

Endoscopic Ultrasonography-guided Drainage of Pancreatic Collections, Including the Role of Necrosectomy



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KEYWORDS

- Acute pancreatitis • Pancreatic necrosis/therapy • Endoscopic therapy
- Minimally invasive • Pancreatitis/adverse events • Drainage/methods
- Therapeutic irrigation

KEY POINTS

- Pancreatic ductal injury often leads to development of pancreatic fluid collections with or without solid necrotic debris.
- Endoscopic intervention is considered the current standard of care for management of symptomatic pancreatic fluid collections.
- Cross-sectional imaging is paramount before any endoscopic intervention to determine the cavity size, location of potential access sites, and relevant adjacent anatomic structures.
- Direct endoscopic necrosectomy can be performed using various techniques but remains a time-intensive procedure.
- The most common adverse events associated with endoscopic management of pancreatic collections are bleeding and perforation.

INTRODUCTION

Injury to the pancreas may occur as a result of varying insults; however, regardless of the cause, resultant parenchymal inflammation occurs, often leading to disruption of the main pancreatic duct and/or secondary branches. Following ductal

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injury, leakage of pancreatic contents promotes formation of fluid-filled pancreatic or peripancreatic collections with or without the presence of solid debris. A minority of patients (approximately 5%–10%) develop evidence of glandular necrosis, often in combination with necrosis of adjacent structures.¹ Clinically severe acute pancreatitis evolves over several weeks, culminating in walled-off necrosis (WON) in many cases (Fig. 1).^{1,2} The aim of endoscopic therapy in this setting is to provide drainage of liquid contents and mechanical removal of necrotic tissue, if necessary. Endoscopic intervention remains the current standard of care for patients with WON following acute pancreatitis. Minimally invasive approaches, including flexible endoscopic and percutaneous therapy, either alone or in combination, are commonly used by most major medical centers.³ This article focuses on the indications, techniques, and outcomes of endoscopic therapy and management of pancreatic fluid collections (PFCs).

Indications and Timing of Intervention

Cross-sectional imaging should be performed before initiation of endoscopic intervention to assess the properties of the collection (ie, size, shape, wall thickness, contents), discern adjacent relevant vascularity, and ascertain the relationship between the cavity and true gastrointestinal lumen. Thorough review of cross-sectional imaging is crucial. The computed tomography (CT) and MRI appearance of PFCs can vary widely. Compared with CT, MRI reliably delineates liquid and solid components. On CT, nondependent air seen within a cavity indicates the presence of solid debris but does not represent infection with gas-forming microorganisms, as is often cited. Most commonly, such nondependent air enters through a fistulous connection from the gastrointestinal lumen. As described later, this fistulous tract can be used for transmural entry into the cavity, either for egress of liquefied contents or to enable endoscopic debridement. Coronal CT/MRI images can be useful, often complementing the standard axial images (see Fig. 1). Although liquefactive necrosis is generally evident, pancreatic necrosis can appear as nonenhancement of the pancreatic parenchyma and surrounding structures or may be more indistinct, resembling a pseudocyst. This uncertainty often compels therapeutic endoscopists to pursue standard

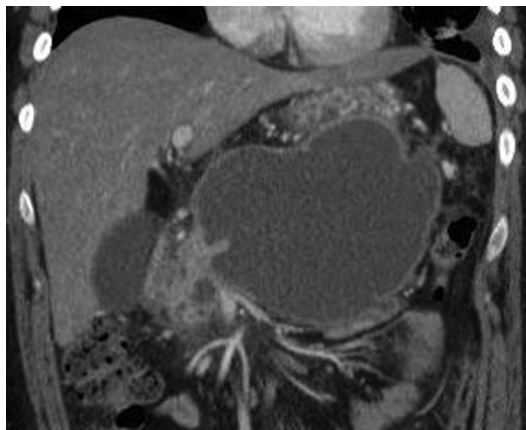


Fig. 1. Coronal computed tomography image of WON. The collection is compressing the stomach, and the patient had clinical gastric outlet obstruction.

pseudocyst drainage methods, which are insufficient at freeing adherent necrotic tissue, and may potentiate serious infection. Understanding the burden of necrosis, the presence or absence of extension into the paracolic gutters, and interactions between multiple cavities, if present, guides the index procedure and streamlines subsequent interventions.

When WON is readily apparent on cross-sectional imaging, consideration can be given to determining the bacteriologic status of the collection, because overt signs/symptoms of infection (eg, leukocytosis, fever) may not be evident. Endoscopic ultrasonography (EUS)-guided drainage or percutaneous fine-needle aspiration (FNA) to sample the contents of the collection are available but are infrequently performed in clinical practice because the decision to intervene is most commonly based on clinical criteria. In addition, EUS-FNA is not sterile and can cause infection of sterile necrosis. When objective findings of infected necrosis are present, urgent intervention is mandatory using either endoscopic (ie, drainage with or without necrosectomy) or percutaneous techniques.

The indications and timing for drainage of sterile fluid or pancreatic necrosis remain controversial. Commonly, peripancreatic collections remain immature and not amenable to endoscopic drainage until at least 4 weeks after the onset of pancreatitis. This interval allows organization of the internal contents of the collection and development of an external rind. Overall, endoscopic intervention should be deferred for as long as possible in patients who remain clinical stable. Common indications for drainage of sterile contents include (1) evidence of gastric outlet obstruction (clinical or radiologic), (2) evidence of biliary obstruction, (3) persistent abdominal discomfort, or (4) failure to thrive (fatigue, anorexia, weight loss). The radiologic appearance (ie, size, shape, location) of a necrotic collection on cross-sectional imaging may be incongruent with the patient's clinical status, and is an insufficient indication for intervention by itself. Historically, a size cutoff of greater than 6 cm was considered an indication for intervention; however, many patients with collections larger than 6 cm may remain asymptomatic with low risk for rupture, bleeding, or infection.

EUS can be used as an adjunct to cross-sectional image before intervention. EUS allows assessment of the presence or absence of significant solid debris that may alter the management strategy. In addition, if there is doubt as to whether the collection represents a true pseudocyst/WON or other noninflammatory cystic lesion, EUS can provide a definitive diagnosis using ultrasonographic features. EUS findings of WON manifest as hyperechoic areas within the collection, which can appear as free-floating debris (Fig. 2) or areas of adherent solid material. This solid material can range from a small percentage to nearly the entire collection with a minimal liquid component. If the diagnosis remains in question, aspiration and analysis of cystic contents, biopsy of the cavity wall, and even probe-based confocal endomicroscopy passed through an FNA needle can also be performed. After verification that the lesion is a PFC, and it is decided to proceed with endoscopic drainage, EUS can guide transmural drainage, as discussed later.

Procedural Technique

Before any intervention, the International Normalized Ratio and platelet count should be assessed and corrected, if necessary. Broad-spectrum antibiotics should be initiated if patients are not already receiving them. Recommended broad-spectrum agents include intravenous penicillins (ie, piperacillin/tazobactam), quinolones (ie, levofloxacin), and carbapenems (ie, meropenem). Antibiotic treatment should

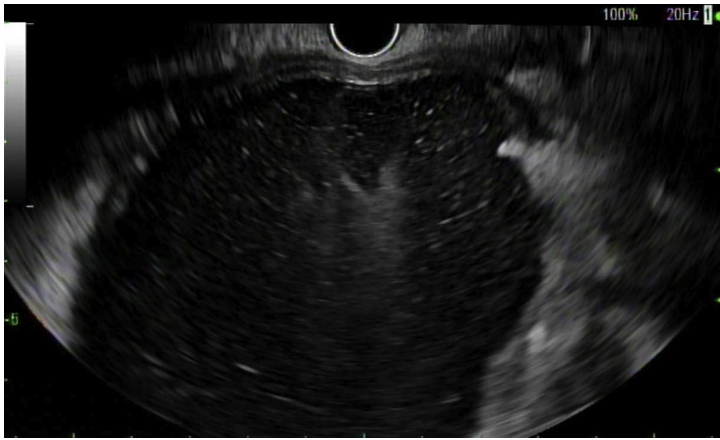


Fig. 2. Echoendoscopic view of WON from patient shown in [Fig. 1](#). Note the presence of scattered debris within the cavity.

subsequently be modified when microbiologic data from intra-procedural cultures are obtained. In general, the authors perform all procedures, pseudocyst drainage, and direct endoscopic necrosectomy (DEN), with anesthesia support given high patient acuity, potential length of the procedure, and increased risk for adverse events compared with other endoscopic procedures.

Endoscopic management of PFCs is predicated on evacuation of liquid and/or solid debris from the cavity. An initial transmural puncture, either transgastric or transduodenal, facilitates access to the collection and drains liquid contents. Collections located within or adjacent to the pancreatic body or tail are drained transgastrically, whereas transduodenal access is best for collections located near the pancreatic head and genu. For PFCs composed predominately of liquefied material, transpapillary drainage may be a viable option either alone or in conjunction with transmural drainage.

Several methods to obtain transmural access have been described. When extrinsic compression leads to endoscopically evident luminal protrusion, non-EUS-guided punctures aided by fluoroscopic guidance can be successfully performed (>95%) with low adverse event rates (<5%) when performed by experienced endoscopists.⁴ However, most endoscopists concur that EUS-guided access is superior and should be used whenever available. EUS guidance allows precision targeting of the cavity while mitigating the risk of inadvertent injury to adjacent vasculature or intraabdominal structures. In addition, EUS permits real-time assessment of the extent, volume, and density of material within the collection.⁵ Transmural access can be gained using a variety of endoscopic devices, including electrocautery-based instruments such as needle knives and specialized cystenterostomy devices (Cystotome, Cook Endoscopy, Winston-Salem, NC), and noncautery tools such as EUS-FNA needles. A recently introduced, lumen-apposing metal stent equipped with an electrocautery-enhanced delivery system (described later) has simplified the management of PFCs. On entrance into the cavity there is often visible extravasation of liquefied contents into the lumen. Aspiration of cyst fluid through an FNA needle, and/or the injection of radiopaque contrast in the cavity under fluoroscopy, can also be used to confirm access.

Following drainage of liquefied contents, FNA or other aspiration needles are advantageous because they permit guidewire passage through the needle core into the cavity (ie, Seldinger technique). A specialized 19-gauge FNA needle (EchoTip Ultra

HD ultrasonography access needle, Cook Endoscopy) designed specifically for EUS-guided drainage procedures may be helpful. A generous length of guidewire is then passed into the collection before tract dilation using a biliary dilating balloon. If the guidewire is lost inadvertently, easily reaccessing the cavity may be problematic, despite prior tract dilation. Blind attempts at passage of the guidewire into the cavity may increase the risk for adverse events. Some endoscopists elect to place 1 (or more) double-pigtail plastic stents during the index procedure with a plan for necrosectomy during subsequent procedures, if necessary. For drainage of purely liquid collections (pancreatic pseudocysts), the authors balloon dilate the tract to 8 to 10 mm followed by placement of 2 10-Fr double-pigtail stents (length of 3–5 cm) to mitigate concerns for stent migration into or out of the cavity. Double-pigtail stents also prevent trauma from impaction into the lumen or cavity wall. The authors recommend placing an endoscopically visible, indelible mark at the midpoint of the stent before placement, if markers are not present on the stent. This technique guards against inadvertent deployment of the entire plastic stent within the collection. Small-bore (10 mm), fully covered, biliary self-expandable metal stents (SEMS) can also be placed for management of collections that are predominately liquid. An SEMS with a diameter of 10 mm only requires a 4-mm balloon dilation (to allow passage of the delivery system). An alternative option to plastic stents or smaller bore SEMS is placement of a large-caliber (16–23mm midbody diameter) SEMS across the dilated lumen wall.^{6–10} Use of large-diameter, covered esophageal SEMS facilitates DEN procedures, at the index procedure and/or in subsequent procedures, and circumvents balloon dilation of the tract before each debridement.⁷ The shortest available SEMS lengths are 6 to 7 cm, often resulting in excess stent length protruding into gastrointestinal lumen or the necrotic cavity, and possibly leading to impaction as the cavity collapses. Stents can be trimmed using argon plasma coagulation, although minimal disruption of the SEMS interstices is paramount. A double-pigtail plastic stent can also be placed within the deployed SEMS to serve as a buffer between the stent flange and the lumen/cavity wall, and to inhibit necrotic debris from occluding the SEMS.

The recent development of lumen-apposing stents (LAMS) (AXIOS; Boston Scientific, Marlborough, MA) provides solutions to many of the limitations of previous drainage techniques (Figs. 3 and 4). These stents are currently available with midbody



Fig. 3. Echoendoscopic view after deployment of LAMS from same patient. Note a large piece of dense solid debris (hyperechoic) within the cavity.

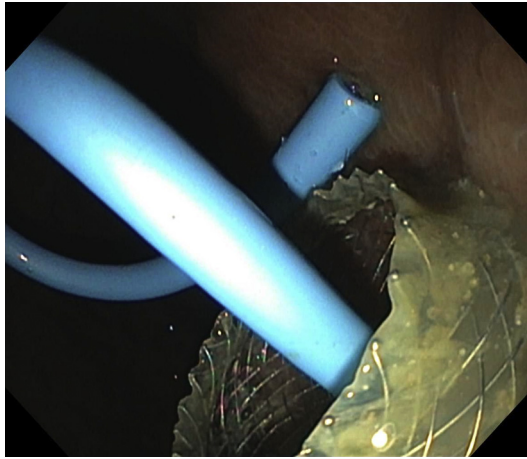


Fig. 4. Endoscopic view of deployed LAMS with 15-mm diameter from same patient as seen from the stomach. An indwelling 10-Fr plastic double-pigtail stent is seen within the LAMS.

luminal diameters of 10 and 15 mm and corresponding external flange diameters of 21 and 24 mm, respectively, with total stent length between the flanges of 1 cm. The short length of these LAMS is ideal for DEN. In addition, the 15-mm version affords apposition of the gastric wall and cavity wall while allowing repeated endoscope passage during debridement procedures.^{11,12} A 20-mm iteration of the device is US Food and Drug Administration approved and expected to be commercially available soon. There are 2 types of AXIOS stent delivery systems. The initial iteration requires a placement approach similar to plastic stent or standard SEMS placement (ie, 1-puncture, 2-guidewire placement; 3-tract dilation, 4-stent deployment), whereas the newer version includes an electrocautery-enhanced tip allowing for puncture and tract dilation in 1 step, followed by stent deployment, with or without the use of a guidewire. Many endoscopists place 1 double-pigtail plastic stent within the LAMS (see Fig. 4) to maintain stent patency, prevent stent impaction, facilitate removal if a buried stent occurs, and leave room for plastic pigtail stents to treat disconnected ducts as the cavity resolves.

Various techniques can be used for removal of solid debris from necrotic collections. A 7-Fr nasocystic irrigation tube can be placed into the cavity, adjacent to transmural stents, to permit intermittent irrigation with escape of disrupted necrosis through 1 or more transmural exit sites.^{13,14} Up to 200 mL of normal saline (with or without 3% hydrogen peroxide) is vigorously infused through the tube every 2 to 4 hours initially to lavage debris from the cavity. Nasocystic irrigation tubes are rarely used in current clinical practice, mostly because of patient intolerance.¹⁵ Dual-modality therapy is a variation of the nasocystic drainage technique that uses the combination of endoscopic and percutaneous therapy, in lieu of a transnasal tube.¹⁶ This technique combines percutaneous drain placement, used as the irrigation conduit, and endoscopic transmural drainage, for egress of debrided necrotic tissue. As mentioned earlier, spontaneous fistulous tracts can provide egress for liquefied debris and allow access for debridement of necrosis, in select cases.¹⁷ If possible, the tract should be balloon dilated to a diameter greater than or equal to 15 mm to allow egress of the remaining liquid and facilitate DEN.

The objective of each DEN procedure should be to remove all possible necrosis. DEN is a labor-intensive intervention that is performed by passing an endoscope

transmurally into the collection. Both diagnostic and therapeutic endoscopes can be used, each with intrinsic benefits and limitations. Diagnostic endoscopes have better flexibility but a smaller working channel compared with therapeutic endoscopes. Depending on the manufacturer, each can offer a high-flow water jet that is used to fragment and irrigate necrotic debris. As previously alluded to, the use of hydrogen peroxide lavage may aid in liquefying necrotic tissue during DEN, although evidence from comparative trials is lacking.¹⁸ Mechanical debridement can be accomplished with various endoscopic accessories (eg, stone retrieval baskets, polypectomy snares, polyp retrieval nets, grasping forceps). Regardless of the device, once the necrotic tissue is freed, it is extracted from the cavity and deposited in the lumen. Larger pieces may be cut into smaller pieces using a polypectomy snare with or without electrocautery, then cleared from the collection to avoid unnecessary transmural passage into and out of the cavity. The consistency of necrotic tissue is variable from one patient to another, ranging from solid debris that is densely adherent to tissue that is loosely attached and easy to remove. Some endoscopists opt to perform DEN immediately after the initial transmural puncture, whereas others advocate debridement starting with the subsequent procedure; however, no data exist to advocate one approach rather than the other.

Assuming clinical stability and absence of intraprocedural adverse events, patients may resume (or initiate) oral intake on the day of the procedure. The authors routinely continue peroral antibiotics for several weeks, often until the cavity completely resolves as determined by cross-sectional imaging. Repeat interventions are almost universally necessary for WON when plastic stents are used, compared with large-diameter SEMs, and include stent removal, followed by debridement, then stent replacement. Future procedures can be scheduled if incomplete debridement is recognized,¹⁹ or performed as determined by clinical status and/or cross-sectional imaging findings. The overall clinical picture, in conjunction with logistical issues (eg, inpatient/outpatient status, distance from treatment center) often determine the procedure frequency. Patients requiring ongoing hospitalization often require frequent procedures (every 1–2 days), whereas stable outpatients can generally tolerate 1 to 2 weeks between DEN. In patients with persistent collections despite several interventions, endoscopic retrograde cholangiopancreatography should be considered to assess for an ongoing pancreatic duct disruption. Adjunctive transpapillary stenting of the pancreatic duct can be considered; however, stenting only minimizes leakage of additional pancreatic fluid into the cavity, and is insufficient to use as a drainage route for pancreatic debris. As the cavity resolves, external drains should be removed before removal of internal drains. Internal drains are then endoscopically removed after complete resolution of the collection. This approach is intended to prevent formation of gastrocutaneous/enterocutaneous fistulae.

In our current practice the authors place large-diameter LAMS with an internal 10-Fr double-pigtail plastic stent. This approach is intended to prevent impaction of the necrotic material within the LAMS lumen and allows continued egress of liquid material. The double-pigtail stent also protects the gastric wall and cavity wall as the collection recedes and minimizes the risk of a buried LAMS. An additional advantage of LAMS is the short overall length (~1 cm) and lack of exposed edges that are involuted at full expansion. LAMS also promote a certain degree of procedural efficiency and safety because dilation of the tract is unnecessary before each session. The authors ask patients to discontinue any acid-suppressive medications to promote acid-induced debridement. We reserve DEN for patients who fail to improve or clinically deteriorate. Studies are being performed that suggest that the need for DEN following LAMS placement is based on percentage of necrosis within the WON cavity.

Outcomes

Outcome data following endoscopic intervention of pancreatic pseudocysts is challenging to interpret. For example, there is notable heterogeneity across patient populations and interventions within series. Frequently, studies have included patients receiving both transpapillary and/or transmural drainage. Overall, successful drainage of liquefied collections is achieved in ~90% of patients with acceptable adverse event (5%–10%) and recurrence (5%–20%) rates.^{20–22}

Many case series have shown the efficacy of DEN^{15,23–26} when plastic stents were used as the primary drainage strategy. Patients with WON have substantial variation in: (1) collection size/shape, (2) overall burden of necrosis, (3) extensions of necrosis into the paracolic gutters, (3) medical comorbidities, and (4) time from onset of necrotizing pancreatitis to intervention. Given this patient heterogeneity and varying definitions of success/failure, comparison of outcomes between reported series remains challenging. In available literature, the 2 most widely used definitions of successful outcomes are complete nonsurgical resolution (including percutaneous drainage) and resolution caused by flexible endoscopy alone.¹⁵

Data from 2 systematic reviews suggest that complete resolution of pancreatic necrosis can be obtained in 81% of patients using endoscopy alone with a mean number of 4 procedures necessary for resolution.^{27,28} The adverse event rates from these studies were 21% and 36%. Furthermore, 2 large retrospective studies have shown resolution in approximately 90% of patients with a lower rate of adverse events (~14%).^{15,24}

Limited outcome data in patients treated with transmural placement of esophageal SEMS or LAMS to facilitate DEN have begun to emerge. A recent retrospective study from 2 US medical centers found that resolution could be achieved in 88% of patients using an esophageal SEMS for transmural access.¹⁰ A mean of 5 DEN procedures were required for complete endoscopic resolution, with adverse events occurring in 6% of patients. A similar study from Attam and colleagues²⁹ revealed similar findings (90% resolution, median 3 procedures). Outcomes following LAMS placement for DEN have also been reported with high rates of success (technical >95%; clinical >80%) and acceptable risk of serious adverse events (<7%).^{30,31}

As described, both double-pigtail plastic stents and SEMS/LAMS can be used to establish and maintain tract patency in patients requiring repeated DEN. Clinical judgment should be used to determine the optimal strategy on a case-by-case basis, because both techniques have high clinical resolution rates (>80%).

ALTERNATIVE TREATMENT STRATEGIES

Patients with WON are best managed by a multidisciplinary approach in tertiary care medical centers. Alternative options to endoscopic intervention include (1) nutritional support with parenteral or enteral supplementation, (2) percutaneous drainage, and (3) surgical drainage. A multicenter, randomized controlled trial (Transluminal Endoscopic versus Surgical necrosectomy in patients with infected pancreatic Necrosis [TENSION] trial) designed to compare outcomes between a endoscopic step-up approach (transmural drainage plus or minus DEN) and a surgical step-up approach (percutaneous drainage plus or minus surgical necrosectomy) is ongoing.³²

Percutaneous DEN has previously been described. This technique requires placement of a large-caliber, fully covered SEMS (20–25 mm in diameter) or flexible overtube to perform debridement of WON.^{33,34} The SEMS remains in place between interventions with an overlying ostomy appliance to prevent soiling. The stent can then be removed when the cavity resolves. Video-assisted retroperitoneal debridement is a similar technique performed by gastrointestinal surgeons using rigid endoscopes

through percutaneous tracts to access and treat WON in areas inaccessible from the gastrointestinal lumen.³⁵ This method is most commonly used when treating necrosis that extends into the paracolic gutters. Paracolic gutter extensions can be challenging to manage, especially when the WON extends into the pelvis, and are often unresolved with endoscopic therapy alone.

STRATEGIES ASSOCIATED WITH ENDOSCOPIC INTERVENTION OF PANCREATIC COLLECTIONS

The authors recommend that surgical and interventional radiology support be available during DEN procedures. Life-threatening adverse events can occur when performing endoscopic intervention for WON, either intraprocedurally or postprocedurally. Recent data show a mortality of 6% for patients undergoing DEN.²⁸ The most serious adverse events of necrosectomy include perforation and bleeding.

Bleeding can occur at any time during the intervention (ie, transmural puncture, dilation, necrosectomy) but most frequently occurs at the puncture site. Supportive measures are generally adequate because bleeding is usually self-limited and resolves by the completion of the procedure. Endoscopic hemostasis, surgical intervention, or angiographic embolization may be required in rare instances. Minor recalcitrant bleeding during the procedure can be managed by endoscopic injection of dilute (1:10,000) epinephrine, balloon tamponade, endoscopic clips (either through the scope [TTS] or over the scope), or electrocautery. Severe bleeding occurring at the transmural entry site can be managed by placement of a large-diameter, fully covered esophageal SEMS.^{36,37} Intracavitary bleeding during debridement occurs but is typically self-limited.

Perforation may occur at the transmural access site or within the cavity wall, and can rarely result in tension pneumoperitoneum, a life-threatening emergency requiring needle decompression.³⁸ Perforations at the entry site occur because of separation of the lumen wall and the cavity wall. This condition can occur during creation of the tract or during DEN. Management options for this scenario include TTS endoclips or placement of a large-caliber SEMS,³⁷ similar to management of bleeding described earlier. Egress of gastric contents must be avoided/limited to minimize the risk of peritonitis. The gastric wall of the body and antrum is extremely forgiving and often closes rapidly without clinical consequence. Many patients can be managed with conservative measures (ie, nil per os status, nasogastric suction, antibiotics) alone. Management of transduodenal perforations is a subject of debate. Some endoscopists think that transduodenal perforation may also be managed conservatively, because the perforation occurs into the retroperitoneum. Large perforations through the cavity wall generate more concern, and often require surgical or percutaneous intervention.

Sufficient removal of fluid and solid debris is essential during DEN, because infectious adverse events can occur from inadequate drainage. As mentioned previously, patients should be maintained on antibiotics during the management of WON. Patients showing signs/symptoms of infection (ie, leukocytosis, fever/chills, culture positivity) should have their antibiotic coverage broadened. Patients may require concomitant placement of 1 or more percutaneous drainage catheters to achieve source control. This requirement most commonly occurs in patients with WON expanding into the paracolic gutters.¹³

Less common adverse events include air embolism and stent migration. Fatal air embolism has been described following DEN.³⁹ Because of this concern, nearly all medical centers managing WON have shifted from air to CO₂ for insufflation during

endoscopic intervention. Stent migration (double-pigtail plastic stents or SEMS) may occur during or after endoscopic placement. Stents can migrate into the collection or out of the collection, both with significant clinical implications. Endoscopic retrieval of migrated stents into the cavity is feasible, assuming that migration is identified promptly. Delayed recognition of migration either into the cavity or into the stomach may lead to premature closure of the transmural puncture site, requiring a new puncture to remove inwardly migrated SEMS.

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