Management of acute pancreatitis

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INTRODUCTION

Acute pancreatitis is an acute inflammatory process of the pancreas. Overall mortality rates in acute pancreatitis are approximately 2 percent, but can be as high as 30 percent in patients with persistent organ failure (severe acute pancreatitis) [1].

This topic reviews the management of acute pancreatitis. Our recommendations are largely consistent with the American Gastroenterological Association, the American College of Gastroenterology, and the International Association of Pancreatology/American Pancreatic Association guidelines for the treatment of acute pancreatitis [2-5]. The etiology, clinical manifestations, diagnosis, and assessment of severity of acute pancreatitis are discussed separately. (See "Etiology of acute pancreatitis" and "Clinical manifestations and diagnosis of acute pancreatitis" and "Predicting the severity of acute pancreatitis".)

CLASSIFICATION

According to the Atlanta classification, acute pancreatitis can be divided into two broad categories [6]:

- Interstitial edematous acute pancreatitis, which is characterized by acute inflammation of the pancreatic parenchyma and peripancreatic tissues, but without recognizable tissue necrosis.

- Necrotizing acute pancreatitis, which is characterized by inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis.

According to the severity, acute pancreatitis is divided into the following:

- Mild acute pancreatitis, which is characterized by the absence of organ failure and local or systemic complications.
- Moderately severe acute pancreatitis, which is characterized by no organ failure or transient organ failure (≤48 hours) and/or local complications.
- Severe acute pancreatitis, which is characterized by persistent organ failure (>48 hours) that may involve one or multiple organs.

ASSESSMENT OF DISEASE SEVERITY

At initial evaluation, the severity of acute pancreatitis should be assessed by clinical examination to assess for early fluid losses, organ failure (particularly cardiovascular, respiratory, or renal) (table 1), and systemic inflammatory response syndrome (SIRS) score (table 2) [7].

We perform the following laboratory tests to help establish the severity of acute pancreatitis and guide management. These include a complete blood count, comprehensive metabolic panel, C reactive protein (CRP), and lactate. Although measurement of serum amylase and lipase is useful for diagnosis of pancreatitis, serial measurements in patients with acute pancreatitis are not useful to predict disease severity, prognosis, or for altering management.

Routine abdominal computed tomography (CT) scan is not recommended at initial presentation in patients with acute pancreatitis unless there is diagnostic uncertainty because there is no evidence that CT improves clinical outcomes and the complete extent of pancreatic and peripancreatic necrosis may only become clear 72 to 96 hours after the onset of acute pancreatitis [2]. Several other scoring systems also exist to predict the severity of acute pancreatitis based upon clinical, laboratory, radiologic risk factors, and serum markers but can be used only 24 to 48 hours after disease onset and have not been shown to be consistently superior to assessment of SIRS or the APACHE II score. The assessment of disease severity in acute pancreatitis is discussed in detail, separately. (See "Predicting the severity of acute pancreatitis".)

Indications for monitored or intensive care — Admission to an intensive care unit setting is indicated in the following patients [2,7,8]:

- Patients with severe acute pancreatitis

- Patients with acute pancreatitis and one or more of the following parameters:
    - Pulse <40 or >150 beats/minute
    - Systolic arterial pressure <80 mmHg or mean arterial pressure <60 mmHg or diastolic arterial pressure >120 mmHg
    - Respiratory rate >35 breaths/minute
    - Serum sodium <110 mmol/L or >170 mmol/L
    - Serum potassium <2.0 mmol/L or >7.0 mmol/L
    - PaO_2 <50 mmHg
    - pH <7.1 or >7.7
    - Serum glucose >800 mg/dL
    - Serum calcium >15 mg/dL
    - Anuria
    - Coma

In patients with severe acute pancreatitis, intensive care unit monitoring and support of pulmonary, renal, circulatory, and hepatobiliary function may minimize systemic sequelae [7]. Transfer to a monitored or intensive care unit may be considered in the following patients, although it is not uncommon for these patients to be treated on the floor in centers with significant expertise in acute pancreatitis [9]:

- Persistent (>48 hours) SIRS (table 2)
- Elevated hematocrit (>44 percent), blood urea nitrogen (BUN) (>20 mg/dL), or creatinine (>1.8 mg/dL)
- Age >60 years
- Underlying cardiac or pulmonary disease, obesity

INITIAL MANAGEMENT

Initial management of a patient with acute pancreatitis consists of supportive care with fluid resuscitation, pain control, and nutritional support.

Fluid replacement — The only effective treatment in the first 24 to 48 hours after the diagnosis of acute pancreatitis is intravenous hydration. Significant third space losses due to inflammatory collections, increased permeability of vasculature resulting in transudation of fluid from intravascular to extravascular compartment, nausea and vomiting and inability to ingest adequate amounts of fluids, lead to increases in hematocrit, blood urea nitrogen and creatinine, possible development of necrotizing (pancreatic and/or peripancreatic necrosis)

pancreatitis and acute kidney injury. Retrospective studies revealed that in the initial stages (within the first 12 to 24 hours) of acute pancreatitis, fluid replacement has been associated with a reduction in morbidity and mortality [2,10-12]. Persistent hemoconcentration at 24 hours has been associated with development of necrotizing pancreatitis [13]. Necrotizing pancreatitis results in vascular leak syndrome leading to increased third space fluid losses and worsening of pancreatic hypoperfusion [14].

Despite numerous studies that have evaluated intravenous hydration, the timing, the rate, the type of fluid, the duration of treatment, and the appropriate goal to direct such intravenous hydration is unclear [15]. While previous guidelines have recommended 250 to 500 mL/hour of normal saline during the first 24 to 48 hours (5 to 10 mL per kilogram of body weight per hour), evidence from randomized controlled trials suggest that a lower volume may be used in patients with mild acute pancreatitis [1,2,16,17]. In a randomized trial, 249 patients with acute pancreatitis were randomly assigned to aggressive fluid resuscitation (lactated Ringer's solution bolus of 20 mL/kg followed by 3 mL/kg/hour) versus moderate resuscitation (1.5 mL/kg/hour with a 10 mL/kg bolus only in patients with hypovolemia) [17]. In both groups, initial physical assessment was performed at three hours to evaluate for fluid overload, and goal-directed resuscitation was adjusted 12, 24, 48, and 72 hours based on volume status. Although there was no difference in the incidence of moderately severe or severe pancreatitis or duration of hospitalization between the two groups, the trial was terminated early due to higher rates of fluid overload in the aggressive resuscitation group (20 versus 6 percent).

We use moderate intravenous hydration (1.5 mL/kg/hour with a 10 mL/kg bolus in patients with hypovolemia) with goal-directed therapy for fluid management [3,5]. Fluid requirements are reassessed at frequent intervals in the first six hours of admission and for the next 24 to 48 hours. This is particularly important in older adults and those with a history of cardiac and/or renal disease [5]. The rate of fluid resuscitation is adjusted based on clinical assessment, hematocrit, blood urea nitrogen (BUN), and creatinine values [18]. Adequate fluid replacement can be assessed by an improvement in vital signs (goal heart rate <120 beats/minute, mean arterial pressure between 65 to 85 mmHg), urine output (>0.5 to 1 cc/kg/hour) and reduction in hematocrit (goal 35 to 44 percent) and BUN over 24 hours, particularly if they were high at the onset [2,19]. Monitoring the BUN may be particularly important, as both the BUN at the time of admission and the change in BUN during the first 24 hours of hospitalization predict mortality [20]. Increased fluid resuscitation should be considered in patients whose BUN levels stay the same or increase. It is important to note that a low urine output may reflect the development of acute tubular necrosis rather than persistent volume depletion. In this setting, aggressive fluid replacement can lead to peripheral and pulmonary edema without improving the urine output.

(See "Etiology and diagnosis of prerenal disease and acute tubular necrosis in acute kidney injury in adults".)

Fluid resuscitation with lactated Ringer's solution can reduce the incidence of systemic inflammatory response syndrome (SIRS) as compared with normal saline [5,18,21-23]. Use of lactated Ringer's solution in patients with acute pancreatitis may reduce hospital stay and intensive care unit admissions, however, further studies are needed [23]. In rare patients with acute pancreatitis due to hypercalcemia, lactated Ringer's is contraindicated because it contains 3 mEq/L calcium. In these patients, normal saline should be used for volume resuscitation. Several other approaches to fluid replacement have also been reported in patients with acute pancreatitis [24,25]. The use of hydroxyethyl starch containing fluids should be avoided given the absence of demonstrable mortality benefit and possible risk of multiple organ failure [3,26]. (See "Intraoperative fluid management", section on 'Hydroxyethyl starches'.)

Fluid resuscitation is important in the first 24 to 48 hours after onset of the disease. Continued aggressive fluid resuscitation after 48 hours may not be advisable as overly vigorous fluid resuscitation is associated with an increased need for intubation and increased risk of abdominal compartment syndrome.

Pain control — Abdominal pain is often the predominant symptom in patients with acute pancreatitis and should be treated with analgesics. Uncontrolled pain can contribute to the hemodynamic instability.

- Attention to adequate fluid resuscitation should be the first priority in addressing abdominal pain, as hypovolemia from vascular leak and hemoconcentration can cause ischemic pain and resultant lactic acidosis. (See 'Fluid replacement' above.)

- Opioids are safe and effective at providing pain control in patients with acute pancreatitis [27]. Adequate pain control requires the use of intravenous opiates, usually in the form of a patient-controlled analgesia pump. Hydromorphone or fentanyl (intravenous) may be used for pain relief in acute pancreatitis. Fentanyl is being increasingly used due to its better safety profile, especially in renal impairment. As with other opiates, fentanyl can depress respiratory function. It can be given both as a bolus as well as constant infusion. The typical dose for the bolus regimen ranges from 20 to 50 micrograms with a 10-minute lock-out period (time from the end of one dose infusion to the time the machine starts responding to another demand). Patients on patient-controlled analgesia should be carefully monitored for side effects. (See "Pain control in the critically ill adult patient".)

  Meperidine was favored in the past over morphine for analgesia in pancreatitis because studies showed that morphine caused an increase in sphincter of Oddi pressure. However,

there are no clinical studies to suggest that morphine can aggravate or cause pancreatitis or cholecystitis [28]. In addition, meperidine has a short half-life and repeated doses can lead to accumulation of the metabolite normeperidine that causes neuromuscular side effects and, rarely, seizures.

Monitoring — Patients with acute pancreatitis should be monitored closely in the first 24 to 48 hours. Patients with organ failure will need ongoing monitoring for other complications that might arise. (See 'Management of complications' below.)

- Vital signs including oxygen saturation should be monitored and supplemental oxygen administered to maintain arterial oxygen saturation of greater than 95 percent. Blood gas analysis should be performed if oxygen saturation is less than 90 percent or if the clinical situation demands. Hypoxia may be due to splinting, atelectasis, pleural effusions, opening of intrapulmonary shunts, or acute respiratory distress syndrome (ARDS). Patients with persistent or progressive hypoxia should be transferred to an intensive care unit (ICU) for respiratory support. (See "Acute respiratory distress syndrome: Clinical features, diagnosis, and complications in adults" and "Acute respiratory distress syndrome: Fluid management, pharmacotherapy, and supportive care in adults" and 'Indications for monitored or intensive care' above.)

- Urine output should be measured hourly and fluids should be titrated to maintain urine output (>0.5 to 1 cc/kg/hour) [2]. (See 'Fluid replacement' above.)

- Electrolytes should be monitored frequently in the first 48 to 72 hours and especially with aggressive fluid resuscitation. Hypocalcemia should be corrected if ionized calcium is low or if there are signs of neuromuscular irritability (Chvostek's or Trousseau's sign). Low magnesium levels can also cause hypocalcemia and should be corrected. (See "Treatment of hypocalcemia", section on 'Intravenous calcium dosing'.)

- Serum glucose levels should be monitored hourly in patients with severe pancreatitis and hyperglycemia (blood glucose greater than 180 to 200 mg/dL) should be treated as it can increase the risk of secondary pancreatic infections. Hyperglycemia may result from parenteral nutritional therapy, decreased insulin release, increased gluconeogenesis, and decreased glucose utilization. The management of hyperglycemia is discussed in detail, separately. (See "Glycemic control in critically ill adult and pediatric patients", section on 'Our approach'.)

- Patients in the intensive care unit should be monitored for potential abdominal compartment syndrome with serial measures of urinary bladder pressures [29]. (See 'Abdominal compartment syndrome' below.)

Nutrition — Patients with mild pancreatitis can often be managed with intravenous hydration alone since recovery occurs rapidly, allowing patients to resume an oral diet as soon as possible, if there is no significant nausea and/or vomiting or paralytic ileus. Oral feeding is favored in order to maintain the gut mucosal integrity. Nutritional support is often required in patients with moderately severe pancreatitis if they are unlikely to resume oral intake within five to seven days. Nasojejunal tube feeding (using an elemental or semi-elemental formula) is preferred to total parenteral nutrition (TPN).

Oral — The time to reinitiate oral feedings depends on the severity of the pancreatitis. (See 'Assessment of disease severity' above.)

- In the absence of ileus, nausea or vomiting, oral feeding can be initiated early (within 24 hours) as tolerated, if the pain is decreasing and inflammatory markers are improving [2-4]. We usually start with a low residue, low fat, soft diet, provided there is no evidence of ileus or significant nausea and/or vomiting. We then advance the diet cautiously as tolerated. Traditionally, patients have been advanced from a clear liquid diet to solid food as tolerated. Early refeeding with a solid, low fat diet when patients are subjectively hungry, regardless of resolution of abdominal pain and normalization of pancreatic enzymes, may be safe [30-34].

- In some patients with moderately severe to severe pancreatitis, oral feeding may not be tolerated due to postprandial pain, nausea or vomiting related to gastroduodenal inflammation and/or extrinsic compression from fluid collections leading to gastric outlet obstruction. Such patients require enteral feeding, if they cannot tolerate oral diet by day five [3]. However, when the local complications start improving, oral feeds can be initiated and advanced as tolerated. (See 'Enteral' below.)

In a systematic review of 11 randomized trials that included 948 patients with acute pancreatitis, early refeeding (≤48 after hospitalization), as compared with delayed refeeding, did not increase adverse effects or exacerbate symptoms [35]. In four of seven trials that included patients with mild to moderate pancreatitis, early refeeding was associated with a reduction in length of hospital stay. However, there was significant heterogeneity in feeding protocols and reported outcomes across studies and a high risk of bias in several studies included in the systematic review. Additional randomized trials are needed to define the benefits of early refeeding in patients with acute pancreatitis [36]. However, a multicenter trial comparing enteral nutrition in the first 24 hours with enteral feeding after 72 hours in patients with predicted severe acute pancreatitis did not find any improved clinical outcomes with early enteral feeding [37]. Early refeeding may decrease length of stay and costs without increasing adverse events in mild to moderate AP. [38].

Enteral — Enteral feeding rather than parenteral nutrition is recommended in patients with moderately severe and severe acute pancreatitis who cannot tolerate oral feeding [2,4,16,39,40]. In patients with predicted severe or necrotizing pancreatitis requiring enteral tube feeding, either nasogastric or naso-enteral route may be used. We also initiate enteral feeding when it becomes clear that the patient will not be able to consume nourishment by mouth (eg, transfer to an intensive care unit, development of organ failure, or SIRS persisting for 48 hours). This assessment can usually be made by the fifth day of the illness. (See "Nutrition support in intubated critically ill adult patients: Enteral nutrition".)

Enteral feeding via a nasojejunal route requires radiologic or endoscopic placement of a jejunal feeding tube beyond the ligament of Treitz [3]. Two controlled trials comparing nasogastric with nasojejunal feedings found no significant differences in APACHE II scores, CRP levels, pain, or analgesic requirements [41-43]. However, another small study comparing nasogastric feeding with TPN noted increased pulmonary and total complications in the nasogastric group [44].

We start enteral feeds with a polymeric formulation at 25 cc per hour and advance as tolerated to at least 30 percent of the calculated daily requirement (25 kcal/kg ideal body weight), even in the presence of ileus [45]. Signs that the formula is not tolerated include increased abdominal pain, vomiting (with nasogastric feeding), bloating, or diarrhea (>5 watery stools or >500 mL per 24 hours with exclusion of *Clostridioides* [formerly *Clostridium*] *difficile* toxin and medication-induced diarrhea) that resolves if the feeding is held.

Enteral nutrition helps maintain the intestinal barrier and prevents bacterial translocation from the gut. Another advantage of enteral nutrition is the avoidance of the complications associated with parenteral nutrition including those secondary to venous access and blood stream infections. Consistent with prior meta-analyses, a 2010 meta-analysis of eight trials demonstrated that enteral nutrition significantly reduced mortality, multiple organ failure, systemic infections, and the need for surgery as compared with those who received parenteral nutrition [4,46-49].

The presence of fluid collections or elevated pancreatic enzymes is not necessarily a contraindication to enteral feeding. However, in a subgroup of patients there is clear correlation of pain, recurrence of pancreatitis, or worsening of fluid collections with feeding. These patients often have disrupted pancreatic ducts with fluid collections. Drainage of fluid collections may allow resumption of oral intake. The diagnosis and management of pancreatic duct disruptions is discussed in detail, separately. (See "Pancreatic stenting at endoscopic retrograde cholangiopancreatography (ERCP): Indications, techniques, and complications", section on 'Pancreatic duct leakage'.)

Parenteral — Parenteral nutrition should be initiated only in patients who do not tolerate enteral feeding or if the target rate of enteral feeding is not achieved within 48 to 72 hours, as the use of parenteral nutrition as an adjunct to enteral feeding may be harmful [50,51].

- An observational study that included 2920 mechanically ventilated, critically ill adults compared 60-day mortality in patients who received enteral nutrition alone, enteral nutrition plus early parenteral nutrition, and enteral nutrition plus late parenteral nutrition [51]. Enteral nutrition plus either early or late parenteral nutrition was associated with increased mortality as compared with enteral nutrition alone (35 versus 28 percent).

- In a randomized trial, 4640 critically ill adults receiving enteral nutrition were assigned to supplemental parenteral nutrition initiated early (within 48 hours of ICU admission) or late (after the eighth day of ICU admission) [50]. Compared with the early-initiation group, patients in the late-initiation group had lower rates of ICU infections (23 versus 26 percent), and fewer mechanical ventilation and renal replacement therapy days (relative risk reduction 10 percent). (See "Nutrition support in intubated critically ill adult patients: Initial evaluation and prescription", section on 'Early parenteral nutrition'.)

Antibiotics — Up to 20 percent of patients with acute pancreatitis develop an extrapancreatic infection (eg, bloodstream infections, pneumonia, and urinary tract infections) [52]. Extrapancreatic infections are associated with an increase in mortality [53]. When an infection is suspected, antibiotics should be started while the source of the infection is being determined. However, if cultures are negative and no source of infection is identified, antibiotics should be discontinued.

Prophylactic antibiotics and selective decontamination of the gut are not recommended in patients with acute pancreatitis, regardless of the type (interstitial or necrotizing) or disease severity (mild, moderately severe, or severe) [3,4,16]. The use of antibiotics in patients with suspected infected pancreatic necrosis is discussed separately. (See 'Classification' above and 'Acute necrotic collection and walled-off necrosis' below.)

Other therapies with no role

- Pentoxifylline – Studies are needed to determine the role of pentoxifylline, a nonselective phosphodiesterase inhibitor, in the treatment of acute pancreatitis. In a randomized trial, 28 patients with predicted severe acute pancreatitis were assigned to pentoxifylline or placebo within 72 hours of diagnosis for 72 hours thereafter or until discharge [54]. Patients treated with pentoxifylline had fewer ICU admissions and hospital stays longer than four days as compared with placebo (zero versus four and two versus eight, respectively). However, there were no significant differences in the levels of inflammatory

markers, including circulating tumor necrosis factor-alpha levels, between the two groups. Of note, 102 of the 132 (77 percent) patients approached to enter the study declined to participate.

- **Antifungals** – Administration of prophylactic antifungal therapy (eg, fluconazole) along with prophylactic or therapeutic antibiotics is not recommended [4,16]. Fungal organisms have become increasingly isolated in infected pancreatic necrosis. Studies have reported infection rates of up to 30 percent in primary (without any intervention) and secondary (after intervention of fluid collections) infections in pancreatic necrosis [55]. However, it is not clear if they are associated with higher mortality [56].

- **Protease inhibitors** – The role of protease inhibitors in the treatment of acute pancreatitis remains unclear as evidence from clinical trials and a meta-analysis demonstrated only marginal reduction in mortality in patients with severe pancreatitis. Intra-arterial administration is another disadvantage [57-61].

MANAGEMENT OF COMPLICATIONS

Patients with predicted or established moderately severe or severe acute pancreatitis, signs of sepsis, or clinical deterioration 72 hours after initial presentation should undergo a contrast-enhanced computed tomography scan to assess the presence of pancreatic or extrapancreatic necrosis and local complications. Patients with persistent organ failure and extensive local complications should be transferred to centers of expertise [9]. (See 'Classification' above.)

Local complications — Local complications of acute pancreatitis include acute peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection, and walled-off necrosis (table 3) [6]. While acute peripancreatic fluid collections and acute necrotic collections may develop less than four weeks after the onset of pancreatitis, pancreatic pseudocyst and walled-off necrosis usually occur more than four weeks after the onset of acute pancreatitis.

Acute peripancreatic fluid collection — Fluid collections usually develop in the early phase of pancreatitis. Acute peripancreatic fluid collections (APFC) do not have a well-defined wall, usually remain asymptomatic, and usually resolve spontaneously without the need for drainage (image 1). In a longitudinal study of patients with interstitial pancreatitis, most acute fluid collections resolved within 7 to 10 days, with only 6.8 percent of APFCs persisting beyond four weeks as pancreatic pseudocysts [62].

Pancreatic pseudocyst — A pancreatic pseudocyst is an encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis

(image 2). Pancreatic pseudocysts usually occur more than four weeks after the onset of interstitial edematous pancreatitis. The management of pancreatic pseudocysts is discussed in detail, separately. (See "Approach to walled-off pancreatic fluid collections in adults".)

Acute necrotic collection and walled-off necrosis — Necrotizing pancreatitis most commonly manifests as necrosis involving both the pancreas and peripancreatic tissues. Necrosis may result in an acute necrotic collection (ANC) that contains a variable amount of fluid and necrosis but lacks a definable wall (image 3) or walled-off necrosis (WON), which consists of a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis that has developed a well-defined inflammatory wall. Both ANC and WON are initially sterile but may become infected. The management of walled-off pancreatic fluid collections is discussed in detail, separately. (See "Approach to walled-off pancreatic fluid collections in adults".)

- **Infected necrosis** – The occurrence of pancreatic infection is a leading cause of morbidity and mortality in acute necrotizing pancreatitis (image 4). Approximately one-third of patients with pancreatic necrosis develop infected necrosis [40]. There is no correlation between the extent of necrosis and the risk of infection. Although infection can occur early in the course of necrotizing pancreatitis, it is more often seen late in the clinical course (after 10 days) [63,64]. The majority of infections (approximately 75 percent) are monomicrobial with gut-derived organisms (eg, *Escherichia coli, Pseudomonas, Klebsiella,* and *Enterococcus)*. However, the incidence of gram-positive, multidrug resistant and fungal organisms in infected pancreatic necrosis is rising.

  Infected necrosis (image 4) should be suspected in patients with pancreatic or extrapancreatic necrosis who deteriorate (clinical instability or sepsis physiology, increasing white blood cell count, fevers) or fail to improve after 7 to 10 days of hospitalization. Clinical signs of infection and abdominal imaging demonstrating the presence of gas within the necrosis are reasonably suggestive of infection and antibiotic therapy can be initiated without aspiration and culture [2,5,16]. If empiric antibiotics are initiated, antibiotics known to penetrate pancreatic necrosis (eg, a carbapenem alone; or a quinolone, ceftazidime, or cefepime combined with an anaerobic agent such as metronidazole) should be used.

  In patients who fail to improve in 48 to 72 hours or those who have clinical deterioration, we perform drainage or debridement of pancreatic necrosis (necrosectomy) [59,63]. The role of fine-needle CT-guided aspiration cytology of necrosis is very limited. CT-guided aspiration may be considered in the patients who fail to improve in order to guide antibiotic treatment, before drainage or debridement.

In stable patients with infected necrosis, we attempt to delay drainage/necrosectomy by continuing antibiotics for at least four weeks [5]. Continued conservative management of necrotic fluid collection allows a minimally invasive debridement to be performed at a later date to clear necrotic debris [65-68]. In addition, some patients with infected necrosis clinically improve to an extent that no intervention is necessary. Interim percutaneous drainage may be needed in patients with infected necrosis who exhibit clinical deterioration or fail to improve, but do not have a walled-off necrotic collection. However, routine immediate drainage once infected necrosis is diagnosed does not improve outcomes. This was demonstrated in a multicenter, randomized trial in which 104 patients were randomly assigned to immediate drainage (55 patients) or postponed drainage (49 patients) when necrotic collections were largely walled-off, but there was either clinical deterioration or lack of improvement [69]. There was no difference in the rate of complications or mortality between the two groups, however, the mean number of interventions (catheter drainage and necrosectomy) was higher in the immediate drainage group as compared with the postponed drainage group (4.4 versus 2.6 mean difference, 1.8; 95% CI 0.6-3.0). Thirty-nine percent of infected necrosis improved just with antibiotics without the need for any other intervention. Necrosectomy should be accomplished initially by a minimally invasive approach (endoscopic or percutaneous radiologic). Open or laparoscopic surgical necrosectomy is rarely required [2,70-72]. Step-up approach of drainage first and debridement later, if required, has become a common practice in patients requiring intervention [71]. However, a multicenter, randomized controlled trial in patients with infected pancreatic necrosis demonstrated safety as well as reduced number of interventions with upfront necrosectomy compared to step-up approach [73]. The technique, efficacy, and complications associated with percutaneous, endoscopic, and surgical necrosectomy are discussed in detail, separately. (See "Approach to walled-off pancreatic fluid collections in adults", section on 'Percutaneous drainage' and "Endoscopic interventions for walled-off pancreatic fluid collections" and "Pancreatic debridement".)

- **Sterile necrosis** – If the aspirated material on CT-guided FNA is sterile, we discontinue antibiotics and continue conservative treatment for four to six weeks. The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended. Sterile necrosis does not require therapy.

  Indications for intervention (radiological, endoscopic, or other minimally invasive) in a patient with sterile necrosis with no signs of an infection (eg, fever, hypotension, leukocytosis) include [2,39]:

- Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect at least four weeks after onset of acute pancreatitis.
- Persistent symptoms (eg, abdominal pain, nausea, vomiting, anorexia or weight loss) >8 weeks after the onset of acute pancreatitis.
- Disconnected duct syndrome (full transection of the pancreatic duct) with persisting symptomatic collections with necrosis (eg, pain, obstruction) >4 weeks after the onset of acute pancreatitis.

Peripancreatic vascular complications

Splanchnic venous thrombosis — Splanchnic vein thrombosis (splenic, portal, and/or superior mesenteric veins) is incidentally found on imaging in 1 to 24 percent of patients with acute pancreatitis, depending on the disease severity and the imaging modality [74,75].

Treatment should focus on the underlying pancreatitis as effective treatment may result in spontaneous resolution of the thrombosis. Despite the theoretical possibility of hemorrhage into pancreatic necrosis or fluid collections, anticoagulation should be initiated if there is extension of the clot into the portal or superior mesenteric vein resulting in hepatic decompensation or compromise of bowel perfusion. This complication is more common in necrotizing pancreatitis compared to interstitial pancreatitis. If splenic vein thrombosis is established (usually a few weeks after the diagnosis of acute pancreatitis with collateral formation), the role of anticoagulation is uncertain.

In contrast with patients who have splanchnic vein thrombosis due to chronic pancreatitis, complications such as variceal bleeding are rare and therefore prophylactic splenectomy is not recommended [76]. (See "Acute portal vein thrombosis in adults: Clinical manifestations, diagnosis, and management", section on 'Management'.)

Pseudoaneurysm — Pseudoaneurysms are a rare but serious complication of acute pancreatitis that should be suspected when patients with acute pancreatitis have unexplained gastrointestinal bleeding, an unexplained drop in hematocrit, or sudden expansion of a pancreatic fluid collection. The diagnosis and management of pancreatic pseudoaneurysms are discussed separately.

Abdominal compartment syndrome — Abdominal compartment syndrome is defined as sustained intra-abdominal pressure >20 mmHg with new onset organ failure [2]. Patients with severe pancreatitis are at increased risk for intra-abdominal hypertension and abdominal compartment syndrome due to tissue edema from aggressive fluid resuscitation, peripancreatic inflammation, ascites, and ileus [77]. Patients in the intensive care unit should be monitored for potential abdominal compartment syndrome with serial measures of urinary bladder pressures

[29]. The clinical presentation, diagnosis, and management of abdominal compartment syndrome are discussed in detail, separately. (See "Abdominal compartment syndrome in adults", section on 'Clinical presentation'.)

Systemic complications — Patients with acute pancreatitis are at increased risk for exacerbation of underlying comorbidities (eg, coronary artery disease, chronic lung disease). In addition to treating these exacerbations, patients should be treated for other complications including alcohol withdrawal and hyperglycemia.

Patients with acute pancreatitis are also at an increased risk of developing prediabetes and diabetes after their first episode of acute pancreatitis [78]. In a 2014 meta-analysis of 24 prospective studies that included 1102 patients with a first episode of acute pancreatitis, 15 percent of individuals were diagnosed with new onset of diabetes mellitus within 12 months. The risk of diabetes significantly increased five years after the first episode of acute pancreatitis (RR 2.7, 95% CI 1.9-3.8). (See "Management of moderate and severe alcohol withdrawal syndromes" and "Glycemic control in critically ill adult and pediatric patients", section on 'Our approach'.)

MANAGEMENT OF UNDERLYING PREDISPOSING CONDITIONS

In addition to treating pancreatic inflammation and its associated complications in patients with acute pancreatitis, it is important to address the underlying predisposing factors. For example, drugs associated with acute pancreatitis should be discontinued. (See "Etiology of acute pancreatitis", section on 'Medications' and "Unique aspects of gastrointestinal disease in patients on dialysis", section on 'Acute pancreatitis'.)

Gallstone pancreatitis — In patients with gallstone pancreatitis, most stones pass into the duodenum. However, in a small proportion of patients, obstructive stones in the biliary tract or ampulla of Vater can cause persistent biliary and pancreatic duct obstruction leading to acute pancreatitis and cholangitis. (See "Etiology of acute pancreatitis" and "Clinical manifestations and diagnosis of acute pancreatitis".)

Endoscopic retrograde cholangiopancreatography — Endoscopic retrograde cholangiopancreatography (ERCP) should be performed early in the course (within 24 hours of admission) for patients with gallstone pancreatitis and cholangitis [5]. Non-urgent indications for ERCP include patients with common bile duct obstruction (visible stone on imaging), dilated common bile duct, or increasing liver tests without cholangitis and prior to elective cholecystectomy (if suspicion of stone in the common bile duct is high) [5].

In the absence of common bile duct obstruction, ERCP is not indicated for (mild or severe) gallstone pancreatitis without cholangitis. When in doubt about bile duct obstruction in the absence of cholangitis, liver tests can be rechecked in 24 to 48 hours to determine if they improve or a magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS) could be performed to determine if there are stones in the common bile duct.

- **Indications for EUS/MRCP prior to ERCP** – EUS or MRCP should be performed to determine the need for ERCP in the following patients:

  - Persistent elevation of liver tests and/or dilation of common bile duct without overt cholangitis
  - Pregnant patients
  - Altered anatomy that would make an ERCP technically challenging

  In patients who are found to have stones on EUS or MRCP, ERCP with sphincterotomy and stone extraction is necessary and will prevent future attacks of biliary pancreatitis. However, in the absence of a cholecystectomy, these patients remain at risk for acute cholecystitis, biliary colic, and gallbladder complications of cholelithiasis.

In patients with acute cholangitis and persistent obstruction, urgent (preferably <24 hours) ERCP with papillotomy or surgical intervention to remove bile duct stones may lessen the severity of gallstone pancreatitis [2,79-82].

In patients with gallstone pancreatitis and persistent obstruction **without** cholangitis, urgent ERCP (within 24 hours) is not indicated [3,4,83,84]. In such patients, therapeutic ERCP can be performed either before the cholecystectomy, if there is a strong suspicion of stone in the bile duct, or postoperatively, if intra-operative cholangiogram demonstrates a stone [2,3]. In a systematic review of eight randomized trials, early ERCP in patients without cholangitis did not lead to a significant reduction in the risk of overall pancreatic complications, single organ failure or mortality [4]. However, one trial demonstrated a reduction in the length of hospital stay with urgent ERCP.

Cholecystectomy — Cholecystectomy should be performed after recovery in all patients with gallstone pancreatitis including those who have undergone an endoscopic sphincterotomy to reduce the risk of recurrent pancreatitis [85]. In patients who have had mild, interstitial pancreatitis, cholecystectomy can usually be performed safely in the same index hospitalization [5,86,87]. A randomized controlled trial demonstrated a reduction in composite outcome of mortality and biliary complications and readmissions due to attacks of acute pancreatitis [88].

In those patients initially diagnosed as interstitial acute biliary pancreatitis and undergoing same admission cholecystectomy, a high white count or presence of SIRS indicates evolving necrotizing pancreatitis and cholecystectomy in those patients resulted in higher incidence of organ failure and infected necrosis [89]. Interval cholecystectomy (within eight weeks) is advised in necrotizing pancreatitis when inflammation and fluid collections resolve or subside to a great extent [90].

Failure to perform a cholecystectomy is associated with a 25 to 30 percent risk of recurrent acute pancreatitis, cholecystitis, or cholangitis within 6 to 18 weeks [91]. The risk of recurrent pancreatitis is highest in patients who have not undergone a sphincterotomy. (See "Endoscopic management of bile duct stones", section on 'ERCP-guided stone removal'.)

If the clinical suspicion of common bile duct stones is high (eg, CBD stone on transabdominal ultrasound or cross-sectional imaging, acute cholangitis, or serum bilirubin greater than 4 mg/dL (68 micromol/L) **and** a dilated CBD on ultrasound), a preoperative ERCP is the best test as there is a high likelihood that therapeutic intervention (sphincterotomy, stone extraction) will be required. Patients at intermediate risk of a CBD stone (age >55 years, abnormal liver biochemical tests or dilated CBD on ultrasound or other imaging) should undergo MRCP or EUS to look for choledocholithiasis and, if present, a preoperative ERCP, sphincterotomy and stone extraction. Intraoperative cholangiography or ultrasound is also an alternative [92]. (See "Choledocholithiasis: Clinical manifestations, diagnosis, and management", section on 'Subsequent evaluation and management'.)

Biliary sludge — Most patients with biliary sludge are asymptomatic. However, biliary sludge is not uncommon in patients with acute pancreatitis with no other obvious cause. On ultrasound, sludge appears as a mobile, low-amplitude echo that layers in the most dependent part of the gallbladder and is not associated with shadowing. However, ultrasound has a low sensitivity for biliary sludge. If the cause is not clear, we perform EUS, even after one attack, to look for microlithiasis in the gallbladder or bile duct. In a randomized trial, 85 patients, after their first attack of idiopathic acute pancreatitis, were assigned to laparoscopic cholecystectomy or conservative watchful waiting [93]. During a median follow-up of 36 months, significantly fewer patients who had undergone laparoscopic cholecystectomy had recurrent idiopathic acute pancreatitis as compared with controls (10 versus 30 percent). A total of five patients needed to be treated to prevent one episode of what was thought to be idiopathic acute pancreatitis. However, EUS was not performed to detect small gallstones or biliary sludge. Biliary stones or sludge were detected during surgery in 23 of 39 patients (59 percent) who underwent cholecystectomy. (See "Etiology of acute pancreatitis", section on 'Approach to establishing the

underlying etiology' and "Etiology of acute pancreatitis", section on 'Biliary sludge and microlithiasis'.)

Hypertriglyceridemia — The treatment of hypertriglyceridemic pancreatitis is discussed separately. (See "Hypertriglyceridemia-induced acute pancreatitis".)

Hypercalcemia — Hypercalcemia is a rare cause of acute pancreatitis. If present, treatment should be directed at normalizing serum calcium levels and determining the underlying etiology. (See "Etiology of hypercalcemia" and "Diagnostic approach to hypercalcemia" and "Treatment of hypercalcemia" and "Etiology of acute pancreatitis", section on 'Hypercalcemia'.)

Alcoholic pancreatitis — Patients with alcoholic pancreatitis should receive brief alcohol intervention as inpatients for unhealthy alcohol use [3]. (See "Brief intervention for unhealthy alcohol and other drug use: Goals and components" and "Brief intervention for unhealthy alcohol and other drug use: Efficacy, adverse effects, and administration".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute pancreatitis".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5^{th} to 6^{th} grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10^{th} to 12^{th} grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Acute pancreatitis (The Basics)")
- Beyond the Basics topics (see "Patient education: Acute pancreatitis (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Classification of acute pancreatitis** – Acute pancreatitis is an acute inflammatory process of the pancreas. Acute pancreatitis can be divided into two broad categories: edematous, interstitial acute pancreatitis and necrotizing acute pancreatitis. Mild acute pancreatitis is characterized by the absence of organ failure and local or systemic complications. Moderately severe acute pancreatitis is characterized by no organ failure or transient organ failure (<48 hours) and/or local complications. Severe acute pancreatitis is characterized by persistent organ failure (>48 hours) that may involve one or multiple organs. (See 'Classification' above.)

- **Initial evaluation** – At initial evaluation, the severity of acute pancreatitis should be assessed by clinical examination to assess for early fluid losses, organ failure (table 1), and systemic inflammatory response syndrome (SIRS) score. Routine abdominal computed tomography (CT) scan is not recommended at initial presentation in patients with acute pancreatitis unless there is uncertainty about the diagnosis. (See 'Assessment of disease severity' above and "Predicting the severity of acute pancreatitis".)

- **Indication for monitored or intensive care unit** – Admission to a monitored or intensive care unit is indicated in patients with severe acute pancreatitis and in patients with acute pancreatitis who meet one or more of the following parameters (see 'Indications for monitored or intensive care' above):

  - Pulse <40 or >150 beats/minute
  - Systolic arterial pressure <80 mmHg or mean arterial pressure <60 mmHg or diastolic arterial pressure >120 mmHg
  - Respiratory rate >35 breaths/minute
  - Serum sodium <110 mmol/L or >170 mmol/L, serum potassium <2.0 mmol/L or >7.0 mmol/L, serum glucose >800 mg/dL, serum calcium >15 mg/dL
  - PaO_2 <50 mmHg
  - pH <7.1 or >7.7
  - Anuria
  - Coma

- **Fluid replacement** – Acute pancreatitis is treated with supportive care including pain control, goal-directed intravenous fluids especially during the first 24 hours, and correction of electrolyte and metabolic abnormalities. The majority of patients with mild pancreatitis require no further therapy, and recover within three to seven days. Patients

with moderately severe and severe pancreatitis require more intensive monitoring as they have transient (<48 hours) or persistent (>48 hours) organ failure and local or systemic complications.

- **Pain control** – Abdominal pain is often the predominant symptom in patients with acute pancreatitis. Adequate pain control requires the use of intravenous opiates, such as hydromorphine and fentanyl, usually in the form of a patient-controlled analgesia pump. (See 'Pain control' above.)

- **Nutrition** – In patients with mild pancreatitis, recovery generally occurs quickly, making it unnecessary to initiate supplemental nutrition. A soft diet can be started early (within 24 hours) as tolerated. We usually start with a low-residue, low-fat, and soft diet, provided there is no evidence of ileus or significant nausea and/or vomiting.

  In patients with moderately severe and severe pancreatitis, we recommend enteral nutrition through a nasojejunal tube placed endoscopically or radiologically rather than initiating parenteral nutrition (**Grade 1B**). If the target rate is not achieved within 48 to 72 hours and if severe acute pancreatitis is not resolved, supplemental parenteral nutrition should be provided. (See 'Oral' above and 'Enteral' above and 'Parenteral' above.)

- **Indications for follow-up imaging** – Patients with moderately severe or severe acute pancreatitis, signs of sepsis, or clinical deterioration 72 hours after initial presentation, should undergo a contrast-enhanced CT scan to assess the presence of pancreatic or extrapancreatic necrosis and local complications. Patients with persistent organ failure and extensive local complications should be transferred to centers of expertise. (See 'Management of complications' above.)

- **Complications of acute pancreatitis** – Patients with pancreatitis may develop local or systemic complications. Local complications of acute pancreatitis include acute peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection (ANC), and walled-off necrosis (WON) (table 3). While acute peripancreatic fluid collections and acute necrotic collections may develop less than four weeks after the onset of pancreatitis, pancreatic pseudocyst and walled-off necrosis usually occur more than four weeks after the onset of acute pancreatitis. (See 'Local complications' above.)

- **Patients with infected necrosis** – Both acute necrotic collection and WON are initially sterile but may become infected. The occurrence of pancreatic infection is a leading cause of morbidity and mortality in acute necrotizing pancreatitis. Infected necrosis (image 4) should be suspected in patients with pancreatic or extrapancreatic necrosis who deteriorate (clinical instability or sepsis physiology, increasing white blood cell count,

fevers) or fail to improve after 7 to 10 days of hospitalization. In patients with suspected infected necrosis, we suggest empiric antibiotics rather than CT-guided fine needle aspiration (**Grade 2C**). (See 'Acute necrotic collection and walled-off necrosis' above.)

Patients with infected necrosis who fail to respond to antibiotics or who are clinically unstable, may require pancreatic debridement. Where possible, we attempt to delay intervention until four weeks after initial presentation to allow the infected necrosis to become walled off. We perform necrosectomy with minimally invasive methods (endoscopic, percutaneous, laparoscopic) and reserve open surgical debridement if minimally invasive approaches are not possible or fail. (See 'Acute necrotic collection and walled-off necrosis' above.)

- **Patients with gallstone pancreatitis** – In patients with gallstone pancreatitis, we recommend urgent (<24 hours) endoscopic retrograde cholangiopancreatography and sphincterotomy for patients with cholangitis (**Grade 1B**). Cholecystectomy should be performed after recovery from acute pancreatitis in all operable patients with gallstone pancreatitis or biliary sludge if no other cause is found. (See 'Gallstone pancreatitis' above.)

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Topic 5633 Version 65.0

GRAPHICS

Modified Marshall scoring system for organ dysfunction

Organ system	Score				
	0	1	2	3	4
Respiratory (PaO_2/FiO_2)	>400	301-400	201-300	101-200	≤101
Renal*					
(serum creatinine, micromol/L)	≤134	134-169	170-310	311-439	>439
(serum creatinine, mg/dL)	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiovascular (systolic blood pressure, mmHg)¶	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH <7.3	<90, pH <7.2

For nonventilated patients, the FiO_2 can be estimated from below:

Supplemental oxygen (L/min)	FiO_2 (percent)
Room air	21
2	25
4	30
6-8	40
9-10	50

A score of 2 or more in any system defines the presence of organ failure.

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* A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 micromol/L or ≥1.4 mg/dL.

¶ Off inotropic support.

Graphic 87718 Version 2.0

Defining features of systemic inflammatory response syndrome (SIRS)

Two or more of the following conditions:
Temperature >38.3°C or <36.0°C
Heart rate of >90 beats/minute
Respiratory rate of >20 breaths/minute or $PaCO_2$ of <32 mmHg
WBC count of >12,000 cells/mm^3, <4000 cells/mm^3, or >10 percent immature (band) forms

WBC count: white blood cell count.

Data from: Annane D, Bellissant E, Cavaillon JM. Septic shock. Lancet 2005; 365:63.

Graphic 69207 Version 5.0

Revised definitions of morphological features of acute pancreatitis

1. Interstitial edematous pancreatitis

Acute inflammation of the pancreatic parenchyma and peripancreatic tissues, but without recognizable tissue necrosis

Contrast-enhanced computed tomography criteria:

- Pancreatic parenchyma enhancement by intravenous contrast agent
- No findings of peripancreatic necrosis

2. Necrotizing pancreatitis

Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis

Contrast-enhanced computed tomography criteria:

- Lack of pancreatic parenchymal enhancement by intravenous contrast agent, and/or
- Presence of findings of peripancreatic necrosis (refer to below–acute peripancreatic fluid collection and walled off necrosis)

3. Acute peripancreatic fluid collection (APFC)

Peripancreatic fluid associated with interstitial edematous pancreatitis with no associated peripancreatic necrosis. This term applies only to areas of peripancreatic fluid seen within the first four weeks after onset of interstitial edematous pancreatitis and without the features of a pseudocyst.

Contrast-enhanced computed tomography criteria:

- Occurs in the setting of interstitial edematous pancreatitis
- Homogeneous collection with fluid density
- Confined by normal peripancreatic fascial planes
- No definable wall encapsulating the collection
- Adjacent to pancreas (no intrapancreatic extension)

4. Pancreatic pseudocyst

An encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis. This entity usually occurs more than four weeks after onset of interstitial edematous pancreatitis to mature.

Contrast-enhanced computed tomography criteria:

- Well circumscribed, usually round or oval
- Homogeneous fluid density
- No non-liquid component
- Well-defined wall (ie, completely encapsulated)
- Maturation usually requires >4 weeks after onset of acute pancreatitis; occurs after interstitial edematous pancreatitis

5. Acute necrotic collection (ANC)

A collection containing variable amounts of both fluid and necrosis associated with necrotizing pancreatitis; the necrosis can involve the pancreatic parenchyma and/or the peripancreatic tissues

Contrast-enhanced computed tomography criteria:

- Occurs only in the setting of acute necrotizing pancreatitis
- Heterogeneous and non-liquid density of varying degrees in different locations (some appear homogeneous early in their course)
- No definable wall encapsulating the collection
- Location–intrapancreatic and/or extrapancreatic

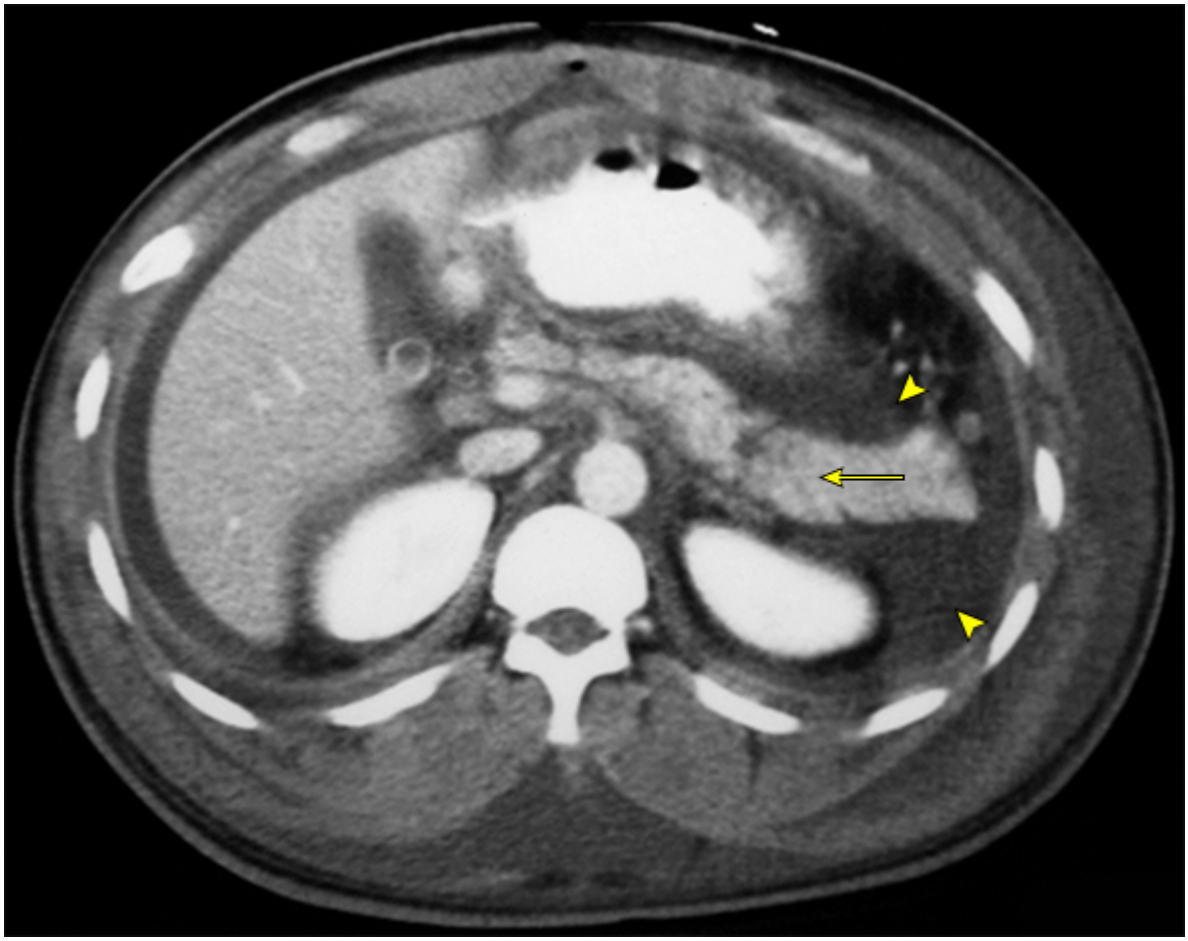
6. Walled-off necrosis (WON)

A mature, encapsulated collection of pancreatic and/or peripancreatic necrosis that has developed a well-defined inflammatory wall. WON usually occurs >4 weeks after onset of necrotizing pancreatitis.
Contrast-enhanced computed tomography criteria:

- Heterogeneous with liquid and non-liquid density with varying degrees of loculations (some may appear homogeneous)
- Well-defined wall, that is, completely encapsulated
- Location–intrapancreatic and/or extrapancreatic
- Maturation usually requires four weeks after onset of acute necrotizing pancreatitis

Graphic 87683 Version 3.0

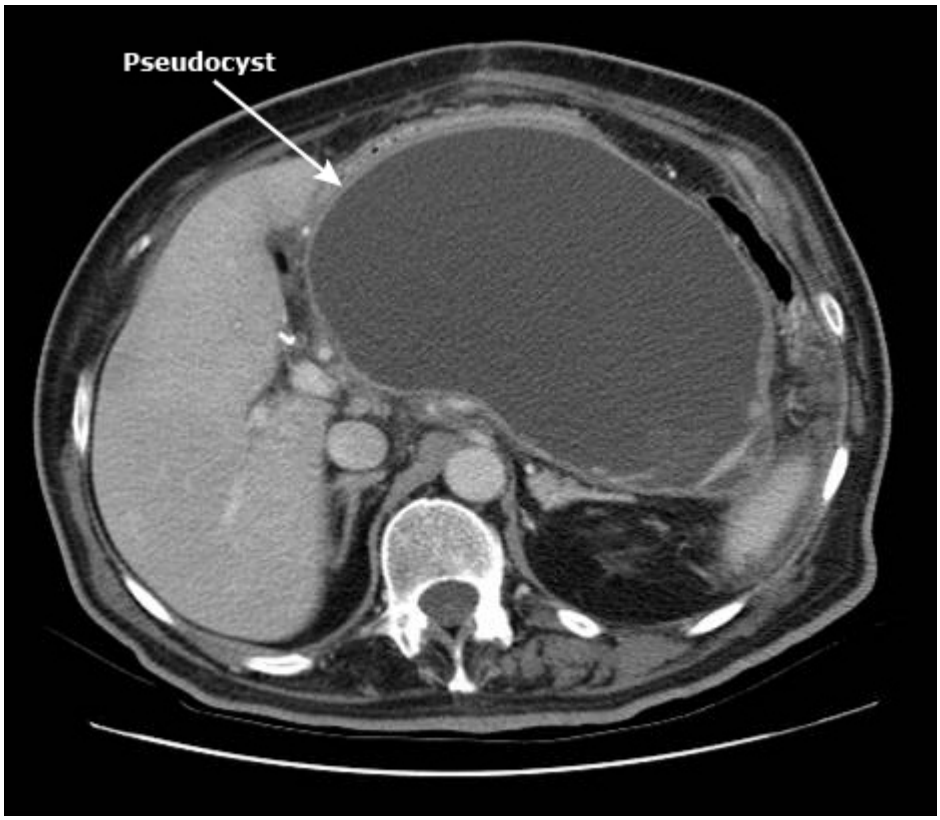
CT scan of acute interstitial pancreatitis with acute peripancreatic fluid collections



Computed tomography (CT) scan reveals acute interstitial pancreatitis with an acute peripancreatic fluid collections (APFC) around the body and tail of the pancreas (arrowheads). There is mild heterogeneity of the enhanced pancreas (arrow).

Graphic 88431 Version 2.0

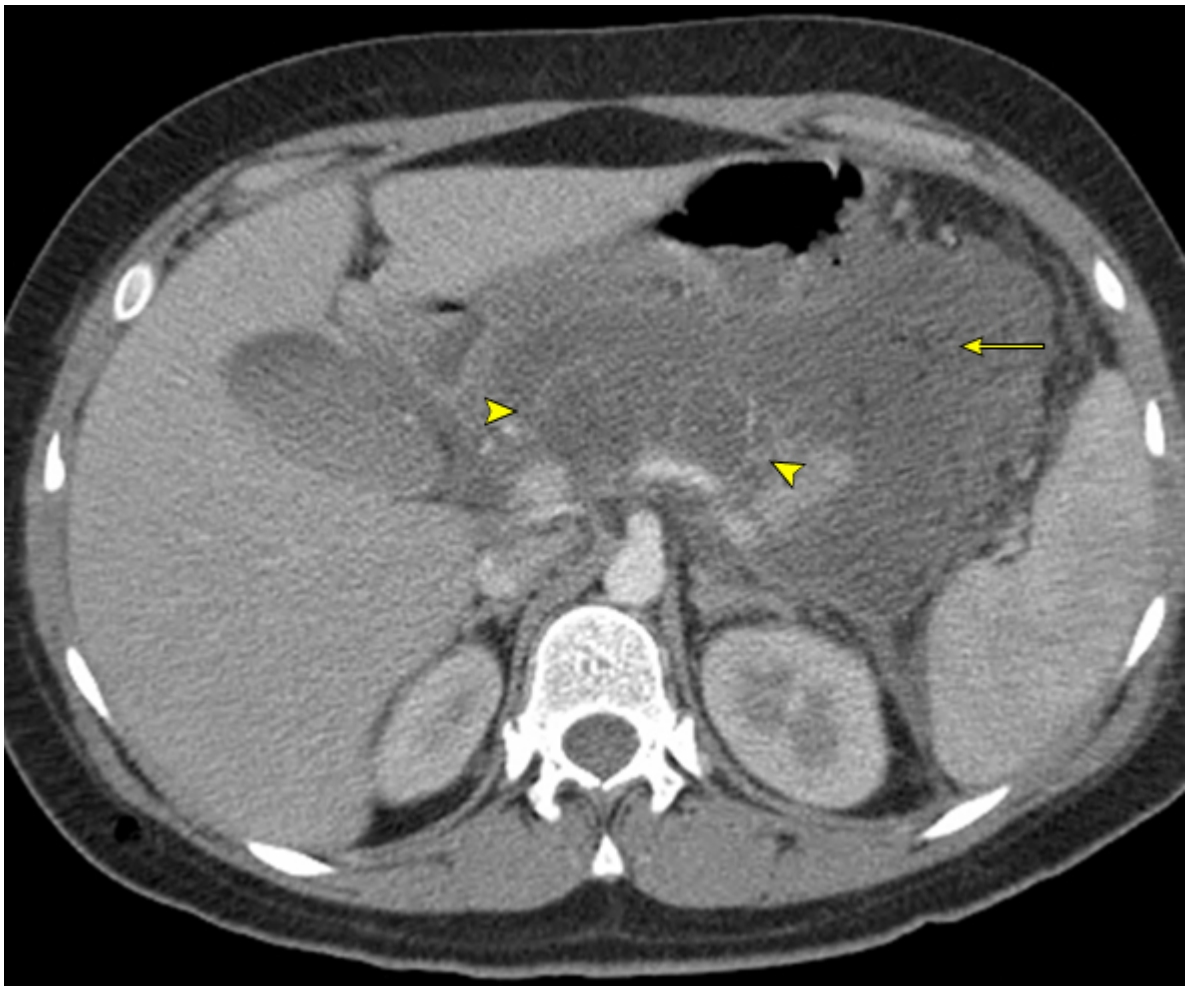
Pancreatic pseudocyst



Computed tomographic scan showing a massive pancreatic pseudocyst compressing the stomach and obliterating the pancreas.

Graphic 80720 Version 5.0

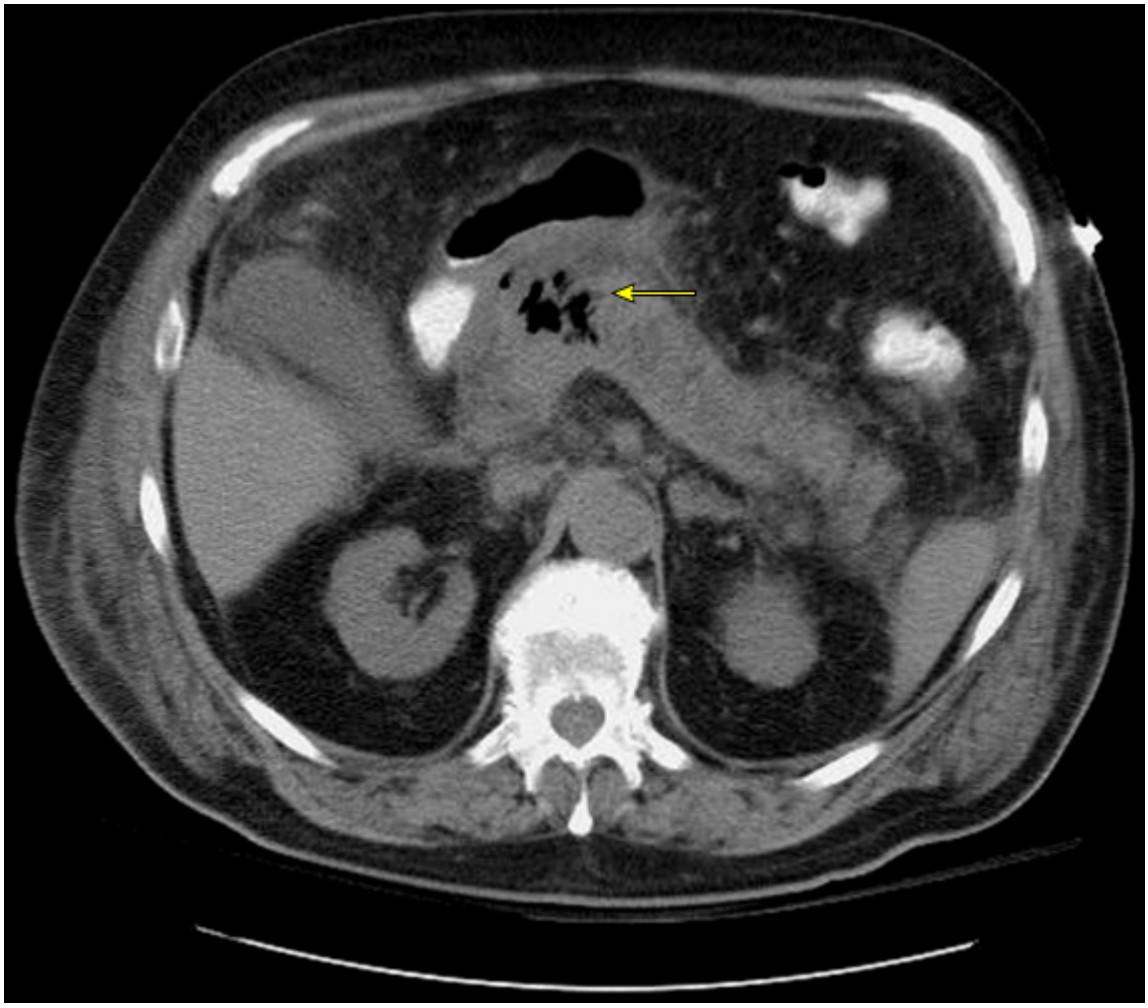
CT scan of acute necrotic collection



Computed tomography (CT) scan reveals an acute necrotic collection in a 20-year-old female with acute pancreatitis. The axial CT image shows pancreatic necrosis with a nonenhancing region in the neck and the body of the pancreas (between arrowheads). In the surrounding anterior pararenal space, there is a large fluid accumulation that contains islands of necrosis (arrow).

Graphic 88434 Version 1.0

CT scan of acute necrotizing pancreatitis complicated by infected pancreatic necrosis



Computed tomography (CT) scan reveals gas bubbles (arrow) within an area of pancreatic necrosis. The presence of gas bubbles is a pathognomonic sign of infection of the necrosis.

Graphic 88436 Version 1.0

Contributor Disclosures

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