Local complications of acute pancreatitis

Acute pancreatitis is seen commonly on the surgical take. It can be complicated by the development of pseudocysts and necrosis. This review discusses each of these in turn and outlines the different management strategies now on offer.

Acute pancreatitis is a common cause of emergency hospital admission, with 150–420 cases per million population per year (UK Working Party on Acute Pancreatitis, 2005). It follows a variable clinical course, being a rapidly resolving condition in the majority of patients who require little more than supportive care. The minority, however, develop systemic or local complications which adversely affect their morbidity and mortality.

Classification of acute pancreatitis and its complications took place at the 1992 Atlanta symposium (Bradley, 1993) in an attempt to agree uniform definitions and, thus, aid comparison and research. This classification was updated in 2012 (Banks et al, 2013) as a result of increased understanding of the pathophysiology as well as improved imaging modalities.

This new classification refined the definitions of the local complications (*Table 1*), but also differentiates interstitial oedematous pancreatitis from that of necrotizing pancreatitis because of their differing clinical course and thus management. It also clarifies the difference in severity, highlighting criteria for mild, moderately severe and severe pancreatitis (*Table 2*).

It is important to remember that this updated classification emerged in 2012, so trials before this time may have included combinations of these complications and clinical severity when comparing management strategies and outcomes. With ongoing research and emerging treatment strategies, there is the potential for further changes in the years ahead.

This review focuses on the local complications of pancreatitis as defined by the 2012 classification and addresses their management strategies.

Table 1. Revised Atlanta classification of the morphological features of acute pancreatitis

Definition	Morphological features
Interstitial oedematous pancreatitis	Acute inflammation of the pancreatic parenchyma and peripancreatic tissues
Necrotizing pancreatitis	Inflammation associated with pancreatic parenchymal and/or peripancreatic necrosis
	Lack of parenchymal enhancement by intravenous contrast on computed tomography
Acute peripancreatic fluid collection	Peripancreatic fluid associated with interstitial oedematous pancreatitis
	Homogenous collection with no definable wall encapsulating the collection
	No associated necrosis
	Only applies within the first 4 weeks after onset of symptoms
Pancreatic pseudocyst	Encapsulated collection of fluid with a well-defined inflammatory wall
	Minimal or no necrosis
	Maturation usually requires >4 weeks after the onset of acute pancreatitis
Acute necrotic collection	Collection containing variable amounts of both fluid and necrosis associated with necrotizing pancreatitis
	Heterogeneous collection of non-liquid density
	No definable wall
Walled-off necrosis	Mature, encapsulated collection of pancreatic or peripancreatic necrosis
	Well-defined wall which usually occurs >4 weeks after the onset of necrotizing pancreatitis

From Banks et al (2013)

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Acute peripancreatic fluid collections

Up to 25% of patients with acute pancreatitis develop collections of fluid in the peripancreatic area. The majority of these are simple collections that lack a granulation or fibrous tissue wall which develop in the first few weeks and resolve spontaneously. They require no additional treatment.

In some patients, these fluid collections fail to resolve and the fluid becomes enclosed within a wall of fibrous or granulation tissue, typically over a period of 4 weeks.

Table 2. Severity of acute pancreatitis

Grade of severity	Features
Mild acute pancreatitis	No organ failure
	No local or systemic complications
Moderately severe pancreatitis	Organ failure that resolves within 48 hours
	Local or systemic complications without persistent organ failure
Severe acute pancreatitis	Persistent organ failure (>48 hours) of a single or multiple organs

From Banks et al (2013)

These fluid collections then become known as pancreatic pseudocysts.

Pancreatic pseudocysts

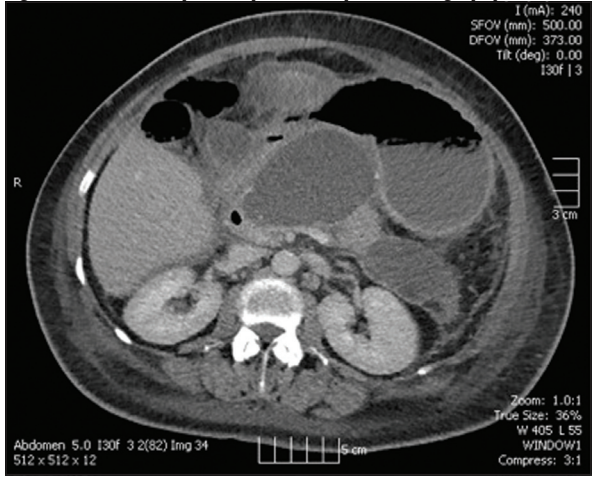
Pancreatic pseudocysts are localized fluid collections that are rich in amylase and other pancreatic enzymes. They are surrounded by a wall of fibrous tissue, yet are not lined by epithelium (*Figure 1*). They are the most common cystic lesion of the pancreas, initially described by Morgagni in 1761.

They can develop following an episode of acute pancreatitis or, more commonly, arise as a result of chronic pancreatitis or pancreatic trauma. Pseudocysts are more common following alcohol-induced pancreatitis as opposed to non-alcohol-related pancreatitis, although the total incidence is low, with only 1.6–4.5% of all acute pancreatitis patients developing a pseudocyst (Habashi and Draganov, 2009). Conversely, 30–40% of patients with chronic pancreatitis will have their clinical course complicated by the occurrence of a pseudocyst (Boerma et al, 2000).

Pseudocysts develop following disruption of the pancreatic duct. In chronic pancreatitis this is secondary to fibrosis and stricturing following chronic inflammation. In acute pancreatitis, pancreatic duct disruption is secondary to increased pancreatic ductal pressure which is a result of calculi or protein plugs blocking the main duct, or as a result of pancreatic necrosis (D'Egidio and Schein, 1991). There remains controversy as to whether there is always pancreatic duct disruption in acute pancreatitis, or whether a proportion of pseudocysts are simply an organized collection of necrotic tissue. The updated Atlanta classification distinguishes walled-off necrosis from a pseudocyst and should aid the understanding and ultimately the management of these two different pathologies.

Traditionally, the treatment of pancreatic pseudocysts was active with the limited evidence indicating that persistent or large (>6 cm) cysts would fail to resolve. Increasingly, however, evidence has shown that the majority of pseudocysts that are a result of acute pancreatitis will resolve spontaneously and thus in the majority of asymptomatic patients, intervention is not recommended.

Figure 1. Pancreatic pseudocyst on computed tomography scan.



Complications of a pancreatic pseudocyst

In some patients the pseudocyst can become problematic, as described in *Table 3*. The size and position of the pseudocyst play a role in this as the cyst can compress the stomach and duodenum leading to gastric outlet obstruction, experienced as early satiety and vomiting. It may also compress the biliary tree, resulting in biliary stasis and obstruction, and lead to ascending cholangitis. Pressure of the pseudocyst on surrounding structures can lead to chronic, and sometimes unmanageable, pain.

Pseudocysts can, in the minority of cases, cause immediate life-threatening complications. The pseudocyst can rupture into the gastrointestinal tract causing sudden abdominal pain and haematemesis. The bleeding is usually from a pseudo-aneurysm in the wall of the cyst itself. Alternatively, the rupture can occur into the peritoneum leading to peritonitis as the cyst contents irritate the peritoneal cavity. This usually requires emergency laparotomy to wash out the abdomen and drain the remaining cyst contents.

The most common complication reported is that of infection of the pseudocyst. This can result in a localized abscess and/or a systemic response. Antibiotics and antifungals are used to control the sepsis, but the source of infection usually needs to be removed by eliminating the pseudocyst.

Management options

The first decision required is to determine which patients require intervention. Complications of pseudocysts as mentioned in the previous section will need intervention, as summarized in *Table 4*. The next step is to determine which method of intervention is most appropriate. The options, in particular endoscopic treatments, have improved in technique and availability in recent years adding to the scope of interventions on offer.

There are now three main modalities of treatment. The most suitable depends on the size and location of the

Table 3. Complications of a pancreatic pseudocyst

Potential complication	Features
Infection	Peripancreatic abscess
	Septic shock
Pressure effects	Biliary compression
	Gastric outlet obstruction
	Chronic pain
Rupture	Peritonitis (intra-peritoneal rupture)
	Gastrointestinal bleeding or internal fistula (gastrointestinal rupture)
Vascular erosion	Pseudocyst haemorrhage or haemoperitoneum

Table 4. Indications for intervention

Complicated pseudocyst	Gastric or duodenal outlet obstruction
	Common bile duct compression
	Infected pseudocyst
	Haemorrhage into cyst
	Pancreatico-pleural fistula
	Compression of large vessels (clinically or radiologically)
Symptomatic pseudocyst (relative indications depending on severity and comorbidities)	Early satiety or vomiting
	Pain
	Upper gastrointestinal bleeding
Asymptomatic pseudocysts (relative indications)	>5 cm, unchanged in size and morphology for more than 6 weeks

pseudocyst as well as local expertise. There are very limited studies directly comparing treatment modalities, particularly in pseudocysts resulting from acute pancreatitis, so recommendations are dependent on centre expertise and experience.

Endoscopic management

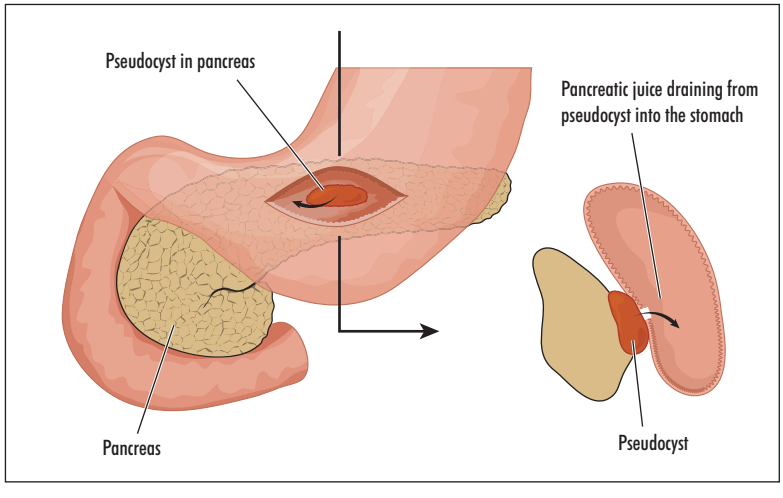
Endoscopic drainage is becoming the preferred treatment as it is minimally invasive and does not require ongoing care of external drains. Two approaches can be used to create a connection between the pseudocyst and gastrointestinal tract through which the cyst contents can drain.

The transpapillary approach involves cannulation of the pancreatic duct through endoscopic retrograde cholangiopancreatography and the placement of a plastic or metal stent into the pseudocyst. This approach is used when the pseudocyst communicates with the main pancreatic duct which tends to be more common in chronic pancreatitis. It cannot be successful if the pancreatic duct is blocked.

The alternative endoscopic approach is to drain the cyst transmurally via the stomach or small bowel, typically the duodenum. A direct connection is formed between the gastrointestinal tract and the cyst and thus the cyst must be located in a position, usually <1 cm from the gastrointestinal wall without any intervening structures, such as vascular structures or varices, for it to be attempted. It can, in a minority, result in upper gastrointestinal bleeding.

In a small series (Hookey et al, 2006), resolution of the pseudocyst occurred in 87.9% of patients following endoscopic drainage, although the success rate was lower in patients with necrotic tissue within the pseudocyst. Complications of this approach are failure of full resolution of the cyst, introduction of infection and stent migration.

Figure 2. Pseudocystogastrostomy.



Percutaneous drainage

If the pseudocyst is sited in a favourable position, a drain can be placed percutaneously using computed tomography or ultrasound imaging to guide placement. This approach, although minimally invasive, has a high risk of infection and can turn a sterile collection into an infected collection. This risk increases with multiple drains and many patients require drain resiting as a result of stent blockage. In addition, some patients find the external drain uncomfortable and difficult to manage. It is, nevertheless, an approach that is particularly useful in infected cysts to gain control of sepsis and stabilize the patient.

Surgical drainage

Surgical drainage creates a communication between the pseudocyst and gastrointestinal tract, known as a pseudocystogastrostomy (*Figure 2*) or pseudocystoduodenostomy. Both of these procedures can be completed laparoscopically, but experience remains limited and long-term outcomes and comparison to other approaches are not yet available. Surgery is now generally reserved for patients in whom the other approaches have failed or cannot be attempted because of the position and/or composition of the pseudocyst.

In summary, the majority of pseudocysts can be managed conservatively, but in those that require intervention, endoscopic approaches are favoured, if possible, because of their minimally invasive nature.

Pancreatic necrosis

Acute pancreatitis can be a fatal illness. Approximately half of the fatalities occur in the first week and are the result of a severe systemic inflammatory response leading to multi-organ failure. There is a second peak of morbidity and mortality which occurs later. The majority of these deaths are the result of the subsequent infection of pancreatic and peripancreatic necrosis.

Necrosis (*Figure 3*) develops in approximately one third of patients who are deemed to have a severe attack of pancreatitis and who have organ failure in the first week of their presentation. The severe inflammatory response results in cell death and subsequent unviable and necrotic tissue. Activation of trypsinogen is the initiating event leading to autodigestion of the pancreas and subsequent

inflammation. The peptide released during the activation of trypsinogen, trypsinogen activation peptide, is therefore indicative of the amount of inflammation and its urinary levels have been shown to be a valuable predictor of severe disease (Neoptolemos et al, 2000), although not yet used in clinical practise.

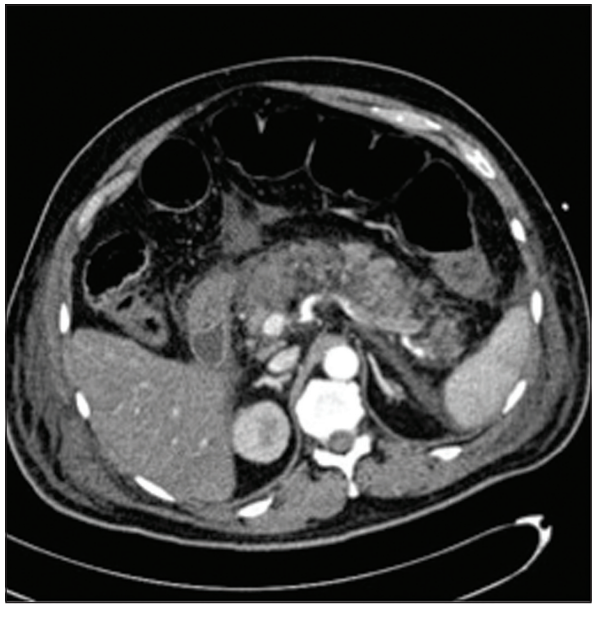
Diagnosing infective necrosis

Sterile pancreatic necrosis does not mandate treatment, particularly if the patient remains in a stable condition. It should be emphasized, however, that sterile necrosis can become infected at any time and the frequency of infection increases with time (Beger et al, 1986). Gram-negative anaerobic bacteria are the most common organisms detected, indicating translocation from the gastrointestinal tract as the primary source. Enteral nutrition maintains mucosal integrity of the gastrointestinal tract, preventing bacterial translocation, and early introduction of enteral nutrition, even at low volumes, appears to reduce sepsis, organ failure and intensive care unit admission rates (Samaraee et al, 2010).

As with other infective conditions, the clinical signs of hypotension, tachycardia and pyrexia aid the detection of infection, although these signs are also present in an inflammatory response without infection. Further aids to identify infection are that of persistently elevated C-reactive protein and the presence of gas within the necrosis on computed tomography scanning. The definitive method for detecting infection is fine-needle aspiration and culture of necrotic tissue.

There have been multiple studies looking at the prevention of infection in pancreatic necrosis. A Cochrane review (Villatoro et al, 2010) showed a significant survival advantage with prophylactic antibiotic therapy, but no significant difference in pancreatic infection rate or operative debridement rate. This may be the result of a reduction in non-pancreatic infections. Previous studies had shown a rise in resistant organisms and fungal infections with antibiotic therapy, yet this was not supported in the Cochrane review. However, the numbers involved in the studies were small.

Figure 3. Pancreatic necrosis on computed tomography scan.



Management of pancreatic necrosis

The presence of infection in pancreatic necrosis is an absolute indication for intervention, although there are isolated case reports of survival following medical therapy alone. Extensive sterile necrosis is a more contentious issue. Failure to improve after 2–3 weeks of supportive treatment, unexplained deterioration and/or necrosis of >50% are felt to be relative indications for surgical intervention (Slavin et al, 2001).

Traditionally open necrosectomy was the only operative intervention which itself carried a high morbidity and mortality risk. Minimally invasive techniques have the potential to reduce this as they reduce the systemic inflammatory and septic response that occurs in an open operation with the release of infected necrosis.

Percutaneous and retroperitoneal approach

The percutaneous approach, analogous to that used for pseudocysts, consists of a drain placed under ultrasound or computed tomography guidance into the necrotic tissue. It is safe and feasible in appropriately located necrosis. Nevertheless, multiple procedures are generally required because solid components within the necrosis cause stent blockage. In most studies, approximately 50% required further treatment, often in the form of surgical necrosectomy. In these patients, percutaneous drainage acts as a temporising method to control sepsis and prevent deterioration before an open operation.

Innovative methods that involve the drainage of collections via a retroperitoneal route have the benefit of avoiding contamination of the peritoneal compartment and the subsequent septic and inflammatory hit that this would give the patient. Minimal access retroperitoneal pancreatic necrosectomy (*Figure 4*) involves placing a guidewire under computed tomography guidance into the necrotic tissue and, at operation, expanding this tract to allow placement of a larger drain through which the tissue is removed. Irrigation of this area is left in place postoperatively to allow the remaining tissue to be liquefied and subsequently drained. Multiple operative procedures may be required. This technique has fewer complications and lower mortality than open necrosectomy (Raraty, 2010).

Endoscopic approach

In the same way as with pseudocysts, the necrotic material can be accessed by making a direct communication between this and the stomach. Endoscopic ultrasonography has been used to allow better definition of the tissue and surrounding vascular structures and guide optimal stent placement. Studies have shown good results

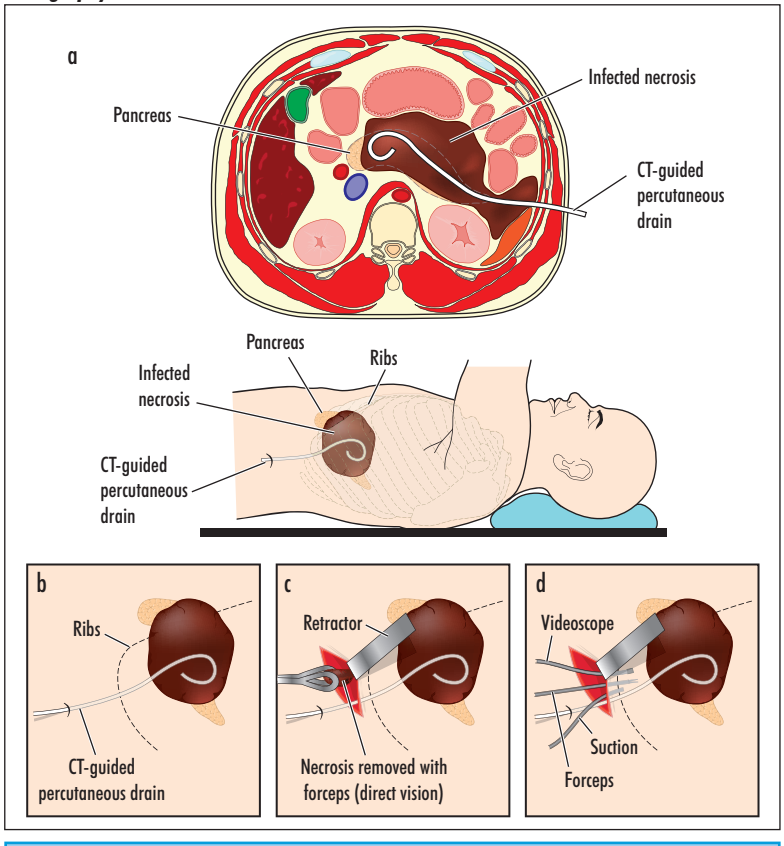
with the majority achieving full resolution of the necrotic material, although often requiring multiple procedures.

Open and laparoscopic necrosectomy

The traditional open necrosectomy involves debriding all necrotic pancreatic tissue and any associated fluid collections. Drains and irrigating catheters are left in the retroperitoneal space with initially continuous irrigation continued postoperatively. Adequate debridement is typically achieved in a single visit to theatre, but access to the necrotic tissue is via the peritoneum and there is an associated septic response as this material is released through the abdomen. Mortality rates are in the order of 20–40%.

Laparoscopic necrosectomy has been used, but it does not eliminate the need for debridement via the peritoneal cavity and the resultant inflammatory response. Small case series have shown good results with thorough debridement achieved, although the patients included may have been more stable as indicated by their ability to tolerate a pneumoperitoneum.

Figure 4. Minimal access retroperitoneal pancreatic necrosectomy. CT = computed tomography.



KEY POINTS

- Significant complications can result from severe acute pancreatitis, leading a second, later peak of mortality.
- Pancreatic pseudocysts can be managed conservatively if they are uncomplicated and asymptomatic.
- When intervention is required, an endoscopic approach, if technically feasible, provides a minimally invasive means of eliminating the cyst.
- Necrotizing pancreatitis has high rates of morbidity and mortality, particularly if infected. There remains controversy as to whether prophylactic antibiotics are beneficial in preventing infection in the presence of necrosis.
- Infected necrosis should be suspected with clinical deterioration, persistently high C-reactive protein levels and/or signs on computed tomography.
- Minimal access techniques have reduced morbidity and mortality, but may require multiple procedures.
- Multidisciplinary teams should be involved in the management decisions of these complex patients.

Conclusions

Acute pancreatitis is a common condition that, in the minority, can have significant complications resulting in high rates of morbidity and mortality. Minimal access techniques have added to the management strategies available for pancreatic pseudocysts and necrosis. Further studies will add clarification and aid decision making in these complex conditions. BJHM

Conflict of interest: none.

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