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# The Role of Endoscopy in the Management of Pancreatic Necrosis

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**Abstract** The management of acute pancreatitis has seen many advances over the past three decades. Attempts to improve care have led to new definitions, classification systems, and treatment strategies. Despite those efforts, considerable morbidity and mortality result from complications of severe acute pancreatitis. Much attention has been given to new ways to treat these complications, including inflammatory pancreatic fluid collections and associated infections. Endoscopy has become one of the established modalities for the treatment of these complications in many expert centers. This chapter will specifically address the role of endoscopy in the management of pancreatic necrosis.

**Keywords** Pancreatic necrosis · Pancreatitis · Pseudocyst · Walled-off necrosis · Endoscopic therapy · Minimally invasive · Drainage

## Diagnosis

Acute pancreatitis is an evolving process, with different clinical symptoms and varying appearances on serial imaging when followed through its course. QueryOf patients with acute pancreatitis, about 15 % have necrotizing pancreatitis. Pancreatic necrosis typically complicates acute pancreatitis late in the course of the disease. Following the onset of pancreatic necrosis, the course is variable. Necrotic pancreatic and peripancreatic tissues can remain solid or become liquid and remain sterile or become infected. Of those with necrotizing pancreatitis 33 % will develop infected necrosis. The mean prevalence of organ failure in necrotizing pancreatitis is 54 % and is very similar or higher in infected necrosis. Although the overall mortality of acute pancreatitis is approximately 5 %, it is 15 % in necrotizing pancreatitis and 30 % in infected necrosis [1]. Since its initial description 25 years ago, endoscopic therapy for complications of pancreatitis has become well accepted in many academic centers [2].

A discussion of pancreatic necrosis must be preceded by an understanding of the current definitions of pancreatic fluid collections. The 2012 revision of the Atlanta classification of acute pancreatitis updated the terminology used to describe inflammatory pancreatic fluid collections [3]. These collections include the simple collections termed *acute peripancreatic fluid* and *pancreatic pseudocysts*. These usually occur with interstitial edematous pancreatitis without associated peripancreatic necrosis, the former within 4 weeks of the onset of disease and the latter occurring more than 4 weeks after the onset of disease. In acute necrotizing pancreatitis, *acute necrotic collections* can be seen containing both fluid and necrotic debris and involve the pancreatic parenchyma and/or the peripancreatic tissues. Early in disease, these collections do not have an encapsulating wall. *Walled-off necrosis* (WON) is the late manifestation of this process, occurring more than 4 weeks after the onset of disease. WON contents are also heterogeneous but have developed a mature capsule. There is often overlap between these entities, sometimes making it difficult to determine the optimal time and modality for intervention.

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These different pancreatic fluid collections can be identified through various imaging modalities. The revised Atlanta guidelines described specific contrast-enhanced computed tomography (CECT) criteria to identify each of these entities [4]. Although not required for the diagnosis of pancreatitis initially, CECT helps determine disease severity by identifying pancreatic and peripancreatic necrosis, as well as the extent of necrosis and other local complications such as venous thrombosis and pseudoaneurysm. Although CECT is usually the exam of choice, it is limited by radiation exposure risks and potential nephrotoxicity associated with intravenous contrast. It is not reliable in detecting underlying necrotic debris particularly in fluid-predominant collections or identifying infection within necrosis prior to the development of intrapancreatic gas. Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) can be better at detecting non-liquid material in fluid collections and are superior at detecting bile duct stones and pancreatic duct anatomy and injury. MRI/MRCP are limited in regular availability, poor patient tolerance with critical illness, potential nephrotoxicity with gadolinium, and contraindication with implanted metal devices [4].

Endoscopic ultrasound (EUS) provides advantages over cross-sectional imaging. EUS is superior to CECT in detecting non-liquid necrosis and debris in pancreatic fluid collections. It can also be used to determine pancreatic duct continuity. The primary advantage of EUS is the ability to utilize image-guided diagnostic and therapeutic modalities. These include fine needle aspiration (FNA) to obtain culture and Gram stain for the diagnosis of infected necrosis. Although empiric treatment of infections has become an acceptable approach, FNA is still helpful in certain situations. For example, FNA alone may be indicated for the suspicion of a fungal infection when broad-spectrum antibiotic therapy fails to improve fevers or leukocytosis in presumed infected necrosis [4]. EUS is also used in peroral endoscopic drainage and necrosectomy to avoid vascular structures and locate the optimal location for the intervention. Though location sometimes can be determined by simply observing an indentation or bulge into the gastric or duodenal lumen, studies have suggested that there are fewer complications and higher success rates when EUS was used to localize the most appropriate access site [5, 6].

## Indications for Intervention

Understanding the indications and timing for endoscopic treatment in pancreatic necrosis is critical to achieving good outcomes and minimizing complications. A multidisciplinary consensus conference in 2010 attempted to define when intervention is indicated for pancreatic necrosis [4]. Using the then proposed revised Atlanta classification for inflammatory pancreatic fluid collections, the consensus conference observed two central principles in the management of pancreatic fluid collections. The first principle is to determine whether the fluid is infected or sterile. The second is choosing the optimal timing for an intervention if it is indicated. The conference concluded that sterile acute necrotic collections almost never require early intervention. Sterile symptomatic pseudocysts and WON may require intervention if there is intractable pain or obstruction of the bowel or bile duct. This is optimally delayed for 4 to 6 weeks after disease onset to allow for capsule maturity. Asymptomatic WON regardless of size usually does not require intervention and may resolve itself with time.

Infected acute necrotic collections may need early intervention, but radiological or endoscopic drainage should be used before surgery to minimize the high morbidity and mortality associated with early open surgery. Even in infected necrosis, there is convincing evidence that delayed intervention is superior to early intervention. In a 2011 prospective observational study of 639 patients with necrotizing pancreatitis, patients with longer times between admission and intervention had lower mortality. Of the 208 (33 %) patients who received intervention, there was 19 % mortality. Catheter drainage was the first intervention in 63 % of cases without additional necrosectomy in 35 % of patients and with fewer complications than those who underwent primary necrosectomy (42 vs 64 %, $p$=0.003) [7]. Intervention of any method is optimal when necrotic collections are walled-off and mature, with at least partial liquefaction and encapsulation. Again, this usually does not occur until 4 to 6 weeks after the onset of disease.

Goals of therapy should be considered for each clinical situation [8]. If controlling a source of infection is the goal, then perhaps simple decompression or drainage is adequate. However, with symptomatic large fluid collections resulting in gastric outlet or biliary obstruction, simple drainage is unlikely to be adequate. With these fluid collections often recurring, complete tissue removal is usually necessary. This can be difficult in patients with fluid collections that extend into the pelvis, possibly making peroral endoscopic intervention alone problematic. The goal of each intervention should influence the modality and aggressiveness of the considered therapies.

## Modalities of Intervention

There are different approaches when intervening on pancreatic and peripancreatic necrosis, including open surgical, minimally invasive surgical, image-guided percutaneous, peroral flexible endoscopic, and hybrid techniques. Minimally invasive surgical techniques include laparoscopic and retroperitoneal sinus tract endoscopy (i.e., videoscope-assisted retroperitoneal

debridement [VARD]) [4, 9]. When an intervention is required for pancreatic cysts that communicate with the pancreatic duct, one can consider transpapillary stent placement via endoscopic retrograde cholangiopancreatography (ERCP). Although not the preferred method of drainage as it does not allow for the placement of multiple stents or necrosectomy, it can provide continuous anatomic drainage allowing for the resolution of ductal disruption that likely caused the pseudocyst. This is most likely to be used in combination with another less invasive modality.

There is great variation conceptually and technically between these techniques, and their use is often determined by institutional preferences, equipment availability, local expertise, and subspecialty background and interest of the involved physicians. Thus, a multispecialty team should be employed in caring for patients with necrotizing pancreatitis including gastroenterologists trained in advanced endoscopic techniques, intensive care physicians, interventional radiologists, and surgeons. Appropriate parties should be made aware of scheduled procedures so they can be available for backup assistance when requested [4, 8].

## Endoscopic Drainage and Necrosectomy

Interventions for necrotizing pancreatitis were dominated by open and subsequently laparoscopic surgical techniques through the 1970s and early 1980s. Then, with the advent of EUS, transmural endoscopic therapy started to play a role, first in evaluation only, then therapeutically. This first occurred through transpapillary or transmural techniques. It was soon evident, however, that simple drainage of many fluid collections was not adequate for full resolution. The placement of nasocystic tubes to drain WON was described in 1996 [4]. Since then, multiple case series and some comparative trials have looked at the effectiveness of endoscopic drainage with these techniques. When compared to surgical interventions, endoscopic drainage is generally equally effective. However, endoscopic therapy is associated with advantages such as shorter hospital stays, better physical and mental health of patients, and lower costs [10].

With successful endoscopic irrigation and drainage of both simple cysts and some WON, more aggressive therapy was attempted to treat more complicated fluid collections. The first direct endoscopic necrosectomy was reported in 2000 by Freeman et al., from Germany [4]. Since that small series, other case series and a few randomized control trials have demonstrated that peroral endoscopic necrosectomy for necrotizing pancreatitis can be also successful when compared to surgical therapies. Of these, the largest to date is from Gardner et al. in 2011 [11]. They reported on a series of 104 patients who underwent endoscopic cystenterostomy with direct endoscopic necrosectomy. There was successful resolution in 91 % with a mean number of procedures of 3.7 and 2.5 debridements. The complication rate was 14 %. Of note, the median number of days from acute pancreatitis to first endoscopic intervention was 46 days, reinforcing the notion that success comes when one intervenes late in the course of disease, once encapsulation has occurred.

Direct comparisons between surgical and less invasive modalities have been few. Most studies have diverse patient populations, definitions, and procedures and are thus not readily comparable. The Dutch Acute Pancreatitis Study Group studied 88 patients with necrotic pancreatitis and suspected or confirmed infection in a multicenter, randomized, prospective study and compared open necrosectomy to a step-up approach [12]. This approach has been advocated to decrease morbidity associated with higher-risk procedures. The step-up started with percutaneous drainage, followed by minimally invasive retroperitoneal necrosectomy, if needed. The authors reported that new-onset multisystem organ failure occurred less often and there were fewer major complications and deaths in the step-up group compared to the open necrosectomy group.

The same Dutch group subsequently published the PENGUIN trial looking at endoscopic transgastric versus surgical necrosectomy [13]. This prospective, randomized trial of 22 patients with infected pancreatic necrosis found that compared to the surgical group, endoscopic necrosectomy reduced postprocedural pro-inflammatory response and a predefined endpoint in major complications (including new-onset multiple organ failure, intraabdominal bleeding, enterocutaneous fistula, or pancreatic fistula) or death. A third study by this group, the TENSION trial, was underway as of 2013 and was to look directly at transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotizing pancreatitis [14].

## Procedural Techniques

When considering peroral endoscopic necrosectomy or drainage, Gardner reported several preprocedural issues to consider [8]. First was again to consider the goal of the intended therapy and that a multimodality approach has been considered. Ensure that imaging is consistent with pseudocyst or WON and not a pancreatic cystic neoplasm. If there is doubt, consider biopsy before attempting the planned intervention. Ensure there is adequate backup from other specialties, including surgery, interventional radiology, and the hospital blood bank. Be sure the endoscopy staff is familiar with the plan and equipment. Finally, spend adequate time with the patient on informed consent, including the alternatives, possible risks, and expected successes of the procedure.

To minimize potential complications, standard protocols for peroral endoscopic drainage and necrosectomy should

include the administration of antibiotics. Periprocedural antibiotics should be given if the patient is not already on broad-spectrum antibiotics for suspected or proven infection. Anticoagulants and antiplatelet agents should be held per current recommendations. To minimize the potential risk of air embolism, the routine use of $CO_2$ for insufflation has been recommended [4, 8]. Also, patient positioning should be optimized to facilitate drainage. This would usually be prone positioning, if the patient can tolerate it, as the fluid collections are retroperitoneal. Finally, include in your plan appropriate sedation or anesthesia given the patient's comorbidities and aggressiveness of the planned procedure.

The approach or choice of endoscopic drainage or necrosectomy will depend on the location of fluid collection. Patients with pancreatic pseudocysts that communicate with the pancreatic duct can be considered for transpapillary drainage. Although this carries decreased risk for bleeding compared to a transmural puncture, it carries risk of infection, particularly thought of when dealing with residual debris such as with WON.

Transmural puncture through the stomach or duodenal wall is performed once the appropriate location is found, as noted above. EUS guidance is recommended. The most appropriate site is through a wall that is less than 10 mm in thickness. Sometimes, multiple tracts may be appropriate. The puncture has been performed with various tools, including needle-knife electrocautery, cystotome, and needle aspiration. As most of these are now being done with EUS, a 19-gauge FNA needle is frequently used for both puncture and initial dilation with the needle sheath. Aspiration of fluid contents or contrast injection into the fluid collection under fluoroscopy can confirm correct access. The remainder of the procedure can be performed with the therapeutic linear array echoendoscope, or the echoendoscope can be exchanged via a rendezvous technique for a side-viewing duodenoscope.

Once the collection is accessed, a guidewire is advanced under fluoroscopy. The fistula tract then is created, usually by dilating the tract with low-profile biliary dilators. Larger dilations with hydrostatic balloons at least 10 mm in size are then used to increase the diameter of the tract. Generally, the goal is to dilate the tract up to 20 mm if there are no contraindications. Draining liquid can then be aspirated until dry. At this point, debridement of the intracavitary necrosis can commence, driving a forward-viewing endoscope through the dilated tract directly into the cavity and removing debris. Tools to remove debris can include balloons, snares, baskets, and forceps. Debridement is not usually completed with a single procedure and often requires repeat intervention. Hydrogen peroxide lavage has been reportedly used for debridement, but its safety has not yet been fully evaluated [8]. The goal of debridement is to eventually uncover pink granulation tissue lining the wall of the collection.

After debridement, stents are left in place for ongoing drainage and to keep the tract patent. This allows for the collection to collapse while preventing reaccumulation and infection. There are various stenting practices currently performed. Among them is the standard use of at least two parallel double-pigtail stents. Many more stents can be used and directed to the various portions of the fluid collection to ensure complete drainage. With most necrotic lesions, a nasobiliary drain is placed to permit the lavage of the fluid collection. This is often used for a few days but can be used longer for larger lesions. The use of covered self-expanding metal biliary and enteral stents (SEMS) to maintain the fistula tract is gaining popularity as these stents have also been found effective at maintaining a conduit for drainage and can easily be removed thereafter. In the authors' experience, the use of fully covered esophageal SEMS with aggressive debridement at the initial procedure can abrogate the need for continuous drainage via use of a nasobiliary drain. These large stents allow efficient access to the necrosis and maintain patency for drainage. Stents are left in place for at least 4–6 weeks after complete drainage and/or necrosectomy and followed by serial cross-sectional imaging to watch for collection collapse. Longer maintenance of the stents may be needed when there has been pancreatic duct disruption, providing a long-term conduit for proximal pancreatic drainage.

Devices specifically designed for the drainage of pancreatic fluid collections have started to appear and gain approval for use from the US Food and Drug Administration (FDA). The NAVIX system is a single-step, fully integrated transluminal access device. It creates and dilates an access tract and can then facilitate the placement of two guidewires [8]. In late 2013, the AXIOS stent and delivery system was approved by the FDA for the drainage of pancreatic pseudocysts [15]. This stent is a self-expanding metal stent designed with two large bilateral anchors to maintain tissue apposition and prevent migration.

## Complications

Complications that can occur during and after endoscopic drainage and necrosectomy procedures are specific to the techniques performed. For all of these, failure of resolution and recurrence must be listed as potential complications. Infection is a common complication, particularly if the fluid collection was sterile prior to the intervention. This can usually be treated with antibiotics and further drainage, if necessary. Bleeding can be a major complication and is usually due to the inadvertent puncture of blood vessels. This can be severe, particularly if a pseudoaneurysm is punctured. Bleeding can be controlled endoscopically through epinephrine injection, following which hemostatic clips or cautery is applied. If hemostasis is not obtained, then angiography and

embolization or surgery may be indicated. Perforations and pneumoperitoneum can occur but can often be managed conservatively. Other complications can include air embolism, pancreatitis, aspiration, stent migration/occlusion, pancreatic duct damage, and complications of sedation. The generally accepted complication rate of transmural drainage is 15–25 % [4, 8].

## Conclusion

Therapeutic endoscopists at expert centers now routinely perform endoscopic drainage of bland peripancreatic fluid collections and are increasingly offering endoscopic drainage and necrosectomy of complex peripancreatic fluid collections. With guidance from expert consensus guidelines, best practices for these procedures are just starting to be defined [4]. There will be continued refinement of patient selection, timing of intervention, and the most effective modality for preventing morbidity and mortality and minimizing loss of quality of life. The early experience with endoscopic management of pancreatic necrosis is very encouraging. Where available, these patients should be referred to a center capable of these techniques.

### Compliance with Ethics Guidelines

**Conflict of Interest** Aaron Lewis and Brett Partridge declare no conflict of interest. Oleh Haluszka serves as a consultant for Boston Scientific, Covidien, and Fujinon outside of the submitted work.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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