Chapter

Medical Treatment of Acute Pancreatitis

Gulcin Ercan

Abstract

This chapter comprehensively examines the current approaches to managing acute pancreatitis (AP), a complex and potentially life-threatening inflammatory condition. It encompasses the fundamental principles of initial clinical assessment, fluid resuscitation, and pain management while emphasizing evidence-based strategies for nutritional support and pharmacological interventions. Additionally, the chapter explores the judicious use of antibiotics, considerations for minimally invasive and surgical interventions, and the management of systemic and local complications such as infected pancreatic necrosis and vascular complications. Special focus is placed on tailoring treatments based on the etiology of AP, including hypertriglyceridemia-induced AP, and addressing emerging therapeutic modalities such as low-molecular-weight heparins and enteral nutrition techniques. By integrating the latest evidence and expert consensus, this chapter aims to enhance understanding and optimize clinical outcomes for patients with both mild and severe forms of AP.

Keywords: acute pancreatitis, medical management, inflammatory response, pancreatic enzymes, fluid resuscitation

1. Introduction

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas, with mortality rates ranging from 3 to 17%, depending on the severity of the disease and associated complications [1, 2]. Although there are regional and local variations, gallstones and alcohol remain the most common causes of AP [3, 4]. Gallstone-related cases account for 40–60% of AP occurrences, alcohol accounts for 10–20%, and hypertriglyceridemia accounts for 5–10% [3]. While alcohol-induced AP is generally associated with daily alcohol consumption exceeding 50 grams, it is worth noting that less than 5% of chronic alcoholics may develop AP for unexplained reasons [5, 6].

In cases where there is no history of gallstones or significant alcohol use, a serum triglyceride level exceeding 1000 mg/dL suggests hypertriglyceridemia-related AP. Although pancreatitis has been reported due to various agents and medications, the most commonly implicated agents include 6-mercaptopurine, azathioprine, isoniazid, loop diuretics, and didanosine [7, 8].

Recent epidemiological data have indicated that the incidence of AP is increasing globally, with rates ranging from 5 to 80 cases per 100,000 individuals [9]. This rise is attributed to factors such as obesity, metabolic syndrome, and increased alcohol consumption. Notably, AP is among the most common gastrointestinal causes of hospitalizations in the United States, with an annual incidence estimated at 13 to 49 per 100,000 persons. The risk of AP is similar among men and women and increases with age [10].

Understanding the pathophysiology of AP is crucial for effective management. The disease is initiated by prematurely activating digestive enzymes within the pancreas, leading to autodigestion and inflammation. This process can result in systemic inflammatory response syndrome (SIRS) and, in severe cases, multiorgan dysfunction. Early recognition and intervention are vital to prevent progression and reduce mortality [10].

This chapter provides a comprehensive overview of the current strategies for managing acute pancreatitis, a severe inflammatory condition of the pancreas. The chapter covers key aspects such as initial clinical assessment, fluid resuscitation, pain management, nutritional support, and pharmacological agents. It also explores the role of antibiotics, the management of complications such as infected pancreatic necrosis, and the criteria for surgical intervention. Emphasizing evidence-based practices, this chapter aims to outline the most effective treatment approaches, addressing both mild and severe forms of acute pancreatitis, to optimize patient outcomes.

2. Treatment of acute pancreatitis

The primary therapeutic interventions for patients diagnosed with AP include fluid resuscitation, pain management, and nutritional support.

2.1 Fluid resuscitation

Aggressive fluid resuscitation is essential to counteract hypovolemia resulting from third-space fluid losses and decreased intravascular volume [11]. In the absence of contraindications such as cardiovascular, renal, or other significant comorbid conditions, it is recommended to administer isotonic crystalloid solutions—either normal saline or Ringer's lactate—at a rate of 5–10 mL/kg per hour. For patients presenting with hypotension and tachycardia, a more aggressive approach may be warranted, such as an initial bolus of 20 mL/kg over 30 minutes. However, in cases of hypercalcemia, Ringer's lactate is contraindicated due to its calcium content [12].

The choice between normal saline and Ringer's lactate for fluid resuscitation in AP remains a subject of ongoing research. While some studies suggest that Ringer's lactate may reduce systemic inflammation compared to normal saline, the American Gastroenterological Association's 2018 guidelines indicate no definitive superiority of one crystalloid solution over the other [13]. Therefore, the selection should be individualized based on patient-specific factors and clinical judgment [14].

Regarding the use of hydroxyethyl starch (HES) in AP, evidence indicates that it does not confer a mortality benefit and may, in fact, increase the risk of multi-organ failure. Consequently, the administration of HES is generally not recommended in the management of AP [15].

Fluid requirements should be reassessed frequently during the first 6 hours after presentation and subsequently over the next 24–48 hours [16]. Targeted therapy can

be adjusted based on parameters such as heart rate, mean arterial pressure, central venous pressure (CVP), urine output, blood urea nitrogen (BUN), and hematocrit levels. Adequate fluid resuscitation is particularly important when initial vital signs are abnormal. The goals include achieving a heart rate below 120 beats per minute, maintaining the mean arterial pressure between 65 and 85 mmHg, ensuring urine output exceeds 0.5–1 mL/kg/hour, keeping hematocrit levels between 35% and 44%, and normalizing BUN levels. Changes in BUN, especially at admission and within the first 24 hours of hospitalization, are effective predictors of mortality [17]. Patients with stable or increasing BUN levels may require additional fluid resuscitation. However, it is important to recognize that low urine output may reflect acute tubular necrosis rather than persistent volume depletion. In such cases, aggressive fluid administration may lead to peripheral and pulmonary edema without improving urine output [17].

Inadequate fluid resuscitation can result in hypotension and acute tubular necrosis [18]. Hemoconcentration persisting beyond 24 hours has been associated with the development of necrotizing pancreatitis, which leads to vascular leak syndrome, third-space fluid loss, and impaired pancreatic perfusion. Therefore, it is crucial to limit aggressive fluid resuscitation to the first 24–48 hours after disease onset. Excessive fluid administration beyond 48 hours is not recommended, as it increases the risk of intubation and abdominal compartment syndrome [19].

In summary, the cornerstone of AP management involves prompt and adequate fluid resuscitation tailored to the patient's clinical status, alongside appropriate pain control and nutritional support. Ongoing assessment and adjustment of therapy are crucial to optimize outcomes and minimize complications.

2.2 Pain control

In patients with AP, abdominal pain is one of the main symptoms, and managing pain is crucial for maintaining hemodynamic stability. Considering the pathophysiology of the disease, the ischemic process caused by vascular leakage and hemoconcentration may lead to pain and, subsequently, lactic acidosis. From this perspective, early fluid replacement is essential not only for hemodynamic stability but also for pain palliation [19].

Several small randomized controlled trials (RCTs) comparing different opioid and non-opioid analgesics in AP patients have not demonstrated any significant superiority of one analgesic over another in terms of efficacy or safety [20–22]. Additionally, a study comparing non-opioid analgesics (intravenous paracetamol, dexketoprofen) with tramadol in AP found them to be similarly effective for pain control [22]. Another study highlighted that, in AP patients, epidural anesthesia was effective not only for pain management but also for improving pancreatic arterial perfusion [23].

Opioids are considered safe and effective agents for pain control in AP patients [20]. Hydromorphone or fentanyl (intravenous) can be used for pain palliation in AP. Fentanyl, in particular, is increasingly preferred due to its better safety profile in patients with renal insufficiency. However, it is important to note that fentanyl, like other opioids, may cause respiratory depression. Fentanyl can be administered in both bolus doses and continuous infusion, and patients should be closely monitored for potential side effects [19].

In recent years, the use of meperidine in AP has increased, as studies suggest that it does not cause an increase in the sphincter of Oddi pressure, unlike morphine [23].

Nevertheless, there is no clinical evidence to suggest that morphine can cause or exacerbate pancreatitis or cholecystitis. Meperidine has a short half-life, and repeated doses may lead to neuromuscular side effects as well as the accumulation of its metabolite, normeperidine, which, though rare, can cause seizures. This risk should be kept in mind when using meperidine [19].

2.3 Nutrition

In patients diagnosed with AP, initiating enteral nutrition as early as possible is crucial due to its protective effects on the intestinal barrier and its role in preventing bacterial translocation. In mild acute pancreatitis (MAP) patients, recovery generally occurs rapidly, and oral feeding is typically feasible within one week, making management with intravenous hydration alone sufficient [24].

In patients with moderately severe acute pancreatitis (MSAP), nutritional support is required if oral intake is unlikely to be sustained within 5–7 days. If the patient does not exhibit ileus, nausea, or vomiting, and if pain severity decreases along with improvements in inflammatory markers, oral feeding can be initiated early (within 24 hours) with a low-fat, soft diet [25, 26].

For some MSAP and severe acute pancreatitis (SAP) patients, oral feeding may not be tolerated due to postprandial pain, nausea, or vomiting caused by luminal compression from fluid collections leading to gastroduodenal inflammation and/or gastric outlet obstruction. If these patients cannot tolerate an oral diet by day 5, enteral nutrition may be necessary. However, once local complications begin to resolve, oral feeding can be resumed as tolerated [19].

2.3.1 Oral nutrition

In a systematic review evaluating randomized studies on patients with (AP), early oral feeding (within ≤48 hours of hospital admission) was found not to increase adverse effects or exacerbate symptoms when compared to delayed oral feeding [27]. In four out of seven studies involving patients with MAP and MSAP, early oral feeding was associated with a reduction in hospital length of stay.

However, conflicting results have been reported in SAP. In a multicenter study comparing early oral feeding (within the first 24 hours) to delayed oral feeding (after 72 hours) in SAP patients, no significant clinical superiority was observed between the groups [28]. In contrast, studies comparing parenteral nutrition and delayed oral feeding (after 48 hours) with early oral feeding (within the first 48 hours) demonstrated the superiority of early oral feeding in terms of reduced rates of infected necrosis, organ failure, hospital length of stay, and mortality [29].

2.3.2 Enteral nutrition

In patients with MSAP and SAP who cannot tolerate oral feeding, enteral nutrition is recommended over parenteral nutrition [4, 30]. In patients with severe or necrotizing pancreatitis who require tube feeding, a feeding tube can be placed either nasogastrically (directly into the stomach) or nasojejunal (beyond the ligament of Treitz) *via* radiological or endoscopic methods. Enteral nutrition is also preferred for patients in intensive care settings, particularly those with organ failure or SIRS, who are unable to tolerate oral intake [19].

Two controlled studies comparing nasogastric and nasojejunal feeding reported no significant differences between the groups in terms of APACHE II scores, CRP levels, pain, or analgesic requirements [31, 32]. However, another small study comparing nasogastric feeding with parenteral nutrition recorded increased pulmonary and total complications in the nasogastric feeding group [33].

Enteral nutrition helps maintain the integrity of the intestinal barrier and prevents bacterial translocation. Compared to parenteral nutrition, enteral feeding has the added advantage of avoiding complications associated with venous access, such as vascular infections. A meta-analysis of eight studies demonstrated that enteral nutrition significantly reduces mortality, multiple organ failure, systemic infections, and the need for surgical interventions compared to parenteral nutrition [34, 35].

Due to reduced pancreatic enzyme secretion in AP, high-protein, low-fat, semi-elemental feeding formulas are preferred as enteral solutions. Enteral feeding should begin at a rate of 20–25 cc per hour and be gradually increased as tolerated to meet daily caloric requirements (25 kcal/kg of ideal body weight). If the patient experiences abdominal pain, vomiting, bloating, or diarrhea, enteral feeding should be discontinued [19].

2.3.3 Parenteral nutrition

Parenteral nutrition should be initiated only in patients who cannot tolerate enteral nutrition or fail to achieve the targeted enteral feeding rate within 48–72 hours, as the addition of parenteral nutrition to enteral feeding may cause adverse effects [36]. Studies conducted on intensive care unit (ICU) patients have reported higher rates of mortality, ICU-associated infections, and the need for renal replacement therapy in those receiving parenteral nutrition compared to enteral nutrition [37].

2.4 Antibiotic therapy

In patients with AP, prophylactic antibiotic use is not recommended regardless of the type (interstitial or necrotizing) or severity (mild, moderate, or severe) of the disease [4]. Even in SAP, studies evaluating the clinical benefits of prophylactic antibiotics have shown no improvement. Furthermore, these studies demonstrated significantly higher mortality and morbidity rates in patients treated with prophylactic antibiotics compared to those who were not [38, 39].

Approximately 20% of AP patients develop extrapancreatic infections, including bloodstream infections, pneumonia, and urinary tract infections [40]. Extrapancreatic infections are associated with increased mortality [17]. When an infection is suspected, antibiotics should be initiated while simultaneously identifying the source of infection. If cultures return negative and no infectious source is identified, antibiotics should be discontinued [19].

2.5 Other treatments

2.5.1 Pentoxifylline

Pentoxifylline, a nonselective phosphodiesterase inhibitor, requires further studies to determine its role in the treatment of AP. In a randomized study with a small sample size involving 28 patients with SAP, pentoxifylline was compared to a placebo when

administered within 72 hours of diagnosis or until hospital discharge. The study reported that the number of patients requiring intensive care (0 vs. 4 patients) and those hospitalized for more than 4 days (2 vs. 8 patients) was lower in the pentoxifylline group. However, no significant difference was observed between the two groups in terms of inflammatory marker levels, including circulating tumor necrosis factor-α (TNF-α) [41].

2.5.2 Somatostatin and its analogues

The pathogenesis of AP involves pancreatic autolysis secondary to the activation of digestive enzymes. Somatostatin, a potent inhibitor of pancreatic enzyme secretion, can suppress the activity of the sphincter of Oddi, significantly reduce basal sphincter pressure, stimulate the reticuloendothelial system, protect gastrointestinal mucosal cells and hepatocytes, and decrease interleukin (IL)-6 secretion induced by TNF-α in human pancreatic periacinar myofibroblasts. However, studies have shown that somatostatin does not have a significant effect on complication rates, mortality, pancreatic fistula, or enterocutaneous fistula associated with AP. Additionally, studies investigating its efficacy in preventing post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) have reported conflicting results. Therefore, based on the current evidence, the routine use of somatostatin in the treatment of AP or the prevention of PEP is not recommended [42, 43].

2.5.3 Antifungals

The use of prophylactic antifungal therapy (e.g., fluconazole) alongside prophylactic or therapeutic antibiotics is not recommended. Fungal infections occur in approximately 9% of cases with necrotizing pancreatitis. However, it remains unclear whether these infections are associated with higher mortality rates [44].

2.5.4 Protease inhibitors

The role of protease inhibitors in the treatment of AP remains uncertain. Meta-analyses have shown that protease inhibitors provide only a marginal reduction in mortality in patients with SAP. Additionally, arterial administration presents another drawback [45]. At present, routine use of protease inhibitors in clinical practice is not recommended [19].

2.5.5 Probiotics

Although the use of probiotics in AP has been increasingly studied in recent years, evidence suggests that their effectiveness is limited. In the largest double-blind RCT conducted by Besselink et al., probiotic prophylaxis was found not to reduce the risk of infectious complications [46]. Moreover, it was associated with a higher incidence of intestinal ischemia and increased mortality. Similarly, a systematic review by Gou et al. reported that probiotics did not reduce the rates of pancreatic infections, hospital length of stay, or mortality [47].

2.5.6 Low molecular weight heparins (LMWH)

In the pancreatic circulation, thrombosis associated with endothelial cell damage, sludge formation, and stasis occurs early in the course of AP, as early as mucous

swelling in the acini. The damage starts peripherally and extends toward the center, with fibrin accumulating at the distal end of the thrombus. Factor Xa catalyzes the conversion of prothrombin to thrombin, leading to the formation of fibrin clots. Low molecular weight heparins (LMWH) are molecules that bind to antithrombin III (ATIII) and enhance their activity. By activating ATIII, LMWH strengthens the inhibition of clotting factors Xa and IIa. The heparin-ATIII complex reduces trypsin and chymotrypsin activity and inhibits trypsinogen activation. The anti-inflammatory properties of heparin are distinct from its anticoagulant activity. Heparin reduces leukocyte adhesion to the site of injury and vascular endothelial cells, thereby mitigating inflammatory responses [48].

LMWH has been shown to downregulate endothelin-1 (ET-1), TNF-α, and IL-6, leading to improved microcirculation by reducing microthrombosis formation [49]. Additionally, heparin inhibits pancreatic enzymes and accelerates pancreatic regeneration during the disease course [50]. Experimental and clinical studies have explored the protective effects of heparin in the treatment of AP. Qiu et al. demonstrated the protective effects of LMWH against the development of pancreatic encephalopathy in rats with SAP [51]. Another study showed that LMWH reduces TNF-α and ET-1 levels, positively influencing morphological changes and vascular flow in SAP-induced rats [52]. In a study by Lu et al. involving 256 SAP patients, LMWH significantly reduced the incidence of pancreatic encephalopathy and improved survival rates in SAP [53]. Another study by Lu et al. on SAP patients reported that LMWH reduced mortality rates [54]. In an RCT conducted by Tozlu et al. on patients with MSAP and SAP, while no statistically significant reduction in mortality was observed, LMWH demonstrated significant effects in reducing both local and systemic complications [55].

2.6 Treatments based on etiology

2.6.1 Management of Hypertriglyceridemia

Hypertriglyceridemia is observed in patients with primary or secondary lipid metabolism disorders, including excessive alcohol consumption and poorly controlled diabetes [56]. When triglyceride levels exceed 1000 mg/dL and 2000 mg/dL, the risk of AP is reported to be approximately 5% and 15%, respectively [57]. A recent epidemiological study has found that even a mild increase in triglyceride levels is associated with an elevated risk of AP in susceptible individuals [58]. Another prospective study reported a higher risk of SAP and an increased need for intensive care in patients with hypertriglyceridemia-induced AP [59]. In patients with severe hypertriglyceridemia, maintaining triglyceride levels below 200 mg/dL significantly reduces the risk of recurrent AP episodes [60].

The triglyceride threshold for causing AP is defined as at least 1000 mg/dL by the American Gastroenterological Association (AGA) and the Endocrine Society, and at least 885 mg/dL by the European Society of Cardiology and the European Atherosclerosis Society. Recent systematic reviews have indicated that hypertriglyceridemia-induced AP can be significantly more severe compared to AP caused by other etiologies [61].

As with other causes of AP, the initial treatment of hypertriglyceridemia-induced AP focuses on fluid replacement and pain management. The primary treatment strategies for hypertriglyceridemia include apheresis and insulin therapy. However, no randomized trials have been conducted to directly compare the efficacy of these

treatments. The initial therapeutic approach for such patients should be tailored based on the severity of AP and clinical features. If clinical findings include hypocalcemia, lactic acidosis, signs of SIRS, or organ failure, therapeutic plasma exchange (TPE) should be initiated promptly. In patients with MAP or those unable to tolerate TPE, intravenous insulin therapy can be administered to lower triglyceride levels to below 500 mg/dL [62].

2.6.2 Apheresis

Apheresis is a procedure that involves passing blood through a medical device to separate a specific component and returning the remaining components to the body. In patients with hypertriglyceridemia, TPE involves the removal of plasma and its replacement with a colloid solution (albumin or plasma). Currently, no studies directly compare the replacement fluids used in TPE (albumin versus fresh frozen plasma) in hypertriglyceridemic patients. Moreover, the efficacy of TPE in reducing the severity of hypertriglyceridemia-induced AP or other clinically significant endpoints, such as mortality, remains unclear. In a study comparing 20 patients treated with TPE to a control group, no significant differences were found in mortality or systemic complications [63].

2.6.3 Insulin therapy

In SAP associated with hypertriglyceridemia, the goal of insulin therapy is to counteract the stress-induced release of fatty acids from adipocytes, promote intracellular triglyceride formation in adipocytes, and enhance fatty acid metabolism in insulin-sensitive cells. Insulin reduces serum triglyceride levels by increasing the activity of lipoprotein lipase, an enzyme that accelerates the conversion of chylomicrons and very low-density lipoproteins into glycerol and free fatty acids [64]. Additionally, insulin inhibits hormone-sensitive lipase, a key enzyme responsible for breaking down triglycerides in adipocytes and releasing free fatty acids into circulation. Since hypertriglyceridemia is often seen in patients with uncontrolled diabetes, insulin can effectively lower both triglyceride and glucose levels. In this context, a treatment regimen similar to that used in diabetic ketoacidosis can be employed, aiming to maintain blood glucose levels between 150 and 200 mg/dL. This can be achieved by maintaining high plasma insulin levels while preventing hypoglycemia using dextrose-infused solutions as needed. Intravenous insulin is more effective than subcutaneous insulin in cases of severe hypertriglyceridemia, and its titration is easier to manage. Once triglyceride levels fall below 500 mg/dL, insulin therapy can be discontinued [65, 66].

2.6.4 Other treatments

Standard heparin and hemofiltration have also been used in the management of hypertriglyceridemia-induced AP. However, data regarding their use and efficacy remain limited [67].

2.7 Management of Complications

In patients with MSAP or SAP, if signs of sepsis or clinical deterioration are present 72 hours after initial admission, contrast-enhanced abdominal CT imaging is

recommended to evaluate for the presence of pancreatic or extrapancreatic necrosis and other local complications [19].

2.7.1 Local complications

The local complications of AP include peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection (ANC), and walled-off necrosis (WON). Acute peripancreatic fluid collections and ANCs typically develop within the first 4 weeks after the onset of pancreatitis, while pancreatic pseudocysts and WON generally occur 4 weeks or more after the onset of the disease [30].

2.7.2 Acute Peripancreatic fluid collection

Acute peripancreatic fluid collections typically develop during the early phase of PEP. These collections lack a well-defined wall, are usually asymptomatic, and often resolve spontaneously without the need for drainage. In a study involving patients with interstitial pancreatitis, most acute fluid collections resolved within 7–10 days, and pancreatic pseudocysts developed in only 6.8% of these patients [68].

2.7.3 Pancreatic Pseudocyst

A pancreatic pseudocyst is a well-defined, encapsulated fluid collection with a distinct inflammatory wall, typically located outside the pancreas and containing little to no necrotic material. Pancreatic pseudocysts generally develop more than 4 weeks after the onset of interstitial pancreatic edema. Even when detected *via* ultrasound, it is essential to differentiate pseudocysts from cystic neoplasms, pseudoaneurysms, or duplication cysts using cross-sectional imaging methods such as contrast-enhanced CT or magnetic resonance imaging (MRI). MRI has superior diagnostic accuracy compared to CT for distinguishing WON from simple pseudocysts. However, endoscopic ultrasonography is often sufficient for the diagnostic evaluation of cystic lesions identified on imaging, and additional imaging may not be necessary [69].
On cross-sectional imaging, pancreatic pseudocysts typically exhibit the following characteristics:

- They are generally round or oval in shape and well-demarcated.
- They are typically located outside the pancreas (extraparenchymal).
- The fluid density is homogeneous.
- There are no non-fluid components within the fluid collection.
- A well-defined wall completely encapsulates the fluid.
- No internal septations are present within the cyst cavity [70].

For patients with pancreatic pseudocysts, supportive treatments may include:

- Nasoenteral feeding: Provides pain palliation and nutritional support.

- Proton pump inhibitors (PPIs): Reduce gastric acid secretion and subsequent pancreatic bicarbonate secretion in response.

Drainage is indicated for patients with symptomatic, rapidly enlarging pseudocysts; those with systemic illness due to infected pseudocysts; or those who do not respond to medical therapy. Currently, endoscopic approaches, and less commonly percutaneous drainage, have largely replaced surgical techniques. Criteria for endoscopic drainage are

- The cyst must be mature (with a well-defined wall).
- It must be adjacent to the gastric or duodenal wall.
- The size should be greater than 6 cm.

Endoscopic interventions for pancreatic pseudocysts are

1. Transmural drainage: Accessing the cyst through the gastric or duodenal wall. Balloon dilation followed by the placement of one or more stents.
2. Transpapillary drainage: Draining cysts that are associated with the pancreatic duct. Involves placing a pancreatic stent, with or without pancreatic sphincterotomy [70].

The overall success rate of endoscopic methods for mature pancreatic fluid collections exceeds 90%. Procedure-related outcomes report morbidity rates of 10–15%, resolution rates of 70–80%, and recurrence rates of 10–15% [71, 72]. Endoscopic drainage methods have replaced percutaneous drainage due to lower morbidity, shorter hospital stays, and reduced catheter dwell times. However, percutaneous drainage can still be utilized for accessing retroperitoneal fluid collections, stabilizing septic patients before surgical debridement, or addressing immature collections where endoscopic access is not feasible [73]. In such scenarios, percutaneous catheter drainage serves as a bridging technique for patients too unstable for surgical debridement. In some cases, it may also act as a standalone therapeutic approach [74].

2.7.4 Acute necrotic collections (ANC) and walled-off necrosis (WON)

Necrotizing pancreatitis can present as necrosis involving both pancreatic and peripancreatic tissues. Necrosis can appear as ANC, which contains variable amounts of fluid and necrotic debris but lack a well-defined wall, or as WON, which is characterized by encapsulated pancreatic and/or peripancreatic necrosis with a mature, well-defined wall (**Figure 1**) [19].

Both ANC and WON on imaging share the following features:

- Heterogeneous fluid collections with varying densities of fluid and non-fluid components.
- A well-defined wall completely encapsulating the fluid collection.
- Presence within pancreatic or peripancreatic regions.
- No internal septations in the cyst cavity [19].

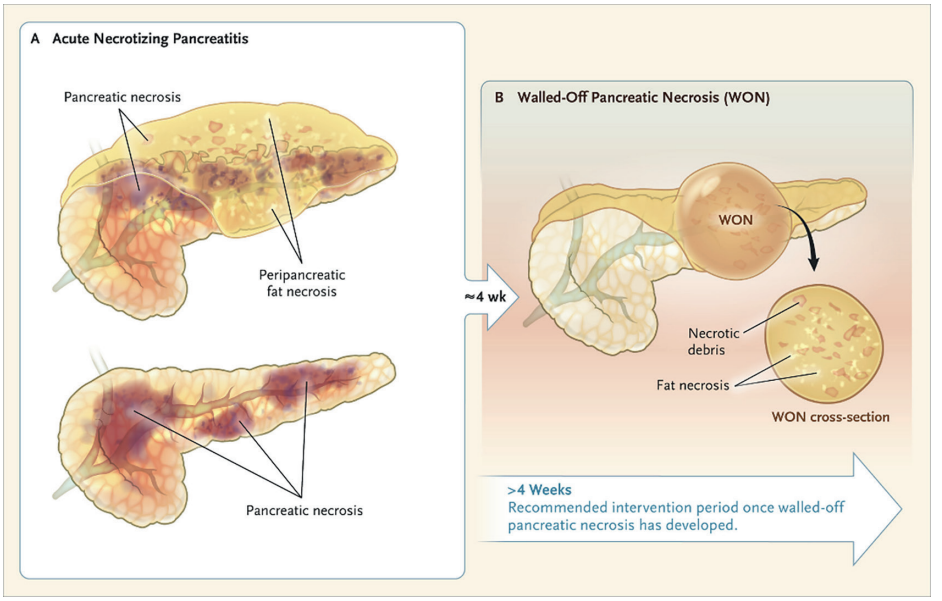

Figure 1.
The progression from acute necrotizing pancreatitis to walled-off pancreatic necrosis (WON). (A) Pancreatic necrosis and peripancreatic fat necrosis are characteristic of acute necrotizing pancreatitis. The necrotic regions seem inflammatory and are limited to the pancreas and surrounding fat tissue. (B) Necrotic pancreatic tissue can develop into walled-off pancreatic necrosis about 4 weeks following acute necrotizing pancreatitis. The picture depicts a well-defined, enclosed area with necrotic debris and fat necrosis. A cross-sectional image reveals the WON's interior structure. Interventions are indicated after ≥4 weeks, when the necrotic tissue has developed a mature wall, making treatments safer [74].

For the treatment of WON, minimally invasive techniques such as percutaneous drainage, endoscopic transmural drainage, and minimally invasive retroperitoneal necrosectomy have been developed. These techniques are as effective as minimally invasive surgery in terms of clinical success for infected and/or symptomatic WON [75]. However, endoscopic approaches have demonstrated lower rates of pancreatic fistulas and reduced hospital stay durations [2]. In a prospective long-term follow-up of 35 patients with SAP, those in the endoscopic approach group exhibited lower rates of diabetes, exocrine insufficiency, and hospital readmissions [76]. The challenges of suboptimal drainage in WON using plastic double-pigtail stents have been recently addressed with the advent of lumen-apposing metal stents (LAMS). LAMS achieves technical success rates exceeding 90%, with numerous studies supporting its clinical efficacy (**Figure 2**) [77, 78].

Complications associated with LAMS include bleeding (1–7%), perforation (1–2%), stent migration (1–6%), and infection (1–11%) [79]. In a randomized controlled trial (RCT) involving 60 patients undergoing endoscopic drainage, no differences in clinical success were observed between the groups treated with LAMS or double-pigtail plastic stents. However, stent-related adverse events were significantly higher with LAMS (32.3%) compared to double-pigtail plastic stents (6.9%) [80].

To minimize adverse events with LAMS, patients should be reassessed within 3–4 weeks, and the stents should be removed if WON has fully or partially resolved. If WON is only partially resolved, replacing the LAMS with double-pigtail plastic stents is recommended, as most of these patients are at risk of developing disconnected duct syndrome [19].

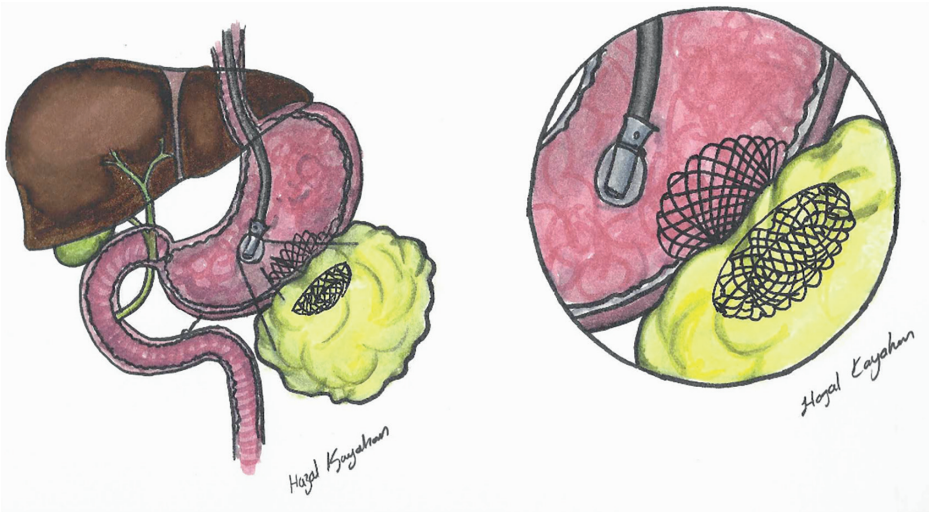

Figure 2.
Creation of a cystgastrostomy with EUS-guided placement of a lumen-apposing metal stent.

2.8 Surgical indications in acute pancreatitis

Conventional absolute indications for surgery in acute pancreatitis include hemorrhage unsuitable for angioembolization, bowel infarction, and perforation. SAP is a risk factor for abdominal compartment syndrome due to visceral and retroperitoneal edema. In cases where nonsurgical treatment fails, surgical abdominal decompression may be required [81].

Other indications for surgical debridement and decompression include infected pancreatic necrosis and symptomatic sterile necrosis characterized by persistent low-grade fever, nausea, lethargy, and anorexia. The goal of pancreatic debridement is to preserve viable pancreatic tissue, control potential pancreatic fistulas, and limit collateral organ damage while removing all necrotic pancreatic and peripancreatic tissue [82]. The surgical indications in acute pancreatitis are summarized:

- Hemorrhages not amenable to angioembolization, bowel infarction, and perforation.
- Infected pancreatic necrosis or symptomatic sterile necrosis characterized by chronic low-grade fever, nausea, lethargy, and anorexia, unresponsive to percutaneous or endoscopic interventions.
- Abdominal compartment syndrome.
- Hemorrhages refractory to endovascular approaches.
- Bowel ischemia or acute necrotizing cholecystitis developing during acute pancreatitis.
- Bowel fistula extending into a peripancreatic collection [19].

2.8.1 Infected necrosis

Pancreatic infection is a leading cause of morbidity and mortality in acute necrotizing pancreatitis. Approximately one-third of patients with pancreatic necrosis develop infected necrosis [83]. There is no correlation between the degree of necrosis and the risk of infection. Although infection can occur early during necrotizing pancreatitis, it is more commonly observed in the late phase (after 10 days) [84]. Most infections (approximately 75%) are monomicrobial and are caused by gut-derived organisms, such as *Escherichia coli*, Pseudomonas, Klebsiella, and Enterococcus. In patients with worsening clinical status (e.g., clinical instability, sepsis physiology, increased white blood cell count, fever) 7–10 days after hospital admission and with evidence of pancreatic or extrapancreatic necrosis, infected necrosis should be suspected [85].

Pancreatic infection should also be considered in the presence of clinical signs of infection and gas-containing necrotic areas on abdominal imaging. In such cases, antimicrobial therapy can be initiated without aspiration for culture sampling [86]. For empirical antibiotic therapy, agents that penetrate pancreatic necrosis should be chosen. Options include monotherapy with a carbapenem or a combination therapy with quinolone, ceftazidime, or cefepime paired with an anaerobic agent such as metronidazole. Some patients with infected necrosis improve clinically without any intervention. However, in certain cases of infected necrosis without WON, temporary percutaneous drainage may be required [87].

2.8.2 Sterile necrosis

If aspirated material is sterile, antibiotics should be discontinued, and conservative management can continue for 4–6 weeks. Antibiotics are not recommended for patients with sterile necrosis to prevent the development of infected necrosis. Sterile necrosis does not require treatment [19].

Intervention (radiological, endoscopic, or surgical) for patients with sterile necrosis without signs of infection (e.g., fever, hypotension, and leukocytosis) is indicated in the following situations:

- 4 to 8 weeks after the onset of AP: Persistent gastric outlet obstruction, bowel obstruction, or biliary obstruction due to mass effect.

- After 8 weeks: Persistent symptoms, including abdominal pain, nausea, vomiting, anorexia, or weight loss.

- After 8 weeks: Symptomatic necrotic collections (pain or obstruction) associated with disconnected duct syndrome (complete transection of the pancreatic duct) [88].

2.9 Peripancreatic vascular complications

2.9.1 Splanchnic venous thrombosis

Splanchnic vein thrombosis (involving the splenic, portal, and/or superior mesenteric veins) is a complication that can occur in 1–24% of patients with AP, depending on the severity of the disease and the imaging modality used [89].

Treatment should focus on the underlying pancreatitis, as thrombosis may resolve spontaneously. Despite the potential risk of bleeding into pancreatic necrosis or fluid collections, anticoagulation should be initiated if the thrombus extends to the portal or superior mesenteric vein or if signs of decompensation due to impaired bowel or liver perfusion are present. In contrast to patients with splanchnic vein thrombosis secondary to chronic pancreatitis, complications such as variceal bleeding are rare in AP patients. Therefore, prophylactic splenectomy is not recommended in AP [90].

2.9.2 Pseudoaneurysms

Pseudoaneurysms are rare but serious complications of AP. They should be suspected in patients with unexplained gastrointestinal bleeding, a sudden drop in hematocrit levels, or a rapid increase in peripancreatic fluid collections [19].

2.9.3 Abdominal compartment syndrome

Abdominal compartment syndrome is defined as a sustained intra-abdominal pressure > 20 mmHg accompanied by new-onset organ failure. Patients with SAP are at high risk of developing intra-abdominal hypertension and abdominal compartment syndrome due to aggressive fluid resuscitation, peripancreatic inflammation, ascites, and ileus-related tissue edema [91]. Patients in the intensive care unit should be monitored for possible abdominal compartment syndrome through serial bladder pressure measurements [92].

2.10 Systemic complications

Patients with AP are at high risk for exacerbations of underlying comorbidities, such as coronary artery disease and chronic lung disease. In addition to treating these exacerbations, management should address other complications, including alcohol withdrawal and hyperglycemia. AP patients also face an increased risk of developing prediabetes and diabetes after the first episode of AP. A meta-analysis of 24 prospective studies involving 1102 patients with a first episode of AP reported that 15% of cases were diagnosed with new-onset diabetes mellitus (DM) within 12 months [93].

3. Conclusions

The management of acute pancreatitis requires a multidisciplinary and evidence-based approach that addresses both the underlying pathology and the systemic complications associated with the disease. This chapter highlights the critical importance of early intervention through adequate fluid resuscitation, pain control, and the timely initiation of enteral nutrition to maintain gut integrity and prevent complications. For severe cases, particularly those involving infected necrosis or SIRS, individualized treatment strategies incorporating antibiotics, minimally invasive procedures, or surgery may be necessary. Advances in understanding the pathophysiology of AP have expanded therapeutic options, such as the targeted use of low-molecular-weight heparins and apheresis for hypertriglyceridemia-induced cases. Ongoing research and refinement of clinical guidelines will continue to shape the management of AP, improving survival rates and reducing the burden of complications. Ultimately,

personalized care, informed by patient-specific factors and disease severity, remains pivotal to optimizing outcomes in acute pancreatitis.

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Conflict of interest

The author declares no conflict of interest.

Appendices and nomenclature

AP	acute pancreatitis
MAP	mild acute pancreatitis
MSAP	moderately severe acute pancreatitis
SAP	severe acute pancreatitis
WON	walled-off necrosis
ANC	acute necrotic collection
SIRS	systemic inflammatory response syndrome
TPD	therapeutic plasma exchange
LAMS	lumen-apposing metal stent
CT	computed tomography
MRI	magnetic resonance imaging
US	ultrasound
ET-1	endothelin-1
TNF-α	tumor necrosis factor-alpha
IL-6	interleukin-6
PPIs	proton pump inhibitors
DM	diabetes mellitus
BISAP	bedside index for severity in acute pancreatitis
CECT	contrast-enhanced computed tomography
ATIII	antithrombin III

Author details

Gulcin Ercan
Department of General Surgery, Sultan 2. Abdulhamid Khan Training and Research Hospital, Istanbul Provincial Directorate of Health, Istanbul, Turkey

*Address all correspondence to: ghepgul@hotmail.com

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