The Management of Pancreatic Pseudocyst

Katherine A. Morgan, MD, and
David B. Adams, MD, FACS

"The fascination that pseudocysts hold for surgeons is beyond comprehension."

Robert Zollinger, MD

OVERVIEW

The pancreatic pseudocyst is a collection of pancreatic secretions contained within a fibrous sac comprised of chronic inflammatory cells and fibroblasts in and adjacent to the pancreas contained by surrounding structures. Why a fibrous sac filled with pancreatic fluid is the source of so much interest, speculation, and emotion amongst surgeons and gastroenterologists is indeed hard to understand. Do we debate so vigorously about bilomas, urinomas, or other abdominal collections of visceral secretions? Perhaps it is because the pancreatic pseudocyst represents a sleeping tiger, which though frequently harmless, still can rise up unexpectedly and attack with its enzymatic claws into adjacent visceral and vascular structures and cause life-threatening complications. Another part of the debate and

puzzlement about pancreatic pseudocysts is related to confusion about pancreatic pseudocyst definition and nomenclature.

The Atlanta classification, developed in 1992, was a pioneering effort in describing and defining morphologic entities in acute pancreatitis. Since then, a working group has been revising this system to incorporate more modern experience into the terminology. In the latest version of this system, pancreatitis is divided into acute interstitial edematous pancreatitis (IEP) and necrotizing pancreatitis (NP), based on the presence of pancreatic tissue necrosis. The fluid collections associated with these two "types" of pancreatitis are also differentiated. Early (<4 weeks into the disease course) peripancreatic fluid collections in IEP are referred to as acute peripancreatic fluid collections (APFC), whereas in NP, they are referred to as postnecrotic peripancreatic fluid collections (PNPFC). Late (>4 weeks) fluid collections in IEP are called pancreatic pseudocysts, and in NP, they are called walled-off pancreatic necrosis (WOPN). These latter two entities are the subject of this chapter.

Acute pancreatitis represents a broad spectrum of disease. Although the disease course may smolder, typically an initial inciting event results in organ injury, which sets into play the evolving clinical course. The early phase of disease is marked by the inflammatory mediators from damaged pancreatic tissue, resulting in variable degrees of systemic inflammatory response. The later phase is determined by the morphology of organ injury, specifically with regard to tissue ischemia and necrosis. The outcome of this later phase is often impacted by local or systemic infection.

Peripancreatic fluid collections can occur in both the early and the late phases of disease. They presumably occur from injury to or ischemia of the main pancreatic duct or a side branch duct, although some, particularly early on, may be the result of third-space edema fluid. Peripancreatic fluid collections represent a heterogeneous entity. Definition of peripancreatic fluid collections is essential in determination of clinical decision making.

PATHOPHYSIOLOGY

Pancreatic pseudocysts develop as a consequence of pancreatic duct disruption and can occur in the setting of acute pancreatitis, chronic pancreatitis, or pancreatic trauma. In acute pancreatitis, ischemia, inflammation, and increased pressure may play a role in ductal injury. In chronic pancreatitis, ductal pathology from postinflammatory fibrosis can lead to ductal compromise. With duct disruption, pancreatic exocrine fluid leaks and pools. The pancreatic enzyme-rich fluid incites an inflammatory response with fibroblast-mediated extracellular matrix formation and the development of a fibrous capsule. Pseudocysts are defined microscopically by this inflammatory fibrous lining, which lacks an epithelial layer. The fluid content of walled-off pancreatic necrosis may develop from a similar pathophysiology, although in the presence of necrosis, or it may be the result of liquefaction necrosis of pancreatic or peripancreatic tissue after severe acute pancreatitis.

The natural history of the pseudocyst is determined by the resultant state of the underlying pancreatic duct. The duct injury may heal on its own, or a persistent fistula or ductal stricture may develop, which impedes resolution of the pseudocyst.

PRESENTATION

A pseudocyst may commonly present as persistent or worsening abdominal or back pain, bloating, early satiety, nausea, vomiting, or failure to thrive after a significant bout of pancreatitis or pancreatic trauma. A pseudocyst in the head of the pancreas can cause biliary obstruction with jaundice or duodenal obstruction with intolerance of oral diet. Mechanical compression from a pseudocyst or the associated inflammatory reaction can result in mesenteric venous thrombosis with variceal bleeding or ascites. The inflammatory pseudocyst can erode into surrounding structures, including the small bowel or colon, to develop an enteric fistula. The pseudocyst can also erode into surrounding vessels (including the splenic artery, gastroduodenal artery, and superior mesenteric artery) to cause a pseudoaneurysm and potentially life-threatening hemorrhage. In addition, the cyst may rupture into the peritoneal cavity to result in pancreatic ascites or the thoracic cavity to result in a pleuropancreatic fistula. Finally, a pseudocyst may be asymptomatic and discovered incidentally on imaging.

DIAGNOSTIC EVALUATION

The goals of the diagnostic evaluation of the pancreatic pseudocyst include defining the disease process at hand, determining the need for intervention, and assessing the options for therapy. Distinguishing a pseudocyst or WOPN from a cystic neoplasm is an essential first step in this diagnostic process. Often history alone can make this determination, but radiography should be consistent with this distinction. Radiography is also effective in differentiating a pseudocyst from WOPN with the presence of necrosis. This important distinction has significant implications in the need for and approach to intervention. Finally, the evaluation of the anatomy of the underlying pancreatic duct and its relationship to the pancreatic pseudocyst is vital to clinical decision making.

Contrast-enhanced computed tomographic (CE-CT) scan is the modality of choice for the frontline evaluation of a pancreatic pseudocyst in the modern era. On CE-CT scan, a pseudocyst appears as a uniform, rounded, fluid-filled mass with a thickened, hyperdense capsule that may take on the morphology of the surrounding structures (Figure 1, *A*). WOPN is marked by associated necrosis, most often visualized as heterogeneity of the cyst fluid with solid matter and particulate debris (Figure 2, *A*). Pseudocysts most commonly occur in the lesser sac, although they may occur in the paracolic gutters, at the base of the mesentery, anterior to the stomach, or even more remotely from the pancreas deep in the retroperitoneum. CE-CT scan allows for the assessment of the pancreatic pseudocyst and its relationship to surrounding structures. It may show evidence of hyperdense material within the cyst, raising concern for hemorrhage from an associated pseudoaneurysm. It may show air within the pseudocyst, indicating infection or the presence of a fistula with the gastrointestinal tract. CE-CT scan can show evidence of pancreatic parenchymal atrophy or calcifications suggestive of underlying chronic pancreatitis. It can also show abnormalities of the underlying pancreatic duct or biliary system, although with less sensitivity and detail than magnetic resonance.

Magnetic resonance cholangiopancreatography with secretin stimulation (ssMRCP) is also a useful modality for the evaluation of a pancreatic pseudocyst (Figure 1, *B*). It can show more detailed morphology of cystic structures, improving the differentiation of the pseudocyst from neoplasm and detecting solid debris in WOPN, distinguishing it from the simple fluid of a pseudocyst (Figure 2, *B*). In addition, ssMRCP can help to delineate the anatomy of the pancreatic duct and its relationship to the pseudocyst.

Endoscopic retrograde cholangiopancreatography (ERCP) is used less commonly as a diagnostic tool in the modern era given the chance for inciting a bout of pancreatitis or for introducing enteric organisms into the pseudocyst or WOPN with the potential for infection. ERCP is well used therapeutically, however, in pseudocysts with a connection to the main pancreatic duct that may be amenable to endoscopic stenting or sphincterotomy for resolution.

Endoscopic ultrasound (EUS) may be useful in the evaluation of the pseudocyst, particularly in distinguishing it from a pancreatic cystic neoplasm. EUS examination can elucidate cyst morphology, including solid nodules or septations, and cyst relationship to the pancreatic duct and identify the presence of pancreatitis in the surrounding pancreatic parenchyma. EUS-guided fine-needle aspiration of fluid can also be helpful. High amylase fluid indicates the cyst is

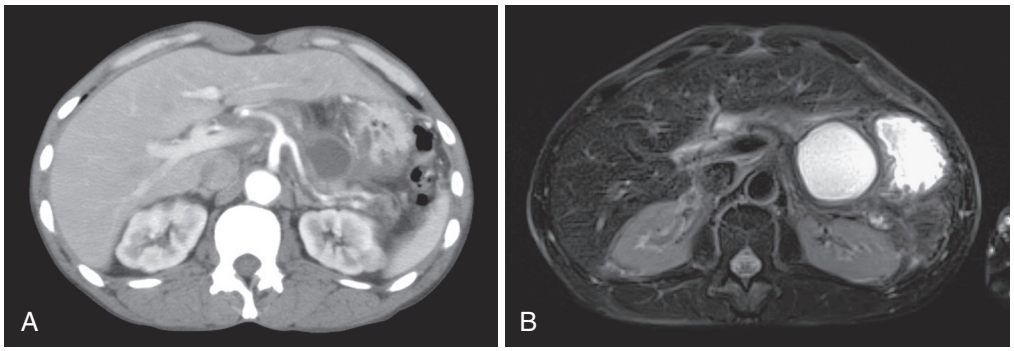

FIGURE 1 A pancreatic pseudocyst is well visualized with contrast-enhanced computed tomographic scan **(A)** as a simple fluid-filled structure with a hyperdense fibrous capsule in the body of the pancreas and with magnetic resonance **(B)** on T2-weighted imaging as a round, homogeneously enhancing lesion.

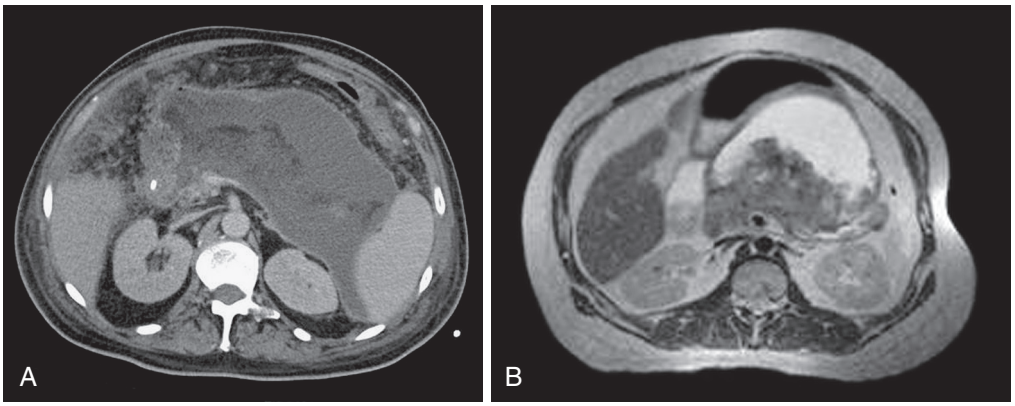

FIGURE 2 Walled-off pancreatic necrosis is shown on contrast-enhanced computed tomographic scan **(A)** as a peripancreatic fluid collection containing heterogeneous material representing solid necrotic debris and with magnetic resonance **(B)** on T2-weighted imaging as a rounded enhancing fluid-filled collection containing nonenhancing solid necrosis.

or has been in communication with the pancreatic duct. Cyst fluid high in carcinoembryonic antigen suggests the presence of a mucinous neoplasm. EUS can also be useful in the therapeutic management of pseudocysts in endoscopic cystoenterostomy.

MANAGEMENT

Pseudocysts (After Acute Interstitial Edematous Pancreatitis)

The natural history of pseudocysts in most cases involves spontaneous resolution over time. In persistent cases, however, intervention may be indicated. Historically, a pseudocyst greater than 6 cm or persistent over time (greater than 6 weeks) was considered to warrant intervention. Modern experience, however, has shown that watchful waiting is appropriate, particularly in small asymptomatic pseudocysts.

There are many reasons not to undertake operative internal drainage of a pseudocyst. The patient may be acutely and chronically unwell and a poor operative risk. The diagnosis may be incorrect despite evaluation with modern imaging studies. The collection may not be a pseudocyst as the acute fluid collection seen early in acute pancreatitis, the so-called pseudo-pseudocyst, does not need operative drainage. A sterile postnecrotic fluid collection or the pancreatic sequestrum may not need drainage. Beware of the cystic neoplasm. Many patients with mucinous cystic neoplasms have undergone cystogastrostomy with perilous outcomes. Most important is to remember that cyst internal drainage procedures do not correct an underlying pancreatic ductal disorder, and the cystoenteric or cystogastric anastomosis may not be effective long-term drainage of an obstructed pancreatic duct. A pancreatic pseudocyst that does not communicate with the main pancreatic duct can be eradicated with a number of minimally invasive techniques.

Symptomatic pseudocysts that cause pain, obstruction (biliary, enteric, mesenteric venous), hemorrhage, or perforation (enteric fistula, pancreatic ascites, pleuropancreatic fistula) warrant intervention. Delineation of the anatomy with MRCP or ERCP is the first step in management. A pseudocyst in connection with the main pancreatic duct and with otherwise normal pancreatic duct anatomy can often be well treated with ERCP-guided sphincterotomy or transpapillary stent placement, altering the pressure differential across the ampulla and allowing for preferential drainage of the pseudocyst into the duodenum with resolution of the pancreatic duct disruption.

A pseudocyst without communication to the pancreatic duct or that has failed transpapillary endoscopic management can often be managed then with drainage. Endoscopic cystogastrostomy or duodenostomy involves placing a stent with endoscopic guidance through the back wall of the stomach or duodenum into a closely opposed retrogastric pseudocyst. Both open and laparoscopic surgical approaches to cystogastrostomy and duodenostomy are also well used, with the advantage of a larger anastomosis for a more durable drainage effect and better control of hemostasis. For all cystogastrostomies and cystoduodenostomies, the stomach or duodenum must be densely adherent to the pseudocyst, or the posterior enterotomy is at risk for postoperative leak and sepsis. In this procedure, an anterior gastrotomy is performed for access to the posterior gastric wall. The flat, firm, bulging surface on the back of the gastric wall represents the underlying pseudocyst. A posterior gastrotomy is then made with cautery (or another energy device for hemostasis). A cyst wall biopsy is included to rule out a cystic neoplasm and the cystoenteric anastomosis is oversewn to ensure hemostasis. The anterior gastrotomy is sewn or stapled securely closed. Open and laparoscopic Roux-en-Y cystoenterostomies are also used for drainage of the pseudocyst that is not well adherent to the stomach into a jejunal limb, with a similar technique.

In cases with the underlying pancreatic duct pathology visualized on preoperative MRCP or ERCP (stricture, obstruction), drainage alone may result in long-term failure of the operation with pseudocyst recurrence. If the pancreatic duct pathology is in the body or tail of the pancreas, distal pancreatectomy is a better, more durable operation than a cystoenterostomy.

Walled-Off Pancreatic Necrosis (After Acute Necrotizing Pancreatitis)

Walled-off pancreatic necrosis in many cases resolves spontaneously over time. In patients with evidence of infected necrosis, either by aspiration and culture or by visualized air within the collection on cross-sectional imaging, drainage or débridement is indicated. In the patient with sterile necrosis who is persistently unwell, marked by pain or nutritional failure with continued disease burden, intervention is also warranted.

The multiple approaches to the treatment of WOPN include the classic open necronectomy, the transgastric approach (either open, laparoscopic, or endoscopic), percutaneous drainage, and the retroperitoneal approach (open or videoscopic). The choice of approach is dependent on the anatomy and distribution of the necrosis, other patient-related factors (body mass index [BMI], surgical history, comorbidities), and importantly, surgeon experience and preference.

Similar to the pancreatic pseudocyst, the initial step in planning intervention in WOPN is to define the underlying pancreatic ductal anatomy with MRCP (or ERCP). Failure to address pancreatic ductal pathology may lead to primary operative failure and recurrent problems.

Open necrosectomy remains the mainstay of management of pancreatic necrosis. In this approach, the lesser sac is entered and gentle blunt débridement undertaken. The placement of large catheters for postoperative drainage and lavage is a classic component of this technique. Laparotomy allows for access to the entire peritoneal cavity for optimal débridement and safe accomplishment of hemostasis. In addition, concomitant cholecystectomy and enteral feeding access are easily obtained.

Open necrosectomy is always a good approach to pancreatic necrosis, even in this modern era. It is particularly suited for the patient with a large, diffuse disease burden, including both paracolic gutters and the root of the mesentery, which are not easily reached with less invasive techniques.

Transgastric necrosectomy emerges from the experience with transgastric drainage of pseudocysts. This technique can be accomplished in an open fashion or laparoscopically. An anterior gastrotomy is performed to gain access to the posterior gastric wall. The site of the WOPN is identified as a firm bulge in the wall of the stomach. The cavity is then entered with cautery or other energy sources (i.e., ultrasonic shears). This posterior gastrotomy is best made in a generous fashion to allow for thorough inspection and débridement of the necrosis cavity. The posterior gastrotomy and cavity wall opening are then secured together for hemostasis with a running absorbable suture. The anterior gastrotomy is closed either with a running suture or with a stapler. The endoscopic approach entails an endoscopically created posterior gastrotomy into the necrosum, often with the use of cautery and pneumatic dilation. Débridement is undertaken with endoscopic instrumentation and can be time and resource intensive.

The transgastric approach is well suited for the patient with disease burden primarily limited to the lesser sac and with a posterior mass effect on the gastric wall. An advantage of the transgastric approach includes the potential creation of a pancreatogastric fistula in cases of a disconnected left pancreatic remnant, potentially avoiding the need for distal pancreatectomy or fistula-enterostomy down the road.

In selected patients with pancreatic necrosis, image-guided percutaneous drainage can be an effective means of therapy. Percutaneous drains have the obvious advantage of avoiding the insult of surgical or even endoscopic intervention. Percutaneous drains serve to drain any liquid component of the necrosum but do not serve well to remove solid necrotic tissue. Several studies have shown significant percentages of patients with WOPN with response to percutaneous drainage alone without surgery (15% to 45%). At a minimum, percutaneous drainage can provide temporization for an ill patient early in the course of necrosis to allow for physiologic recovery and a delayed débridement. Drains are also an essential component of the retroperitoneal approach to pancreatic débridement.

The retroperitoneal approach to pancreatic débridement has been described with an open technique but is more commonly applied with laparoscopic guidance. It has been referred to as videoscopic-assisted retroperitoneal débridement (VARD) by the group in Seattle and as the step-up approach by the Dutch. This technique involves placing percutaneous catheters, typically in the left flank, as an initial attempt at drainage. In those patients with continued solid disease burden, the catheter track is then used as a guide into the necrosis cavity through the left flank into the lesser sac. The laparoscope is used for visualization, and laparoscopic instruments are used for the débridement. A large-bore catheter is left behind for postoperative irrigation and drainage. The retroperitoneal approach is best suited for patients with WOPN that extends into the left paracolic gutter. It can have limited effectiveness with disease burden at the base of the mesentery or into the right paracolic gutter.

Disconnected Left Pancreatic Remnant

In severe cases of acute pancreatitis, significant parenchymal inflammation and necrosis may result in obliteration of the main pancreatic duct, typically at the neck of the pancreas, resulting in a disconnected left pancreatic remnant. This viable body and tail tissue continues to have exocrine production, which does not have an avenue for drainage. The result is a midbody pseudocyst or persistent pancreatic fistula if a drain is in place (Figure 3). Patients with this problem may present several months after the resolution of severe pancreatitis with the signs and symptoms of a pseudocyst and are well treated with resection of the tail remnant. If there is a significantly large segment of disconnected pancreas, a cyst enterostomy can be undertaken to preserve pancreatic endocrine function. Alternatively, a distal pancreatectomy with islet autotransplantation is an option. If this anatomy is apparent at the time of initial débridement, the patient can undergo combined open distal pancreatectomy and débridement if they are physiologically fit for this potentially morbid operation. Alternatively, a transgastric débridement approach may be considered to allow for the creation of a pancreatogastric fistula and the internal drainage of this remnant.

Pseudocysts Associated With Chronic Pancreatitis

In the setting of chronic pancreatitis, delineation of the underlying pancreatic ductal anatomy is essential to the proper management of the pseudocyst. Unaddressed obstruction from stricture or stone is likely to result in long-term management failure. Endoscopic intervention with stenting or stricture dilation is a good initial approach, particularly in patients with small duct disease involving the pancreatic head. In small duct disease with a stricture in the body or tail, left-sided resection may be appropriate. In the setting of dilated duct pancreatitis, a drainage procedure consisting of a lateral pancreaticojejunostomy is a good option.

CONCLUSION

Peripancreatic fluid collections are heterogeneous. Most are benign and resolve spontaneously. Some, however, are complex, with significant potential for morbidity, and can be vexing in management. Proper categorization can aid in clinical decision making, as

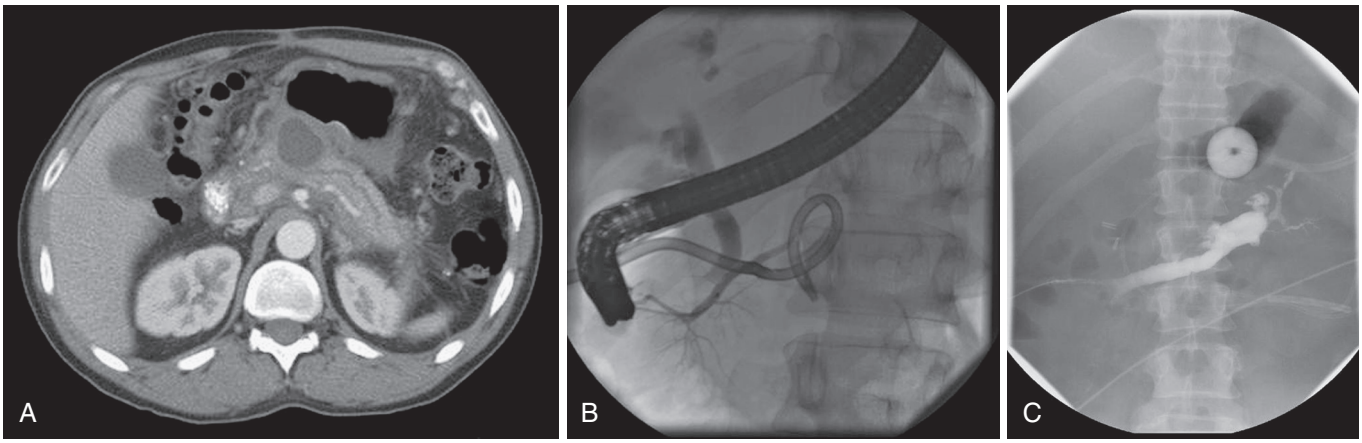

FIGURE 3 A disconnected left pancreatic remnant occurs after necrosis in the neck of the pancreas with resultant obliteration of the main pancreatic duct. The disrupted pancreatic duct from the viable left pancreas, now not in continuity, leaks and results in a midbody pseudocyst. This condition is visualized on contrast enhanced computed tomographic scan **(A)**. It is shown by an abrupt cut-off of the pancreatic duct at the neck on endoscopic retrograde pancreatography **(B)** and by a drain track fistulagram filling only a small tail remnant **(C).**

can determination of the underlying pancreatic ductal anatomy. Symptomatic pseudocysts can be drained, but the underlying pancreatic duct pathology should be considered and may warrant a distal resection. Infected pancreatic necrosis and sterile necrosis with persistent illness require drainage or débridement. There are multiple effective approaches to pancreatic débridement in the modern era.

Suggested Readings

Bradley EL III, Allen K: A prospective longitudinal study of observation versus surgical intervention in the management of necrotizing pancreatitis, *Am J Surg* 161:19–25, 1991.

Freeny PC, Hauptmann E, Althaus SJ, et al: Percutaneous CT-guided catheter drainage of infected acute necrotizing pancreatitis: techniques and results, *Am J Roentgenol* 170:969–975, 1998.

Horvath K, Freeny P, Escallon J, et al: Safety and efficacy of video-assisted retroperitoneal debridement for infected pancreatic collections: a multicenter, prospective, single arm phase 2 study, *Arch Surg* 145:817–825, 2010.

Howard TJ, Moore SA, Saxena R, et al: Pancreatic duct strictures are a common cause of recurrent pancreatitis after successful management of pancreatic necrosis, *Surgery* 136:909–916, 2004.

Kozarek RA, Call TJ, Patterson DJ, et al: Endoscopic transpapillary therapy for disrupted pancreatic duct and peripancreatic fluid collections, *Gastroenterology* 100:1362–1370, 1991.

Nealon WH, Bhutani M, Riall TS, et al: A unifying concept: pancreatic ductal anatomy both predicts and determines the major complications resulting from pancreatitis, *J Am Coll Surg* 208:790–801, 2009.

Nealon WH, Walser E: Main pancreatic ductal anatomy can direct choice of modality for treating pancreatic pseudocysts (surgery versus percutaneous drainage), *Ann Surg* 235:751–758, 2002.

Uhl W, Warshaw A, Imrie C, et al: IAP guidelines for the surgical management of acute pancreatitis, *Pancreatology* 2:565–573, 2002.

van Santvoort HC, Besselink MG, Bakker OJ, et al: A step-up approach or open necrosectomy for necrotizing pancreatitis, *N Engl J Med* 362:1491–1502, 2010.

Warshaw AI, Rattner DW: Timing of surgical drainage of pancreatic pseudocyst, clinical and chemical criteria, *Ann Surg* 202:720–724, 1985.