

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: John Baillie, MB ChB, FRCP

Endotherapy for Organized Pancreatic Necrosis



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G&H What is organized pancreatic necrosis, and how does it differ from a pseudocyst?

RK There are over 200,000 hospitalizations for pancreatitis in the United States yearly, and 20–25% of these cases involve severe acute pancreatitis. Most severe acute pancreatitis cases are associated with the loss of perfusion, or death, of part of the pancreas, a marker of and a prerequisite for pancreatic necrosis. This condition is usually diagnosed 1–2 weeks after a patient presents to the hospital in this setting. Computed tomography (CT) shows the failure to perfuse part of the pancreas. Pathologically, there may be significant dead tissue with or without a concomitant fluid collection.

Organized pancreatic necrosis, which is also known as walled-off pancreatic necrosis, usually occurs after 4–6 weeks of severe pancreatitis, in which the body forms a rim or shell around a collection of necrotic tissue containing a variable amount of enzyme-rich fluid. This condition differs from a pseudocyst, which has a fibrous capsule or wall and primarily fluid internal contents. The internal contents of organized pancreatic necrosis have a liquid component but also contain a lot of dead tissue; thus, the 2 conditions cannot be treated the same way. Pseudocysts can be poked percutaneously, transgastrically, or transduodenally in order to insert a tube that will allow collapse and disappearance of the pseudocyst. With organized pancreatic necrosis, the fluid component can be drained, but the solid component has the potential for infection if it does not drain.

G&H How can endotherapy be used to manage organized pancreatic necrosis?

RK Endotherapy is just one tool in our armamentarium. Other tools are used before drainage of the necrosis; just

because there is necrosis does not mean that it has to be drained. However, it may be relatively asymptomatic and resolve spontaneously. If a patient is quite ill, several endoscopic interventions are available. If the pancreatitis is caused by common bile duct stones, an endoscopic retrograde cholangiopancreatography (ERCP) could be performed to remove choledocholithiasis. If the endoscopic necrosis is associated with a partial ductal disruption, a transpapillary pancreatic duct stent could be endoscopically placed in order to reduce the ongoing pancreatic duct leak feeding the necrotic area and limiting pancreatic enzyme egress outside the pancreas and progressive necrosis of pancreatic and intrapancreatic tissues.

If the necrosis itself has to be approached, most endoscopists and surgeons now support waiting as long as possible to drain the necrotic tissue. Thus, drainage usually occurs at 4–6 weeks, when the necrotic collection is adherent to a contiguous loop of gut or there is enough of a rim that drainage of the necrosis will not leak throughout the retroperitoneal space. Historically, this procedure was performed via open surgery, but there are currently other methods of facilitating drainage, including laparoscopic drainage anteriorly or via the retroperitoneum to debride necrotic tissues. Percutaneous drainage can also be performed alone, with very large bore tubes. In addition, drainage can be performed transgastrically or transduodenally, whereby a hole is poked through the stomach or duodenum into the cavity. A variety of techniques are subsequently used to remove adherent debris, such as the placement of pigtail stents or expandable metal stents across the lumen into the cyst (or necrotic) cavity.

Thus, endoscopic interventions can be performed early to treat the cause (such as stones) or consequences of severe pancreatitis (such as ductal disruptions), or they can be performed 4–6 weeks later to drain the necrosis itself.

G&H What are the indications for the use of endotherapy in sterile organized pancreatic necrosis, which in the past was left alone using a wait-and-watch approach?

RK There are several indications for endotherapy in uninfected necrosis. One indication is the clinical deterioration of a patient (eg, the presence of systemic inflammatory response syndrome, or progressive leukocytosis, despite a negative Gram stain and culture of the necrosis). Another indication is an enlarging collection, suggesting an ongoing leak from the pancreatic duct, which may result in the development of gastric outlet obstruction with nausea, vomiting, and the inability to eat. Endotherapy is also indicated when pressure develops on contiguous organs (eg, obstructive jaundice related to bile duct obstruction) or fistulization into contiguous areas such as the bile duct, colon, or skin. Vascular structures can erode with the development of a pseudoaneurysm. In this setting, the pseudoaneurysm is usually embolized and necrosis needs to be drained, even if it is not infected. Finally, sterile necrosis is drained if a patient is not doing well clinically and there is delayed functional improvement after months.

G&H What are the pros and cons of using large self-expanding metal mesh stents to endoscopically establish transgastric or transenteric tracts in organized pancreatic necrosis?

RK In theory, the pro is that the large diameter of the stent allows the endoscope to be placed through the prosthesis to mechanically debride the necrosis. Theoretically, this should be better than keeping the tract open with several pigtail stents and may facilitate improved drainage of the lesser sac contents or the collection. Currently, the most effective of these prostheses are called yoyo-type stents because they have very broad flanges to keep them from being pulled in and out of the cyst as the endoscopist works through the prosthesis.

The cons of this approach are that the stents can still be displaced (even by experienced endoscopists) and that they are not currently marketed in the United States. Endoscopists in the United States have to use stents that are designed for other indications, usually the esophagus, and these prostheses are too long to be useful in the long run; even with a 6-cm stent, there is a possibility that the necrotic collection will fall away from the stomach.

G&H Have initial concerns regarding the use of endotherapy for organized pancreatic necrosis been addressed?

RK When early data on endotherapy for organized pancreatic necrosis were published nearly 20 years ago, I wrote an editorial advising caution for several reasons. One was that

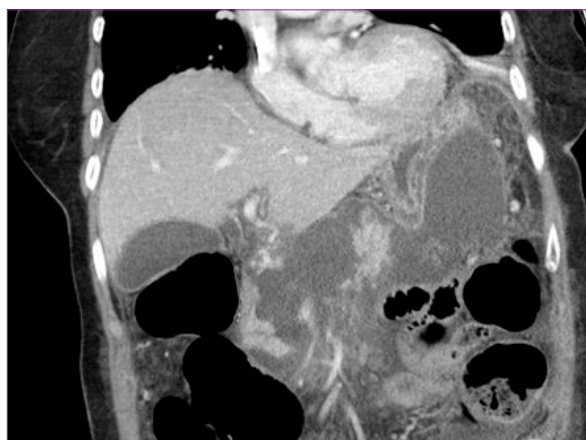


Figure 1. Severe necrotizing pancreatitis related to gallstones in an 89-year-old woman.

endoscopists were initially performing endotherapeutic procedures too early; thus, these procedures were associated with an inadequate rim to the necrotic cavity, which caused peritonitis and leakage of the debris. Endoscopists have learned to wait 4–6 weeks to avoid these complications. Another early problem was the risk of air embolism, which resulted in deaths in Europe and the United States. To decrease this risk, endoscopists have now switched to carbon dioxide during mechanical endoscopic debridement.

The third concern was whether it made sense to perform a procedure that requires multiple repeat studies. In many of the early individual series and both the combined US series and the combined European series, the number of procedures required to endoscopically remove necrotic debris was 3–6. Bringing patients back on a daily or every-other-day basis during the first week or 10 days of treatment in order to complete the debridement of a necrotic cavity was a significant commitment for an endoscopy suite. Therefore, I raised the question—and still raise it—of how cost-effective endotherapy is for managing organized pancreatic necrosis, given limited resources and the need to perform other procedures in the endoscopy suite. However, it should be noted that more recent studies have reported the need for only 3–4 procedures, as opposed to the original series, which reported the need for as many as 11 procedures in order to obtain adequate debridement.

The final concern was that, by definition, pancreatic necrosis is associated with a pancreatic duct leak. Thus, if there is a disconnection between the pancreatic gland in the setting of central pancreatic necrosis, performing endotherapy and then pulling out the stents will often result in the development of a recurrent fluid collection from the disconnected tail, which has nowhere to drain. A central pancreatic necrosis with a recurrent fluid collection is a problem, whether drainage is achieved surgically, endoscopically, percutaneously, or via a combination of endoscopic and percutaneous methods (which is done at my institution).

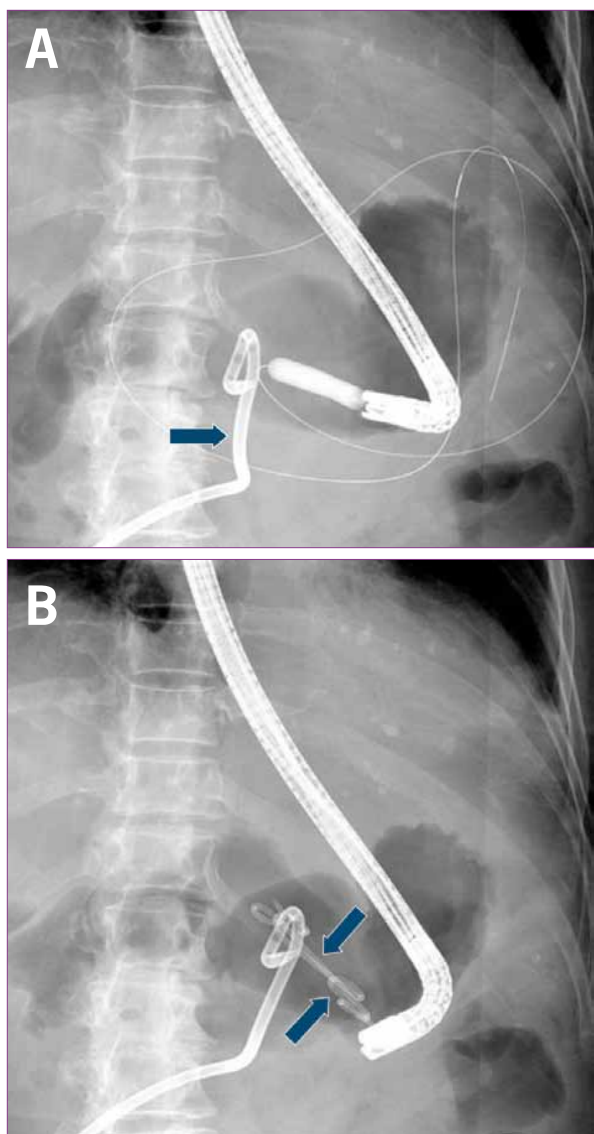


Figure 2. A percutaneous drain (arrow) and guidewire in a large necrotic cavity accessed with an 8–10 mm dilating balloon (A) and two 7-French pigtail stents (B; arrows).

G&H Currently, what are the basic requirements for offering a pancreatic necrosectomy service?

RK I think that patients with organized pancreatic necrosis should be managed by a multidisciplinary team that includes a pancreatic surgeon, therapeutic endoscopist, and interventional radiologist. This team approach should be used when managing severely ill patients with pancreatic necrosis, who historically have a 1-in-4 likelihood of dying from their disease. Published data from my institution suggest that dual-modality drainage, as opposed to historical percutaneous drainage with wide-bore tubes, is associated with statistically significant improvement with shorter hospitalization stays, a

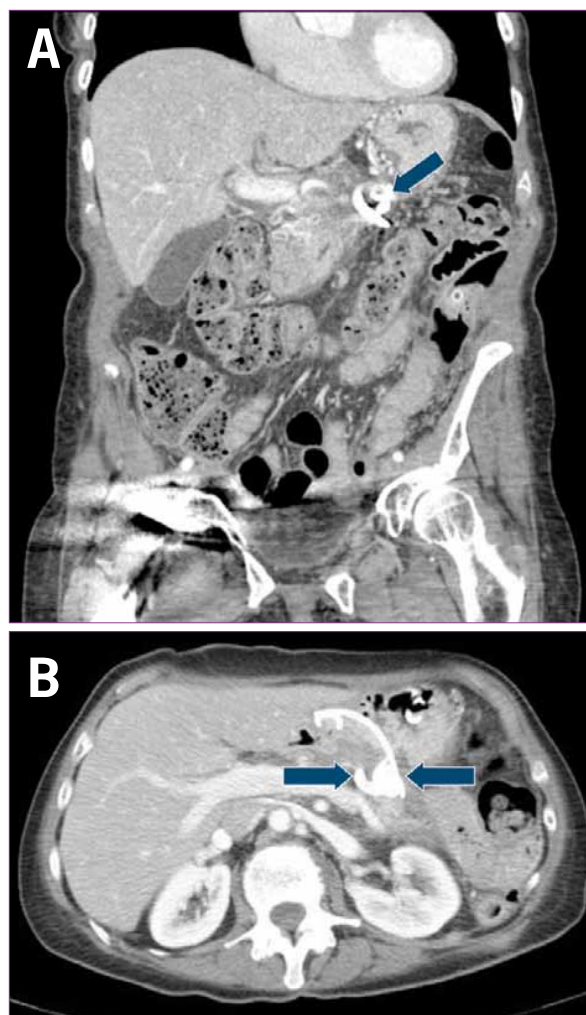


Figure 3. A coronal section demonstrating necrosis resolution and residual transgastric stents (A; arrow). Residual transgastric stents and resolved necrosis (B; arrows).

(All images courtesy of M. Gluck, MD, Virginia Mason Medical Center, Seattle, Washington.)

decrease in the utilization of resources, fewer CT scans, fewer ERCPs, fewer tube checks, and an incidence of subsequent external fistula that has fallen to 0, all with a mortality rate close to 5% (Figures 1–3).

G&H What are the next steps in research?

RK There are many issues involving organized pancreatic necrosis that require further research. A better yoyo-type stent is needed, as are better tools for endoscopic debridement of necrosis; in fact, a variety of tools are currently in the development process. Because manual debridement is somewhat archaic, research is currently being conducted to develop an agent that could be placed in the necrotic cavity to liquify nonviable tissue without damaging viable tissue.

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Another area of research is examination of the following question: If pancreatic necrosis is associated with a leak in the vast majority of patients, what will happen if patients who present to the hospital with severe acute pancreatitis—most of whom will have necrotizing pancreatitis—are randomized to a transpapillary stent or no stent. Although it is not clear whether the leak is the cause or the effect of necrosis, I predict that endoscopic placement of a stent would lead to decreased severity of the illness, the length of hospitalization, and the degree of necrosis. Nevertheless, there would still be an inherent risk that an endoscopic procedure might worsen the pancreatitis or iatrogenically infect the necrosis. More research is needed to definitively answer this question.

Because there are multiple ways to approach and drain necrosis, another interesting area of research involves a recent Dutch study that was published in the *New England Journal of Medicine*. In this study, patients who presented with pancreatic necrosis and became sick were randomized to open necrosectomy or initial placement of a percutaneous tube and subsequent open debridement (“step-up treatment”) if there were ongoing problems. The patients who were randomized to the step-up group did much better than those who underwent open necrosectomy during the index time frame, when they became sick, and 40% of the patients avoided any type of surgery. There

should be further research comparing these approaches as well as comparing the endoscopic approach versus the laparoscopic or retroperitoneal laparoscopic approach (video-assisted retroperitoneal debridement).

In addition, there will likely be additional studies looking at more effective antibiotics because of the debate over whether patients with necrosis should be routinely put on antibiotics. Meta-analyses have yielded conflicting data on this issue.

Suggested Reading

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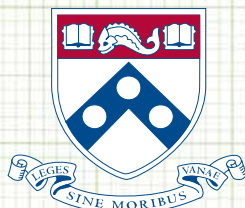
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