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Acute pancreatitis: a review of etiology, diagnosis and management of local complications

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Abstract:

Background: Acute pancreatitis (AP) is an inflammatory disease primarily caused by gallstones and alcohol consumption. Its clinical presentation varies significantly, ranging from mild interstitial edematous pancreatitis to severe necrotizing forms. The Revised Atlanta Classification establishes the standard for defining the severity of the disease and categorizing its local complications into four distinct types: acute peripancreatic fluid collections (APFC), acute necrotic collections (ANC), pancreatic pseudocysts, and walled-off necrosis (WON).

Aim: The aim of this study was to review the current literature regarding the epidemiology, pathophysiology, diagnostic criteria, and management strategies for the local complications of acute pancreatitis.

Materials and Methods: The review included scientific papers sourced from the PubMed and Google Scholar databases.

Results: The diagnosis and characterization of local complications rely heavily on imaging modalities. While Contrast-Enhanced Computed Tomography remains the standard tool, Magnetic Resonance Imaging and Endoscopic Ultrasound demonstrate superior accuracy in detecting solid necrotic debris. Distinguishing between fluid-only collections (APFC, pseudocyst) and those containing necrosis (ANC, WON) is critical, as it dictates the therapeutic approach. The review highlights that while APFCs often resolve spontaneously, necrotic collections carry a higher risk of infection and mortality. Management strategies have evolved significantly, moving away from open surgery toward minimally invasive methods.

Conclusions: Accurate classification of local complications based on the Revised Atlanta Classification is essential for guiding clinical decision-making. Contemporary management of AP complications favors a "step-up" approach, prioritizing conservative treatment and minimally invasive endoscopic interventions over traditional surgical necrosectomy to reduce morbidity and improve patient outcomes.

Key words: Acute Pancreatitis, AP local complications, Pancreatic Pseudocysts, Acute Peripancreatic Fluid Collection, APFC, Walled off Necrosis, WON, Acute Necrotic Fluid Collection

Introduction:

Acute pancreatitis (AP) is defined as an inflammatory disease of the pancreas. The most common causes of AP include gallstones and the overconsumption of alcohol. Other factors which may contribute to the onset of the disease include tobacco smoking, hypertriglyceridemia, hypercalcemia, certain medications, genetic and autoimmune factors. (Heckler et al., 2020). Those trigger factors lead to the activation of trypsinogen and the destruction of secretory cells. In turn cytokines and inflammatory mediators are released. This leads to acinar cell death and then both localized and systemic inflammatory response. Initially, the most prominent features are distant organ dysfunction notably the lungs and kidneys, which in most cases is of short duration (< 48 h). Calcium overload, mitochondrial dysfunction, impaired autophagy, endoplasmic reticulum stress, and exosomes are other factors in pathogenesis of the disease. (Raray et al., 2004; Szatmary et al., 2022).

To diagnose acute pancreatitis 2 out of 3 of the following criteria must be met. 1. upper abdominal pain of acute onset often radiating through to the back, 2. serum amylase or lipase activity greater than 3 times normal, and 3. findings on cross-sectional abdominal imaging consistent with acute pancreatitis. If the first two criteria are met it is not obligatory to perform radiology imaging. According to the Atlanta Criteria AP can be divided into interstitial edematous pancreatitis and necrotizing pancreatitis. The former being both more common (80-90% of patients can be diagnosed with this type) and milder. The latter occurs less frequently but it is more severe. (Sarr, 2012). The patient's outcome can be attributed both to the severity

of the disease and its aetiology. There are several scoring systems developed, their aim being predicting which patients are at risk of a more severe course of the disease. Examples of those systems are : Ranson, APACHE II, Glasgow-Imrie, SOFA, Balthazar, BISOP (Zerem et al., 2023).

A large epidemiology study from 2018 by Roberts et al. looked at studies from 1970 to 2015 in order to review the incidence of AP. The incidence of acute pancreatitis was reported from 17 countries across Europe and ranged from 4.6 to 100 per 100 000 population. Incidence ranged from 4.6 per 100 000 in Tirana, Albania (from 2005 to 2012), to 100 per 100 000 in the Świętokrzyskie Voivodeship province of Poland in 2011. They also found that the highest ratios of gallstone to alcohol aetiologies were identified in southern Europe (Greece, Turkey, Italy and Croatia) with lowest ratios mainly in eastern Europe (Latvia, Finland, Romania, Hungary, Russia and Lithuania). (Roberts et al., 2018).

The 2012 revision of Atlanta classification of acute pancreatitis defines local complications of AP as: acute peripancreatic fluid collections (APFCs), pancreatic pseudocysts, acute necrotic collections (ANCs), and walled-off necrosis (WON). Other complications include colonic necrosis, splenic/portal vein thrombosis, and gastric outlet dysfunction. (Sarr, 2012). A 2018 meta analysis by Miko et al. found that patients with preexisting diabetes have a higher chance of developing both local and systemic complications if diagnosed with AP (OR, 1.267 [95% CI, 0.964–1.659]; $p = 0.090$). Patients suffering from diabetes also stayed in a hospital longer (standardized mean difference, 0.217 [95% CI, 0.075–0.360]; $p = 0.003$). (Miko et al., 2018).

Diagnosis of local complications of AP relies heavily on radiology imagining. The standard imagining tool is computed tomography (CT) however it carries the burden of radiation and may require use of iodized contrast media in order to achieve a better diagnostic image. Some researchers suggest the use of magnetic resonance imagining for the detection and characterization of local complications. The general MRI sequences for pancreatitis require the combined use of T1-weighted, T2-weighted sequences, and magnetic resonance cholangiopancreatography (Xiao et al., 2010).

Research materials and methods

A comprehensive literature review was conducted using the PubMed and Google Scholar databases. The search focused on systematic reviews, meta-analyses, and key clinical trials published on the topic of local complications of acute pancreatitis. To cover all relevant aspects, the search strategy included keywords such as "acute pancreatitis", "acute pancreatitis local complications" "acute peripancreatic fluid collection", "APFC" "pancreatic pseudocyst" "walled off necrosis", "acute necrotic fluid collection".

Acute Peripancreatic Fluid Collection (APFC)

According to the Revised Atlanta Classification, Acute Peripancreatic Fluid Collections (APFCs) are defined as fluid collections that develop during the early phase of acute pancreatitis (typically within the first 4 weeks of symptom onset). They occur specifically in the setting of interstitial edematous pancreatitis (IEP) and are characterized by the absence of pancreatic or peripancreatic necrosis (Bansal et al., 2022). Morphologically, APFCs are homogenous, fluid-filled collections that lack a well-defined inflammatory wall or capsule, instead being confined by normal fascial planes within the retroperitoneum (Solakoglu et al., 2023). It is crucial to

distinguish APFCs from Acute Necrotic Collections (ANCs), which contain solid necrotic debris and occur in the setting of necrotizing pancreatitis (Bansal et al., 2022).

APFCs are the most frequently observed local complication of acute pancreatitis, with reported incidence rates ranging from 30% to 50%. In a recent retrospective study of 132 patients, APFCs were detected in 38.6% of cases (Solakoglu et al., 2023). While the development of APFCs does not appear to significantly impact mortality rates or the necessity for intensive care unit admission, it is associated with a significantly longer duration of hospital stay compared to patients without fluid collections (Solakoglu et al., 2023).

The diagnosis and characterization of APFCs rely heavily on imaging modalities. Contrast-enhanced computed tomography (CECT) is the standard method for assessment. On CECT, APFCs appear as homogenous collections with low attenuation values and without well-defined walls (Dhaka et al., 2015).

Differentiating APFCs from ANCs can be challenging during the first week of the disease. However, this distinction is vital as management strategies differ significantly based on the presence of solid necrotic debris. While transabdominal ultrasound is useful for monitoring, it may be limited by bowel gas. Magnetic Resonance Imaging (MRI) and Endoscopic Ultrasound (EUS) have shown higher accuracy than CECT in quantifying solid debris, which is the key differentiator between simple fluid collections and necrotic collections (Dhaka et al., 2015).

The vast majority of APFCs remain sterile and asymptomatic, requiring no specific intervention (Bhakta et al., 2022). They often resolve spontaneously without treatment (Khizar et al., 2023). Intervention is generally reserved for rare cases where the collection becomes infected or causes severe symptoms. In one study, rapid resolution of fluid was documented in 68.6% of patients within two weeks (Lenhart et al., 2008). Consequently, in patients with milder forms of pancreatitis, routine follow-up imaging is generally indicated only for those with fluid collections to document resolution or the development of complications.

If an APFC does not resolve spontaneously within 4 weeks, it may mature into a pancreatic pseudocyst, which will be discussed later.

Acute Necrotic Collection (ANC)

Acute pancreatitis is a disease with a high chance for resolving itself, with limited medical intervention. However, recent data suggests that even 20% of patients who develop acute pancreatitis see the progression into necrotizing pancreatitis (Puschke et al., 2022), which increases mortality rate even up to 39% (Rainho et al, 2025). The necrotic regions can remain sterile or get infected by bacteria or fungi, further increasing the mortality rate.

Acute necrotic collections (ANCs) occur only in patients with acute pancreatitis and start forming within the first 4 weeks of the disease onset. They can usually be found in the lesser sac, pararenal spaces and might extend into the pancreas through the affected parenchyma. The ANCs are multiple sacs filled with a variable amount of fluid and most of them contain necrotic debris. If the necrosis persists, the affected area starts forming a thick wall, enclosing itself in a pseudocyst or might become a so-called WON (walled-off necrosis) (Foster et al., 2016).

Up to a third of patients with acute pancreatitis develop a superinfection with bacteria and/or fungi within 2 to 4 weeks of the symptoms onset (Rainho et al, 2025). It is linked with a mortality rate of 35% in comparison to 20% in patients with sterile necrosis.

The diagnosis is typically based on clinical symptoms indicating sepsis (Rainho et al, 2025), however some sources suggest the use of MRI imaging as a helpful tool for diagnosis

(Heckler et al., 2020). The bacteria most frequently found in infected pancreatic necrosis include *Escherichia coli*, *Enterococcus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, *Pseudomonas spp.* and *Streptococcus spp.* The infection should initially be treated empirically with antibiotics covering a whole spectrum of bacteria; aerobic and anaerobic, Gram-positive and Gram-negative, for example Imipenem or Ciprofloxacin. (Purschke et al., 2022). Despite the idea for prophylactic use of antibiotics in necrotic pancreatitis seeming promising, it has been proven that it does not affect the mortality rate (Rainho et al, 2025). Secondarily to the bacterial infection, fungal infection might appear. Its appearance significantly increases the mortality rate and requires aggressive systemic anti-fungal therapy (Heckler et al., 2020).

Apart from systemic treatment, there are also surgical methods of managing the necrosis. Historically the surgery to remove the necrotic tissues was linked with up to 50% mortality rate. Plenty of research has led to the realisation that the timing of the surgery plays an important role. If possible, the surgery is recommended after around 4 weeks since the symptoms appeared, due to a previously mentioned formation of walled-off necrosis. The surgery is an open pancreatic necrosectomy and includes transection of the gastro-colic and duodenal-colic ligaments to expose the necrotic tissue and later careful dissection of the necrosis walls and debridement. However, with the progress of laparoscopy, and computer tomography, minimal access retroperitoneal pancreatic necrosectomy became one of the most promising techniques. It minimises the risk of potential septic shock due to its extra peritoneal approach while still allowing to safely decompress the necrotic cavity. (Heckler et al., 2020).

Pancreatic Pseudocyst:

Pancreatic pseudocyst is a localized fluid collection which may form in the pancreas as a result of both acute and chronic pancreatitis. Contrary to a true cyst its wall is lined with fibrous tissue and does not contain epithelium. Its contents are rich in pancreatic enzymes, mainly amylase and may also contain necrotic debris (Bradley, 1993). Pseudocysts are connected with the pancreatic duct system, either as a direct communication or indirectly via the pancreatic parenchyma. They are caused by pancreatic ductal disruption following increased pancreatic ductal pressure, either due to stenosis, calculi or protein plugs obstructing the main pancreatic ductal system, or as a result of pancreatic necrosis following an attack of acute pancreatitis. In order to diagnose this complication a collection of fluid should persist for at least 4-6 weeks. (Habashi et al., 2009). The incidence of pseudocysts is less common in acute pancreatitis compared to chronic pancreatitis. Studies show that it occurs more frequently in AP caused by alcohol overconsumption compared to other etiologies. The total incidence is low, 1.6%-4.5%, or 0.5-1 per 100 000 adults per year (Pitchumoni et al., 1999' Wade et al., 1985).

The clinical presentation of pancreatic pseudocyst can range from asymptomatic patient to major abdominal catastrophe due to complications. Acute complications include bleeding (usually from splenic artery pseudoaneurysm), infection, and rupture. On physical examination there are no specific symptoms which may suggest the incidence of this complication. Patients may have a tender abdomen, sometimes an abdominal mass may also be palpable. However it is also possible for a patient with a large pseudocyst to be asymptomatic. (Habashi et al., 2009)

Therefore a diagnosis of pseudocyst must be done after performing imaging. There are a number of techniques in which this fluid collection can become visible. On abdominal ultrasound a pseudocyst will appear as an echoic structure with an oval or round smooth wall. Internal echoes may be present if the cyst contains necrotic debris, blood or becomes infected. Sensitivity rates for ultrasound imaging in the detection of pancreatic pseudocysts are between

75% and 90%. Limitations of this method include the presence of overlying bowel gas which decreases the sensitivity of diagnosis. In addition to that ultrasound examinations are highly operator dependent (Pitchumoni et al., 1999).

Computed tomography is a more accurate method of imaging pancreatic pseudocysts. This method is most often used in a clinical setting. It does not have the limitations of ultrasonography. In addition to that a CT scan shows the surrounding anatomy more clearly and can reveal additional pathology, including pancreatic duct dilatation and calcifications, common bile duct dilatation, and extension of the pseudocyst outside the lesser sac. Limitations of CT imaging include the negative effect of iodized contrast media on the kidneys and its inability to differentiate pseudocysts from cystic neoplasms (Siegelman et al., 1980). End-stage renal failure is also common in chronically ill patients, which prevents the administration of contrast and limits the sensitivity and specificity of this method.

MRI and magnetic resonance cholangiopancreatography (MRCP) are sensitive diagnostic modalities for pancreatic pseudocysts. The main additional data which may be drawn from MRCP compared to routinely used CT is a clear appearance of choledocholithiasis if present (Habashi et al., 2009).

Traditional open surgical approaches to acute, symptomatic pseudocysts include cyst-gastrostomy, cyst-duodenostomy, Roux-en-Y cyst-jejunostomy, and, in rare cases, external drainage (Cannon et al., 2009). However, the preferred method for draining a pseudocyst is the endoscopic approach. That is because it is invasive, does not require external drain and has a high long-term success rate. A 2008 study compared the outcomes in patients with pancreatic pseudocysts treated with surgical and endoscopic methods. It revealed a significantly shorter hospital length of stay in the endoscopic group (2.65 versus 6.5 days, $p= 0.008$) (Varadarajulu et al., 2008). Endoscopic pseudocyst drainage can be performed through a transpapillary and transenteric approach. The transpapillary approach can only be used in pseudocysts which communicate with the main pancreatic duct. After the drainage a stent may be placed in the pancreatic duct. The transenteric endoscopic approach requires either an endolumenal bulge or a confirmed adherence between the cyst and the wall of either the stomach or the duodenum. The pseudocyst may then be punctured and its contents aspirated. In this approach, similarly to the transpapillary approach a stent may be placed between the cyst and the digestive track. (Cannon et al., 2009).

Walled off Necrosis (WON):

Walled-off pancreatic necrosis (WON) is a late, local complication of acute pancreatitis (AP). According to the revised Atlanta classification, WON is defined as a mature, encapsulated collection of either pancreatic or peripancreatic necrosis. It is surrounded by a well-defined inflammatory wall. This complication typically occurs at least four weeks after the onset of the disease. (Cunha et al., 2014; Shah et al., 2017).

It is crucial to distinguish WON from a pseudocyst before taking further action. While both present as well separated collections of fluid, pseudocysts contain homogenous fluid with no solid material. In contrast, WON contains a heterogeneous mixture of liquid and solid necrotic debris (Cunha et al., 2014). Misdiagnosing WON as a pseudocyst can lead to treatment failure, as standard drainage techniques may be insufficient to evacuate solid necrotic material (Stamatakos et al., 2010; Papachristou et al., 2007).

Contrast-enhanced computed tomography (CT) is the standard imaging technique for identifying the extent of necrosis. However, CT may occasionally fail to differentiate between liquid and solid contents. Magnetic Resonance Imaging (MRI) or Endoscopic Ultrasound (EUS)

are superior for characterizing the content of the collection, specifically detecting solid debris which dictates the need for aggressive debridement rather than simple drainage (Cunha et al., 2014; Dalsania et al., 2019).

WON does not require intervention in every case. About 50% of patients are asymptomatic and they are more likely to experience a spontaneous resolution. Medical management of WON includes nutritional support and antibiotics for suspected infection. (Dalsania et al., 2019). Intervention is indicated in the presence of infection, gastric outlet or biliary obstruction, or persistent symptoms such as intractable pain, anorexia, and failure to thrive (Shah et al., 2017; Ramai et al., 2023). The standard of care is to delay drainage until the wall matures, which takes at least 4 weeks. However, recent data suggests that earlier intervention may be indicated in selected unstable patients without increased adverse events (Ramai et al., 2023).

In the past, open surgical necrosectomy was the standard treatment but it was associated with high morbidity and mortality (Stamatakos et al., 2010). Currently the "step-up" approach is favoured. It prioritizes minimally invasive endoscopic techniques to treat WON.

EUS-guided transmural drainage is now the preferred first-line therapy. This involves creating a tract between the gastrointestinal tract (stomach or duodenum) and the necrotic cavity. While double-pigtail plastic stents were used historically, they are prone to occlusion by solid debris. Current practice increasingly favors Lumen-Apposing Metal Stents (LAMS). LAMS provide a larger diameter conduit, which not only facilitates better passive drainage but allows the endoscope to enter the cavity for Direct Endoscopic Necrosectomy (DEN) (Shah et al., 2017; Ramai et al., 2023). Because WON contains solid debris, simple drainage may be unsuccessful in the treatment. DEN is frequently required; it utilizes tools such as snares, baskets, and forceps to manually remove necrotic tissue (Papachristou et al., 2007). Recent advancements in DEN include the use of hydrogen peroxide lavage in order to loosen debris. Another method includes the use of novel mechanical debridement devices (e.g., EndoRotor) to pulverize necrotic tissue (Ramai et al., 2023). Additionally, nasocystic irrigation may be used to both continuously flush the cavity and prevent stent occlusion (Papachristou et al., 2007).

A significant challenge in managing WON is Disconnected Pancreatic Duct Syndrome (DPDS), where a viable segment of the pancreas is isolated from the main duct. If not identified and properly treated, DPDS often leads to recurrent fluid collections. Management often requires the use of long-term transluminal stents in order to maintain drainage (Dalsania et al., 2019; Papachristou et al., 2007). Successful management of WON requires a multidisciplinary team to navigate the complex decisions regarding timing, nutritional support, and the specific technique of debridement.

Conclusions:

Acute pancreatitis remains a complex inflammatory disorder with a heterogeneous clinical course, ranging from mild interstitial edematous pancreatitis to severe necrotizing forms associated with significant morbidity and mortality. As evidenced by the literature, the accurate classification of local complications based on the Revised Atlanta Classification is crucial for guiding appropriate clinical management. The distinction between fluid-only collections (APFC and Pseudocysts) and those containing necrotic debris (ANC and WON) has a very high significance in therapeutic decision-making.

While contrast-enhanced computed tomography (CT) serves as the standard diagnostic imaging option, the role of MRI and Endoscopic Ultrasound (EUS) has become increasingly vital in characterizing the content of these collections, particularly in identifying solid necrotic debris

that may be missed in a CT scan. The management of these complications has undergone a paradigm shift in recent decades. There is a clear movement away from open surgical interventions which have a higher risk of adverse effects including morbidity. Instead a "step-up" approach is implemented, which favors conservative management and minimally invasive endoscopic techniques such as LAMS and Direct Endoscopic Necrosectomy. Ultimately, the successful treatment of acute pancreatitis and its local complications relies on precise imaging, timely diagnosis of superinfection, and a multidisciplinary strategy that prioritizes the least invasive and, at the same time, effective intervention.

Disclosure

Author's contributions

Conceptualization:VP;
Methodology:VP, ES;
Software:VP;Check:ES;
Formal analysis:ES
Investigation:ES,VP
Resources:ES,VP
Data curation:VP;
Writing-rough preparation:ES
Writing-review and editing:ES,VP
Supervision:VP

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