WON is the mainstay of LAMS. The European Society of Gastrointestinal Endoscopy (ESGE) suggests using either plastic stents (PS) or LAMS for initial endoscopic transmural drainage (4). In this setting, studies comparing both approaches have reported conflicting results. Bang JY et al. (5), in a randomized, controlled trial concluded that there was no significant difference in treatment outcomes between LAMS and PS. Conversely, a higher clinical success, shorter procedure time, lower need for surgery and lower rate of recurrence have been reported in a recent multicenter retrospective study (6). In addition, as suggested by a recent cost-effectiveness analysis, a higher LAMS efficacy could be obtained at the expense of higher overall costs (7). Finally, it is important to point out that safety data are still lacking and that most available studies have been focused on intraoperative adverse events. The single-step procedure of Hot Axios™ LAMS with an electrocautery-tipped delivery system (Boston Scientific, Marlborough, MA, USA) decreases the number of accessories to be exchanged, which may potentially reduce complication rates (8). Little is known about the time a LAMS should be removed in PFCs/WON, and how to prevent delayed complications such as bleeding or LAMS occlusion. Although a four-week interval has been proposed, there is no consensus on whether and when LAMS removal should be performed (5). A recent systematic review and meta-analysis including eleven studies with 688 patients, and comparing LAMS with multiple PS, concluded that LAMS has an excellent efficacy and safety profile in the management of PFCs and may be preferred over PS, as it is associated with better clinical success and lesser adverse events (9). However, higher rates of procedure-related bleeding and a greater need for repeat endoscopic procedures as compared to PS have also been reported (10).

In the current issue of *The Spanish Journal of Gastroenterology (Revista Española de Enfermedades Digestivas)*, Bazaga Pérez de Rozas et al. (11), reporting on a multicenter study of 179 patients who underwent an Axios™ LAMS placement, conclude that delayed complications are uncommon but may be serious. This original work analyzes the safety profile of the device over the whole lifespan of the stent after deployment, including the patients who underwent stent removal and those who did not. The authors report a median stent patency period of 8.3 weeks in 93 patients (52%) who underwent stent removal, and an association between stent duration and complications was not found. Removal was uneventful in 95% of patients and the complication rate was 5%. The most frequent complication was bleeding, and it was solved endoscopically in most cases.

Endoscopic options to solve LAMS-related delayed complications are relatively limited (12). In the present study, stents were not removed in almost half of the patients as they were placed with permanent intent (e.g., gallbladder drainage, gastrojejunostomy). The overall complication rate during the stent indwelling period (excluding removal) was 10.9%. However, the crucial point of the timing of complication occurrence has not been addressed. A survival analysis according to LAMS indication and permanent placement intention would have been of great interest to get a better understanding of stent patency and procedure-related complications during the LAMS indwelling period.

The group of Hospital Río Hortega previously reported that LAMS migration occurred in 14% of cases and may be more common in PFCs. An 8.4% cumulative risk of migration has been described for LAMS placed over longer durations (13). Similarly, in the present study migration was more frequent in fluid collections, whereas only 1.7% of patients with encapsulated necrosis experienced migration during follow-up. Not surprisingly, most delayed stent migrations were non-symptomatic as they were probably secondary to PFC regression. However, other authors have reported that the risk of migration in WON was 17.4%, compared to 2.3% for pancreatic pseudocysts (14). It is also interesting to note that a recent multicenter study found EUS-guided LAMS for PFCs to be associated with a low incidence of delayed adverse events (15). It is therefore likely that other risk factors besides type of collection or presence of necrosis may play a significant role.

Pérez de Rozas reports stent occlusion in 4.5% of patients, most of them presenting with WON. This complication led to some severe events such as relapsing cholecystitis after gallbladder drainage, but most cases of stent obstruction were

associated with WON drainage and solved endoscopically. In the literature, this outcome has been identified in 30% and 18% of patients with WON and PP, respectively (15), but the definition of this outcome is not homogeneous, and its incidence varies widely across different studies. A double pigtail plastic stent placed across the LAMS lumen is an easy and common way to prevent LAMS migration or treat occlusion.

The authors describe a 3.9% bleeding rate, with all cases being solved using conservative measures or endoscopic therapy. As previously reported by other authors (16), this complication usually occurred in the first weeks following deployment. It can also be a severe complication, sometimes beyond the reach of the endoscopist, due to the erosion of a large vessel in the necrotic cavity or the rupture of a pseudoaneurysm. This complication is a major concern in LAMS therapy, and can be prevented by early LAMS removal or insertion of a coaxial pigtail stent.

Delayed perforation may occur due to the passage of penetrating devices during endoscopic transluminal necrosectomy, or spontaneously due to the prolonged irritation of the WON cavity by the LAMS. Early stent migration may also lead to peritonitis with fatal consequences, particularly in gastrojejunostomy and gallbladder drainage. However, no delayed perforations are described in these series during the stent patency period (before removal).

Most current data assessing LAMS-related adverse events have been reported in the PFC/WON drainage setting during deployment. However, there is a growing number of reported cases where LAMS is indicated with permanent intent, and both patency time and delayed procedure-related adverse events in these new scenarios remain uncertain. Indeed, more studies are needed regarding the long-term patency of LAMS in specific indications such as gastrojejunostomy. In the present study, all perforations were related to stent removal in gallbladder drainage or gastrojejunostomy.

In conclusion, the present study reduces the gap in evidence regarding LAMS safety in the long term, but at the same time raises new questions. What is the threshold of complications to consider LAMS placement as a safe procedure? How can delayed complications be effectively prevented? At what time are they most likely to occur? To address these concerns we probably need a wide consensus on the definition of reported complications, as well as a list of key performance measures for LAMS placement, as the ESGE and other societies have already suggested for other procedures. In addition, there are different LAMS sizes, different drainage modalities (coaxial stent, dilation of stent after placement, etc.), and different possible protocols for the timing of endoscopic procedures with LAMS (necrosectomy, ERCP after Roux-en-Y bypass, etc.), all of which may influence the incidence of delayed complications and should be considered.

Another crucial point is that not all procedure-related complications have the same clinical impact. Indeed, some of them (e.g., spontaneous delayed migration in PFCs) should be probably considered as a technical issue rather than a real complication (17), while others (e.g., delayed perforation and hemorrhage by arterial erosion) may be fatal. Thus, it seems very risky to interpret the overall complication rate in a broad sense, as the settings where LAMS may be used are very specific, leading to different safety profiles and concerns in each individual scenario.

LAMS represent one of the most significant recent innovations in endoscopy, as they have opened new avenues of intervention that previously belonged to the realm of surgery. We will thus probably see more long-term indications for LAMS as well as new devices in the near future. Meanwhile, removing a LAMS within eight weeks of WON/PFC drainage and necrosectomy seems reasonably safe and should in our view be recommended. Multicenter RCTs comparing LAMS and conventional methods are urgently needed, as well as large, long-term prospective studies to confirm the results and the large experience obtained from this multicenter study.

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