

Endoscopic management of pancreatic walled-off necrosis

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Abstract

Pancreatic walled-off necrosis (WON) is a complication of severe pancreatitis. Endoscopic transmural drainage has been recognized as the first-line treatment for pancreatic fluid collections. Endoscopy offers a minimally invasive approach when compared to surgical drainage. Today, endoscopists may choose to use self-expanding metal stents, pigtail stents, or lumen-apposing metal stents to facilitate drainage of fluid collections. Current data suggest that all 3 approaches yield similar outcomes. It was previously thought that drainage should be performed 4 weeks from the initial event of pancreatitis, theoretically allowing the capsule to mature. However, current data show that both early (<4 weeks) and standard (≥4 weeks) endoscopic drainage are comparable. Herein, we provide an up-to-date state-of-the-art review of the indications, techniques, innovations, outcomes, and future perspectives following drainage of pancreatic WON.

Keywords Pancreatitis, walled-off necrosis, pancreatic fluid collection, endoscopic transmural drainage, stent

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Introduction

Approximately 20% of patients with acute pancreatitis will develop pancreatic necrosis and one third of these patients will develop infected pancreatic necrosis, which is associated with high rates of morbidity and mortality [1-4]. Infected pancreatic necrosis generally requires interventional treatment [5,6]. Over the past 15 years, the treatment of infected pancreatic necrosis has changed dramatically. In the past, percutaneous and invasive surgical approaches were used; however, with the development of lumen-apposing metal stents (LAMS), an endoscopic step-up approach is favored and has become the standard of care [7,8].

As a result, endoscopic transluminal drainage by direct endoscopic necrosectomy (DEN) through LAMS is the preferred therapeutic option for treating patients with walled-off necrosis (WON) [5,7-10]. Following endoscopic ultrasound (EUS)-guided transgastric or transduodenal drainage, a pancreatic fluid collection (PFC) cavity can be entered with a standard forward viewing endoscope to perform DEN. As a rule, multiple sessions of DEN are required for complete removal of the necrosis; the mean number of DEN sessions varied from 1-15 in a meta-analysis by Puli *et al* with a weighted mean of 4.09 procedures [11].

The guidelines of the International Association of Pancreatology (IAP), American Pancreatic Association (APA), and American Gastroenterological Association suggest that

endoscopic treatment for WON should be delayed until at least 4 weeks after the onset of pancreatitis whenever possible, to allow the encapsulation of necrotic tissue [3,12]. While debridement is recommended after 4 weeks, earlier debridement may be warranted if there is a strong indication [12].

Classification of PFCs

The classification of pancreatic and peripancreatic fluid collections plays a large role in the understanding of acute pancreatitis and its treatment options. In 2012, the Atlanta classification was revised to represent our knowledge of the pathogenesis of acute pancreatitis more accurately [13] (Table 1).

The Atlanta classification divided PFCs into 4 categories. It is first divided into acute (<4 weeks) or chronic (≥4 weeks). Acute fluid collections are then further separated into acute peripancreatic fluid collections (APFC) and acute necrotic collections (ANC). Chronic collections are divided into pancreatic pseudocysts (PP) and pancreatic WON. Classification into these categories is based upon how long the collection has existed and its histological features. Fluid collections that contain both fluid and necrotizing components can be categorized as either ANC or WON, depending upon their duration and the presence of a well-defined wall (as seen only in WON). Fluid collections with no presence of necrosis would be divided into APFC or PP: APFC do not have a well-defined wall, whereas PP do [13-15] (Fig. 1).

However, in clinical practice, endoscopists often find that many PFCs do not fit exactly into the above-mentioned system. Pseudocysts identified on cross-sectional imaging (particularly computed tomography [CT] scans) are often found to contain substantial solid material at the time of EUS-guided transmural drainage, requiring debridement and DEN [16]. Thus, proper

characterization of PFCs is important prior to subjecting patients to drainage.

Indications for drainage

Initially, the fluid collection is monitored and managed with enteral feedings and pain control. In cases of mild to moderate acute pancreatitis, enteral or oral feeding should be initiated as soon as pain is controlled. In more severe cases, patients may remain nil *per os* to allow rest and prevent further pancreatic inflammation from auto digestion by pancreatic enzymes [17].

In many cases, acute PFCs will resolve spontaneously and do not require intervention [18]. Drainage is recommended in patients who develop symptoms including persistent pain; signs of gastric outlet obstruction such as nausea, vomiting or early satiety; or signs of biliary obstruction such as jaundice [19]. To this end, the presence of a PFC alone is not an indication for drainage; however, PFCs larger than 6 cm are often symptomatic, thus requiring drainage [20,21].

When PFCs become infected, patients can be treated with antibiotics and, if stable, can be followed clinically [3]. Signs of infected necrosis include sepsis, declining clinical status despite medical support, and no other source of infection. On

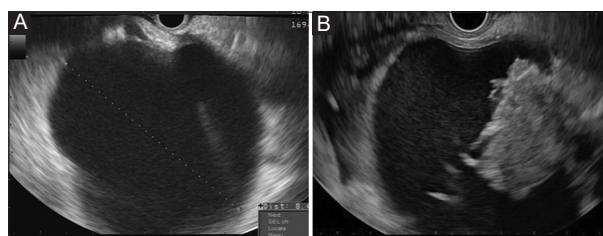


Figure 1 Endoscopic ultrasound imaging of pancreatic cyst without solid debris (A) and pancreatic walled-off necrosis with necrotic debris within the cyst cavity (B)

Table 1 Fluid collections according to the revised Atlanta classification of pancreatic fluid collections

Type of Collection	Time (weeks)	Necrosis	Location	Appearance	Infection
APFC	<4	No	Adjacent to pancreas. Extrapancreatic only	Homogenous, fluid attenuation, no liquefaction, not encapsulated	Rare
Pseudocyst	>4	No	Adjacent or distant to pancreas	Homogenous, fluid attenuation, no liquefaction, not encapsulated	Rare
Sterile ANC	<4	Yes	In parenchyma and/or extrapancreatic	Mixed (can be homogenous early and heterogeneous later) non-liquefied material, variably loculated, not encapsulated	No
Infected ANC	<4	Yes	In parenchyma and/or extrapancreatic	Mixed (can be homogenous early and heterogeneous later) non-liquefied material, variably loculated, not encapsulated	Yes
Sterile WON	>4	Yes	In parenchyma and/or extrapancreatic	Mixed (can be homogenous early and heterogeneous later) non-liquefied material, variably loculated, encapsulated	No
Infected WON	>4	Yes	In parenchyma and/or extrapancreatic	Mixed (can be homogenous early and heterogeneous later) non-liquefied material, variably loculated, encapsulated	Yes

APFC, acute pancreatic fluid collection; ANC, acute necrotic collections; WON, walled-off necrosis

radiologic imaging, gas bubbles within the PFC can sometimes be appreciated [18]. In cases of clinical deterioration, early drainage may be needed [22].

Non-endoscopic techniques

Percutaneous catheter drainage (PCD)

PCD is a common initial intervention during which a catheter is inserted into a PFC under guidance of imaging [23]. Keshavarz *et al* performed a meta-analysis of 32 studies, containing a total of 1398 patients, and concluded that PCD alone was effective in 63% of patients with pancreatic necrosis and PP [24].

Video-assisted retroperitoneal debridement (VARD)

Another technique to treat pancreatic necrosis is via VARD. During this intervention, the previously placed catheter within the percutaneous tissue is advanced to enter the necrotic tissue [25]. VARD is a combination of sinus tract endoscopy and an open translumbar approach. Research has shown it to be an effective and easy alternative to the traditional methods [26].

EUS-guided drainage

Endoscopic guided drainage is regarded as the standard of care in the treatment of WON. Traditionally, the method for drainage of the fluid collections was surgical. However, in recent years first-line treatment has shifted to endoscopic procedures. Both methods have been shown to have similar efficacy rates. Saluja *et al* compared endoscopic vs. surgical drainage of pseudocysts in 55 patients and found that the technical success rate in patients undergoing endoscopic treatment was 89% (31 of 35) compared to 100% (20 of 20) patients for surgical treatment [27]. It was also recorded that successful drainage occurred in 78% of patients undergoing endoscopic treatment compared to 100% of those with surgical treatment. This study indicates that endoscopic drainage is a comparable first-line treatment option. Furthermore, endoscopy may offer other benefits to patients, including a shorter hospital stay and lower cost [28,29].

One advantage to EUS-guided drainage is the ability to visualize the fluid collection without it bulging into the lumen [30]. This technique starts with visualization through ultrasound technology to assess a target site. Once a location is chosen that is in contact with the gastric or duodenal walls, a 19-G needle is introduced and fluid can be aspirated from the PFC [25,29,31]. This approach was then expanded by Seifert *et al*, who described DEN as an adjunct procedure that can improve patient outcomes [32]. The AGA regards this practice as an appropriate technique in patients who do not respond appropriately to EUS-guided drainage, and it is best used in

patients who have limited necrosis [12]. Studies have illustrated that DEN has high clinical success rates [33-35] (Fig. 2).

Step-up approach

The step-up approach was first described by the Dutch Acute Pancreatitis Study Group in 2010. It was described as a method that focused on controlling infection by gradually escalating treatment methods to more invasive ones (Fig. 3). The goal is to limit invasive surgical procedures [5]. This technique was found by Jain *et al*, in their observational study of 415 patients with acute pancreatitis, to have a 79.2% success rate in the treatment of infected necrotizing pancreatitis [36]. Other step-up approaches have illustrated high success rates, with low mortality rates ranging from 2-6% [37-40].

Drainage and stent types

EUS-guided pancreatic drainage can be performed under either conscious sedation or general anesthesia. Prophylactic antibiotics are usually administered. Next, ultrasound images are obtained to identify an appropriate window for drainage that would not compromise the surrounding structures and

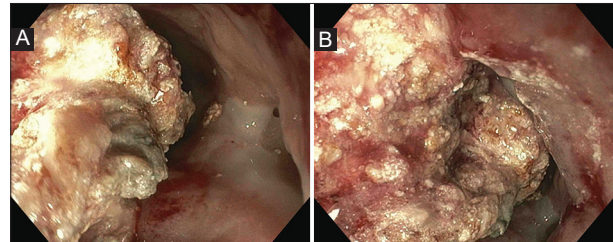


Figure 2 (A,B) Pancreatic necrotic tissue

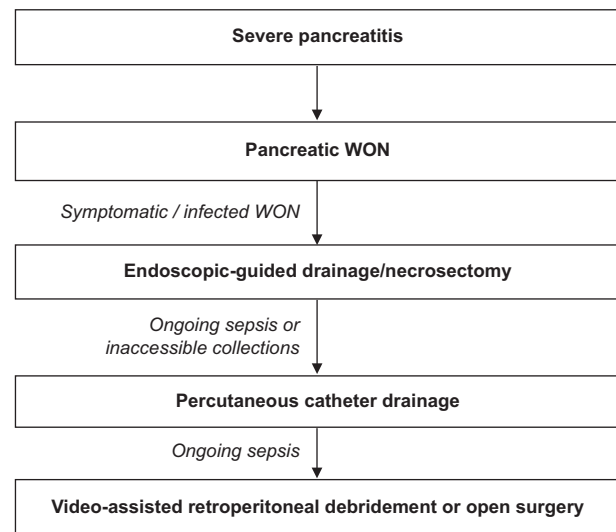


Figure 3 Schematic diagram of step-up approach
WON, walled-off necrosis

is free of interposed vasculature. Once a suitable location for cystogastrostomy has been identified, a needle is introduced and punctures the fluid collection. A guidewire is then inserted, and a fistula is created between the lumen of the gastrointestinal tract and the PFC [31]. There are 3 different types of stents that can be inserted: plastic pigtail stents, self-expanding metal stents (SEMS), and LAMS (Fig. 4). If a LAMS with an electrocautery enhanced catheter is used, no wire or dilation is required during cystogastrostomy formation.

Bartholdy *et al* conducted a retrospective study to evaluate the success of EUS-guided drainage in the treatment of WON with the placement of plastic pigtail stents [41]. This study showed favorable outcomes for patients treated with EUS-guided drainage and necrosectomy. The stents were removed one year after the initial procedure and patients were followed for an average of 4.3 years. A total of 125 patients were eligible for follow up and a 7% mortality rate was recorded. Diabetes was the most common complication observed, while the prevalence of exocrine insufficiency during follow up was 18% [41].

SEMS can be used for drainage of PFCs. Vazquez-Sequerios *et al* studied 211 patients to analyze the effectiveness and safety of fully covered SEMS for drainage of different types of PFCs (pseudocyst/pancreatic WON: 53%/47%) [42]. The fully covered SEMS used were straight biliary (66%) or lumen-apposing (34%). Technical success was achieved in 97% of patients (95% confidence interval [CI] 93-99%). Short- and long-term clinical success were obtained in 94% (95%CI 89-97%) and 85% (95%CI 79-89%) of patients, respectively [42]. Similar outcomes have been reported in the literature [43].

LAMS are the most common stent used for drainage of PFCs. A survey found that 16 of 22 advanced endoscopists believed that LAMS should be the standard of care for WON [44]. Khan *et al* noted that EUS-guided PFC drainage with LAMS was effective in all 4 classifications of PFC, with a technical success rate of 202/208 (97.1%) [45]. Anderloni *et al* evaluated the safety of the largest available diameter LAMS (22 mm) [46]. This multicenter retrospective study concluded that large-diameter LAMS matched small-diameter LAMS in terms of safety and efficacy.

Wang *et al* reported outcomes in 160 patients with PFC, including 62 patients drained with plastic stents, 28 with fully covered SEMS and 70 with LAMS [47]. The technical success (93.5% vs. 96.4% vs. 94.3%, $P > 0.99$) and treatment success rates (84.6% vs. 85.2% vs. 89.2%, $P = 0.763$) were similar among

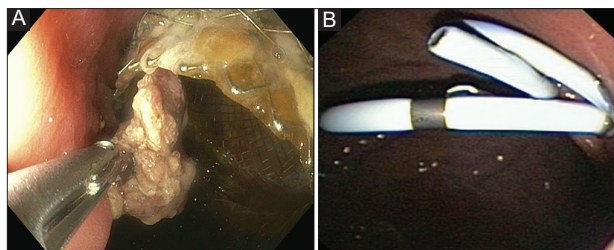


Figure 4 (A) Rat-tooth grasping necrotic tissue through a cystogastrostomy using an Axios stent. (B) Plastic stents inserted into pancreatic walled-off necrotic cavity

all stent types. Zhou *et al* reported greater clinical success with the use of metal stents compared to plastic (92% vs. 82%) [48]. WON were also found to resolve with fewer procedures when LAMS was used as opposed to plastic stents or SEMS [49]. However, Lang *et al* found that higher rates of bleeding occurred with the use of LAMS [50].

A meta-analysis of 30 studies, including one randomized controlled trial (total 1524 patients), showed that LAMS were associated with similar risks of bleeding (2.5% vs. 4.6%, $P = 0.39$) and perforation (0.5% vs. 1.1%, $P = 0.35$) compared to double pigtail plastic stents [51]. WON resolution (87.4% vs. 87.5%, $P = 0.99$), number of procedures to achieve resolution (2.09 vs. 1.88, $P = 0.72$), stent migration (5.9% vs. 6.8%, $P = 0.79$), and stent occlusion (3.8% vs. 5.2%, $P = 0.78$) were similar for both cohorts.

Results from the Tension trial by Boxhoorn *et al* showed that the need for endoscopic transluminal necrosectomy in patients with infected necrotizing pancreatitis treated with LAMS was not lower compared with plastic stents (odds ratio 1.21, 95%CI 0.45-3.23) [52]. Furthermore, the trial showed that the total number of interventions, length of hospital stay and total healthcare costs, as well as complications (especially bleeding), also did not differ between groups. Some concerns over procedural standardizations have been raised, emphasizing the need for larger studies on the topic [22,53].

Given that clinical and technical outcomes appear to be similar among LAMS and plastic stents, the decision to use either method is typically driven by endoscopists' experience and availability. However, the economic burden of such innovative accessories and procedures is not negligible. In fact, there is evidence that the cost of LAMS may be greater than that of plastic stents. Chen *et al* used a decision-tree model to compare LAMS to plastic stents in inpatients over a 6-month period following stent insertion [54]. The study reported that the respective costs per successful drainage were US \$18,129 (LAMS) and US\$10,403 (plastic stent), and concluded that plastic stents should be used in the initial management of PFCs. Indeed, while plastic stents may be more cost-effective than LAMS, anecdotally, the ease of inserting LAMS must be highlighted, which may have led to their widespread adoption.

Multiple transluminal gateway technique (MTGT) drainage

In most cases, a single pigtail stent or LAMS placed transmurally across the stomach or duodenum and into the necrotic pancreatic cavity is sufficient. This is referred to as the single transluminal gateway technique. However, in cases where the pancreatic collection is complex or multiloculated, placing multiple pigtail stents or LAMS at different access points may be necessary, referred to as a MTGT [55]. Some authors will automatically use the MTGT approach if collections are > 12 cm [56]. It should be noted that this size is random and larger collections may drain easier with single access, while smaller complex collections may require multiple access points and/or adjunctive interventions. This technique is not

commonly performed at many centers; however, the technique facilitates better drainage of necrotic contents and obviates the need for high-risk interventions such as necrosectomy [57].

Binda *et al* applied MTGT in 6 patients using 2 LAMS [58]. Technical success was 100%. The mean procedure time was 29 min. The mean number of DEN sessions per patient was 2. Two of 6 patients developed adverse events, bleeding in both cases, and were treated endoscopically and surgically, respectively. The mean hospital stay was 52.5 days. No patients had residual necrosis or WON recurrence. Despite the limited number of patients, the single-step MTGT using electrocautery-LAMS can be considered a feasible and well-tolerated treatment option for patients with complex WON.

Early (<4 weeks) vs. standard (≥4 weeks) drainage

Early drainage of PFCs is classified as drainage that occurs earlier than 4 weeks. IAP/APA guidelines recommend that fluid collections with complications of necrosis wait for drainage until week 4, when the collections become walled off—i.e., have a mature wall [3]. However, there has been very little research into the risks and benefits of conducting this drainage earlier than 4 weeks, if necessary. Chantarojanasiri *et al* compared the safety and efficacy of early (<4 weeks) vs. delayed (≥4 weeks) drainage of PFCs [59]. Technical success was achieved in both the early and delayed groups and complication rates were similar between groups.

Trikudanathan *et al* used an endoscopically centered step-up strategy to compare drainage at <4 weeks or ≥4 weeks from the onset of pancreatitis [60]. The study reported that early (<4 weeks) interventions were more often performed for infection and organ failure, with no more complications, similar improvement in organ failure, slightly greater need for surgery, and relatively low mortality. The study concluded that early endoscopic drainage ± necrosectomy should be considered when there is a strong indication for intervention, and this indeed reflects current practice.

A meta-analysis looking at any early intervention (endoscopy, interventional radiology or surgery) for draining walled-off PFCs showed that early interventions (≤4 weeks) were associated with higher mortality rates and did not reduce adverse events or improve clinical success [61]. However, a recent meta-analysis by Ramai *et al* reported that endoscopy (only) early (<4 weeks) and standard (≥4 weeks) drainage of walled-off PFCs offered similar technical and clinical outcomes, as well as comparable adverse events [62]. The study concluded that patients requiring endoscopic drainage should not be delayed until 4 weeks.

Hydrogen peroxide (H₂O₂) lavage of PFC cavities

Endoscopic necrosectomy is often the preferred treatment of WON. H₂O₂ can serve as an agitator and as a bactericidal agent (Fig. 5). Individual formulations vary, but sterile saline is

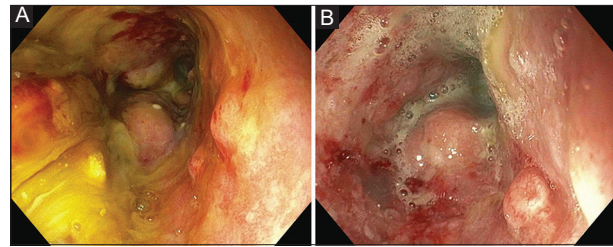


Figure 5 (A) Pancreatic cavity post debridement. (B) Pancreatic cavity sprayed with hydrogen peroxide

used to dilute a 3% H₂O₂ solution in a 2:1 or 3:1 ratio. No firm guidelines exist on the volume to be injected for lavage, but typically several hundred cc are used.

The use of diluted H₂O₂ lavage during this procedure has shown promising results. Messallam *et al* found a higher clinical success rate of 93.8% in the H₂O₂ group, compared to 78.9% in the non-H₂O₂ group [63]. Garg *et al* reported that the most common associated adverse events were bleeding and stent migration [64].

A recent meta-analysis studying the pooled clinical outcomes of H₂O₂-assisted DEN for pancreatic WON showed that the pooled rate of technical success was 95.8% (95%CI 88.5-98.5), clinical success was 91.6% (95%CI 86.1-95), and cumulative rate of overall adverse events was 19.3% (95%CI 7.6-41). The pooled rate of bleeding was 7.9% (95%CI 2.4-22.7), stent migration was 11.3% (95%CI 4.9-23.9), perforation 5.4% (95%CI 1.7-15.7), infection 5.7% (95%CI 2-15.1), and pulmonary adverse events 2.9% (95%CI 1.3-6.1) [65].

Mechanical debridement

One of the main limitations of endoscopic necrosectomy is the lack of dedicated, on-label instruments to remove necrotic tissue from within PFCs. For this purpose, various instruments originally designed for other indications—including endoscopic retrograde cholangiopancreatography and colonoscopy, among other procedures—are widely used. These devices, including biliary stone baskets, rat-tooth forceps, retrieval nets and polypectomy snares, are able to grasp and remove solid necrotic material. Liquid contents in the PFC can be directly aspirated through the endoscope.

The EndoRotor (Interscope Medical, Inc., Worcester, MA, USA) is a novel automated mechanical endoscopic system designed for use in the gastrointestinal tract for tissue dissection and resection with a single device (Fig. 6). The EndoRotor was approved by the Food and Drug Administration for the removal of dead pancreatic tissue via DEN in December 2020 [66].

The EndoRotor is inserted through the working channel of a therapeutic endoscope across a cystogastrostomy and advanced into the PFC collection cavity, where it operates under direct endoscopic visualization. The device features a rotating serrated tip on a hollow catheter connected to suction. As the catheter rotates, it breaks up solid necrotic material and suctions it into a trap where its volume can be assessed. The

catheter is stiff but relatively atraumatic. Various speeds of rotation can be set by the user (Fig. 7).

The standard debridement catheter has an external diameter of 3.1 mm and has been used with endoscopes that have a 3.2 mm or larger working channel. It has a fixed outer cannula with a hollow inner cannula that can be set at rotation speeds of 1000 (low) or 1700 (high) revolutions per min. Typically, as outlined in the electronic control console, cutting ranges from 2-4 mm of tissue per sec [67]. The necrotic tissue is sucked into the catheter using negative pressure and cut by the rotating blade from the inner cannula. Tissue is transported to a standard vacuum container. Suction is typically set between 500 and 620 mmHg, the maximum achievable negative pressure level [68,69].

The catheter shaft is flexible and can tolerate endoscope bending or manipulation up to greater than 160 degrees. If greater manipulation is required, a longer catheter can be used to reduce the torsional stress on the device. Three catheter lengths accommodate Olympus and Pentax long colonoscopes (1890 mm), and Fuji (1240 mm), Olympus and Pentax (1270 mm) gastroscopes [69]. Both the cutting tool rotation and the activation/deactivation of suction are controlled by the endoscopist using 2 separate foot pedals. The foot pedal has a twin pedal design: blue (activate rotor) and orange (activate vacuum) [69].

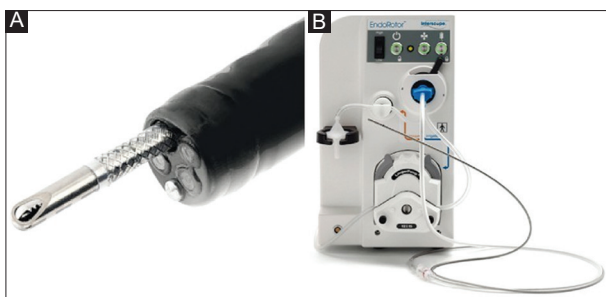


Figure 6 EndoRotor mechanical debridement system (A-catheter and B-console; source: Interscope INC)



Figure 7 EndoRotor being used to mechanically debride necrotic tissue

Stassen *et al* evaluated the use of the EndoRotor to remove solid debris under direct endoscopic visualization using a 3.1-mm debridement catheter [70]. The prospective trial involved 10 international sites, which enrolled 30 patients (mean age 55 years, 60% male) with pancreatic WON ranging in size from 6-22 mm, with a >30% solid component based on CT. The authors reported that 15/30 (50%) achieved complete debridement in 1 session, and 21/30 (73%) achieved complete debridement after 2 sessions. Additionally, mean total procedure time was 117 min (standard deviation [SD] 50), mean EndoRotor time was 71 min (SD 36), and overall median percent necrotic debris removed per procedure was 66% (interquartile range 65).

Recently, a 5.1-mm debridement catheter was introduced that has a greater volume and faster rates of necrotic tissue removal. A study abstract that described the clinical use of this device reported a significant (>50%) single-session decrease in the percent of solid debris, a nearly 70% single-session decrease in the WON area, and an average of 2 endoscopic necrosectomies to achieve WON resolution with minimal complications [71]. The average duration of EndoRotor therapy was 65 min.

Using direct endoscopic visualization, the EndoRotor device is designed to facilitate removal of dead tissue in patients with pancreatic WON. Overall, with the limited data available, the EndoRotor resection system appears to be safe and effective. Large, randomized trials are required to confirm these favorable observations. Furthermore, the costs associated with this technology may hinder its adoption, limiting its use to highly specialized centers. Cost analyses comparing EndoRotor to traditional endoscopic methods of debridement are needed.

Another mechanical device, currently in experimental form, is the waterjet necrosectomy device (WAND) [72]. This instrument can deliver a continuous stream of water with a surface pressure of 0.72 bar at a flow rate of 0.37 L/min. The device delivers irrigation capable of fragmenting necrotic debris while avoiding trauma to healthy nontargeted tissue. Future in-human studies are awaited to assess the efficacy and safety of the WAND for endoscopic pancreatic necrosectomy.

Management of disconnected pancreatic duct syndrome (DPDS)

Disruption or DPDS is a potential complication of WON. Roughly 30-50% of patients with pancreatic necrosis may experience DPDS and are more likely to require additional therapeutic interventions, rescue surgery and/or an extended hospital stay [73,74].

When the main pancreatic duct is partially (incomplete) disrupted, transpapillary stenting may be effective. If the endoscopic interventions fail and a recurrent fluid collection occurs, surgery such as distal pancreatectomy and Roux-en-Y drainage can offer an alternative. If transpapillary stenting of a partial disruption fails, or where there is complete disruption, EUS-guided main pancreatic duct drainage can be considered.

However, EUS-guided pancreatic duct drainage is a relatively new procedure and remains one of the most technically challenging therapeutic EUS interventions, as evidenced by the multiple concerns associated with device selection and the risk of severe complications [75]. Furthermore, because of the lack of larger, more controlled studies, the exact efficacy and the safety of this procedure have yet to be determined [76].

An international survey identified a clinically relevant lack of expert consensus on diagnosing and treating pancreatic duct disruption or disconnection in patients with necrotizing pancreatitis [77]. However, magnetic resonance imaging/magnetic resonance cholangiopancreatography was the preferred diagnostic modality, while endoscopic transluminal drainage was the preferred intervention for patients with DPDS. However, diabetes almost always occurs in these patients. Thiruvengadam *et al* reported that, in patients with necrotizing pancreatitis and DPDS, the risk of new-onset diabetes after pancreatitis was 5 times higher compared to patients without DPDS (adjusted hazard ratio 5.63, 95%CI 1.69-18.74; P=0.005) [78].

Concluding remarks

While most PFCs resolve spontaneously, pancreatic WON is associated with debilitating symptoms that may require drainage. To this end, drainage of pancreatic necrotic collections is managed using an endoscopy-centered approach, limited to endoscopists who are experts in this subspecialized area. SEMS, plastic stents and LAMS all appear to have comparable results in facilitating drainage; thus, the choice of stent type is based solely on the endoscopist's preference. Advances in mechanical debridement (i.e., EndoRotor, WAND) are promising and may add to the endoscopic armamentarium.

References

1. Mederos MA, Reber HA, Girgis MD. Acute pancreatitis: a review. *JAMA* 2021;**325**:382-390.
2. Toouli J, Brooke-Smith M, Bassi C, et al; Working Party of the Program Committee of the Bangkok World Congress of Gastroenterology 2002. Guidelines for the management of acute pancreatitis. *J Gastroenterol Hepatol* 2002;**17**(Suppl): S15-S39.
3. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatol* 2013;**13**:e1-e15.
4. van Santvoort HC, Bakker OJ, Bollen TL, et al; Dutch Pancreatitis Study Group. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology* 2011;**141**:1254-1263.
5. van Santvoort HC, Besselink MG, Bakker OJ, et al; Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med* 2010;**362**:1491-1502.
6. Adler DG, Chari ST, Dahl TJ, Farnell MB, Pearson RK. Conservative management of infected necrosis complicating severe acute pancreatitis. *Am J Gastroenterol* 2003;**98**:98-103.
7. Bakker OJ, van Santvoort HC, van Brunschot S, et al; Dutch Pancreatitis Study Group. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *JAMA* 2012;**307**:1053-1061.
8. van Brunschot S, van Grinsven J, Voermans RP, et al; Dutch Pancreatitis Study Group. Transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotising pancreatitis (TENSION trial): design and rationale of a randomised controlled multicenter trial [ISRCTN09186711]. *BMC Gastroenterol* 2013;**13**:161.
9. Bugiantella W, Rondelli F, Boni M, et al. Necrotizing pancreatitis: a review of the interventions. *Int J Surg* 2016;**28**(Suppl 1):S163-S171.
10. Gurusamy KS, Belgaumkar AP, Haswell A, et al. Interventions for necrotising pancreatitis. *Cochrane Database Syst Rev* 2016;**4**:CD011383.
11. Puli SR, Graumlich JF, Pamulaparthi SR, Kalva N. Endoscopic transmural necrosectomy for walled-off pancreatic necrosis: a systematic review and meta-analysis. *Can J Gastroenterol Hepatol* 2014;**28**:50-53.
12. Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association clinical practice update: management of pancreatic necrosis. *Gastroenterology* 2020;**158**:67-75.
13. Bezmarević M, van Dijk SM, Voermans RP, van Santvoort HC, Besselink MG. Management of (peri)pancreatic collections in acute pancreatitis. *Visc Med* 2019;**35**:91-96.
14. Tyberg A, Karia K, Gabr M, et al. Management of pancreatic fluid collections: A comprehensive review of the literature. *World J Gastroenterol* 2016;**22**:2256-2270.
15. Banks PA, Bollen TL, Dervenis C, et al; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102-111.
16. Adler DG, Siddiqui AA. What's in a name? Pancreatic pseudocysts, walled-off necrosis, and pancreatic fluid collections. *Endosc Ultrasound* 2016;**5**:215-217.
17. Goodgame JT, Fischer JE. Parenteral nutrition in the treatment of acute pancreatitis: effect on complications and mortality. *Ann Surg* 1977;**186**:651-658.
18. Muthusamy VR, Chandrasekhara V, Acosta RD, et al; ASGE Standards of Practice Committee. The role of endoscopy in the diagnosis and treatment of inflammatory pancreatic fluid collections. *Gastrointest Endosc* 2016;**83**:481-488.
19. Bhakta D, de Latour R, Khanna L. Management of pancreatic fluid collections. *Transl Gastroenterol Hepatol* 2022;**7**:17.
20. Yeo CJ, Bastidas JA, Lynch-Nyhan A, Fishman EK, Zinner MJ, Cameron JL. The natural history of pancreatic pseudocysts documented by computed tomography. *Surg Gynecol Obstet* 1990;**170**:411-417.
21. Libera ED, Siqueira ES, Morais M, et al. Pancreatic pseudocysts transpapillary and transmural drainage. *HPB Surg* 2000;**11**:333-338.
22. Larghi A, Facciorusso A. Lumen-apposing metal stents versus double-pigtail plastic stents for infected necrotising pancreatitis: more doubts than answers. *Gut* 2022;gutjnl-2022-328149. [Online ahead of print]. doi: 10.1136/gutjnl-2022-328149
23. Gupta P, Gupta J, Kumar C, et al. Aggressive percutaneous catheter drainage protocol for necrotic pancreatic collections. *Dig Dis Sci* 2020;**65**:3696-3701.
24. Keshavarz P, Azrumelashvili T, Yazdanpanah F, et al. Percutaneous catheter drainage of pancreatic associated pathologies: A systematic review and meta-analysis. *Eur J Radiol* 2021;**144**:109978.
25. van Brunschot S, Bakker OJ, Besselink MG, et al; Dutch Pancreatitis Study Group. Treatment of necrotizing pancreatitis. *Clin Gastroenterol Hepatol* 2012;**10**:1190-1201.
26. Van Santvoort HC, Besselink MGH, Horvath KD, et al. Videoscopic assisted retroperitoneal debridement in infected necrotizing pancreatitis. *HPB (Oxford)* 2007;**9**:156-159.

27. Saluja S, Srivastava S, Govind S, et al. Endoscopic cystogastrostomy versus surgical cystogastrostomy in the management of acute pancreatic pseudocysts. *J Minim Access Surg* 2019;**16**:126-131.
28. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. *Gastroenterology* 2013;**145**:583-590.e1.
29. Ang TL, Teoh AYB. Endoscopic ultrasonography-guided drainage of pancreatic fluid collections. *Dig Endosc* 2017;**29**:463-471.
30. Yasuda I, Takahashi K. Endoscopic management of walled-off pancreatic necrosis. *Dig Endosc* 2021;**33**:335-341.
31. Puri R, Thandassery RB, Alfadda AA, Kaabi SA. Endoscopic ultrasound guided drainage of pancreatic fluid collections: Assessment of the procedure, technical details and review of the literature. *World J Gastrointest Endosc* 2015;**7**:354-363.
32. Seifert H, Wehrmann T, Schmitt T, et al. Retroperitoneal endoscopic debridement for infected peripancreatic necrosis. *Lancet* 2000;**356**:653-655.
33. Feng L, Guo J, Wang S, et al. Endoscopic transmural drainage and necrosectomy in acute necrotizing pancreatitis: a review. *J Transl Intern Med* 2021;**9**:168-176.
34. Kaczmarek D, Nattermann J, Strassburg C, et al. Endoscopic ultrasound-guided drainage and treatment of symptomatic pancreatic fluid collection following acute or acute-on-chronic pancreatitis – a single center case series. *Zentralbl Chir* 2018;**143**:577-585.
35. Yan L, Dargan A, Nieto J, et al. Direct endoscopic necrosectomy at the time of transmural stent placement results in earlier resolution of complex walled-off pancreatic necrosis: Results from a large multicenter United States trial. *Endosc Ultrasound* 2019;**8**:172-179.
36. Jain S, Padhan R, Bopanna S, et al. Percutaneous endoscopic step-up therapy is an effective minimally invasive approach for infected necrotizing pancreatitis. *Dig Dis Sci* 2020;**65**:615-622.
37. Liu ZW, Yang SZ, Wang PF, et al. Minimal-access retroperitoneal pancreatic necrosectomy for infected necrotizing pancreatitis: a multicentre study of a step-up approach. *Br J Surg* 2020;**107**:1344-1353.
38. Luckhurst CM, El Hechi M, Elsharkawy AE, et al. Improved mortality in necrotizing pancreatitis with a multidisciplinary minimally invasive step-up approach: comparison with a modern open necrosectomy cohort. *J Am Coll Surg* 2020;**230**:873-883.
39. Jones JD, Clark CJ, Dyer R, Case LD, Mishra G, Pawa R. Analysis of a step-up approach versus primary open surgical necrosectomy in the management of necrotizing pancreatitis: experience in a cohort of patients at a US academic medical center. *Pancreas* 2018;**47**:1317-1321.
40. Aparna D, Kumar S, Kamalkumar S. Mortality and morbidity in necrotizing pancreatitis managed on principles of step-up approach: 7 years experience from a single surgical unit. *World J Gastrointest Surg* 2017;**9**:200-208.
41. Bartholdy A, Werge M, Novovic S, et al. Endoscopic treatment with transmural drainage and necrosectomy for walled-off necrosis provides favourable long-term outcomes on pancreatic function. *United European Gastroenterol J* 2020;**8**:552-558.
42. Vazquez-Sequeiros E, Baron TH, Pérez-Miranda M, et al; Spanish Group for FCSEMS in Pancreas Collections. Evaluation of the short- and long-term effectiveness and safety of fully covered self-expandable metal stents for drainage of pancreatic fluid collections: results of a Spanish nationwide registry. *Gastrointest Endosc* 2016;**84**:450-457.
43. Shah RJ, Shah JN, Waxman I, et al. Safety and efficacy of endoscopic ultrasound-guided drainage of pancreatic fluid collections with lumen-apposing covered self-expanding metal stents. *Clin Gastroenterol Hepatol* 2015;**13**:747-752.
44. Guo J, Saftoiu A, Vilmann P, et al. A multi-institutional consensus on how to perform endoscopic ultrasound-guided peri-pancreatic fluid collection drainage and endoscopic necrosectomy. *Endosc Ultrasound* 2017;**6**:285-291.
45. Khan S, Chandran S, Chin J, et al. Drainage of pancreatic fluid collections using a lumen-apposing metal stent with an electrocautery-enhanced delivery system. *J Gastroenterol Hepatol* 2021;**36**:3395-3401.
46. Anderloni A, Fabbri C, Nieto J, et al. The safety and efficacy of a new 20-mm lumen apposing metal stent (lams) for the endoscopic treatment of pancreatic and peripancreatic fluid collections: a large international, multicenter study. *Surg Endosc* 2021;**35**:1741-1748.
47. Wang Z, Zhao S, Meng Q, et al. Comparison of three different stents for endoscopic ultrasound-guided drainage of pancreatic fluid collection: A large retrospective study. *J Gastroenterol Hepatol* 2019;**34**:791-798.
48. Zhou X, Lin H, Su X, et al. Metal versus plastic stents for pancreatic fluid collection drainage: a systematic review and meta-analysis. *J Clin Gastroenterol* 2021;**55**:652-660.
49. Siddiqui AA, Kowalski TE, Loren DE, et al. Fully covered self-expanding metal stents versus lumen-apposing fully covered self-expanding metal stent versus plastic stents for endoscopic drainage of pancreatic walled-off necrosis: clinical outcomes and success. *Gastrointest Endosc* 2017;**85**:758-765.
50. Lang GD, Fritz C, Bhat T, et al. EUS-guided drainage of peripancreatic fluid collections with lumen-apposing metal stents and plastic double-pigtail stents: comparison of efficacy and adverse event rates. *Gastrointest Endosc* 2018;**87**:150-157.
51. Chandrasekhara V, Barthet M, Devière J, et al. Safety and efficacy of lumen-apposing metal stents versus plastic stents to treat walled-off pancreatic necrosis: systematic review and meta-analysis. *Endosc Int Open* 2020;**8**:E1639-E1653.
52. Boxhoorn L, Verdonk RC, Besselink MG, et al. Comparison of lumen-apposing metal stents versus double-pigtail plastic stents for infected necrotising pancreatitis. *Gut* 2023;**72**:66-72.
53. Tiwari A, Shah A, Singh J. LAMS versus plastic stents for infected pancreatic walled off necrosis (WON): has the addition of the TENSION trial to the AXIOMA study eased the tension? *Gut* 2022;gutjnl-2022-328148. [Online ahead of print]. doi: 10.1136/gutjnl-2022-328148
54. Chen YI, Khashab MA, Adam V, et al. Plastic stents are more cost-effective than lumen-apposing metal stents in management of pancreatic pseudocysts. *Endosc Int Open* 2018;**6**:E780-E788.
55. Varadarajulu S, Phadnis MA, Christein JD, Wilcox CM. Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis. *Gastrointest Endosc* 2011;**74**:74-80.
56. Bang JY, Holt BA, Hawes RH, et al. Outcomes after implementing a tailored endoscopic step-up approach to walled-off necrosis in acute pancreatitis. *Br J Surg* 2014;**101**:1729-1738.
57. 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* 2019;**68**:1200-1209.
58. Binda C, Dabizzi E, Anderloni A, et al. Single-step endoscopic ultrasound-guided multiple gateway drainage of complex walled-off necrosis with lumen apposing metal stents. *Eur J Gastroenterol Hepatol* 2020;**32**:1401-1404.
59. Chantarojanasiri T, Yamamoto N, Nakai Y, et al. Comparison of early and delayed EUS-guided drainage of pancreatic fluid collection. *Endosc Int Open* 2018;**6**:E1398-E1405.
60. Trikudanathan G, Tawfik P, Amateau SK, et al. Early (<4 weeks) versus standard (≥4 weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. *Am J Gastroenterol* 2018;**113**:1550-1558.
61. Nakai Y, Shiomi H, Hamada T, et al; WONDERFUL study group in Japan. Early versus delayed interventions for necrotizing pancreatitis: A systematic review and meta-analysis. *DEN Open* 2023;**3**:e171.

62. Ramai D, Enofe I, Deliwala SS, et al. Early (<4 weeks) versus standard (≥ 4 weeks) endoscopic drainage of pancreatic walled-off fluid collections: a systematic review and meta-analysis. *Gastrointest Endosc* 2022 Nov 14 [Online ahead of print]. doi: 10.1016/j.gie.2022.11.003
63. Messallam AA, Adler DG, Shah RJ, et al. Direct endoscopic necrosectomy with and without hydrogen peroxide for walled-off pancreatic necrosis: a multicenter comparative study. *Am J Gastroenterol* 2021;116:700-709.
64. Garg R, Gupta S, Singh A, Simonson MT, Rustagi T, Chahal P. Hydrogen peroxide assisted endoscopic necrosectomy for walled-off pancreatic necrosis: A systematic review and meta-analysis. *Pancreatology* 2021;21:1540-1547.
65. Mohan BP, Madhu D, Toy G, et al. Hydrogen peroxide-assisted endoscopic necrosectomy of pancreatic walled-off necrosis: a systematic review and meta-analysis. *Gastrointest Endosc* 2022;95:1060-1066.
66. Food and Drug Administration. FDA authorizes marketing of new device designed to remove dead pancreatic tissue. 2020. Available from: <https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-new-device-designed-remove-dead-pancreatic-tissue> [Accessed 19 December 2022].
67. Pinto S, Bellizzi S, Badas R, et al. Direct endoscopic necrosectomy: timing and technique. *Medicina (Kaunas)* 2021;57:1305.
68. Ramai D, Adler DG. Endoscopic management of pancreatic necrosis using the EndoRotor resection system. *Pract Gastroenterol* 2021;45:54-67.
69. Interscope. EndoRotor® DEN Microdebrider. 2021. Available from: <https://static1.squarespace.com/static/5cde1ad25312b90001d33766/1558139748829/NEW-2.pdf> [Accessed 19 December 2022].
70. Stassen PMC, de Jonge PJJ, Bruno MJ, et al. Safety and efficacy of a novel resection system for direct endoscopic necrosectomy of walled-off pancreas necrosis: a prospective, international, multicenter trial. *Gastrointest Endosc* 2022;95:471-479.
71. Shinn B, Burdick JA, Berk K, et al. Safety, efficacy and clinical utility of the 5.1 mm endorotor powered debridement catheter for treatment of walled off pancreatic necrosis. *Gastrointest Endosc* 2022;95:AB235-AB236.
72. Yachimski P, Landewee CA, Campisano F, Valdastrì P, Obstein KL. The waterjet necrosectomy device for endoscopic management of pancreatic necrosis: design, development, and preclinical testing (with videos). *Gastrointest Endosc* 2020;92:770-775.
73. Bang JY, Wilcox CM, Navaneethan U, et al. Impact of disconnected pancreatic duct syndrome on the endoscopic management of pancreatic fluid collections. *Ann Surg* 2018;267:561-568.
74. Vanek P, Trikudanathan G, Freeman ML. Diagnosing disconnected pancreatic duct syndrome: many disconnects, few answers. *Dig Dis Sci* 2021;66:1380-1382.
75. Giovannini M. EUS-guided pancreatic duct drainage: ready for prime time? *Gastrointest Endosc* 2013;78:865-867.
76. Khan Z, Hayat U, Moraveji S, Adler DG, Siddiqui AA. EUS-guided pancreatic ductal intervention: a comprehensive literature review. *Endosc Ultrasound* 2021;10:98-102.
77. Boxhoorn L, Timmerhuis HC, Verdonk RC, et al. Diagnosis and treatment of pancreatic duct disruption or disconnection: an international expert survey and case vignette study. *HPB (Oxford)* 2021;23:1201-1208.
78. Thiruvengadam NR, Forde KA, Miranda J, et al. Disconnected pancreatic duct syndrome: pancreatitis of the disconnected pancreas and its role in the development of diabetes mellitus. *Clin Transl Gastroenterol* 2022;13:e00457.