

Management of (Peri)Pancreatic Collections in Acute Pancreatitis

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Keywords

Acute pancreatitis · Fluid collection · Management · Surgery · Minimally invasive procedure

Abstract

The development of (peri)pancreatic fluid collections are frequent local complications in acute pancreatitis. These collections are classified as early (acute peripancreatic fluid collection or acute necrotic collection) or late (walled-off necrosis or pseudocyst). The majority of pancreatic fluid collections resolve spontaneously and do not require intervention. However, infection may require intervention. Interventions may include endoscopic or percutaneous catheter drainage, or in a next step endoscopic or surgical necrosectomy, minimally invasive or open. The best timing for the first intervention is still under investigation. Whereas some use antibiotics to postpone intervention until the stage of walled-off necrosis, others drain earlier. Endoscopic drainage of (peri)pancreatic fluid collections is now the preferred approach of drainage due to reduced morbidity as compared to surgical or percutaneous drainage. However, each collection must be treated according to a tailored approach. The final treatment should take into consideration anatomic characteristics, patient preference, comorbidity profile of the patient, and physician discretion. This review summarizes the current evidence on the treatment of (peri)pancreatic fluid collections.

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Introduction

Acute pancreatitis (AP) accounts for over 50% of all hospital admissions for pancreatic disease and still represents one of the most unpredictable diseases of the digestive system [1]. As such, AP can be associated with various local or systemic complications, and in its most severe form, it can lead to multiple organ failure and even death [1–4]. Moderate severe pancreatitis is defined as AP that is accompanied with local complications (e.g., necrosis) of the pancreatic and/or peripancreatic tissue and transient organ failure, and severe pancreatitis is defined as local complications in combination with persistent organ failure [2]. Approximately 15–20% of patients develop moderate severe or severe form of the disease. In nearly one-third of this group, infection of the (peri)pancreatic necrosis occurs, which is associated with mortality rates varying from 15% to 39% [4–8]. Approximately half of AP deaths occur within the first 2 weeks of the disease, mostly due to multiple organ failure as a result of severe systemic inflammatory response. The remainder of deaths occur later from complications secondary to the infection of (peri)pancreatic necrosis and the subsequent interventions [9, 10].

Effective management requires accurate diagnosis and treatment by a multidisciplinary team of specialized surgeons, gastroenterologists, intensivists, and radiologists working in tandem to minimize morbidity and mortality

rates. Over the last decades, treatment has evolved from aggressive open surgery to a more conservative approach with minimally invasive techniques. This review will provide and summarize the existing evidence on the treatment of (peri)pancreatic fluid collections and comment on the challenges that lie ahead.

Definitions of Peripancreatic Fluid Collections

One of the most frequent local complications in AP is the development of (peri)pancreatic fluid collections (PFC). According to the 2012 revised Atlanta classification [2], PFC can be classified based on acuity and content into four distinctive categories: acute peripancreatic fluid collection (APFC), acute necrotic collections (ANC), pancreatic pseudocysts (PP), and walled-off necrosis (WON). According to this classification, PP is defined as well-circumscribed, homogeneous fluid collection surrounded by a well-defined wall without associated necrotic tissue in this collection and is seen >4 weeks after onset of interstitial edematous pancreatitis. A PP will have a strictly liquid substance, and will therefore by definition never occur in necrotizing pancreatitis. Prior to 4 weeks after onset of AP, these fluid collections are termed APFC and have no wall [2, 11]. APFC and PP may arise from the rupture of the main pancreatic duct or one of the smaller peripheral side branches of the pancreatic ductal system. It is not necessary that all APFC and PP have direct communication with a pancreatic duct, as they also may arise from local edema secondary to pancreatic inflammation [2, 12]. Usually, these collections will resolve spontaneously [2, 13, 14].

ANC can occur as a result of necrotizing pancreatitis. These collections have both fluid and necrotic components. This can be seen as a more heterogeneous presentation on abdominal imaging (e.g., contrast-enhanced computed tomography or magnetic resonance imaging). The necrosis will develop in the first 3–5 days after onset of disease, and therefore an early scan may underestimate the amount of necrosis. It is therefore advised to perform imaging after 5 days after onset of disease. In the acute phase, it can be difficult to differentiate between a APFC and ANC. It may take 1–2 weeks after initial diagnosis of a fluid collection to make a clear distinction [2, 14]. Necrotic pancreatitis may present as necrosis of the pancreatic parenchyma, usually accompanied with peripancreatic necrosis. In a small group of patients, there will be solely extrapancreatic necrosis (EXPAN), without necrosis of the parenchyma. Around 2–6 weeks after onset of AP, the necrotic tissue begins to liquefy giving the appearance of both liquid and solid components in clearly demarcated area (WON) [15]. Hence, the term WON refers to a matured ANC that has well-demarcated and thickened wall between the necrotic and viable pancreatic tissue [2].



Fig. 1. CT scan of a pancreatic fluid collection in a 63-year-old male 56 days after onset of acute pancreatitis. Ultrasound or MRI is required to exclude the presence of pancreatic necrosis in this collection.

Indication and Timing for Intervention of (Peri) Pancreatic Fluid and Necrotic Collections

The indication for intervention of PFCs has evolved over the years. Previously [16], PFCs were considered for drainage based on the presence of symptoms and/or complications such as abdominal pain, gastrointestinal obstruction, vascular compression, biliary obstruction, or infection, as well as on the size of the collection. However, guidelines have evolved into the situation that drainage is only necessary in infected collections, or in the exceptional case of symptomatic fluid collections, after a long period of conservative treatment [17].

Generally, intervention in PFCs is deemed preferable if is performed after the collection is encapsulated or demarcated (generally after around 4 weeks). This facilitates entering into the collection with a lower probability of free perforation, and a higher likelihood of successful drainage due to greater adherence of collection to the gastrointestinal lumen for endoscopic approach, for example [18]. Furthermore, postponing the intervention decreased mortality due to reduced proinflammatory response in already critically ill patients, reduced postoperative complications, and is technically more easy to perform with a reduced number of adverse events [19, 20]. However, these arguments have all been extrapolated from direct open surgical necrosectomy. It is unclear if the same applies for the current minimally invasive procedures.

PP is an encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas without necrosis. This entity usually requires >4 weeks after onset of interstitial edematous pancreatitis to mature [2]. PP on contrast-enhanced CT is presented as

well-circumscribed, usually round or oval homogeneous fluid density without non-liquid component (Fig. 1) [2, 11, 21]. Spontaneous resolution of PPs ranges from 8 to 70% and depends on several factors: presence of multiple cysts, location in the pancreatic tail, communication with the main pancreatic duct and co-existence of stricture, and increasing size during follow-up [22–24]. Intervention should be delayed up to 6 weeks from onset of AP, in order to let the PP wall mature [3, 12, 24]. This delay of intervention aids in the success of any type of drainage [25]. Exception of this delay is occurrence of life-threatening events such as erosion of the surrounding blood vessels with hemorrhage with or without cyst rupture; however, this is very uncommon. PPs less than 3 cm in diameter are usually asymptomatic and do not require intervention. There is no absolute size at which intervention is mandated; however, increased risk of complications has been reported of cyst >5 cm in diameter, especially in the absence of decreasing cysts size over 6 weeks [2, 18, 24, 26]. Uncomplicated and asymptomatic PPs, remaining stable or even diminishing in size, can be managed conservatively. PPs that are larger in size may become symptomatic and are a relative indication for intervention. Symptoms include persistent abdominal pain, flank or back pain, partial or complete gastric or duodenal outlet obstruction with early satiety, anorexia, weight loss, abdominal distension, vomiting or reflux, biliary obstruction, and jaundice. As mentioned, more severe complications include PP infection, bleeding into cyst, PP rupture, and gastroduodenal and/or splenic artery erosions [18, 27–29], where intervention is necessary.

During the first 2–4 weeks after occurrence of ANC, it will either resolve or become encapsulated (Fig. 2). Most of ANCs are sterile and will resolve with conservative management, but in cases with infection, further intervention will be required [17]. An asymptomatic WON does not require intervention regardless of its size, because it may resolve spontaneously over time [8, 30]. Even in large collections, the majority will resolve spontaneously. However, it has been shown that larger size of WON, extension of WON to the paracolic gutter, and extension of necrosis are associated with the need for intervention [31–33]. Intervention in a sterile collection carries the risk of secondary iatrogenic infection, with all its associated morbidity and mortality. A symptomatic sterile necrotic collection (e.g., abdominal pain or mechanical obstruction) may require intervention; however, due to the risk of secondary iatrogenic infection, the focus should be on conservative management and interventions should be delayed for 6–8 weeks or longer [8]. In nearly 30% of patients, the (peri)pancreatic necrosis will become infected, requiring intervention in the vast majority of patients (Fig. 3). Only a small percentage of patients can be treated with antibiotics only [34, 35]. Since

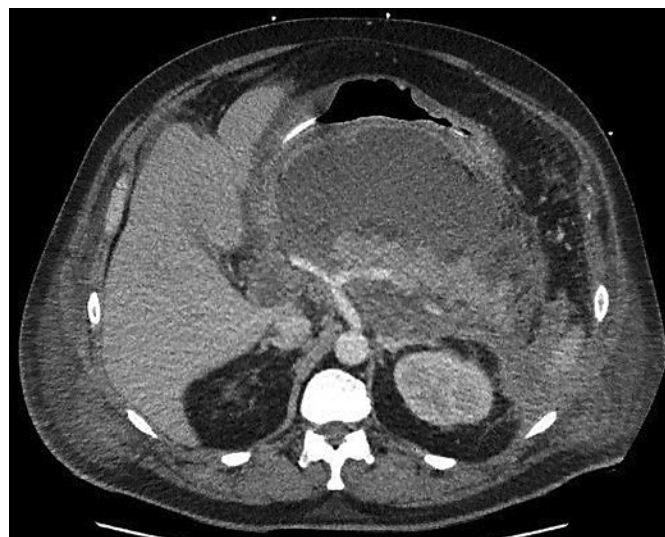


Fig. 2. Acute necrotic collection in a 57-year-old male 17 days after onset of acute pancreatitis.

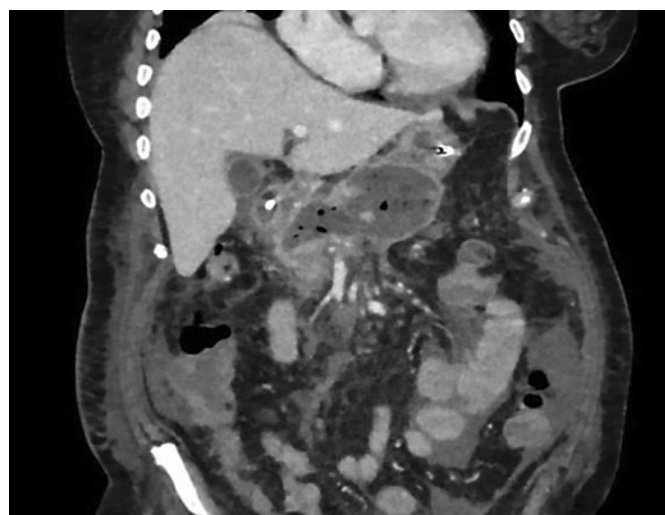


Fig. 3. Walled-off necrosis with infection as documented by the impact gas in a 74-year-old female 27 days after onset of acute pancreatitis.

early open surgery is associated with high morbidity and mortality, it should be avoided whenever possible. Mesenteric ischemia and abdominal compartment syndrome as a direct consequence of AP may represent only two absolute indications for early open surgical intervention [36]. Nerosotomy in the first 2 weeks carries a high risk of morbidity and mortality and therefore should be avoided [19, 20, 36]. Percutaneous drainage, however, can be performed early in the course of infected necrotizing pancreatitis. Currently, the Dutch Pancreatitis Study Group is performing the POINTER trial (<http://www.isrctn.com/ISRCTN33682933>), which randomizes 104 patients between the immediate catheter drainage after diagnosing infected necrosis versus current standard treatment

with postponing catheter drainage under antibiotic treatment (preferably until walled-off necrosis). If necessary, a necrosectomy will be performed and postponed, if feasible, until the stage of walled-off necrosis in both treatment arms. This trial has currently recruited over 75% of patients and results are expected in 2020.

Management of Acute Peripancreatic Fluid Collections and Pancreatic Pseudocysts

As stated above, APFC do not require any intervention and can be treated conservatively. If there is an indication for intervention of a PP, there are several techniques available, including percutaneous, endoscopic, and surgical drainage. Endoscopic transmural drainage has essentially replaced surgical and percutaneous drainage.

In the last two decades, studies comparing the different treatment techniques show significant heterogeneity in the included studies and a clear conclusion cannot be made [37–45]. The adequate technique which should be used depends on anatomy, PP localization, size, content, and communication with the main pancreatic duct. In one of the largest studies comparing percutaneous and surgical drainage of PPs, Morton et al. [44] concluded that surgical approach has fewer complications, less inpatient mortality, and reduced hospital stay. Similar results were published by Heider et al. [45] who favored surgical over percutaneous approach. Only two studies published almost 3 decades ago favored percutaneous over surgical approach in terms of higher mortalities, morbidities [46], and re-interventions [47]. Regarding the success rate, it seems that surgical approach has had higher rate of clinical success, but the overall success rate has been equivalent across all techniques [40–45]. On the other hand, surgical drainage may still be preferred because it avoids the need of an external catheter and reduces the risk of developing external pancreatic fistula. When comparing endoscopic procedures with other techniques for PP treatment, endoscopic transmural approach has showed benefit in hospital stay reduction, treatment costs, and quality of life [37–39, 41, 46]. Therefore, endoscopic approach is preferred when anatomy of the PP allows for direct drainage into the stomach or duodenum. Only if the cyst is located away from the stomach or duodenum, surgical or percutaneous approach should be considered. Also, percutaneous drainage can be helpful in cases of fragile patients with severe comorbidities who cannot tolerate any other procedure; however, due to the risk of pancreatocutaneous fistula, this is not the preferred treatment route. It is important to evaluate the communication between PPCs and main pancreatic duct due to decreased rate of clinical success of transmural drainage alone, in cases in which this communication is present. In such cases, combined endoscopic

transmural and transpapillary drainage may have benefit over single approach modality [48]. However, another study could not find any benefit from combination of transpapillary and transmural over transmural drainage alone [49], and at the moment, the use of this combined approach remains ambiguous.

Management of Acute Necrotic Collections and Walled-Off Necrosis

Invasive interventional procedures for acute necrotizing pancreatitis include radiological, endoscopic, and surgical approach. Previously, a primary open necrosectomy was the preferred treatment of choice. This was associated with high rates of mortality and morbidity. Currently, the treatment of choice is the step-up approach, in which the necrotic collections are primarily drained, and in case of no clinical improvement, there is a “step-up” towards necrosectomy. This step-up approach reduces the rates of new-onset multiple organ failure, morbidity, serious adverse events, and lower costs [50, 51] as compared to primary open necrosectomy, which has since largely been abandoned.

In the step-up approach, nearly half of the patients can be treated with drainages alone, the other half require additional different procedures for the final treatment, including percutaneous, endoscopic, open, or minimally invasive surgery [17, 50, 52, 53]. In a systematic review including 10 retrospective series and one RCT with 384 patients who underwent percutaneous drainage because of acute necrotizing pancreatitis, percutaneous drainage was sufficient as definitive treatment in 56% of patients [54]. Another analysis showed that percutaneous drainage along with antibiotics was successful treatment in 50% of patients [55]. There are no comparative trials yet regarding catheter diameter, but large-bore catheters seem to less frequently obstruct by the necrotic debris. Upgrading drains to a larger diameter could be beneficial for the outcomes [35, 50, 54, 56]. If the patient does not recover with drainage alone, necrosectomy is required. The traditional open necrosectomy has been largely replaced by minimally invasive techniques [6, 50, 51]. Of these, the most commonly used techniques include sinus tract endoscopy and video-assisted retroperitoneal debridement (VARD) [57, 58]. These techniques showed reduced morbidity and mortality, especially in high-risk groups of patients [59].

In the last decades, endoscopic transmural (i.e., transgastric) management of acute necrotizing pancreatitis is being increasingly performed. Various endoscopic techniques are used for the treatment of WON, all of these include transmural access to the cavity with or without endoscopic ultrasound (EUS). EUS-guided drainage and/or necrosectomy has had advantage over conventional

transmural endoscopic approach due to higher technical success [40, 42, 60]. Compared to surgical necrosectomy, an endoscopic approach significantly reduces proinflammatory response and improves clinical outcome in ANP patients [52]. However, when used as a single modality approach, it requires more sessions of necrosectomy for definitive treatment than in combination with other interventional procedures [53, 61–63]. A large meta-analysis found that endoscopic necrosectomy has success rate of 81% as a single treatment modality with a complication rate of 36% [64]. In the largest randomized controlled trial, comparing endoscopic step-up approach with surgical step-up approach [53], both procedures have similar mortality rates and major complications. The surgical step-up approach, however, had a higher incidence of pancreaticocutaneous fistula [51, 53].

Conclusion

The management of pancreatic fluid collections needs to be tailored for each patient. Multidisciplinary approach is crucial for adequate and timely treatment. Asymptomatic collections do not need drainage irrespective of their size. Infected collections may require intervention. Delaying intervention at least for 3–4 weeks after AP onset allows better decision in the selection of interventional approach. A minimally invasive step-up approach is superior to primary open surgery in terms of morbidity for all peripancreatic fluid collections and should be the treatment of choice. Decision on surgical/percutaneous or endoscopic treatment should be made on anatomy, location of the collection, and local expertise of endoscopists, radiologists, and surgeons.

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