

Endoscopic Management of Peri-Pancreatic Fluid Collections

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In the past decade, there has been a progressive paradigm shift in the management of peri-pancreatic fluid collections after acute pancreatitis. Refinements in the definitions of fluid collections from the updated Atlanta classification have enabled better communication amongst physicians in an effort to formulate optimal treatments. Endoscopic ultrasound (EUS)-guided drainage of pancreatic pseudocysts has emerged as the procedure of choice over surgical cystogastrostomy. The approach provides similar success rates with low complications and better quality of life compared with surgery. However, an endoscopic “step up” approach in the management of pancreatic walled-off necrosis has also been advocated. Both endoscopic and percutaneous drainage routes may be used depending on the anatomical location of the collections. New-generation large diameter EUS-specific stent systems have also recently been described. The device allows precise and effective drainage of the collections and permits endoscopic necrosectomy through the stents. (**Gut Liver 2017;11:604-611**)

Key Words: Pancreatic pseudocyst; Pancreatic necrosis; Endosonography; Endoscopic ultrasound-guided pseudocyst drainage; Endoscopic necrosectomy

INTRODUCTION

Peri-pancreatic fluid collections is a common complication after acute pancreatitis, with a reported incidence of 30% to 60%.¹⁻⁴ It may cause symptoms of pain, bleeding or gastric outlet obstruction. Management of peri-pancreatic fluid collections has changed significantly over the past decade and endoscopic techniques are increasingly utilized in the management of these conditions. Increased understandings of the condition have also led to refinements in the definitions in the updated Atlanta's classification. This review aims to provide an overview on the

management of peri-pancreatic fluid collections with particular focus on newer endoscopic interventions.

HISTORICAL DEVELOPMENT

The history of endoscopic treatment of peri-pancreatic collections began in 1975.⁵ In the first report, a 31-year-old woman with history of alcoholism had repeated admissions for abdominal pain. Upper gastrointestinal series showed a 10-cm mass with pressure effect onto the stomach, suspicious of a pancreatic pseudocyst. Endoscopic aspiration was performed with a 21-gauge needle that yielded 60 mL of yellow to brown color cloudy fluid. Although the cyst recurred soon afterwards, this was the first report of an attempted endoscopic treatment of pancreatic pseudocysts and the start of many in the years to come. Since then, over the last two decades, we have witnessed the evolution of endoscopic treatment from simple aspiration, fistulotomy, nasocystic catheter drainage, endoscopic ultrasound (EUS)-guided puncture to irrigation, necrosectomy, insertion of metallic stents, multiple gateway access techniques and the development of EUS specific stent systems (Fig. 1).

Endoscopic drainage could be the preferred approach of drainage of peri-pancreatic fluid collections if it could overcome a number of obstacles. First, the approach needs to provide a high precision in drainage. The drainage portal must also be of sufficient size to allow adequate decompression. Furthermore, repeated interventions through the portal should be possible and the risk of adverse events associated with the procedure should be low.

DEFINITIONS OF PERI-PANCREATIC FLUID COLLECTIONS

The Atlanta's classification published in 1992 had been the most utilized classification system for acute pancreatitis.⁶ In 2012, a revised classification system by the acute pancreatitis

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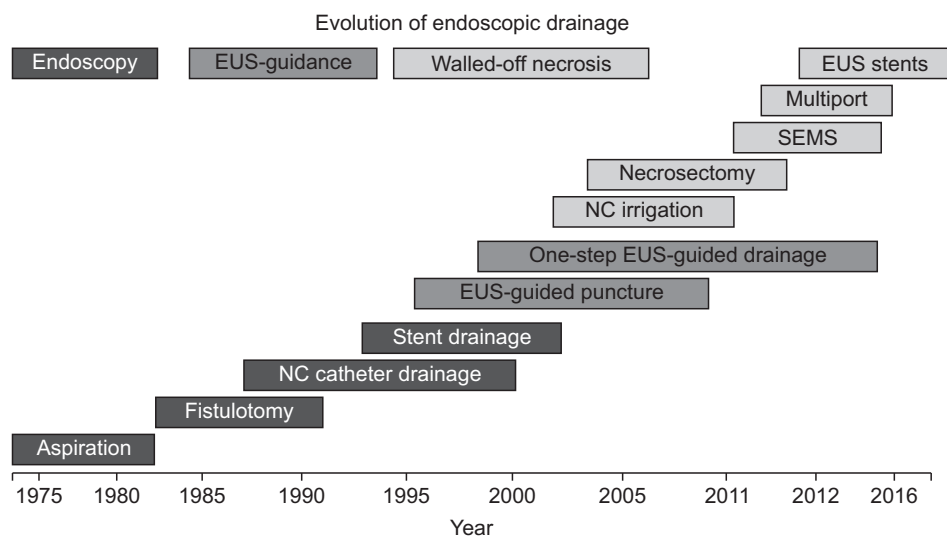


Fig. 1. Evolution of endoscopic treatment of pancreatic fluid collections.

EUS, endoscopic ultrasound; SEMS, self-expanding metallic stents; NC, nasocystic catheter.

Table 1. Revised Atlanta Classification of Pancreatic and Peri-Pancreatic Fluid Collections

Type of collection	Time, wk	Location	Imaging appearance
Interstitial edematous pancreatitis			
Acute peri-pancreatic fluid collection	≤4	Adjacent to pancreas, extrapancreatic only	Homogeneous, fluid attenuation, no liquefaction, not encapsulated
Pseudocyst	>4	Adjacent or distant to pancreas	Homogeneous, fluid attenuation, no liquefaction, encapsulated
Necrotizing pancreatitis			
Acute necrotic collection	≤4	In parenchyma and/or extrapancreatic	Heterogeneous, nonliquefied material, variably loculated, not encapsulated
Walled-off necrosis	>4	In parenchyma and/or extrapancreatic	Heterogeneous, nonliquefied material, variably loculated, encapsulated

Adapted from Thoeni RF. *Radiology* 2012;262:751-764, with permission from Radiological Society of North America.⁸

working group was published.⁷ The most notable difference is the recognition that pancreatic necrosis can exist in both an acute and chronic form, the latter now being defined as walled-off pancreatic necrosis (Table 1).⁸

According to the 2012 updated classification, the following terms have been defined: (1) acute peri-pancreatic fluid collection occurring in interstitial oedematous pancreatitis; (2) pancreatic pseudocyst as a delayed (usually more than 4 weeks) complication of interstitial oedematous pancreatitis; (3) acute necrotic collection in the early phase before demarcation in necrotizing pancreatitis, and (4) walled-off necrosis (WON) being surrounded by a radiologically identifiable capsule which typically develops after 4 weeks from the onset of pancreatitis (Fig. 2).

The new classification scheme provides guidance on the appropriate management of these different conditions. In general, endoscopic drainage is not advised in the early phase of collection formation due to the lack of a well-circumscribed cyst wall. The differentiation between pancreatic pseudocyst and WON is

also important as endoscopic drainage of WON had been demonstrated to have significantly lower success rate, higher adverse events, more frequent reinterventions and longer hospital stay.⁹

DRAINAGE OF PANCREATIC PSEUDOCYSTS

Pancreatic pseudocysts should be drained only if they persist for more than 4 to 6 weeks and are ≥6 cm in size, causing symptoms or complications such as gastric outlet obstruction or biliary obstruction.^{10,11} Drainage of pseudocysts could be performed with surgical, percutaneous and endoscopic approaches. Different endoscopic methods have been employed, including blind endoscopic puncture, endoscopic retrograde cholangiopancreatography (ERCP) or EUS-guided drainage. According to a recent multicenter survey conducted by the Asian EUS group, 77% of the participating Asian endoscopists preferred EUS-guided approach for pseudocyst drainage.¹² Regarding the technical aspects of the procedure, a high variation between dif-

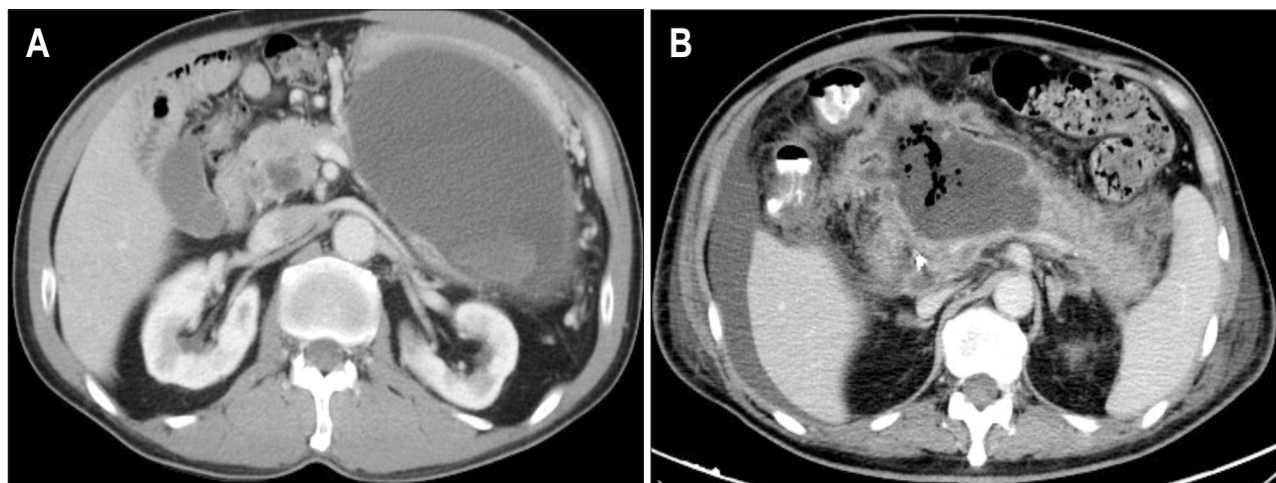


Fig. 2. Computed tomography of (A) pancreatic pseudocyst and (B) walled-off pancreatic necrosis.

ferent centers was observed: 69% would use double guide-wire technique, 84% would dilate the track up to 8 to 10 mm in size, 92% would place plastic stents instead of metallic stents and 61% would keep the stents in place for 3 to 6 months. Forty-six percent of participants believed that ERCP is not essential prior to drainage. This highlighted the current lack of consensus on the optimal method of pseudocyst drainage. A recent randomized controlled trial demonstrated that EUS-guided endoscopic cystogastrostomy had equivalent success rate (95% vs 100%) yet a shorter hospital stay, lower cost and better quality of life scores as compared to surgical cystogastrostomy.¹³ The blind esophagogastroduodenoscopy (EGD)-guided approach, is limited by the lack of visualization of the pseudocyst during puncture. In a meta-analysis by Panamonta *et al.*,¹⁴ EUS-guided puncture had a higher technical success rate, particularly for nonbulging type of pseudocysts. A trend to higher risk of hemorrhage was observed with the blind endoscopic approach (2% to 13% vs 0% to 7%), but the four studies included were underpowered to detect a statistically significant difference. On the other hand, the benefit of performing ERCP and transpapillary pancreatic ductal drainage in addition to EUS-guided transmural drainage was assessed.¹⁵ In 174 patients with pseudocysts, 95 received transmural drainage and 79 received combined drainage. Transpapillary drainage was unsuccessful in more than half of the patients with attempted transpapillary stenting. No difference in long-term resolution rates was observed. In addition, transpapillary drainage was negatively associated with pseudocyst resolution, indicating that the presence of a pancreatic stent may hinder the patency and maturation of the cystoenterostomy fistula. Results from a latest systemic review concerning the optimal approaches for pseudocyst drainage concluded that EUS-guided drainage is the modality of choice in pancreatic pseudocysts that are located adjacent to the stomach or duodenum.¹⁶ In patients with unfavorable anatomy, surgical cystogastrostomy should be the subsequent choice of procedure. Large randomized studies are

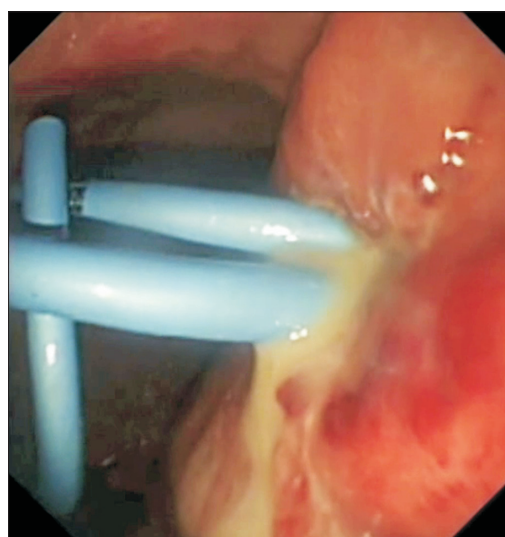


Fig. 3. Endoscopic appearance of an infected pseudocyst after two double pigtail stents were placed.

needed to compare the outcomes of various modalities.

During EUS-guided drainage, the pseudocyst is first visualized using a linear echo-endoscope to determine the best puncture site. In general, transgastric puncture is more preferable than transduodenal puncture owing to more stable position of the endoscope and better luminal visibility in the stomach. Color Doppler mode would be utilized to ensure the absence of aberrant vessels or varices along the intended puncture track. After puncture of the pseudocyst by a 19-gauge needle, the track is dilated with either electrocautery or balloon dilator. One or two double pigtail plastic stents would be placed in the pseudocyst using the double wire technique (Fig. 3).

ROLE OF ENDOSCOPIC DRAINAGE IN PANCREATIC NECROSIS

Pancreatic necrosis is traditionally managed by open necrosectomy. The procedure is associated with a high morbidity and mortality.¹⁷⁻²⁸ Repeated operations are frequently required. The fashioning of a zipper over the anterior abdominal wall was described to allow repeated access to the peritoneal cavity.²⁸ The procedure also posted significant risk of late pancreatic insufficiency. In the recent decade, there has been a paradigm shift on the approach for pancreatic necrosectomy and the procedure is increasing being performed by the endoscopic approach. This could be achieved by either percutaneous retroperitoneal or transgastric approaches. These approaches led to reduced activation of inflammatory markers and local sepsis, thus decreasing the morbidity and mortality associated with the procedure.²⁹

Percutaneous retroperitoneal and transgastric endoscopic approaches are complementary to each other, depending on the location of the pancreatic necrosis (Fig. 4). Transgastric approach is more applicable for centrally locating necrosis behind the stomach, whereas the retroperitoneal approach is suitable for necrosis near the pancreatic tail. The transgastric approach avoids the complications associated with percutaneous puncture

including bleeding, hollow visceral perforation and the risk of pancreatico-cutaneous fistula.²⁹⁻³² It can provide a more direct approach to the necrotic cavity. However, the presence of an iatrogenic fistula may lead to possible contamination of the abscess cavity by gastrointestinal contents. On the other hand, percutaneous retroperitoneal approach allows introduction of open or laparoscopic surgical instruments for effective necrosectomy.³³⁻³⁵ High volume fluid irrigation is possible through large caliber drain for effective necrosectomy and drain output could also be monitored. The “step-up” approach was introduced since the landmark randomized study published by the Dutch group in 2010.³⁶ Patients randomized to the “step-up” approach group underwent necrosectomy via the endoscopic approach (percutaneous retroperitoneal or transgastric) if necessary. These patients suffered from significantly less major complications. New onset multi organ failure was also significantly reduced with this approach, as were the need for intensive care, new onset diabetes and the rate of incisional hernias. Another smaller randomized trial (n=22) compared the outcomes of transgastric endoscopic necrosectomy and retroperitoneal necrosectomy.²⁹ The transgastric endoscopic approach was associated with a significantly less composite end-point of major complications or death. This was mainly attributed by the reduced rate of new onset multiorgan

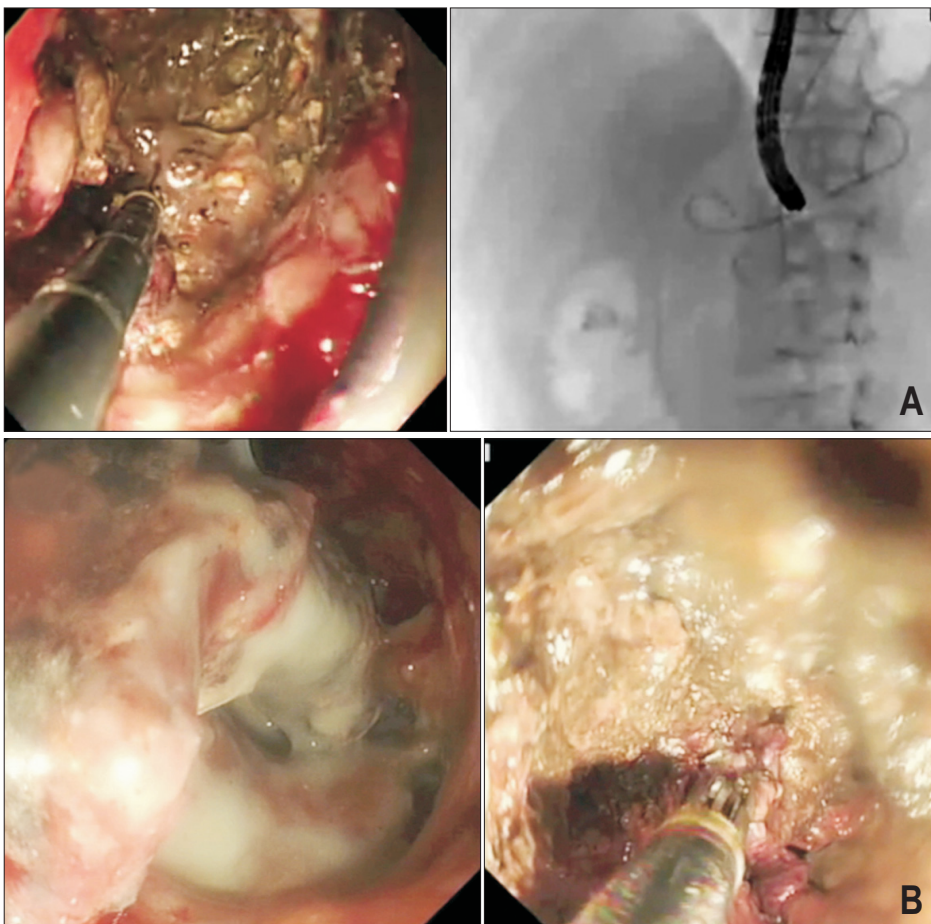


Fig. 4. (A) Transgastric and (B) percutaneous necrosectomy.

failure and pancreatic fistula with this approach.

Current guidelines suggested that for patients with suspected or confirmed infected necrosis, invasive intervention should be delayed where possible until at least 4 weeks after initial presentation to allow the collection to become "walled-off."³⁷ Percutaneous catheter or endoscopic transmural drainage should be the first step in the treatment of patients with suspected or confirmed (walled-off) infected necrotizing pancreatitis, while necrosectomy should be reserved for those who do not improve despite drainage.

RECENT ADVANCES IN ENDOSCOPIC DRAINAGE OF PANCREATIC COLLECTIONS

EUS-guided drainage is traditionally performed by an oblique viewing echo-endoscope. However, the angle of the instrument channel results in tangential puncturing of the collection. This may lead to inadequate transmission of force during insertion of the stents. Furthermore, re-cannulating an angulated track for multiple stent insertion may be difficult after tangential puncturing. Recently, forward-viewing echo-endoscopes have become available. The device allows forward sonographic imaging with in-line axis for puncturing and insertion of stents along the direction of the scanning plane (Fig. 5). This may allow better transmission of force and easier insertion of stents. In a study involving 58 patients from four tertiary centers comparing forwarding viewing and oblique viewing echo-endoscopes in drainage of pancreatic pseudocyst >6 cm in size, no difference in the ease of procedure, procedural time, morbidities and success rates were observed.³⁸ It was concluded that forward viewing endoscopes did not provide any addition benefit. However, one should be aware that only expert endoscopists participated in this study, and their performance may be less affected by the types of endoscopes being used.

On the other hand, endoscopic necrosectomy is cumbersome to perform and the procedure is associated with potential

risks of morbidities, thus the multiple transluminal gateway technique (MTGT) has been described in an aim to reduce the need of endoscopic necrosectomy. The MTGT involves creation of two to three transmural tracts by use of EUS. A nasocystic catheter would be placed across one of the tract for irrigation of normal saline, while plastic stents would be inserted at the other tracts to facilitate drainage of necrotic content after flushing. In a study of 60 patients with symptomatic walled-off pancreatic necrosis, treatment was successful in 91.7% of the patients managed by MTGT versus 52.1% managed by simple continuous drainage.³⁹ One patient in the MTGT cohort required endoscopic necrosectomy while in the simple drainage group, 17 required surgery, three underwent endoscopic necrosectomy, and three died of multiple-organ failure. Treatment success was more likely in patients treated by the MTGT after adjusting for confounding factors.

Recently, multiple small cases series have reported the use of metallic stents for drainage of peri-pancreatic fluid collections.⁴⁰⁻⁴⁴ These stents provide a larger lumen for drainage and may allow the passage of the endoscope for necrosectomy. The treatment success rate ranged from 78% to 100% in these studies using biliary or esophageal metallic stents. However the adverse event rates were also high ranging from 15% to 33%. The main problem of conventional metallic stent insertion lies in the lack of anchorage between the stent, gastric wall and the collection. As the collection collapses after successful drainage, the wall of the collection may push the stent outside the cavity and result in stent migration. The stent may also erode onto the pancreatic bed and cause severe bleeding if blood vessels are injured. Nonetheless, the use of metallic stent carries a few important advantages, including the ease of stent insertion, avoidance of multiple guidewires or excessive dilatation, and possibility of intervention through the stent. As a result, a number of specific metallic stent systems have been designed for EUS-guided drainage of pancreatic collections.

EUS specific stent systems represent the latest technological

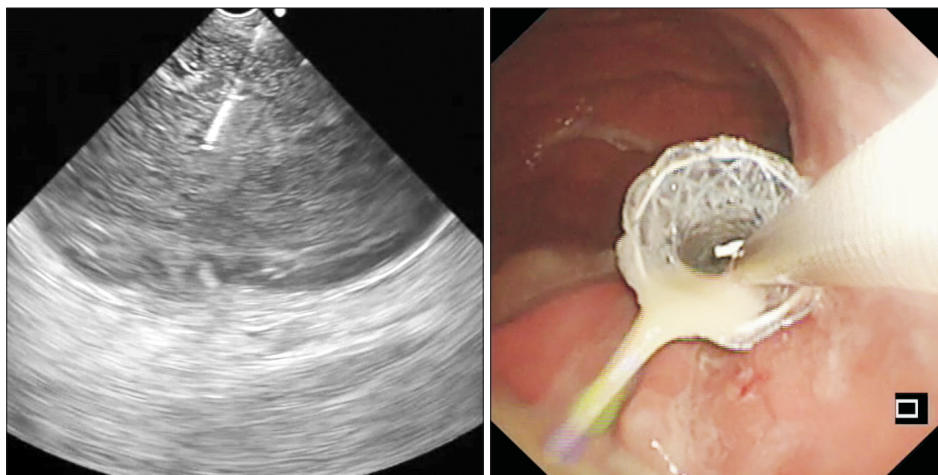


Fig. 5. Drainage with a forward viewing echoendoscope.

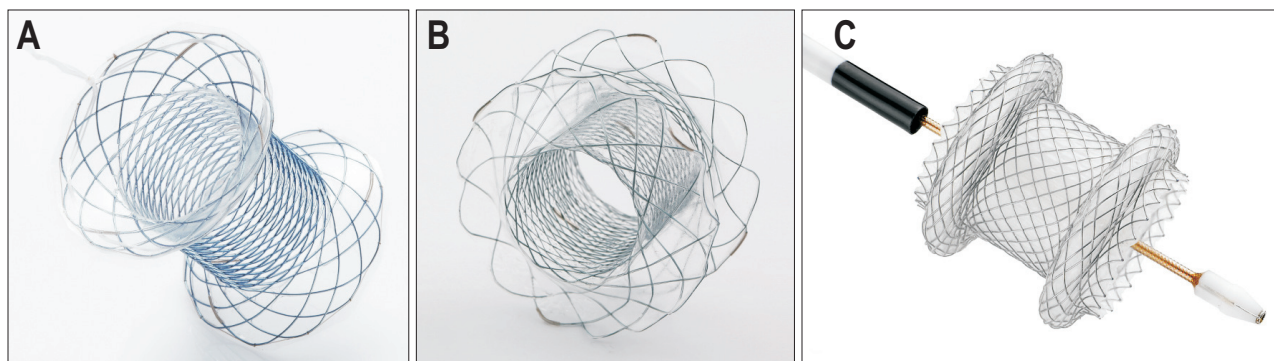


Fig. 6. Endoscopic ultrasound-specific stent systems: (A) NAGI stent, (B) Spaxus stent, and (C) Hot AXIOS stent.

development in EUS-guided drainage (Fig. 6). The described stent systems include the AXIOS stent (Boston Scientific Corp, Marlborough, MA, USA), Niti-S Spaxus stent (Taewoong Medical, Gimpo, Korea) and Niti-S NAGI stent (Taewoong Medical). These systems share several common design elements. Firstly, the stents could be deployed with EUS guidance. The ends of the stents are flanged and short in length to prevent migration. The stents also enjoy a large internal diameter allowing through the stent endoscopic intervention such as necrosectomy. Two of these systems also possess lumen-apposing capabilities to prevent leakage of gastrointestinal contents. An *ex-vivo* study examining anastomosis created by these stents (gastro-gastrostomy, gastro-jejunostomy, choledocho-gastrostomy, choledocho-duodenostomy) demonstrated that the lumen apposing force generated by the AXIOS and Spaxus stents were significantly higher across all types of anastomosis.⁴⁵

Early studies of these EUS specific stent systems yielded promising results. In two studies involving 24 patients with pancreatic pseudocysts, the use of lumen opposing AXIOS stents resulted in a technical success rate of 95.83% and a clinical success rate of 100%.^{46,47} One patient suffered from complication of stent migration. This was followed by a multitude of studies reporting on the efficacy of lumen apposing stents in pancreatic fluid collections.⁴⁸⁻⁵⁰ Another feasibility study also demonstrated 100% clinical success rate in four patients with pancreatic pseudocysts who underwent EUS-guided drainage by the lumen apposing Spaxus stent.⁵¹ No adverse event was observed and removal of stent was possible in all patients. In another pilot study utilizing the bi-flanged NAGI stents involving nine patients with pancreatic collections (five pseudocysts and four WON) also reported a 100% technical success rate with no early complication.⁵² Two patients suffered from late complications of bleeding and stent migration. This was followed by another study that included 47 patients with pseudocyst. The technical and clinical success was 91.48% and 95.43% respectively and adverse events occurred in two patients.⁵³

On comparing metal stents versus plastic stents for pancreatic fluid collections, results from two studies have become avail-

able.^{54,55} Sharaiha *et al.*,⁵⁴ included 230 patients with pseudocysts that received EUS-guided transmural drainage with double plastic pigtail stents or fully covered metallic stents. The uses of plastic stents were associated with lower complete resolution rates (89% vs 98%, $p=0.01$) but higher procedural adverse events (31% vs 16%, $p=0.006$). On multivariate analysis, the use of plastic stents was 2.9 times more likely to experience adverse events. Regarding WON, no significant differences in the rates of success, adverse events rates or procedural costs were observed between the two groups.⁵⁵ However, the mean procedure times on initial drainage and re-intervention were significantly shorter for the metal stent group.

CONCLUSIONS

Tremendous advancements have been made since the first report of endoscopic drainage of peri-pancreatic collections. Endoscopic drainage is now accurate, adequate, safe and effective with potential for repeated interventions. Tools of the trade will continue to evolve and require future trials to confirm their efficacy.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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