—Commentary—

Pancreatic fluid collections and necrosectomy with plastic stents *versus* lumen-apposing stents

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INTRODUCTION

The incidence of hospitalizations for acute pancreatitis is rising, with 5%–15% of patients with pancreatitis developing pancreatic fluid collections (PFCs).[1,2] In addition to acute pancreatitis, other causes of PFCs include chronic injury, trauma, surgical resection, and/or injury to the pancreas during abdominal surgery.[3,4] Management paradigms for these collections, particularly if they are complicated by infected necrosis, have changed over the past decade. Advances in endoscopic tools have driven a new era of minimally invasive techniques to manage both pancreatic pseudocysts (PPs) and walled-off necrosis (WON). This step-up approach with initial interventions using less invasive procedures rather than surgical necrosectomy was described by van Santvoort *et al.* and has been associated with an overall decreased mortality, fewer number of complications, and lower healthcare costs.[2,5] The primarily liquid content of PP can be drained in a single endoscopic session with a transmural drain to allow for collapse and resolution. However, the solid, necrotic tissue contained within WON often does not drain as easily and has the potential of developing infection, requiring larger caliber transmural drains. Therefore, successful management of PFCs must be tailored based on the characteristics of the collection.

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Website: www.eusjournal.com

DOI: 10.4103/eus.eus_80_17

CONVENTIONAL TRANSMURAL DRAINAGE WITH PLASTIC STENTS

Transenteric drainage of PFC has been described in several series, initially as conventional transmural drainage (CTD) with plastic stents. This requires the PFC to create a visible bulge into the luminal wall to direct the endoscopist to identify where to create the cystgastrostomy or cystduodenostmy fistulous tract. Success rates of CTD with plastic stents have been reported between 70% and 100%, with recurrence rates up to 20%.[6,7] There is also a wide range of reported complication rates for CTD, reported between 2% and 40%, from bleeding, perforation, and infection from stent occlusion or migration.[2,8]

ENDOSCOPIC DRAINAGE OF PANCREATIC FLUID COLLECTIONS THROUGH PLASTIC STENTS

Outcomes of pancreatic fluid collection drainage with plastic stents

Introducing endoscopic ultrasound for PFC drainage (EUD) has improved the technique because endoscopists can now identify the cyst cavity when

How to cite this article: Saumoy M, Arvanitakis M, Kahaleh M. Pancreatic fluid collections and necrosectomy with plastic stents *versus* lumen-apposing stents. Endosc Ultrasound 2017;6:S132-7.

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Received: 2017-07-12; **Accepted:** 2017-08-31

there is no obvious bulge. EUD with plastic stents has been shown to be successful in management of PFCs. Multiple retrospective studies have demonstrated EUD success rates ranging from 80% to 100% and complication rates averaging around 10%. Given the low complication rate and the ease of identification of the PFCs, Kahaleh *et al.* performed a prospective case–control study comparing CTD and EUD in patients with PFC if there was an identifiable bulge. There was no significant difference between CTD and EUD in technical/clinical success or complication rate.[9] However, in 42%–48% of cases, the characteristic bulge is not identifiable, which limits the overall use of the CTD technique.[10] Moreover, subsequent prospective trials have found higher technical success with EUS drainage.[11,12] Therefore, EUD has become standard of care for drainage with PFCs.

Endoscopic ultrasound-guided drainage technique

PFC drainage procedures are typically performed from the stomach or proximal duodenum using endoscopic ultrasound. Color Doppler ultrasound is routinely used to identify regional vasculature. A fistula between the PFC and the stomach or duodenum is created by introducing a 19-gauge needle or a cystotome into the PFC. A guidewire is then introduced through the needle and coiled within the PFC using EUS and fluoroscopic guidance. The cystoenterostomy fistula was dilated with either a wire-guided balloon or the large portion of the cystotome. The balloon or cystotome is then exchanged off the guidewire and one or two 10-Fr double-pigtail endoprostheses are placed across the cystoenterostomy fistula at the discretion of the endoscopist.[9]

BIFLANGED METAL STENTS

There is a growing body of evidence demonstrating that the use of large caliber metal stents is both technically feasible and allow for a significant rate of resolution of PFC and particularly of WON.[13-16] Initially, endoscopists demonstrated success with the use of fully covered self-expanding metal stents (FCSEMS).[17] Biliary and esophageal FCSEMS provided a large diameter for drainage as compared with plastic stents, and esophageal FCSEMS allowed for endoscopically directed mechanical debridement of WON.[18-21] However, both stents were limited by the risk of migration.

Advances in endoscopic tools have led to the development of multiple novel stents that are designed for deployment under endoscopic ultrasound guidance, and ideal for the management of PFCs. These stents have a large diameter which prevents obstruction from necrotic material as well as fully covered to allow for ease of debris removal.[22] Finally, these stents have two large flanges to allow for apposition of the collection to the stomach or duodenum and prevent migration. There are an increasing number of the commercially available covered biflanged metal stents: Axios (Boston Scientific, Marlborough, Massachusetts), Nagi and Spaxus (Taewoong Medical, Gyeonggi-do, South Korea), Hanaro stent (M. I. Tech Seoul, South Korea), and Aix stent PPS (Leufen Medical, Aachen, Germany) [Table 1]. However, at this time, only the Axios stent is available in the United States.

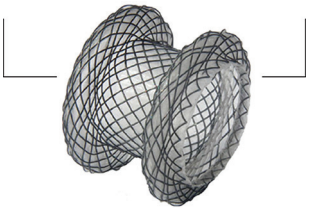
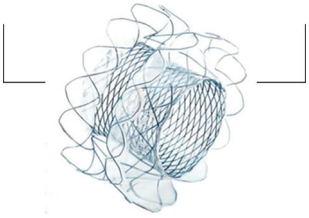
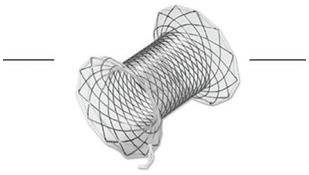
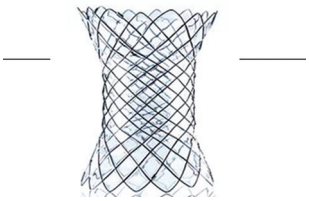
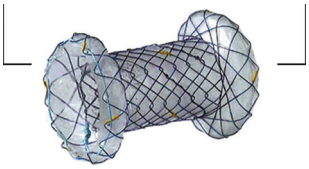
One key difference between the stents is the angled biflanged design *versus* the flat anchoring flanges, which have been coined lumen-apposing metal stents (LAMS). The perpendicular flanges allow for strong tissue wall apposition. Teoh *et al.* demonstrated that the Axios and Spaxus stent generated a larger lumen-apposing force when attempting to pull apart a simulated anastomosis as compared with the Nagi stent.[23] When shortening the stent by dilating the internal diameter to its maximal size, there is a mechanical force applied to the anastomosis by the opposing ends of the stent. This applies an even pressure on the luminal walls.[24] The covering of the metal stent and the fusion of the two lumens generate an intact fistulous tract to prevent leakage as well as prevent tissue ingrowth. Further, the "dog bone" shape of the stent also potentially decreases the risk of migration. Finally, these stents are easily removable after resolution of the PFC. Therefore, these stents should be preferentially used when creating anastomosis between a nonadherent collection and a luminal organ, with a goal to generate enough force to hold the cyst cavity against the stomach or duodenum despite *in vivo* peristalsis. Most of the currently published literature with LAMS for PFC is using the Axios stent, likely because of its wider commercial availability.

ENDOSCOPIC DRAINAGE OF PANCREATIC COLLECTIONS THROUGH LUMEN-APPOSING METAL STENTS

Technique

After the implementation of the Atlanta classification in 1992 and the revised classification in 2012, endoscopists have been able to classify types of PFCs and determine when a collection requires intervention.[4,25] On

Table 1: Commercially available biflanged and lumen apposing metal stents

Stent	Image	Internal Diameter (mm)	Length between flanges (mm)
Lumen apposing metal stents			
Axios (Boston Scientific, Malborough, Massachusetts USA)		10, 15	10
Spaxus (Taewoong Medical, Gyeonggi-do, South Korea)		8, 10, 16	5
BiFlanged Metal Stents			
Nagi (Taewoong Medical, Gyeonggi-do, South Korea)		10, 12, 14, 16	10, 20, 30
Aix PPS (Leufen Medical, Aachen, Germany)		10, 15	30
Hanaro stent BCF (M.I. Tech Seoul, South Korea)		14	10, 20, 30

determination, the endoscopist can use an echoendoscope to identify an appropriate access point for transmural drainage. The collection is punctured with a 19-guage needle, and a guidewire is coiled within the collection. The fistulous tract is then dilated with a dilating balloon and/or electrocautery device and the LAMS is deployed across the fistula tract. In particular, the Axios delivery system has been modified with a cautery device integrated into the nosecone at the catheter tip. This enables transmural advancement of the stent without preliminary tract dilation and without over-the-wire exchanges of separate cautery devices. Alternatively, the cautery-assisted Axios delivery system can be used "freestyle" without initial needle puncture. After the LAMS is deployed, the large diameter of the stent allows for direct visualization within the cavity for endoscopic necrosectomy [Figure 1].

Outcomes of pseudocyst drainage with lumen-apposing metal stents

PP drainage with LAMS has been shown to be both clinically and technically successful in published retrospective case series. Itoi *et al.* described the first case series of LAMS for drainage of PP. Fifteen patients underwent LAMS for drainage and demonstrated a 100% clinical success rate, but a 26.7% complication rate.[26] Other published case series have described a combination of WON and PP. For example, Rinninella *et al.* described a 93 patient case series, with 18 patients who had PP. There was an overall 92.5% clinical success and only 1 of the 18 PP patients (5.56%) had an adverse event.[27] Walter *et al.* conducted a multicenter prospective trial of 61 patients, with 14 patients who had PP. They described a 93% clinical success rate in

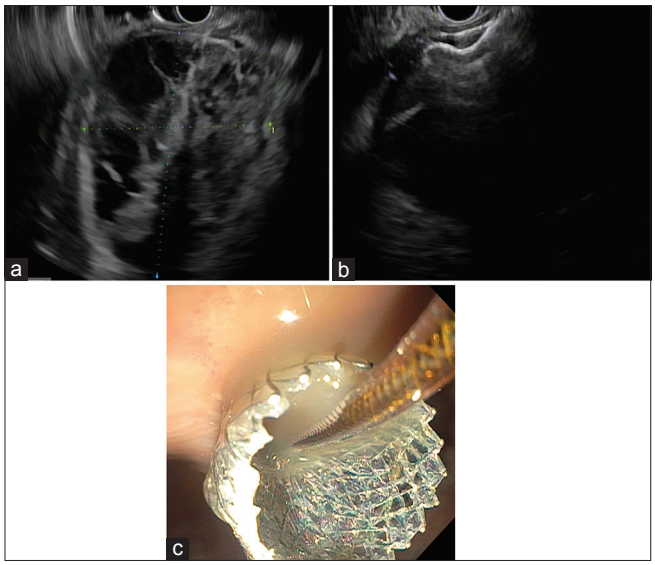


Figure 1. (a) Endosonographic visualization to identify a pancreatic fluid collection, (b) endosonographic visualization of the distal flange of the lumen-apposing metal stents deployed within the pancreatic fluid collection, (c) endoscopic visualization of the proximal flange deployed within the stomach

the PP group, and none of the PP patients required additional endoscopic intervention to achieve clinical success. There was one patient (7.14%) who had a perforation after stent deployment, which was the only major complication.[28] Siddiqui *et al.* also performed a multicenter retrospective trial of 14 patients with PP and 68 patients with WON, all drained with LAMS. Two of the 14 patients (14.3%) with PP had stent misdeployment, (85.7% technical success), 1 of the 14 patients (7.1%) had self-limited bleeding, and 1 of the 14 patients (7.1%) developed infection of the PP cavity. The patients with successful PP stent placement with 100% clinical success, with 83.3% of patients requiring only one endoscopic session for PP resolution.[13]

Comparison of plastic and lumen-apposing metal stents for pancreatic pseudocysts drainage

Bang *et al.* conducted a retrospective case–control study, comparing patients who underwent PFC drainage with LAMS with plastic stents according to PFC type. Using a 1:2 comparison, 7 patients had LAMS drainage of PP and 14 patients had plastic stent drainage of PP. LAMS patients had a 100% clinical success rate with no adverse events. There was no statistically significant difference between LAMS and plastic stents for PP, and they also suggested a lower overall cost with plastic stents compared to LAMS.[29]

Overall, PP drainage with LAMS has been demonstrated in retrospective trials to be safe and effective. However, the case–control study from Bang *et al.* suggests that there may not be a difference in PFC resolution from plastic stents. Given the cost differential, at this time, PP drainage with plastic stents is likely the most cost-effective option. However, randomized control trials with an associated cost analysis are necessary to definitely compare types of stents in the management of PP to determine the appropriate role of LAMS.

Outcomes of walled-off necrosis with lumen-apposing metal stents

Symptomatic WON (especially infected WON) has significant morbidity and mortality.[30] Direct endoscopic necrosectomy with debridement of WON using an endoscope that is inserted directly into the collection through the LAMS. Before LAMS, direct endoscopy necrosectomy for WON was associated with 80% clinical success, but a 26% complication rate and a 7.5% mortality rate at 30 days.[31] However, in recent case series, necrosectomy through a LAMS has been associated with similar, if not higher, clinical success rate, and a lower complication rate.

The previously described series by Rinninella *et al.* demonstrated an adverse event rate of 3 of 52 patients (5.77%) with WON.[27] Similarly in the prospective trial by Walter *et al.*, clinical success was achieved in 81% of the patients (35 of 43) with WON. Four patients (7.02%) had complications with new-onset infection of the collections requiring endoscopic necrosectomy, antibiotics, and nasocystic drainage. In total, 43% of patients required either an additional necrosectomy and/or irrigation to achieve clinical success.[28] The multicenter case series by Siddiqui *et al.* reviewed 68 patients with WON drained with LAMS. Five of 68 (7.3%) had self-limited bleeding and 4 of 68 (5.9%) patients had infection of the necrotic cavity. They had an 88.2% clinical success rate, and patients with WON required a higher number of endoscopic sessions (mean 2.8 sessions) for resolution as compared to PP though this was not statistically significantly different.[13]

Bang *et al.* compared 13 patients with LAMS to 26 patients with plastic stent drainage for WON. In their case–control study, they demonstrated a clinical success rate of 92.3% in both groups, with an adverse event rate of 15.4% in the LAMS group. There was no statistically significant difference between the LAMS and plastic stent group in either adverse event, number of

reinterventions performed, or length of stay.[29] Sharaiha *et al.* published the largest case series to date of 124 patients with only WON drained by LAMS. These patients had a high clinical success rate (86.3%) with a low rate of adverse events (18.5%).[15] And finally, a randomized control trial (NCT02685865) is currently recruiting patients to compare plastic stents *versus* LAMS for WON. Interim analysis of the 21 recruited patients reported a 50% adverse event rate (bleeding, biliary obstruction, or buried stent syndrome) in the LAMS group requiring the investigators to change their clinical practice protocol to include a CT scan 3 weeks post-LAMS drainage.[32]

The data are varied among clinicians reporting overall complication rates for management of WON with LAMS. Complications reported are typically bleeding, perforation, infection of the cavity after obstruction of the LAMS, stent misdeployment, or migration/dislodgement. Similar to PP, additional randomized control trials are needed to evaluate the role of LAMS, and whether specific protocols for follow-up imaging, or even additional double pigtail plastic stents through the LAMS, are necessary to further decrease complication rates.

CONCLUSIONS

In this new era of advances in endoscopic devices, management of PFCs is rapidly expanding the domain of therapeutic endoscopists. Primary drainage is a key in the management of PFCs. Minimally invasive techniques are gaining favor because of significant morbidity and mortality associated with surgical drainage and the poor success rate of percutaneous catheter drainage.[5,33] In addition, complication rates can vary by the type of PFC, with a lower documented complication rate of PP compared to WON.[34] To decrease the risk of complications, the use of these specifically designed, saddle-like LAMS is now becoming the mainstay for management, particularly of WON. Future randomized control trials will determine when the use of LAMS is the most effective. Moreover, in the coming years, novel endoscopic devices, similar to the transformative LAMS, will only further improve procedural safety and efficacy when managing patients with PFCs.

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