Endoscopic Therapy of Necrotizing Pancreatitis and Pseudocysts

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KEYWORDS

• Therapeutic endoscopy • Pancreatitis • Pancreatic fluid collection
• Necrotizing pancreatitis • Walled off necrosis • Pancreatic pseudocyst
• Endoscopic ultrasound

KEY POINTS

- In the last several years, endoscopic management of pancreatic pseudocysts and walled-off necrosis has come to serve as an important primary interventional technique for therapeutic gastroenterologists.
- Although a primary means of treatment at many centers, it additionally serves as an adjunct to other minimally invasive interventional techniques, such as percutaneous drainage or laparoscopic necrosectomy and video-assisted retroperitoneal debridement.
- Endoscopic drainage and debridement are most clearly indicated in patients with well-encapsulated pancreatic or peripancreatic collections of fluid or necrotic debris with signs of infection and clinical deterioration, luminal or biliary obstruction, or severe pain.
- To ensure optimal patient outcomes, the use of periprocedural antibiotics, endoscopic ultrasonography guidance for localization of puncture site, multiple pigtail drains or enteral stents at the fistula site, serial direct endoscopic necrosectomy as needed, and serial imaging is recommended.
- The endoscopist should be prepared to repeat procedures as needed depending on the patient's clinical status and imaging results.
- Although more prospective comparative trials are needed to refine future practice guidelines, endoscopic management of pancreatic pseudocysts and walled-off necrosis is a safe and effective therapeutic option in the appropriate patient population.

INTRODUCTION

The endoscopic management of pancreatic fluid collections (PFC) and walled-off necrosis (WON) has become increasingly common and frequently within the capability of the therapeutic endoscopist.[1–6] New tools, such as linear-array endoscopic

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ultrasonography (EUS), retroperitoneal sinus tract endoscopy, and video-assisted retroperitoneal debridement (VARD), have revolutionized retroperitoneal access to treat PFCs and WON.[7–11] Based on mounting evidence, a recent international consensus of leading surgeons, interventional endoscopists, interventional endoscopists, and pancreatologists concluded that minimally invasive routes of necrosectomy, and especially endoscopic transluminal necrosectomy, is now the procedure of choice for the management of WON in most circumstances.[12]

Although therapeutic endoscopists have been performing these procedures for 2 decades, there are several issues that still need to be addressed before these procedures are widely adapted and accepted.[13] Although progress has been made with the more appropriate definitions for pancreatic collections per the recently published revised Atlanta Classification of acute pancreatitis, these definitions have yet to be adapted universally.[14] In addition, the timing and indications for intervention are not universally defined and agreed on. Furthermore, it is unclear if formal therapeutic endoscopic training is necessary to credential providers or whether these procedures should be offered by the general gastroenterologist or surgeon. Finally, although there have now been 2 prospective trials comparing single-modality endoscopic techniques (one retroperitoneal as an adjunct to VARD, and the other transluminal direct endoscopic necrosectomy) with surgical techniques, these have yet to be comprehensively evaluated outside the Dutch Pancreatitis Study Group.[8,9]

This article highlights the techniques used for endoscopic management of PFC and WON. It provides information regarding patient selection criteria, indications and timing of interventions, procedural technique, periprocedural management, and review of potential complications of endoscopic management. It is hoped that the reader will be left with both an understanding of the benefits of minimally invasive techniques and an appreciation and respect for the potential risk and complications inherent in these procedures.

PATIENT EVALUATION OVERVIEW

Patient Selection

It is essential to have standard definitions of WON and PFCs to select patients appropriately for this procedure. For example, it is no longer acceptable to use the term "pseudocyst" to describe the entire spectrum of PFC, which is a common practice among radiologists, surgeons, and gastroenterologists. PFC by definition occur when there is fluid leakage from the pancreas or liquefaction of pancreatic necrosis as a result of some type of pancreatic injury or damage. The new Atlanta Classification, listed as follows, provides characterization of PFCs in standardized fashion based on the presence or absence of necrosis and the time from injury.[14]

- Acute fluid collection: interstitial pancreatitis; less than 4 weeks since injury; no encapsulated wall
- Acute necrotic collection: necrotic pancreatitis; less than 4 weeks since injury; no encapsulated wall
- Pseudocyst: interstitial pancreatitis; greater than 4 weeks since injury; encapsulated wall; no solid debris. Usually extrapancreatic, but can occasionally be intrapancreatic as a result of "disconnected pancreatic duct, especially after surgical debridement"
- Walled-off necrosis: necrotic pancreatitis; greater than 4 weeks since injury; encapsulated wall; solid debris. Can be pancreatic and/or extrapancreatic, extending far into the pelvis or elsewhere in the abdomen.

When there is acute pancreatic injury and leakage from the pancreatic duct, that injury can be caused by either necrotic or interstitial disease. If interstitial, the resulting fluid collection is termed an acute fluid collection, which can be peripancreatic or pancreatic. If necrotic, this collection is termed an acute necrotic collection. Most acute fluid and acute necrotic collections will resolve spontaneously. However, if they do not resolve after 4 weeks, the acute fluid collection will be labeled a pseudocyst as long as there is no evidence of solid debris. The acute necrotic collection will be termed walled-off necrosis if the collection develops an encapsulated wall and contains solid debris. WON may involve the pancreas only (rarely), pancreas plus extrapancreatic tissues (most commonly), or extrapancreatic tissues alone (uncommonly). It is important therefore to recognize and define properly the collection so that the appropriate intervention can then be performed. **Fig. 1** demonstrates representative computed tomographic (CT) scan images of the 4 types of collections.

It should also be noted that it is critical to make sure that all fluid collections are inflammatory in nature. Patients with fluid collections thought secondary to inflammation should have an antecedent history of pancreatic injury. Unfortunately, patients are sometimes misdiagnosed with inflammatory collections when in fact they actually have premalignant or malignant cystic pancreatic lesions, such as mucinous cystic neoplasms, islet cell neoplasms with cystic degeneration, or intraductal papillary mucinous neoplasms.[15–18]

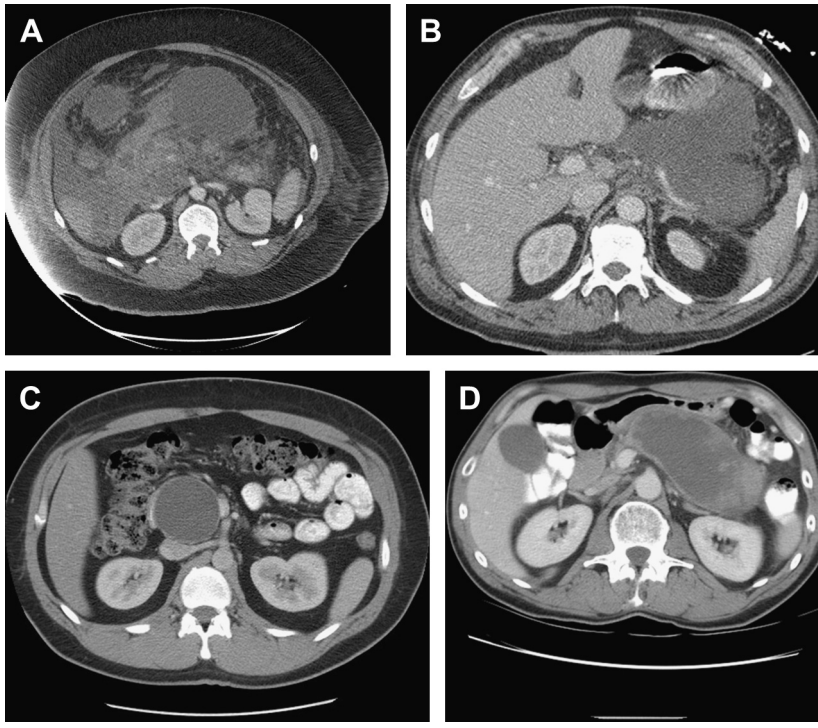

Fig. 1. Representative examples of postacute pancreatitis fluid collections as defined by the revised Atlanta classification. (*A*) Acute fluid collection. (*B*) Acute necrotic collection. (*C*) Pancreatic pseudocyst. (*D*) WON.

Therefore, in summary, patients on whom endoscopic therapy is being considered must have a PFC that arises from pancreatic duct injury and not a spontaneous premalignant or malignant lesion. The collection should have an encapsulated wall and therefore ideally should have resulted from an injury at least 4 weeks before the planned intervention, although that may not be feasible in some cases. As discussed later, the patient should also have an appropriate indication and an experienced provider performing the proposed procedure.

Indication and Timing of Intervention

There are usually several interventional methods for the management of pancreatic pseudocysts and WON that can be used effectively. Therefore, coordination among the surgeon, gastroenterologist, and interventional radiologist is critical to a positive outcome for the patient. It is imperative to choose the technique that is not only the most appropriate for that particular patient's clinical situation but also with which the treating institution has the most familiarity and past success.

In addition to classifying fluid collections and necrosis accurately, it is also critical to define the indication for and timing of endoscopic intervention.[19–21] Without exception, the most important urgent indication for treating a pseudocyst or WON is the presence, or suspected presence, of infection, especially those with systemic clinical deterioration despite maximal medical support. Although the case is sometimes made that infected pancreatic necrosis can be treated with antibiotics and supportive care alone, removal of infected tissue is still often required.[22] In addition, other indications, such as luminal or biliary obstruction from external compression, undiagnosed sepsis syndrome, persistent pain requiring narcotics, or recurrent acute pancreatitis, can also drive the need for drainage or debridement.[13] The algorithm in **Fig. 2** displays this treatment modality.

The goals of treatment might also determine which type of procedure is required and generally focus on the need to either *control* or *remove* the source of infection. For example, the need to control the source of infection, rather than complete removal, may be important in a hospitalized patient with a known sepsis syndrome in which the infected pancreatic necrosis is not well encapsulated. In this situation, it may be safer and more efficacious to debride the collection percutaneously. Conversely, in an ambulatory patient with a symptomatic gastric outlet obstruction from WON, the goal may be to remove this tissue completely and this can likely be accomplished with a single endoscopic modality. Not only will goals of care influence the type of intervention, they will also determine the timing and aggressiveness of treatment. Location of the collection—extension into the pelvis, for example—may also determine the type of therapy.

Time to treatment has been an important controversy in the evaluation of endoscopic efficacy.[12,22–24] Interventions within the first few weeks for necrotizing pancreatitis, especially single-modality endoscopic techniques, are generally associated with poor outcomes and should be reserved for infected necrosis in a severely ill patient with clinical deterioration. Poorly organized or liquefaction necrosis ismore difficult to manage by any method compared with necrosis containing a well-encapsulated rim. Therefore, the guiding principle for timing of debridement is to delay, if at all possible, any intervention until the collection has become encapsulated. Although encapsulation can occur in some patients as early as 1 week after the onset of acute pancreatitis, this is unusual, and typically encapsulation does not occur until at least 4 weeks after the initial injury.[23]

Ample literature supports the importance of timing.[12] In a retrospective series from the Mayo Clinic Rochester, 138 patients with pancreatic necrosis, acute pseudocysts,

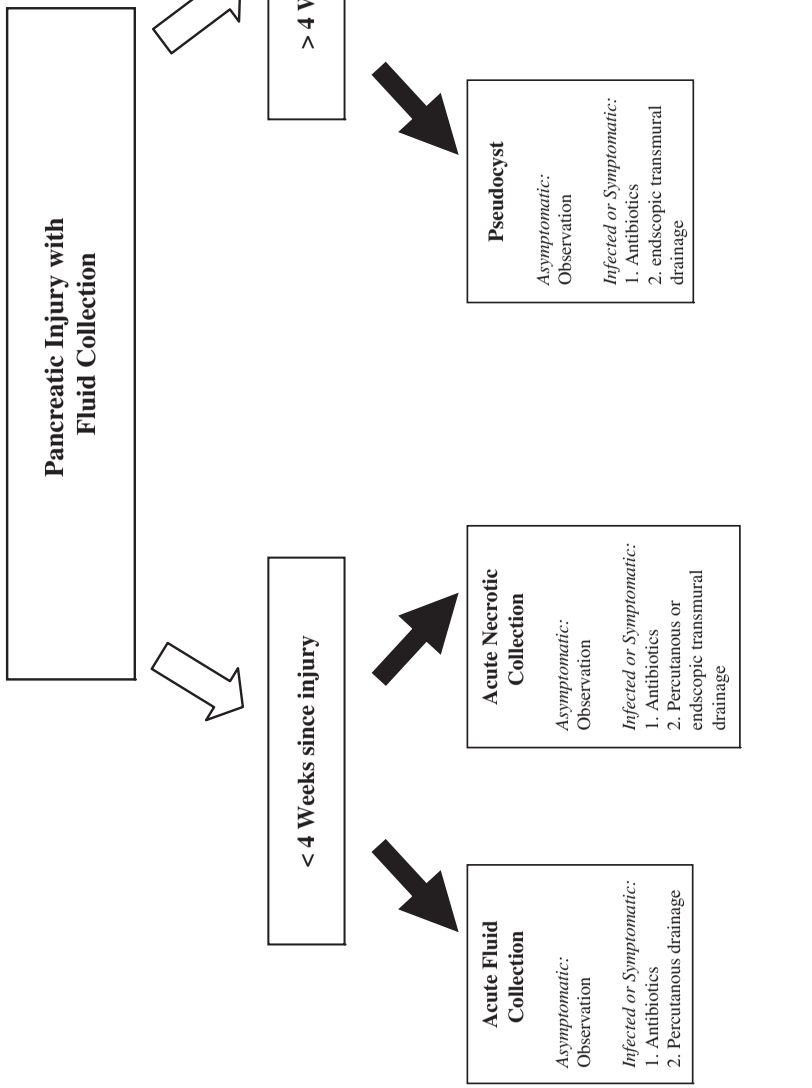

Fig. 2. Treatment modality as determined by type of pancreatic injury.

or chronic pseudocysts underwent endoscopic therapy. Resolution was significantly more frequent in patients with chronic pseudocysts (59/64, 92%) than acute pseudocysts (23/31, 74%, $P = .02$) or necrosis (31/43, 72%, $P = .006$). Waiting for encapsulation, or "walling off," therefore, is critical to the success of primary endoscopic therapy.[25,26]

As increasingly it is being reported that nonoperative management of infected pancreas necrosis is not only feasible, but also appropriate, it is critical to understand the nuances of indication and timing.[27–29] The single-modality endoscopic approach is best reserved for patients who have a well-encapsulated rim around the collection, which usually occurs several weeks after the initial insult. Although the degree of solid debris should not generally dictate the approach, having an appropriate site for fistula tract creation is critical to using endoscopic therapy (see **Fig. 2**).

The decision to proceed with a certain type of therapy should be guided by (1) the goals of therapy (ie, control of infection vs removal of the cavity), (2) the proper procedural indication, (3) preservation of organ function (pancreas and spleen), and (4) patient preference.

PROCEDURAL TECHNIQUE

Historical Context

Since the 1970s, the management of PFCs and WON has transitioned from a purely surgical technique, to percutaneous interventional techniques, to endoscopic therapy.[30–33] With each of these techniques, there have been permutations, including the development of VARD, which is a technique used to perform percutaneous debridement using a retroperitoneal approach in which both laparoscopes and endoscopes have been used.

PFC were initially drained using a transpapillary approach during endoscopic retrograde cholangiopancreatography (ERCP).[34] Although this was an important advance in the endoscopist's ability to manage PFC, the revolution in endoscopic drainage of PFCs really came with the development of EUS in the 1980s, allowing endoscopists the ability to define the collection precisely, as well as outline the associated structures, such as blood vessels, which needed to be avoided during intervention.[35,36] The breakthrough came with the advent of the linear EUS endoscope, which allowed drainage of PFCs via the gastrointestinal lumen. Multiple series subsequently established EUS-guided pseudocyst drainage as a firstline therapy.[37–40]

In 1996, Baron and colleagues reported the first experience with endoscopic management of WON in 11 patients by performing a standard cystgastrotomy with nasocystic tube irrigation.[15] Subsequent endoscopists reported their experiences with direct endoscopic necrosectomy, consisting of transmural endoscopic entry into the cavity and debridement with a variety of accessories. From those reports, multiple case series have been generated, but few comparative efficacy trials have been performed.

A major development has been the development of the "step-up approach" in which a minimally invasive technique is initially used for drainage of WON, which is definitive in about one-third of cases, with progression to minimally invasive necrosectomy (by endoscopic, sinus tract endoscopy, VARD, or open surgery) as needed.[41]

It is possible but not well studied that combining techniques may achieve better results than a single approach alone. For example, sinus tract endoscopy combined with direct endoscopic necrosectomy may be more beneficial than single strategies alone, especially for the management of extensive WON deep into the pelvis.[42–45]

Preparation

Before the endoscopic drainage of a PFC or WON, the following issues should be addressed by the treating endoscopist:

- Define whether the procedure is being performed for source control or removal of the collection. The goals of therapy will undoubtedly drive which intervention is selected.
- Make sure the timing of intervention is appropriate. For example, has the wall of the collection been allowed enough time to mature if endoscopic transmural drainage is being considered?
- Be clear that the patient does not have any obvious medical contraindications to the procedure—coagulopathy, for example.
- Be certain that the procedure is within the realm of the endoscopist's, and the facility's, realm of expertise. In addition, all assisting nurses and technicians should have experience with the procedure.
- Make sure the collection is an inflammatory collection and not a premalignant condition, such as a mucinous cystic neoplasm or intraductal papillary mucinous neoplasm.
- Clearly define the risks and benefits of the procedure with the patient and take time obtaining and documenting the patient's informed consent.
- Discuss with colleagues in surgery and interventional radiology the plans for the procedure and make sure appropriate backup is available.
- Be certain that an anesthesia team generally is managing the patients with appropriate airway protection because there is the potential for extensive reflux and subsequent aspiration of fluid following initial cavity puncture.
- Be certain to have availability of appropriate endoscopic expertise following the procedure (ie, planning to leave town in the period following the procedure is not advised in case there are complications that need to be managed).

Patient Positioning

Positioning of the patient should generally be determined based on the clinical scenario. In hemodynamically unstable patients, supine positioning is generally safer. In stable patients, prone positioning may allow for better gravitational drainage from posteriorly located collections and decrease the incidence of fluid reflux and aspiration. All patients should have general endotracheal intubation for airway protection.

Technique

Although the endoscopic technique for management is fairly standardized, there are several variations at each stage of the procedure. Presented are the standard means by which drainage is performed, with variations highlighted at each step where applicable (**Fig. 3**).

1. Initial endoscopy: Initial endoscopy is performed using a therapeutic, side-viewing video duodenoscope, gastroscope, or echoendoscope. Although not every provider uses EUS to puncture the cavity initially and create the fistula tract, there is evidence that EUS-guided drainage of PFCs is substantially more effective and less prone to complications than "conventional" techniques.[46,47]
2. Procedural considerations:
   a. Routine antibiotic use is recommended for those not already receiving broad-spectrum antibiotics for presumed or documented infection.

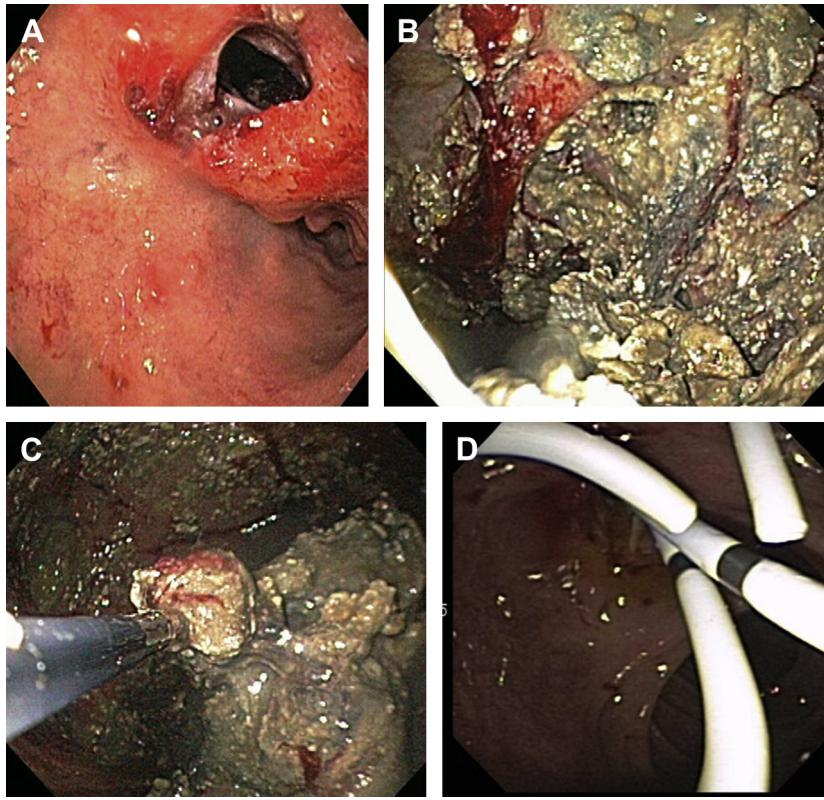

Fig. 3. Images demonstrating the technique for necrosectomy. (*A*) The fistula tract following creation of the cystenterostomy. (*B*) Inside the cavity demonstrating necrotic debris. (*C*) Debriding the cavity with a snare. (*D*) Stents in place into the cystenterostomy following debridement.

   b. If possible, CO_2 insufflation should be used to help minimize the risk of air embolism, a rare but potentially catastrophic complication.[13]
3. Assessment of the pancreatic duct: Integrity of the pancreatic duct can be assessed by CT, magnetic resonance cholangiopancreatography, EUS, or ERCP. Whether to perform direct pancreatography using ERCP at the time of initial drainage is subject to variable opinion, but does require a subsequent endoscopy for transpapillary stenting if the duct is later found to have a persistent leak. In general, though, in ill patients with infected necrosis, ERCP should generally be avoided at the initial intervention and postponed until after the infection is controlled. If evidence of a disconnected duct is found on ERCP, an attempt should be made to stent across the site of disruption (see below).
4. Identification of the fistula site: Localization of the most appropriate access site from within the gastric or duodenal lumen should be performed under EUS, because there is considerable agreement that, at least in PFCs, EUS allows for higher success rates and trends toward less complications, especially for nonbulging collections, collections in the tail, and those patients with varices.[46,47]
   a. With EUS: Endosonography is used to identify the appropriate site of transmural puncture. It is important to ensure that the cyst lumen is well approximated

against the luminal gastroinestinal tract; the most appropriate site of transmural puncture should ideally be through a combined wall of 10 mm or less in thickness, although in some circumstances up to 20 mm may be acceptable.

b. Without EUS: External compression of the gastric or duodenal wall is determined endoscopically while referencing the most recent cross-sectional imaging.[48]

5. Puncture: When the appropriate site of puncture is identified, the gastric or duodenal walls are targeted and punctured. The choice of instrument to puncture is at the discretion of the endoscopist, and multiple sites of puncture can be performed for certain large collections.[49]
   a. With EUS: Transmural puncture is performed under direct EUS guidance, with use of color-flow to avoid disruption of mural blood vessels at the time of wall puncture.[13] Most endoscopists use a 19-gauge fine-needle aspiration needle for puncture, and subsequently the needle sheath for initial dilation. Aspiration of cavity contents and/or demonstration of contrast injection into the cavity under fluoroscopic guidance confirms cavity access and allows collection of liquid for microbial culture. Recently, many endoscopists have been using a nonbeveled needle to avoid shearing of the hydrophilic coating that is present on many wires.
6. Fistula tract creation: Once the collection is accessed, any standard-sized guidewire (as small as 0.018 inch) is advanced into the collection under fluoroscopic guidance. Care should be used with a 0.035-inch guidewire, as these are fairly tight in a 19-gauge needle and can easily shear. Enlarging the fistula tract can be accomplished with several devices—simple low-profile dilating balloon, dilating catheter, or if resistant to those techniques, a wire-guided needle knife, fistulotome, or Soehendra screw-type stent retriever to act as a dilator. The entire sequence of procedures can be performed entirely through a therapeutic EUS scope, or, once the fistula and wire are in place, after exchange for a therapeutic duodenoscope.
7. Fistula tract dilation: Next, the tract is dilated to at least 10 mm in size using sequentially larger hydrostatic balloons. If purely liquid pseudocyst drainage is the goal, further dilation is not generally necessary. However, if endoscopic debridement is to be performed, the fistula tract must be dilated to at least 12 mm to allow passage of the endoscope into the collection. Therefore, as long as there is no contraindication—bleeding, disrupted fistula tract, patient instability, etc—generally the goal is to dilate the fistula tract fully to 20 mm at the time of the first endoscopy.
   a. If bleeding occurs during fistula puncture or dilation from the fistulous tract, bleeding can be controlled by prolonged balloon tamponade, epinephrine injection, or rarely, thermocoagulation or clip placement. Immediate bleeding from within the cavity, as a result of a pseudoaneurysm, which can be more easily identified during EUS puncture of a cavity, is more difficult to manage, sometimes requiring cavity entry and direct hemostasis, or even angiographic embolization.
8. Stent placement for drainage: If draining a pseudocyst, the next step is to place stents to maintain the patency of the fistula tract and not necessarily act as a conduit for drainage. Current stenting practices vary, but the standard use of at least 2 parallel double-pigtail stents allow the fistula tract to drain even if the stents become occluded due to the space between the round catheters. Placement of one stent is fraught with occlusion risk and increases the risk of treatment failure. It is important that the fistula tract be kept patent so that fluid can escape from the

collection, pus can be released into the lumen, and the collection can be allowed to collapse. The authors generally recommend 10-F double-pigtail stents of 2 to 4 cm length, preferably of soft material to minimize trauma to the back wall of the cavity or intestinal obstruction if the stents migrate spontaneously. Alternatives are placement of a fully covered biliary type metallic stent, or even various forms of larger enteral or esophageal metallic stents to create a larger fistula.[50]

a. Recently, a single-step system called the NAVIX system (Xlumena, Mountain View, CA) has been US Food and Drug Administration approved for chronic pseudocyst drainage. A fully integrated transluminal access device that creates and dilates an access tract, then facilitates placement of 2 guidewires, it is the first device specifically approved for pseudocyst drainage.

9. Debridement of WON: WON requires the additional step of debriding the intracavitary solid debris because the necrosis will often not resolve with the simple creation of a fistula tract.[13] Debridement of the intracavitary solid debris is performed by driving a gastroscope or duodenoscope through the dilated fistula tract into the necrotic cavity. The fluid contents within the necrotic cavity are then aspirated through the endoscope until dry, and devitalized necrotic tissue is then removed. The devitalized pancreatic tissue can be removed via a combination of several accessories including balloons, snares, waterjets, and baskets, and cap-suction techniques. The goal is to remove as much of the devitalized necrotic tissue as possible from the cavity, but without disrupting a major vessel or the wall of the cavity, potentially leading to perforation, bleeding, or air embolus.
   a. At the conclusion of each debridement session, stents must be left in place to allow the fistula tract to remain patent. Although the authors' choice is to use pigtail stents as with the pseudocyst drainage, many types of stents can be used per endoscopist preference, including fully covered metal stents, which may allow for dissolution of solid necrosis by gastric and bile acids over several weeks to months; the stent is subsequently removed once the collection has resolved.
10. Disconnected pancreatic duct: Most often, PFC arise in the context of some degree of pancreatic ductal disruption. Commonly, a disconnected duct will serve as a "feeding source" to the collection. Before effective endoscopic cystgastrotomy, endosocpists attempted to bridge the disruption with pancreatic duct stent placement. However, creating a cystenterotomy fistula tract will usually allow for adequate pancreatic drainage and general current practice it to leave the stents across the fistula tract permanently to allow for adequate pancreatic drainage proximal to the site of disruption.[51]

COMPLICATIONS AND MANAGEMENT

The interventional nature of endoscopic therapy for PFCs and necrosis does lend itself to potential complications. For example, the largest case series reported a major complication rate of 13%, including 5 patients with pneumoperitoneum/perforation (all of which were managed nonoperatively) and one periprocedural death, which was believed to be from an air embolism.[52] Eighteen percent of patients developed bleeding requiring endoscopic intervention and in 2 patients bleeding could not be controlled by endoscopic means and embolization by interventional radiology was necessary. Similar complication rates have been found in the other large series and generally the complication rate of transmural drainage is believed to be approximately 15% to 25%.[8,9,52–58]

It is imperative for endoscopists to recognize these life-threatening complications and to act accordingly. In the case of bleeding, every attempt should be made to control the bleeding endoscopically using closure devices, such as endoclips, and pharmacologic therapies, such as epinephrine. In the case of bleeding that is unable to be controlled endoscopically, interventional radiology should be consulted for embolization. Again, this underscores the importance of alerting the interventional radiologists before any attempt at drainage or debridement.

If pneumoperitoneum does occur, it is important to recognize the source immediately. In the case of fistula tract disruption, this can usually be managed nonoperatively with nasogastric tube suction, antibiotics, and conservative therapy. However, if the wall of the collection becomes disrupted (ie, during debridement) surgical intervention will usually be necessary.

As mentioned above, there is the potential for air embolism during these procedures and every attempt should be made to use CO_2 insufflation if possible. Although CO_2 does not reduce the risk of gas embolism per se, the rapidity at which CO_2 is cleared from the bloodstream, compared with oxygen, makes the hemodynamic effect of an air embolism with CO_2 generally less profound.

To prevent infection, broad-spectrum antibiotics should be given at least periprocedurally. Although there are limited data on whether long-term antibiotics are effective or appropriate, general consensus is that antibiotics should be prescribed for at least 2 to 3 days following the procedure.

Finally, it cannot be emphasized enough that before undertaking any definitive drainage of PFC or WON, the diagnosis should be firmly established as an inflammatory collection, and not intraductal papillary mucinous neoplasms or cystadenocarcinoma. Fine-needle aspiration of the collection with cytopathologic inspection can easily confirm this.

POSTOPERATIVE CARE

In an uncomplicated procedure, hospital admission is generally not necessary, even when performing an initial debridement for necrosis. Following an uncomplicated pseudocyst drainage, cross-sectional imaging should be repeated in 2 to 4 weeks to make sure resolution or near resolution of the cavity has occurred. If there has been complete resolution, no further treatment is necessary, including the removal of the plastic stents, which will typically migrate through the intestinal tract spontaneously without complication. If the collection recurs, consideration must be made for repeat transmural drainage, with possible transpapillary drainage as well if pancreatic ductal disruption is suspected.

Following an initial uncomplicated necrosectomy procedure, serial cross-sectional imaging with CT or magnetic resonance imaging every 1 to 2 weeks is performed to evaluate the status of the collection until resolution. Most often, repeat debridement will need to occur within 1 to 2 weeks after the initial cystenterostomy has been performed. At each debridement, the steps outlined above should be followed, as often there will need to be repeat dilation of the fistula tract. Each session should attempt to remove progressively more devitalized tissue.

One technique that the authors find especially helpful is to stop patients from taking any acid-suppressive therapy as the collection is resolving. Their belief is that gastric acid allows for further debridement of the collection, which in turn facilitates more rapid resolution. As with pseudocysts, plastic stents to do not need to be removed endoscopically on cavity resolution; they will usually migrate spontaneously.

In addition, if the collection fails to resolve or reaccumulates, alternative therapies, such as retroperitoneal catheter-based adjunctive techniques, such as sinus tract endoscopy, or VARD should be considered. Pancreatic ductal disruption should again always be considered as a cause of reaccumulating collections and dealt with accordingly.

OUTCOMES

There have been very few prospective, comparative effectiveness trials evaluating the success of minimally invasive approaches for PFCs and WON. In fact, effectiveness data for endoscopic therapy are limited to mostly single-center case series. However, in recent years, there have been a few trials that have laid the foundation for further endoscopic research in this field.

For pancreatic pseudocysts, the most robust study was a retrospective case-controlled study at a single center that matched 10 patients who underwent surgical cystgastrostomy with 20 patients who underwent an EUS-guided cystgastrostomy.[55] Although there were no significant differences in rates of treatment success (100% vs 95%, $P = .36$), procedural complications (none in either cohort), or reinterventions (10% vs 0%, $P = .13$) between surgery versus an EUS-guided cystgastrostomy, the mean length of a postprocedure hospital stay for an EUS-guided cystgastrostomy was significantly shorter than for surgical cystgastrostomy (2.65 vs 6.5 days, $P = .008$). In addition, the average direct cost per case for EUS-guided cystgastrostomy was significantly less when compared with surgical cystgastrostomy ($9077 vs $14,815, $P = .01$), which corresponded to a cost savings of $5738 per patient. A prospective, randomized trial comparing EUS-guided versus open surgical cystgastrostomy for the treatment of pseudocysts has been reported in abstract form and is in press (Varadarajulu). This study showed significant advantage of EUS-guided drainage over surgery with respect to cost, hospital stay and quality of life, with no differences in treatment success or recurrence.

The only randomized, prospective study comparing minimally invasive techniques with open necrosectomy is a study of 88 hospitalized patients from the Dutch Acute Pancreatitis Study Group.[8] In this multicenter study, 88 patients with pancreatic necrosis with suspected or confirmed infection were randomized to open necrosectomy or a step-up approach of percutaneous drainage followed by, if necessary, minimally invasive retroperitoneal necrosectomy. The authors found that in patients treated with the "step-up" approach, 35 were treated with percutaneous drainage only, new-onset multisystem organ failure occurred less often, and major complications and death were significantly lower (40% vs 69%, $P = .006$) compared with the open necrosectomy group.

The same group has also subsequently published the PENGUIN trial, a prospective, randomized trial of 22 patients hospitalized with infected pancreatic necrosis.[9] Patients underwent percutaneous catheter drainage, with a step-up approach, and if they failed to respond to simple catheter drainage, they were randomized to endoscopic transgastric or surgical necrosectomy. Endoscopic necrosectomy consisted of transgastric puncture, balloon dilatation, retroperitoneal drainage, and necrosectomy. Surgical necrosectomy consisted of VARD or, if not feasible, laparotomy. The authors found that endoscopic necrosectomy reduced the postprocedural proinflammatory response as measured by serum interleukin-6 levels and a predefined composite end point of major complications (new-onset multiple organ failure, intra-abdominal bleeding, enterocutaneous fistula, or pancreatic fistula) or death compared with the surgical group.

Given the small number of comparative effectiveness trials, it is critical for the endoscopic community to continue to collaborate on the design and implementation of more robust studies.

CURRENT CONTROVERSIES/FUTURE DIRECTIONS

Although the development of endoscopic therapies for PFCs and WON has revolutionized the care of patients, there still remain several controversies, questions, and limitations that need to be addressed because these techniques become more commonplace as detailed below:

- Robust comparative effectiveness studies evaluating the efficacy of transmural endoscopic techniques versus other minimally invasive techniques
- To what extent must providers be credentialed/trained
- Whether all facilities should be allowed to perform these procedures
- Improving on the debridement tools for necrosectomy
- The role of placing metallic stents and allowing natural debridement versus performing serial endoscopic necrosectomy
- Whether EUS localization needs to be used for every drainage procedure
- Should CO_2 be required to prevent air embolus during every procedure
- Further defining the role of pancreatic duct drainage in managing PFCs and WON
- How best to manage disconnected duct syndrome (ie, leaving cystgastrostomy stents in place indefinitely vs transpapillary pancreatic duct stenting).

SUMMARY

In the last 3 decades, the endoscopic management of pancreatic pseudocysts and necrosis has become increasingly common. Not only are therapeutic endoscopists draining simple collections but have recently begun extraluminal debridement of pancreatic necrosis with good success. Although these techniques are promising, further prospective trials are necessary to validate their effectiveness, cost, and safety when compared with standard operative and percutaneous techniques.

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