Published online: 2019-09-16

Lumen-Apposing Metal Stent: Not the Answer for Every Pancreatic Fluid Collection!!

Acute pancreatitis (AP), especially acute necrotizing pancreatitis, is a potentially life-threatening condition with high morbidity and mortality.[1] Peri-pancreatic fluid collections (PFCs) are one of the common local complications of AP and according to the revised Atlanta classification, they have been classified into four types depending on the content and presence or absence of well-formed wall.[1] Walled of necrosis (WON) develops in the delayed phase of illness in patients with acute necrotizing pancreatitis. It is an encapsulated collection of fluid and solid necrotic material that usually develops after 4 weeks of an attack of acute necrotizing pancreatitis.[1] Majority of PFCs including asymptomatic WON resolve spontaneously without any need of intervention.[2,3] However, in the presence of symptoms such as persistent significant pain, infection, gastric outlet obstruction, or biliary obstruction, the PFC requires drainage and it can be achieved using radiological, endoscopic, or surgical means.

The management algorithm of symptomatic PFCs has evolved from primarily invasive surgical necrosectomy to minimally invasive and now endoscopic step-up approach.[4-6] A multicentric randomized trial comparing open necrosectomy versus minimally invasive step-up approach has shown decreased risk of new-onset organ failure, new-onset diabetes mellitus, or death in minimally invasive step-up approach, comprising initial percutaneous catheter drainage followed by laparoscopic or surgical necrosectomy, if required.[6] Recently, endoscopic step-up approach has also shown a technical success rate of 98%–99% and a clinical success rate up to 95%.[4,5]

The face of endoscopic step-up approach has changed in the last decade due to the introduction of lumen-apposing metal stents (LAMS) such as Axios stent (Boston Scientific, Natick, MA, USA) and Niti-S Spaxus stent (Taewoong Medical, Gyeonggi-do, South Korea). Recently, the introduction of electrocautery-enhanced delivery system has made insertion of Axios as well as Spaxus stent even simpler with minimal technical complications. As WON is a mixture of solid as well as liquid necrotic materials, LAMS are preferred as their large diameter is expected to be beneficial for effective drainage of solid necrotic material and also, if required, allow easy direct endoscopic necrosectomy (DEN) without the need of repeated large diameter balloon dilatations.

In a recent retrospective comparison between LAMS and double-pigtail plastic stents (DPPSs) in 94 patients, the authors have shown that WON resolution rate without DEN was higher with LAMS compared to DPPSs (60.4% vs. 30.8%; $P = 0.01$), with lower need for repeated necrosectomy and decreased incidence of intervention-related hemorrhage.[7] Despite few disadvantages of LAMS such as higher cost and stent blockade by necrotic debris requiring repeated endoscopic interventions, it appeared that we have finally developed an ideal stent for the management of WON. However, recent concerns about the serious adverse effects because of prolonged duration of transmural stenting by LAMS have dampened this initial enthusiasm with LAMS. In this news and views, we will discuss two recent studies on the endoscopic management of WON with LAMS and have highlighted LAMS-related serious complications. Bang *et al*. conducted a prospective randomized trial comparing LAMS and DPPSs in patients with WON,[8] whereas Brimhall *et al*. conducted a retrospective study comparing LAMS and DPPSs in patients with WON.[9]

Bang *et al*. enrolled sixty patients of WON prospectively and randomized them to endoscopic ultrasound-guided drainage using LAMS or plastic stents. The patients had symptomatic WON either in the form of infection or persistent pain requiring narcotics at least three times per day. All patients underwent transmural drainage using either LAMS (Hot Axios (Boston Scientific, Natick, Massachusetts, USA); 15 mm in diameter and 10 mm in length) or DPPSs (7F 4 cm). In patients with WON >120 mm in size, multigate technique was used using the same stent type. In addition, nasocystic catheters (10 Fr) were inserted for lavage of necrotic cavity. Patients with inadequate response as defined by persistent or new-onset systemic inflammatory response syndrome (SIRS) underwent computed tomography (CT) scan at 72 h postintervention. If CT showed <25% decrease in WON size, then the patient underwent creation of additional transmural tract using the same stent technique or DEN depending on the content of WON. Patients were followed up at 6 weeks postintervention with CT scan to see for WON size and endoscopic retrograde cholangiopancreaticogram to look for pancreatic duct integrity. In the presence of resolution of WON with intact main pancreatic duct, transmural stents were removed. In the presence of disconnected pancreatic duct syndrome (DPDS) with resolution of WON, plastic stents were left *in situ* indefinitely and LAMS were replaced with plastic stents. In the presence

of partial disruption, transpapillary stent was placed. Treatment success was defined as resolution of WON on CT scan with resolution of symptoms at 6 months. Treatment failure was defined as need of rescue surgery or death due to disease or intervention.

There were 31 patients in the LAMS group and 29 patients in the plastic stent group. Both the groups were identical in baseline characteristics including a mean size of WON (10.2 ± 4.6 vs. 10.7 ± 6.8 cm; $P = 0.784$). In the LAMS group, 29% of patients had ongoing SIRS or organ failure, and the median degree of necrosis was 40% (interquartile range [IQR] 20) prior to intervention. Multigate technique was used in 9.7% of patients, and a mean of 2.8 procedures were required to achieve a clinical success rate of 93.5%. In view of inadequate response at 72 h, two patients underwent percutaneous drainage catheter placement, two patients underwent creation of additional transmural track, and four patients underwent DEN. Stent-related adverse events occurred in ten (32.2%) patients. Two patients presented with stent buried in the gastric wall and three patients presented with massive gastrointestinal (GI) bleed requiring intensive care unit admission and blood transfusion. In all the three patients with bleed, endoscopic ultrasonography examination showed the presence of interlacing vessels within the distal flange of LAMS. CT angiography followed by glue embolization of pseudoaneurysm was required in all the three patients. Three patients presented with obstructive jaundice due to mechanical obstruction by LAMS when it was deployed via the duodenal bulb. All these adverse events were observed in the LAMS cohort at 3 or more weeks postprocedure. Hence, the study protocol was changed as per the safety board recommendation, and CT scan was obtained at 3 weeks followed by stent removal if there was resolution of WON. After these changes, only two patients had stent-related adverse events: one patient presented with stent migration in GI tract with obstructive symptoms and another patient had bled from the gastric mucosa while using electrocautery-enhanced delivery system. Pancreatography showed normal duct in 9 patients, DPDS in 13 patients, partial duct disruption in 6 patients, and duct status was unknown in 3 patients. Out of the 13 patients with DPDS, transmural plastic stent exchange was not possible in six patients due to collapse of the necrotic cavity. All patients with partial leak were treated with transpapillary stent bridging the leak.

In plastic stent group, ongoing SIRS was present in 44.8% of patients, and the median degree of necrosis was 50% (IQR 20). Multigate technique was used in 31% of patients, and a mean of 3.2 procedures were required to achieve a treatment success rate of 96.6%. In view of inadequate response at 72 h, five patients underwent percutaneous drainage catheter placement, five patients underwent creation of additional transmural track, and six patients underwent DEN. Stent-related adverse events occurred in two patients, both presented with migration of stents in the jejunum which were retrieved using rat tooth forceps. Pancreatography revealed normal pancreatic duct in 9 patients, DPDS in 17 patients, partial duct disruption in 2 patients, and ductal status was unknown in 1 patient. Both patients with partial disruption were treated with bridging transpapillary stents, and the stents were left *in situ* in patients with DPDS.

At 6 months postprocedure, both groups (LAMS and plastic groups) had similar clinical success (93.5% vs. 96.6%; $P = 0.99$), length of hospital stay (6.2 ± 9.0 vs. 12.2 ± 21.1 days; $P = 0.129$), and total number of procedures required (2.8 ± 1.2 vs. 3.2 ± 1.5; $P = 0.192$). Although overall adverse events were similar in both the groups ($P = 0.077$), stent-related adverse events were more frequent in the LAMS group (32.3% vs. 6.9%; $P = 0.014$). However, stent-related adverse events were more frequent in the original protocol ($P = 0.005$), and after change in protocol at 5 months, stent-related adverse event rate was similar in both the groups ($P = 0.999$). The duration of procedure was statistically significantly less in LAMS group (15 vs. 40 min; $P < 0.001$), and the cost of procedure was significantly more in LAMS group (12,155 vs. 6609 USD; $P < 0.001$).

The authors hypothesized that, due to wider diameter, WON resolved rapidly in the LAMS group. By virtue of its lumen-opposing nature, once the necrotic cavity collapses, it gets embedded deeply into the wall or causes compression of the surrounding structures including bile duct or vessels causing obstructive jaundice or pseudoaneurysm, respectively. Moreover, these complications occurred in patients after 3 weeks of placement of LAMS. Hence, the authors recommended doing CT scan at 3 weeks postprocedure and remove LAMS if WON has resolved to reduce stent-related complications. The authors concluded that, except for procedure duration, there was no significant difference in the clinical outcomes of patients with WON treated with LAMS or plastic stents.

Brimhall *et al*. conducted a retrospective study of 249 patients with symptomatic pancreatic pseudocyst or WON: 97 (39%) patients in the LAMS group (10 or 15 mm diameter of LAMS) and 152 (61%) patients in the DPPS group (at least two 7/10F plastic stents).[9] Baseline characteristics including the presence of WON were similar in both the groups (83.3% vs.

76.3%; $P = 0.52$). However, the LAMS group had larger size of fluid collection (80.1 vs. 69.8 mm; $P = 0.001$), more patients with >50% necrosis in WON (56.7% vs. 36.3%; $P = 0.038$), and less patients with chronic pancreatitis (20.6% vs. 38.8%; $P = 0.03$). In the LAMS group, eight patients had DPPSs through LAMS and in the DPPSs group, patients had a median number of two stents placed. Technical success was similar in the LAMS and DPPS groups (90.1% vs. 92.8%; $P = 0.67$). Clinical success (90.1% vs. 91.8%; $P = 0.54$), average number of endoscopic necrosectomies (1.7, range 1–11 vs. 1.9, range 1–19; $P = 0.93$), and stent duration (51.5 vs. 59.8 days; $P = 0.26$) were also similar in both the groups. The authors have also stated that location of fluid collection, overall presence of necrosis, or use of nasocystic drain were not significant factors contributing to technical or clinical success or adverse event occurrence.

Overall adverse events were similar in the LAMS and DPPS groups (24.7% vs. 17.8%; $P = 0.67$). However, in the LAMS group, there was presence of significantly higher rate of bleeding episodes (15.46% vs. 3.28%; $P = 0.0005$) and higher rate of pseudoaneurysmal bleeding (8.2% vs. 0.7%; $P = 0.009$). Overall average time to bleed was 18.5 postprocedure days. Infection (2.0% vs. 3.9%; $P = 0.28$) and perforation rates (0% vs. 2%; $P = 0.22$) were showing higher trend in the DPPS group.

The authors hypothesized that the presence of large peripancreatic fluid collection might compress the vessel, making it more liable to be missed during predrainage cross-sectional imaging. After drainage due to rapid emptying of the cavity size, distal flanges may irritate the cyst wall, promoting pseudoaneurysmal formation. However, though both groups had similar clinical efficacy, the LAMS group had larger collection size with more necrosis content in WON compared to the DPPS group. The authors in this study concluded that LAMS should be used in the presence of collection with larger diameter and more necrosis content as subsequent drainage and endoscopic necrosectomy, if required, can be more feasible. Once there is resolution of collection cavity, LAMS should be removed to reduce the chances of bleeding.

Commentary

The management of pancreatic collection, especially WON, is a challenging task in the management of AP. Patients with WON have variable natural history of progression, with some WON becoming symptomatic, some getting resolved spontaneously, and some getting infected.[10] Moreover, treatment of such symptomatic WON is also a challenging task due to the presence of variable amount of necrotic debris which is difficult to remove by traditional endoscopic or percutaneous approach. The introduction of LAMS was a game changer in the endoscopic management of WON as along with being easier to deploy, it provides wider diameter for drainage of solid necrotic content as well as makes DEN easier, if required. A meta-analysis has shown technical success rate up to 98% and clinical success rate up to 93% in WON using LAMS.[11] However, the use of LAMS is associated with higher cost of procedure as well as various side effects such as bleeding, stent clogging by necrotic debris, and stent migration. Bang *et al*. prospectively compared LAMS with plastic stents and showed that both modalities are associated with similar clinical success rate at 6 months.[10] However, the LAMS group is associated with significantly higher risk of pseudoaneurysm-related bleeding, especially if the stent is kept *in situ* for more than 3 weeks. Brimhall *et al*. in their retrospective study also showed that both types of drainage methods have similar technical and clinical success rates.[9] In this study also, the LAMS group had higher rate of pseudoaneurysm-related bleeding.

In the study by Bang *et al*., the authors suggested that CT scan should be performed at 3 weeks and if it shows resolution of cavity, the LAMS should be removed. The authors have demonstrated that this protocol of removing LAMS at 3 weeks decreased the risk of pseudoaneurysm-related bleeding.[10] Recently, a study by Rana *et al*. suggested a hybrid approach of early removal of metal stents followed by placement of multiple plastic stents in WON. In their study, after placement of fully covered self-expanding metal stent, they have exchanged the clogged SEMS early within 2 weeks (median 10.9 ± 1.3 days) with multiple 10F plastic stents (median of 3). They have compared such hybrid approach ($n = 10$) with the conventional endoscopic de-clogging of SEMS and repeated endoscopic necrosectomy approach ($n = 17$). They found that patients with hybrid approach had faster resolution of collection (20.3 ± 3.1 days vs. 25.6 ± 5.5 days; $P = 0.01$) and required fewer endoscopic procedures (2.6 ± 0.5 vs. 4.1 ± 1.1; $P = 0.0003$). They have hypothesized that early removal of such clogged stent leads to removal of large chunk of adherent necrotic debris, leading to early resolution of collection and thus also avoids the risks of delayed removal of metal stents.[12]

The current evidence suggests that there is probably no significant difference in clinical as well as technical outcome between patients with WON treated with LAMS

versus plastic stents. However, LAMS is technically easier to insert with a shorter procedure time as compared to plastic stents and also provides easy access for DEN, whenever required. The decision of placement of LAMS should be based on larger size of collection with higher percentage of necrotic debris, presence or absence of large vessel or pseudoaneurysm in the vicinity of collection, and financial status of the patient. Given the concerns of bleeding and other complications, LAMS should be removed early, preferably within 3 weeks of insertion.[13] It seems that LAMS are still not an ideal stent for endoscopic treatment of WON and therefore, the search for an ideal stent continues.

Jimil Shah, Surinder Singh Rana

Department of Gastroenterology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence: Prof. Surinder Singh Rana, Department of Gastroenterology, Post Graduate Institute of Medical Education and Research, Chandigarh - 160 012, India.
E-mail: drsurinderrana@gmail.com

References

1. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, *et al.* Classification of acute pancreatitis-2012: Revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-11.
2. Rana SS, Sharma RK, Gupta P, Gupta R. Natural course of asymptomatic walled off pancreatic necrosis. Dig Liver Dis 2018. pii: S1590-8658(18)31204-0.
3. Lenhart DK, Balthazar EJ. MDCT of acute mild (nonnecrotizing) pancreatitis: Abdominal complications and fate of fluid collections. AJR Am J Roentgenol 2008;190:643-9.
4. Lakhtakia S, Basha J, Talukdar R, Gupta R, Nabi Z, Ramchandani M, *et al.* Endoscopic "step-up approach" using a dedicated biflanged metal stent reduces the need for direct necrosectomy in walled-off necrosis (with videos). Gastrointest Endosc 2017;85:1243-52.
5. Rana SS, Sharma V, Sharma R, Gupta R, Bhasin DK. Endoscopic ultrasound guided transmural drainage of walled off pancreatic necrosis using a "step – Up" approach: A single centre experience. Pancreatology 2017;17:203-8.
6. van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, *et al.* Endoscopic or surgical step-up approach for infected necrotising pancreatitis: A multicentre randomised trial. Lancet 2018;391:51-8.
7. Abu Dayyeh BK, Mukewar S, Majumder S, Zaghlol R, Vargas Valls EJ, Bazerbachi F, *et al.* Large-caliber metal stents versus plastic stents for the management of pancreatic walled-off necrosis. Gastrointest Endosc 2018;87:141-9.
8. Bang JY, Navaneethan U, Hasan MK, Sutton B, Hawes R, Varadarajulu S. Non-superiority of lumen-apposing metal stents over plastic stents for drainage of walled-off necrosis in a randomised trial. Gut 2018. pii: gutjnl-2017-315335.
9. Brimhall B, Han S, Tatman PD, Clark TJ, Wani S, Brauer B, *et al.* Increased incidence of pseudoaneurysm bleeding with lumen-apposing metal stents compared to double-pigtail plastic stents in patients with peripancreatic fluid collections. Clin Gastroenterol Hepatol 2018;16:1521-8.
10. Rana SS, Bhasin DK, Reddy YR, Sharma V, Rao C, Sharma RK, *et al.* Morphological features of fluid collections on endoscopic ultrasound in acute necrotizing pancreatitis: Do they change over time? Ann Gastroenterol 2014;27:258-61.
11. Hammad T, Khan MA, Alastal Y, Lee W, Nawras A, Ismail MK, *et al.* Efficacy and safety of lumen-apposing metal stents in management of pancreatic fluid collections: Are they better than plastic stents? A systematic review and meta-analysis. Dig Dis Sci 2018;63:289-301.
12. Rana SS, Sharma R, Gupta R. Early removal of metal stents in walled off pancreatic necrosis. Pancreatology 2018;18:868-9.
13. Rana SS. An overview of walled-off pancreatic necrosis for clinicians. Expert Rev Gastroenterol Hepatol 2019;13:331-43.

Access this article online

Quick Response Code:

Website: www.jdeonline.in

DOI: 10.4103/jde.JDE_16_19

How to cite this article: Shah J, Rana SS. Lumen-apposing metal stent: Not the answer for every pancreatic fluid collection!! J Dig Endosc 2019;10:XX-XX.