

Endoscopic Ultrasound Guided Walled-off Necrosis Drainage



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KEYWORDS

- Walled-off necrosis • Endoscopic drainage • Endoscopic ultrasound
- Endoscopic necrosectomy • Minimally invasive surgery • Debridement
- Percutaneous drainage

KEY POINTS

- Walled-off necrosis is associated with significant morbidity and mortality, particularly in the presence of secondary infection.
- Endoscopy-based interventions are associated with less morbidity and costs compared to minimally invasive surgery.
- EUS-guided lumen-apposing metal stent placement followed by endoscopic necrosectomy is the current standard-of-care with treatment success greater than 90%.
- Evidence-based recommendations are needed to standardize post-procedure care to expedite recovery and reduce resource consumption.

INTRODUCTION

In the United States, acute pancreatitis is the third most common gastrointestinal disorder, requiring 291,915 hospitalizations annually.¹ Necrotizing pancreatitis occurs in about 20% of patients with acute pancreatitis and is associated with a mortality rate of 8% to 40%.² Mortality is more common in patients with secondary infection that may result in sepsis and multiorgan failure. Although traditional treatment has been open surgical necrosectomy, it is associated with high rates of adverse events (34%–95%) and mortality (11%–39%).^{3,4} Recent studies suggest that minimally invasive techniques that incorporate a step-up approach of percutaneous drain placement in conjunction with video-assisted retroperitoneal debridement (VARD) are superior to open surgical necrosectomy with lower rates of postprocedural adverse events (40%) and long-term morbidity.⁵ As an alternative to surgical methods, endoscopic interventions have gained increasing popularity for the treatment of necrotic collections,

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with an adverse event rate between 10.4% and 24.5%, and a mortality rate of less than 10%.^{6–9} In this review, we outline the approach to the management of walled-off necrosis (WON) with a particular focus on endoscopic treatment options. Additionally, the definition, indications for and timing of intervention, description of various procedural techniques, adverse events, and post-procedure management are reviewed.

DEFINITION OF WALLED-OFF NECROSIS

Acute necrotic collections and WON occur as a result of necrotizing pancreatitis and are characterized by the presence of solid, necrotic debris of varying quantities. Acute necrotic collections are present early in the course of necrotizing pancreatitis whereas WON develops a few weeks (usually > 4) after the onset of acute pancreatitis when a mature rim encapsulates the collection.¹⁰ Fig. 1 outlines the differences in characteristics between both fluid collections.

The distinction of a WON from a pseudocyst is important as the treatment outcome varies. Although the majority of pseudocysts can be treated successfully by endoscopic transmural drainage, WON may require multiple treatment sessions that include endoscopic necrosectomy or adjuvant interventions such as percutaneous drainage or VARD.¹¹ The most common initial imaging modality for evaluation of pancreatic fluid collection (PFC) is a contrast-enhanced computed tomography (CT)



Fluid collection	Pancreatitis	Duration in weeks	Wall Maturity	Necrosis	CT
Acute necrotic collection	Necrotizing	<4	Absent	Minimal	
Walled-off necrosis	Necrotizing	>4	Present	Significant	

Fig. 1. Necrotic fluid collections. CT, computed tomogram; CT of acute necrotic collection reveals ill-defined fluid in the setting of parenchymal necrosis (*top image*); CT of WON reveals clear demarcation of the necrotic fluid collection that is conducive for drainage (*bottom image*).

scan of the abdomen, because it is readily available, relatively inexpensive, and can determine presence and extent of necrosis. MRI may be more sensitive for characterizing the contents (solid vs liquid) in a PFC and in determining pancreatic ductal integrity.^{12,13}

Timing of Intervention

Drainage is indicated only for patients who are symptomatic, collections that compress vital structures, or have systemic illness that does not improve with medical management.¹⁴ If patients meet the criteria for drainage, the next question is timing of intervention. Within the first 4 weeks after an acute attack of pancreatitis, the wall of the necrotic fluid collection is immature and so treatment should be temporized if possible,^{15,16} with analgesics, enteral nutrition, and antibiotics. The most common reason for failure of conservative measures is infection, which can be managed by interventional radiology-guided placement of a percutaneous drainage catheter. Beyond the 3- to 4-week period, most collections develop a capsule and are prime for endoscopic drainage provided they are adherent or adjacent to the wall of the stomach or duodenum. In a recent randomized trial that compared immediate versus postponed drainage, no difference in complications was observed between treatment groups and patients with postponed drainage required fewer invasive interventions.¹⁷

IMPORTANT CONSIDERATIONS

Before embarking on a therapeutic intervention, the clinical history, and radiological and laboratory findings should be reviewed. The international normalized ratio and platelet counts should be corrected if abnormal to <1.5 and at least $>50,000/\text{mm}^3$, respectively. Prophylactic broad-spectrum antibiotics are administered to minimize the risk of infection and are to be continued after the procedure¹⁸; the choice of antibiotics and their duration is based on culture and sensitivity results or per infectious diseases recommendations. In cross-sectional imaging studies, evaluating the relationship of WON to the gastrointestinal lumen, presence of collateral vasculature, assessing from where in the pancreas the necrotic collection originates, and its extent, are all important to determine the type and site of potential intervention. Also, cystic pancreatic neoplasms, duplication cysts, and solid necrotic tumors can mimic a PFC on cross-sectional imaging, and therefore, need to be excluded.^{19,20}

Choice of Intervention

Minimally Invasive Surgery: Treatment approaches include laparoscopic cystogastrostomy with transabdominal necrosectomy or VARD. In a recent randomized trial of 66 patients, an endoscopic transluminal approach for infected necrotizing pancreatitis, compared with minimally invasive surgery, significantly reduced major complications, lowered costs, and increased quality of life.²¹ A recent meta-analysis evaluated three randomized trials involving 184 patients who underwent endoscopic or minimally invasive surgery-based interventions in patients with infective necrotizing pancreatitis.²² Although there was no significant difference in mortality, new-onset multiple organ failure, enterocutaneous fistula/perforation, and pancreatic fistula were significantly lower for endoscopic interventions as compared to surgery. There was no significant difference in intraabdominal bleeding, and endocrine or exocrine pancreatic insufficiency between cohorts. The length of hospital stay was significantly shorter for endoscopic approach as compared to surgery. Therefore, when the requisite expertise is available, endoscopic intervention should be undertaken as the first-line therapy in the management of WON.

Percutaneous drainage: Percutaneous drain placement under radiological guidance is being increasingly practiced as initial treatment in the step-up surgical approach or as an adjunctive measure when the collections are not amenable to endoscopic drainage. An advantage of this approach is that necrosectomy can be obviated in up to 50% of patients following drain placement,²³ and in those requiring further interventions, the percutaneous tract can be utilized as a conduit for performing sinus tract necrosectomy or VARD. Adverse events associated with percutaneous drainage range from 22% to 50% and include bleeding, intestinal perforation, and pancreaticocutaneous or pancreaticocenteric fistula formation (Fig. 2A, B).^{23–25} More recent data comparing endoscopic and percutaneous treatment approaches for PFC drainage have observed the percutaneous approach to be an independent risk factor for mortality.²⁶ Therefore, to expedite drainage of infected contents, we recommend the insertion of a large-bore percutaneous drain (16 Fr) as it can be used in conjunction with endoscopic internal transmural drainage as part of a “dual-modality” (endoscopic + percutaneous) approach to achieving optimal outcomes.²⁷

Endoscopic interventions: Before performing an intervention, a thorough EUS examination should be undertaken as EUS has been shown to alter the management in up to 37.5% of patients referred for endoscopic drainage.²⁸ First, the suitability for endoscopic drainage as determined by the presence of a mature wall around the WON that is adherent to the gastric or duodenal wall can be confirmed on EUS, especially if less than 3 to 4 weeks have passed since the inciting event. Second, the presence of malignancy can be excluded as the etiology of the WON on EUS, which has been shown to occur in 1.25% of patients referred for endoscopic drainage.²⁰ Finally, other types of cysts, such as duplication cysts and mucinous cysts, can mimic a WON and can be excluded.¹⁹

There are two methods currently being adopted for performing EUS-guided drainage: multi-step technique using plastic stents and single-step technique using lumen-apposing metal stents (LAMS). However, before undertaking an intervention, it is important to perform a checklist to ensure successful technical and treatment outcomes (Box 1).

Plastic stents—Under EUS guidance, a 19-gauge fine needle aspiration (FNA) device is used to puncture the necrotic cavity. Suction is applied to sample the fluid to rule out infection (cultures, Gram stain) and for confirmation of diagnosis (tumor markers, cytology, biochemistry). A 0.025 inch or 0.035 inch guidewire is passed through the needle and coiled within the cavity. Transmural tract enlargement is performed with

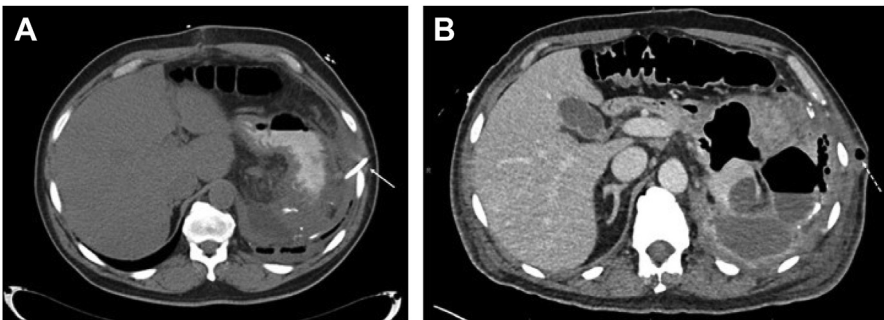


Fig. 2. Computed tomogram of the abdomen showing a percutaneous drain (solid arrow) into a WON (A). A pancreaticocutaneous fistula (dotted arrow) was observed (subcutaneous air bubble) on follow-up imaging (B).

Box 1**Procedural checklist**

- History and clinical examination, with review of vital signs and laboratory investigations to determine appropriateness of indication.
- Review of the cross-sectional imaging to assess for presence of solid debris, confirmation of mature wall, exclusion of cyst neoplasm or intervening vasculature.
- Optimization of coagulation parameters (INR \leq 1.5, platelet count $>$ 50,000/mm³).
- Assess nutritional status to determine need for enteral feeding
- Administration of broad-spectrum intravenous antibiotics prior to instrumentation. Intravenous ciprofloxacin or piperacillin/tazobactam are the preferred antibiotics and should be continued for 3-5 days post-drainage.
- Multidisciplinary care in consultation with pancreatic surgeons and interventional radiologists.

a graded dilation catheter or with the aid of electrocautery until it is large enough for passage of a dilating balloon (6–20 mm). WON drainage can usually be accomplished by the placement of two or more 7 F or 10 F double-pigtail plastic stents, 3 to 5 cm in length. In patients with WON that are non-communicating or very large in size ($>$ 10 cm), it is important to consider augmenting drainage adopting the multi-gate technique.⁶

LAMS: There has been growing interest in placing LAMS for WON drainage as the technique is much simpler than the placement of multiple plastic stents (Fig. 3A, B). LAMS are fully covered with a wide lumen (8–20 mm diameter) to expedite the drainage of necrotic contents and possess bilateral flanges at both ends to minimize the risk of stent migration. LAMS can be equipped with or without an electrocautery-enhanced delivery system. When using the non-electrocautery-based system, the WON is punctured under endosonographic guidance using a 19G FNA needle, followed by the insertion of a guidewire through the needle, which is looped inside the cavity. The transmural tract is then sequentially dilated using graded catheters or a cystotome, followed by a 4 to 6 mm dilating balloon. LAMS on a delivery system are then inserted over the guidewire into the necrotic cavity. The distal flange is deployed first under endosonographic guidance, followed by deployment of the proximal flange under either endosonographic or endoscopic view. When using the cautery-enhanced delivery system, the necrotic cavity is directly punctured using the electrocautery-enhanced tip of the stent delivery system under endosonographic guidance, without the need for a guidewire or pre-deployment dilation (Fig. 4A, B).

Outcomes of drainage: Although the majority of studies pertaining to LAMS for drainage of PFCs are retrospective, registry-based, case-control, or single-arm prospective series, three recent randomized trials comparing LAMS to plastic stents have yielded new information on treatment outcomes.^{29–31} Although the procedural duration for LAMS placement is significantly shorter than for plastic stents, there was no significant difference in rates of technical or treatment success, adverse events, need for necrosectomy, hospital length of stay, or reinterventions between groups. However, the short procedural duration is clinically relevant, particularly when treating sicker patients who cannot withstand prolonged procedures. Another unique advantage pertaining to LAMS is the attribute of a wide lumen which facilitates easy access to the necrotic cavity to perform debridement. As initial reports suggested high rates of post-procedure bleeding (due to pseudoaneurysm) after LAMS

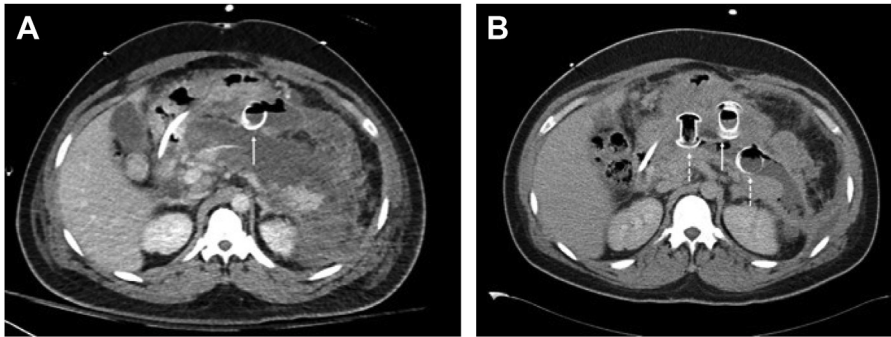


Fig. 3. Multi-gate technique using LAMS for a large WON collection. Despite successful drainage of a first collection using a single LAMS (A, solid arrow), the patient was persistently symptomatic. Two additional LAMS were subsequently placed to achieve optimal outcome (B, dotted arrows showing subsequent LAMS placed after index intervention; solid arrow showing LAMS from index procedure).

placement,³²⁻³⁴ the consensus is that the endoprosthesis be removed within a 3- to 4-week time frame. Given the complexity of clinical presentation, varying extent and severity of disease, and frequent occurrence of pancreatic duct disconnection, we propose a comprehensive management protocol that yields a 6-month treatment success of greater than 95% (Fig. 5).²⁷

Endoscopic necrosectomy: Nearly one-third of patients with WON respond well to transmural drainage alone and do not require direct endoscopic necrosectomy (DEN).^{21,35} DEN is indicated when the WON cavity is filled with solid or infective debris and treatment response to transluminal stenting is suboptimal.^{36,37} DEN is a labor-intensive and resource-consuming procedure involving non-standardized techniques. Consequently, the number of sessions required to achieve radiological resolution of WON ranges from 2 to 7, with a procedural morbidity of 14% to 25% and mortality of 5.6% to 7.5%.^{8,22} Different aspects of the DEN procedure have been addressed with greater detail elsewhere in this issue. In this article, we have presented just a few salient aspects.

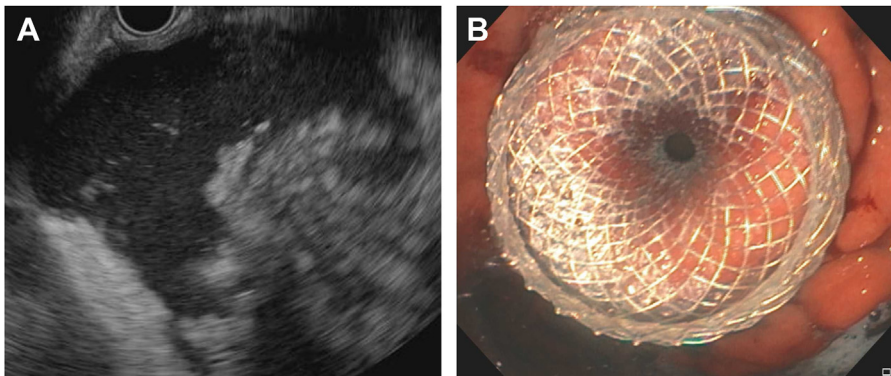


Fig. 4. (A, B). EUS image of a WON as demonstrated by an anechoic fluid collection with debris (3A), treated by deployment of a lumen-apposing metal stent as seen on endoscopic view (3B).

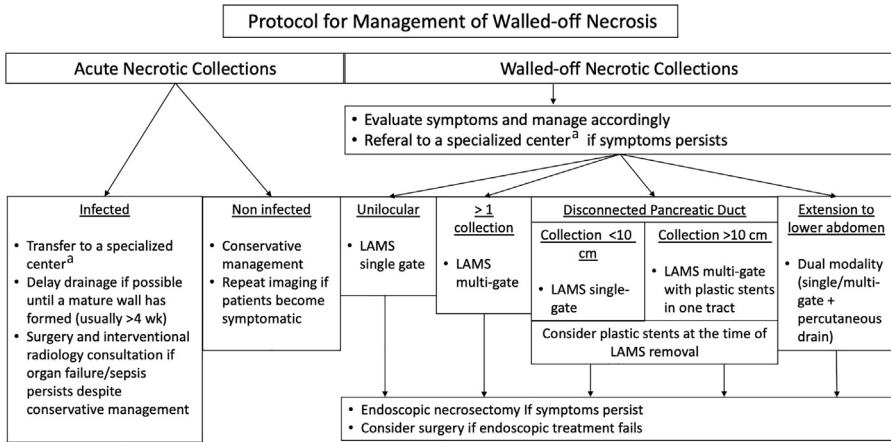


Fig. 5. Protocol-based management of WON. ^aA specialized center should have an experienced multidisciplinary team including therapeutic endoscopists, pancreaticobiliary surgeons, critical care specialists and interventional radiologists.

Technique: There are three critical steps to performing an efficient necrosectomy.³⁸

Debridement (step 1): If the necrotic debris is non-adherent, 15 to 30 mm oval snares may be used. If the necrotic debris is adherent to the WON cavity, removal can be accomplished using 15 to 25 mm round, braided-wire snares. Only the cold snare technique is adopted for debridement unless the necrotic debris is adherent to the cavity. In such instances, electrocautery-assisted debridement may be performed. After placing the polypectomy snare around the base of the necrotic debris, it may be closed tightly and then lifted gently to ensure the absence of entangled vasculature. Electrocautery is administered and the necrotic material is peeled away from the walls of the necrotic cavity. In patients with extensive collateral vasculature, to minimize the risk of snaring a vessel, debridement is performed using wide-jaw, rat tooth forceps. Intra-procedural bleeding when encountered can be managed using the hemostatic forceps.

Extraction of debris (step 2): After necrosectomy, liquefied debris is suctioned using the gastroscope. Solid debris is extracted by suctioning necrotic chunks into the cap with the aid of wide-jaw, rat tooth forceps or polypectomy snares.

Irrigation (step 3): Normal saline can be used intermittently during the procedure for irrigation of the necrotic cavity. About 100 to 200 mL of half-strength hydrogen peroxide mixed in equal volume of normal saline is used to ‘top-off’ the irrigation step at the completion of each necrosectomy session with the intent of sterilizing the WON cavity. Hydrogen peroxide should be used only toward the end of the procedure because the emanating effervescence precludes adequate visualization of the necrotic cavity. A recent retrospective study demonstrated higher rates of treatment success with a shorter time to disease resolution when hydrogen peroxide was used for performing DEN.³⁹

Special Considerations

Disconnected pancreatic duct syndrome (DPDS): DPDS is defined as the complete disruption of the main pancreatic duct with resultant disconnection of the viable upstream distal pancreatic gland from the main pancreatic duct downstream. Consequently, a symptomatic fluid collection can evolve in the disconnected gland. DPDS occurs in nearly 70% of patients with necrotizing pancreatitis.⁴⁰ In a randomized

controlled trial of 46 patients who had successful transmural drainage, stent retrieval was associated with higher rates of PFC recurrence as compared to indwelling stents (38.4% vs 0%).⁴¹ We, therefore, recommend indwelling plastic stents to minimize the chances of PFC recurrence in patients with DPDS.

Discussion of DPDS with greater details is available in an article dedicated to this entity in this issue.

Post-Procedure Care

Although a low-fat diet may be suitable for patients with minimal residual pancreatitis-related symptoms, enteral nutrition should be initiated for patients with ongoing pancreatic inflammation, particularly for those with persistent anorexia or abdominal pain.⁴² There are no evidence-based recommendations for inpatient follow-up or indications for procedural reinterventions. In general, reinterventions are undertaken in patients with ongoing sepsis or systemic inflammatory response syndrome and when there is a suboptimal resolution of the WON on follow-up imaging. Following discharge, cross-sectional imaging study of the abdomen must be obtained at 6 to 8 weeks in patients treated with plastic stents or at 3 to 4 weeks in patients treated with LAMS to evaluate treatment response. If the collection measures less than 2 or 3 cm, and the main pancreatic duct is intact, the transmural stents may be removed. In patients with DPDS, indwelling transmural plastic stents have been shown to decrease the rates of PFC recurrence.⁴¹

SUMMARY

Endoscopic interventions are highly effective for the management of WON. However, outcomes are reliant on correct patient selection, risk stratification, practicing evidence-based procedural techniques, and more importantly pursuing a multidisciplinary treatment approach. Clinical studies to optimize post-procedure care and inpatient follow-up are required to shorten hospital length of stay and minimize resource utilization.

CLINICS CARE POINTS

- Before embarking on an intervention, a thorough EUS examination should be undertaken to exclude occult pancreatic tumor as a cause of acute pancreatitis.
- A protocol-based treatment strategy is important taking into consideration presence of a disconnected duct, the extent and number of fluid collections, as each of these factors determines the overall treatment outcome.
- Multidisciplinary care is an important requisite when caring for patients with necrotizing pancreatitis.

DISCLOSURES

P. Willems: None. S. Varadarajulu: Consultant for Boston Scientific, Medtronic, Fujifilm, Olympus.

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