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Review

Acute pancreatitis: international classification and nomenclature

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The incidence of acute pancreatitis (AP) is increasing and it is associated with a major healthcare concern. New insights in the pathophysiology, better imaging techniques, and novel treatment options for complicated AP prompted the update of the 1992 Atlanta Classification. Updated nomenclature for pancreatic collections based on imaging criteria is proposed. Adoption of the newly Revised Classification of Acute Pancreatitis 2012 by radiologists should help standardise reports and facilitate accurate conveyance of relevant findings to referring physicians involved in the care of patients with AP. This review will clarify the nomenclature of pancreatic collections in the setting of AP.

Introduction

Acute pancreatitis (AP) is a common condition with a highly variable disease presentation, clinically and morphologically, causing significant morbidity and mortality in severe cases.[1–3] Its incidence is reported to be increasing.[1] Almost all patients who present with AP are hospitalised for supportive therapy and optimal management, particularly for the first episode of pancreatitis, to determine the specific cause.[2,3] Consequently, for gastrointestinal disorders AP represents the primary cause leading to hospital admission in the United States, with annual costs of treatment exceeding $2.5 billion.[4,5] The diagnosis of AP is made when two of the following three features are present: (1) characteristic upper abdominal pain; (2) amylase and/or lipase three-times the institutional upper limit of normal; and (3) imaging findings consistent with AP.[1] Disease severity of AP is variable: some 75–80% have a relatively mild clinical course with a ready response to conservative management, resulting in complete recovery and a short hospital stay.[1,3] About one out of four patients develops clinically severe AP associated with major morbidity and mortality, prolonged hospital stay, consuming most of the healthcare expenses in AP.[1–3] Imaging in severe AP is pivotal for local severity assessment, evaluation of pancreatic and extrapancreatic complications, and guiding clinical management.[6] Severity classification of AP is essential for patient triage (to identify those requiring early intensive treatment), patient transfer (to tertiary centres), and allocation of patients to clinical trials (for reliable comparison of data and outcome).[7] Earlier efforts to classify the severity of AP resulted in the 1992 Atlanta Classification.[8] This clinically based classification system defined AP, its severity, and the local pancreatic complications based on clinical criteria.[8] These definitions proved useful initially. Over the last decade, inconsistencies in the Atlanta definitions and ambiguous descriptions of pancreatic collections, mainly by a lack of radiological criteria for characterisation, has become increasingly apparent.[9–11] This, combined with advances in the knowledge of the natural history of AP, improved diagnostic imaging, and the

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development of minimally invasive treatment options for complicated pancreatitis, necessitated an update of disease severity classification and nomenclature of pancreatic collections. An international iterative web-based consultative process resulted in the development of the 2012 Revised Atlanta Classification (RAC) to overcome the aforementioned limitations.[12] For radiologists, the most important part of the RAC concerns the redefinition of morphological types of AP and the revision of pancreatic collections based on their content, wall, site, and evolution by using computed tomography (CT) criteria. Essentially, the RAC pertains to cases of AP. It does not apply for chronic pancreatitis, acute on chronic pancreatitis, and groove pancreatitis, all of which have a different aetiopathogenesis, clinical presentation, imaging findings, therapy, prognosis, and outcome.[6,12,13] This article provides a comprehensive review of the RAC of AP.

Overview of imaging techniques

Imaging techniques commonly used for the diagnosis and severity assessment of AP include abdominal ultrasound, contrast-enhanced CT (CECT), and magnetic resonance imaging (MRI). In the early phase, ultrasound is primarily used for assessment of biliary stones and biliary obstruction to elucidate the aetiology of AP. At a later stage, ultrasound is helpful for characterisation of pancreatic collections, by differentiating fluid from non-liquid material and guiding diagnostic or therapeutic interventions.[6,14] CECT is the imaging method of choice for overall assessment of AP because of its accuracy and wide availability. In the initial phase, CT can provide the diagnosis when in doubt or suggest an alternative diagnosis, help triage patients with different grades of severity, and identify early local complications, such as pancreatic parenchymal necrosis (in short, pancreatic necrosis). In the late phase, CT is essential for assessment of evolution of local complications, guidance of when and how to employ invasive treatment, and monitoring response to treatment.[6,14]

MRI is an acceptable alternative to CT. MRI is as sensitive as CT for diagnosis and severity assessment, but superior to CT in characterisation of pancreatic collections by accurately identifying non-liquefied material (necrotic tissue or debris) within collections.[15] MRI also allows for assessment of pancreatic duct integrity; however, availability, longer scanning time, motion artefacts, the need for specialised MRI-compatible monitoring equipment in critically ill patients, and high costs hamper the widespread use of MRI in AP. Therefore, at present, MRI has a complementary role in AP.[6,14] The RAC regards CT as the frontline imaging technique in AP. Consequently, CT criteria are proposed for the description of morphological types of AP and associated local complications.

Imaging findings of AP

Irrespective of the aetiology (Table 1), the morphological findings of AP can be described in terms of alterations of the pancreatic parenchyma (interstitial oedema and necrosis), peripancreatic tissues (fat stranding and collections), and extrapancreatic abnormalities (involvement of parenchymal organs, biliary system, vascular structures, and gastrointestinal tract). The spectrum of morphological abnormalities is dictated by the severity of the initial attack of AP. In approximately 10–20% of cases, CECT will show equivocal (normal or near normal) findings by which the diagnosis of AP hinges on upper abdominal pain and elevated pancreatic enzymes.[16] Typical findings of morphologically mild AP includes focal or diffuse enlargement of the pancreas, parenchymal inhomogeneity (due to interstitial oedema), irregular gland margins with increased attenuation of peripancreatic fat (peripancreatic fat stranding), and/or collections, usually minor in degree (Fig 1).[16] In around 20% of cases, the inflammation is a focal process, usually involving the head or tail.[16] With increasing severity of the attack, more pronounced abnormalities are observed with development of pancreatic collections and pancreatic necrosis. CT diagnosis of pancreatic necrosis is defined as non-enhancing pancreatic parenchyma. Visual comparison between the degree of pancreatic and splenic

Table 1
Causes of acute pancreatitis.

Common causes (70–80%)
- Gallstones
- Alcohol abuse
Uncommon causes (10–15%)
- Hypercalcaemia
- Hypertriglyceridaemia
- Post-endoscopic retrograde cholangiopancreatography
- Drug induced (e.g., thiazides, azathioprine, tetracycline)
- Abdominal trauma
- Infection (e.g., mumps, coxsackie B virus)
- Tumours (e.g., peri-ampullary tumour, pancreatic cancer)
Idiopathic (10–20%)

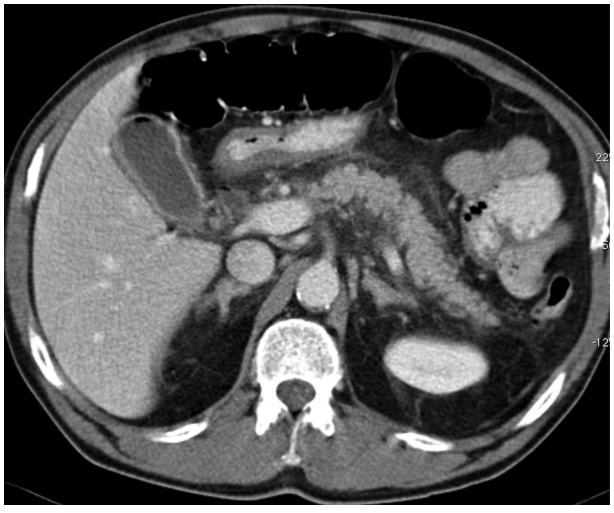


Figure 1 Interstitial pancreatitis with swollen pancreas and peripancreatic fat stranding.

parenchymal enhancement is generally adequate for detection of pancreatic necrosis.[16] Pancreatic necrosis may be focal or multifocal, limited or extensive, confined to the periphery or full thickness. Pancreatic necrosis develops early in the course of AP (within 24–48 hours) and is complete within 72–96 hours after symptom onset.[16–18] Cross-sectional imaging is best performed after this time period, as early CT may miss or overestimate the presence of pancreatic necrosis (Fig 2).[14,16,17,19] When pancreatic necrosis has been definitively established on CECT, it tends to remain stable during the following disease course as opposed to pancreatic collections. Pancreatic necrosis represents the most severe form of AP and forms the basis for most of the systemic and local complications.[16,17] The presence, and possibly the extent, of pancreatic and peripancreatic necrosis, increases the probability of infection. In turn, when pancreatic necrosis becomes infected, it is associated with a two- to threefold increase in mortality: about 20–30% for infected necrosis compared with 9–12% for sterile necrosis.[2,3,20]

CT indications

In the early phase (first week), imaging by means of CT is rarely necessary for clinical management in patients with (mild and severe) AP because local changes still progress, under-staging by CT is common and falsely reassuring clinicians, while morphological findings often do not parallel clinical findings, and thus, patient management will not be influenced by CT findings in stable patients at this stage[2,12,19]; however, CT is indicated in those with uncertain diagnosis or those suspected of having early complications, such as bowel ischaemia or perforation requiring emergency laparotomy.[21] In the later phase (after the first week),

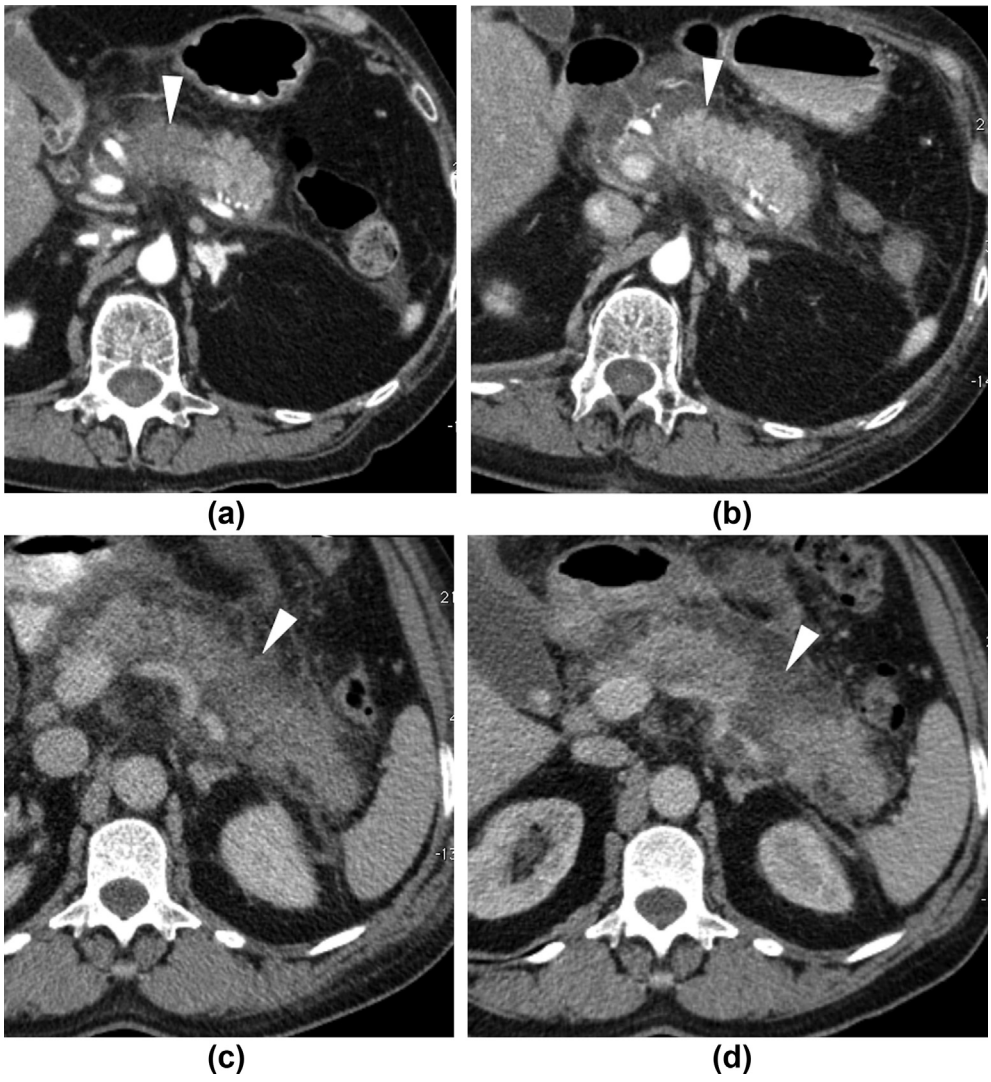


Figure 2 (a–b) False-positive parenchymal necrosis. (a) Early contrast-enhanced CT demonstrates a focal hypodense area at the pancreatic neck and proximal body (arrowhead). (b) Follow-up CT 5 days later shows normal perfused pancreas (arrowhead). (c–d) False-negative parenchymal necrosis. (c) Early contrast-enhanced CT depicts a slightly hypodense area at the body–tail junction (arrowhead), which was not read as parenchymal necrosis in the original report. (d) Follow-up CT 1 week later shows an area of non-enhancement at the body–tail junction (arrowhead) compatible with <30% parenchymal necrosis.

patients with mild or moderately severe AP who fail to respond to supportive therapy and those with predicted or established severe AP (based on clinical parameters, such as systemic inflammatory response syndrome [SIRS] or organ failure) should undergo abdominal CT.[2,12,19] In the former case, CT is needed for unsuspected local complications, in the latter as a baseline study. Follow-up studies are dictated by clinical findings that include sudden-onset or increase of abdominal pain and organ failure, signs of sepsis or other \signs of local complications (e.g., sudden drop of haemoglobin), or when invasive treatment is contemplated.[21]

CT imaging technique

CT protocols for evaluation of AP vary widely in literature and practices worldwide. Some advocate multiphasic CT, but in the author's opinion a monophasic CT protocol after intravenous contrast medium administration is usually sufficient for overall assessment of AP (both as baseline study and follow-up studies).[21–23] Typically, imaging is performed during the pancreatic phase (delay of 40–50 seconds) or portal venous phase (delay 60–70 seconds) from diaphragm to pelvis. Dual-phase studies are helpful in cases of haemorrhage, ischaemia, or suspicion of a pseudoaneurysm or pancreatic mass.

2012 RAC for radiologists

Phases of AP

Clinically severe AP roughly runs a biphasic clinical course with concomitant peaks in mortality.[12] Within the first 1–2 weeks of onset, a cytokine-mediated activation of the inflammatory cascade leads to SIRS and (multi)organ dysfunction. Deaths in this early phase are related to organ dysfunction rather than sepsis or infection. The second phase ensues thereafter and is primarily dictated by sepsis-related complications, often due to infection of pancreatic and peripancreatic tissues, responsible for the second peak in mortality.[12]

Clinical and morphologic severity of AP

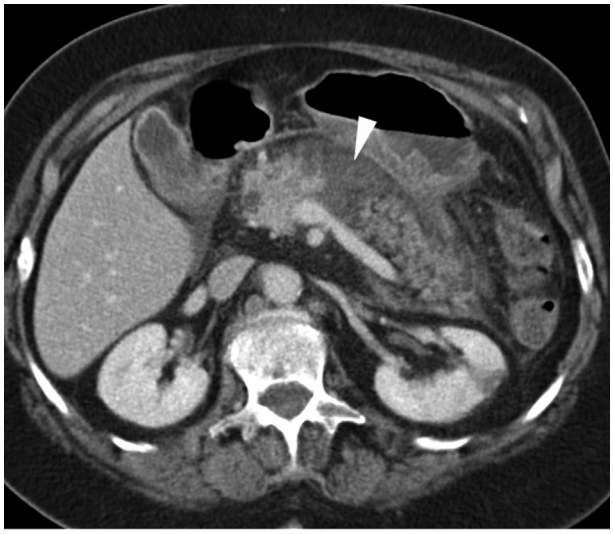
The RAC makes a clear distinction between clinical severity based on clinically based parameters and morphological severity based on imaging (CT) parameters. The RAC defines three categories of clinical severity: (1) mild AP: defined as absence of systemic or local complications; (2) moderately severe AP: this new category has been added, defined as the presence of transient organ failure, deteriorating pre-existing co-morbid disease, and/or presence of local complications requiring prolonged stay or intervention; (3) severe AP: defined as persistent organ failure (>48 hours) during the course of disease.[12] Morphologically, two different types of AP (interstitial or oedematous pancreatitis and necrotising pancreatitis) are discriminated. These entities will be outlined in the following sections. In general, morphological severity closely correlates with clinical severity: patients with necrotising pancreatitis have clinically severe disease, and vice versa. CT findings, however, are not absolutely predictive of outcome for an individual patient. Approximately 5% of patients with minimal changes on CT will have significant complications with mortality of around 1–3%.[24] An even larger number of patients, up to 30%, will have a relatively benign clinical course despite the presence of pancreatic necrosis.[19,25,26] Therefore, ultimate severity of disease is based on clinical parameters, primarily organ failure.

Morphological types of AP

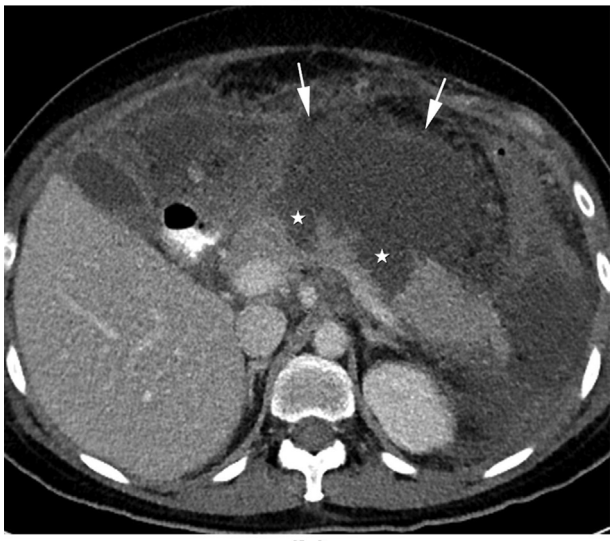
The RAC maintains the distinction between interstitial and necrotising pancreatitis that corresponds well with cross-sectional imaging criteria. In interstitial pancreatitis (Fig 2), the pancreas enhances normally on CECT with or without surrounding peripancreatic inflammatory changes or fluid (acute peripancreatic fluid collections or APFC). In necrotising pancreatitis (Fig 3), there is tissue necrosis subdivided into three forms dependent on whether the necrosis entails the pancreatic parenchyma alone (very rare), peripancreatic tissues alone (also known as extrapancreatic necrosis or EXPN), or combined necrosis of both pancreatic parenchyma and peripancreatic tissue (most common).[12] Isolated EXPN was not recognised in the original 1992 Atlanta Classification and represents a subgroup of patients with intermediate prognosis ranging between patients with interstitial pancreatitis and combined necrosis.[24,27] At CECT, this entity is depicted as a normally enhancing pancreas that is surrounded by pancreatic collections of various densities (acute necrotic collections or ANCs). The distinctions between the various subtypes and complications of AP have important implications for clinical management and prognosis. Interstitial pancreatitis has a mortality of <3% and is generally treated conservatively.[24] Pancreatic necrosis, particularly in the presence of infection, is associated with mortality rates up to 25%, and surgical management may be required.[20] Patients with EXPN have a significant better prognosis than those with combined necrosis if necrosis remains sterile, but have similar rates of morbidity and mortality in case of infected EXPN.[27]

Nomenclature of pancreatic collections in AP

In the RAC, pancreatic collections associated with AP can be categorised temporally (by degree of encapsulation) or morphologically (by content; Fig 4). The various pancreatic collections are either sterile or may become infected during the course of disease. In the early phase, collections that have no or an incomplete wall of granulation tissue are called either APFC or ANC.[12,28] In the late phase when collections are completely encapsulated, these are termed either pseudocyst or walled-off necrosis (WON).[12,28] Morphologically, those collections containing liquid only (APFC and pseudocysts) arise in interstitial pancreatitis, and those containing necrotic tissue (ANC and WON) arise



(a)



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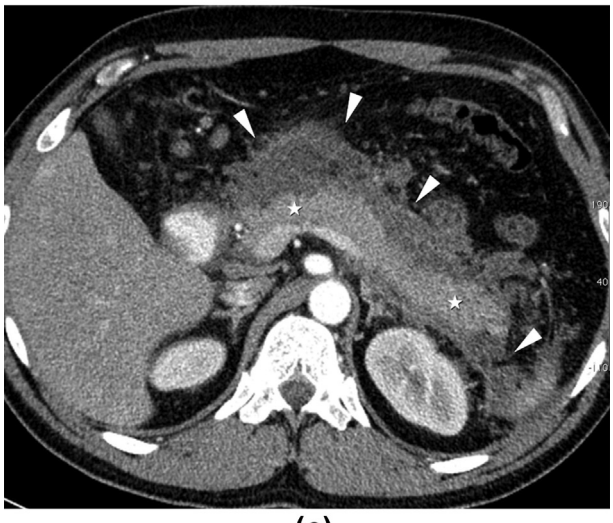

(c)

Figure 3 Three subtypes of necrosis in three different patients. (a) Isolated parenchymal necrosis in a 64-year-old man with a focal area of non-enhancement at the proximal body of the pancreas (arrowhead) without evidence of peripancreatic fat necrosis. (b) Combined necrosis in a 45-year-old man with combined necrosis of pancreatic neck and body (asterisks) and peripancreatic fat necrosis (arrows pointing at the borders). (c) Isolated extrapancreatic fat necrosis (EXPN) in a 53-year-old man with normal perfused pancreas (asterisks) with surrounding heterogeneous collections compatible with EXPN.

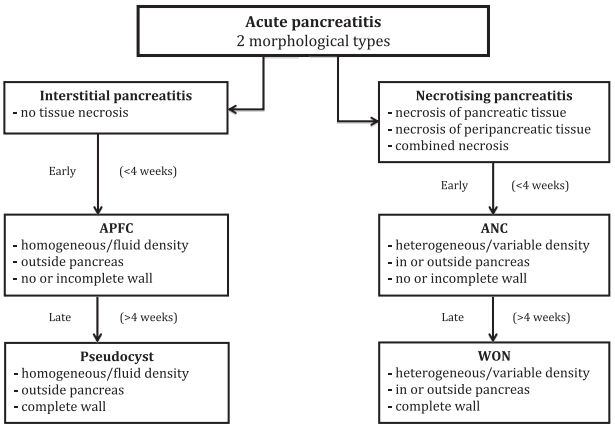

Figure 4 Morphological classification of AP.

exclusively in necrotising pancreatitis. Thus, by convention, an APFC does not occur in necrotising pancreatitis and, likewise, an ANC does not develop in interstitial disease.

Differentiating liquid from necrotic collections in symptomatic patients is important for management purposes; for liquid collections simple drainage procedures suffice, whereas for necrotic collections usually more invasive interventions, like necrosectomy, are needed.

Liquid collections: APFC and pseudocyst

APFCs may be single or multiple, occur early and exclusively in the setting of interstitial pancreatitis, contain fluid only, and have no or incomplete wall of granulation tissue. At CECT, APFCs are variable in size and shape and have a homogeneous appearance with fluid density commonly arising in the lesser sac, retroperitoneum, or mesenteries confined by peritoneal reflections or fascial planes (Fig 5). APFCs often resolve spontaneously and need no intervention. If an APFC persists and acquires a complete encapsulating wall (usually this takes around 4 weeks to develop), it is termed a pseudocyst (Fig 6). Thus, an APFC differs from a pseudocyst only in degree of encapsulation. It must be stressed that a true pseudocyst in AP is a rare occurrence as most persistent collections in AP contain some degree of necrotic material.[12,29] A pseudocyst may also develop many weeks, months or even years after necrosectomy for necrotising pancreatitis involving the central part of the pancreatic gland (neck and/or body) with significant remaining viable pancreatic tail. The isolated remnant tail continues to secrete pancreatic juice, which accumulates in the cavity (now devoid of necrotic tissue) with formation of a post-necrosectomy pseudocyst (Fig 7).[28]

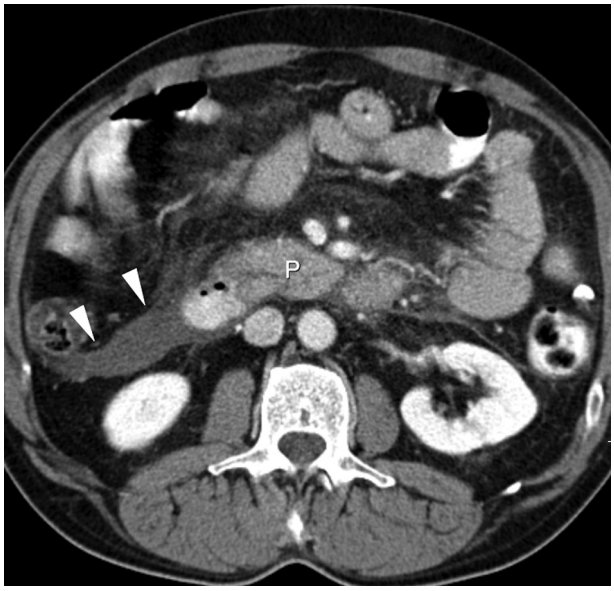

Figure 5 Interstitial pancreatitis with APFC (arrowheads) in the right retroperitoneum. P, pancreatic head.

Necrotic collections: ANC and WON

ANCs may be single or multiple, arise early and solely in the setting of necrotising pancreatitis, contain necrotic material or a combination of fluid and necrotic tissue (with varying amount of each component), and initially have no or an incomplete wall of granulation tissue.[12,28] At CECT, ANCs are variable in size and shape and have a heterogeneous appearance with varying densities; often a mixture of tissue, fat, fluid, and/or higher densities than simple fluid, typically in the range of 20–40 HU (Fig 8).[6,28] ANCs arise intrapancreatically and/or extrapancreatically at the same sites as APFCs. At times, solid necrotic material within ANCs may be non-discernible on CECT due to a homogeneous appearance. In these cases, MRI or ultrasound may assist in establishing the diagnosis. Alternatively, serial imaging beyond the first week will usually show areas of inhomogeneity.[6,12,28] ANCs may resolve spontaneously, persist, or progress. Over time, persisting ANCs will organise and develop a wall of granulation tissue at the border of the necrotic and viable tissue and, if complete, it is termed WON (Fig 9). Thus, an ANC differs from WON only in the degree of encapsulation. Most persisting encapsulated collections in AP contain some necrotic debris, and hence, are WON.

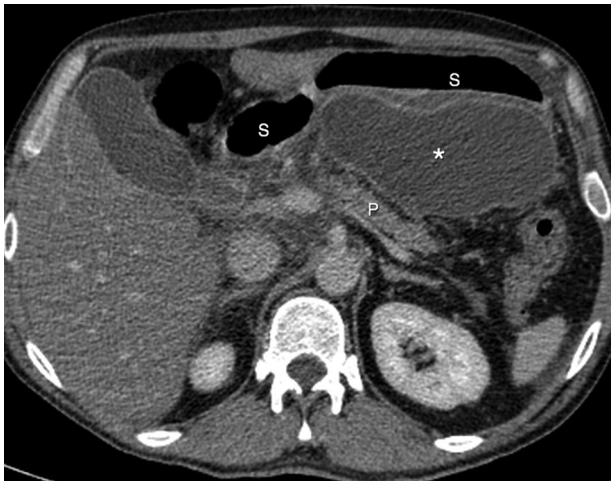

Figure 6 A 67-year-old man with interstitial pancreatitis and development of a pseudocyst (asterisk) in the lesser sac 5 weeks after symptom onset. The collection is homogeneous, has the attenuation of fluid, and is fully encapsulated. P, pancreas; S, stomach.

Natural history of pancreatic collections

Irrespective of the cause triggering an attack of AP, the severity of pancreatic injury relates to the disturbance of acinar cell function leading to the inappropriate activation of pancreatic enzymes and their extravasation in and outside the pancreas, facilitated by a lack of a pancreatic capsule.[1] The release of activated pancreatic enzymes may subsequently cause autodigestion and necrosis of (peri-)pancreatic tissues depending on the intensity of premature activation and magnitude of extravasated enzymes. Pancreatic collections may vary in size, shape, number, and content, and may be localised in or near the pancreatic bed or widespread at remote sites. Initially, they show irregular morphology lacking a well-defined wall contained by anatomical boundaries; typically, they have indistinct margins with adjacent normal fat or organs. Over time, pancreatic collections start to organise with better demarcation between normal and inflamed tissue by formation of a wall (process of encapsulation), which usually takes around 4 weeks (Fig 10).[12,28,30] AP has the unique capability of simultaneously involving different abdominal compartments including the retroperitoneum (primarily the pararenal spaces), subperitoneal spaces of mesenteries of small bowel and transverse mesocolon, and intraperitoneal spaces (primarily the lesser sac) via the enzymatic nature of pancreatic secretions. For a clear understanding of the varying natural history of pancreatic collections, it is essential to realise that their contents broadly depend on two components: fluid and solid necrotic material (the amount of each may vary during the disease course in individual patients). Fluid represents pancreatic secretions, inflammatory exudate, liquefied necrosis, and possibly some haemorrhage. Solid necrotic material represents dead pancreatic parenchyma and/or peripancreatic fat and connective tissue.[16] Pancreatic collections are a spectrum of these components ranging from pure fluid or completely necrotic material at the extremes and anything in between. The advent of ultrasound and, in particular, CT has significantly enhanced our contemporary knowledge on the natural evolution of pancreatic collections. They may resolve spontaneously, diminish in size, or progress potentially leading to various complications. This varying natural history of pancreatic collections largely depends on the following factors: integrity of the pancreatic duct, amount of necrotic material within collections, site and size of the

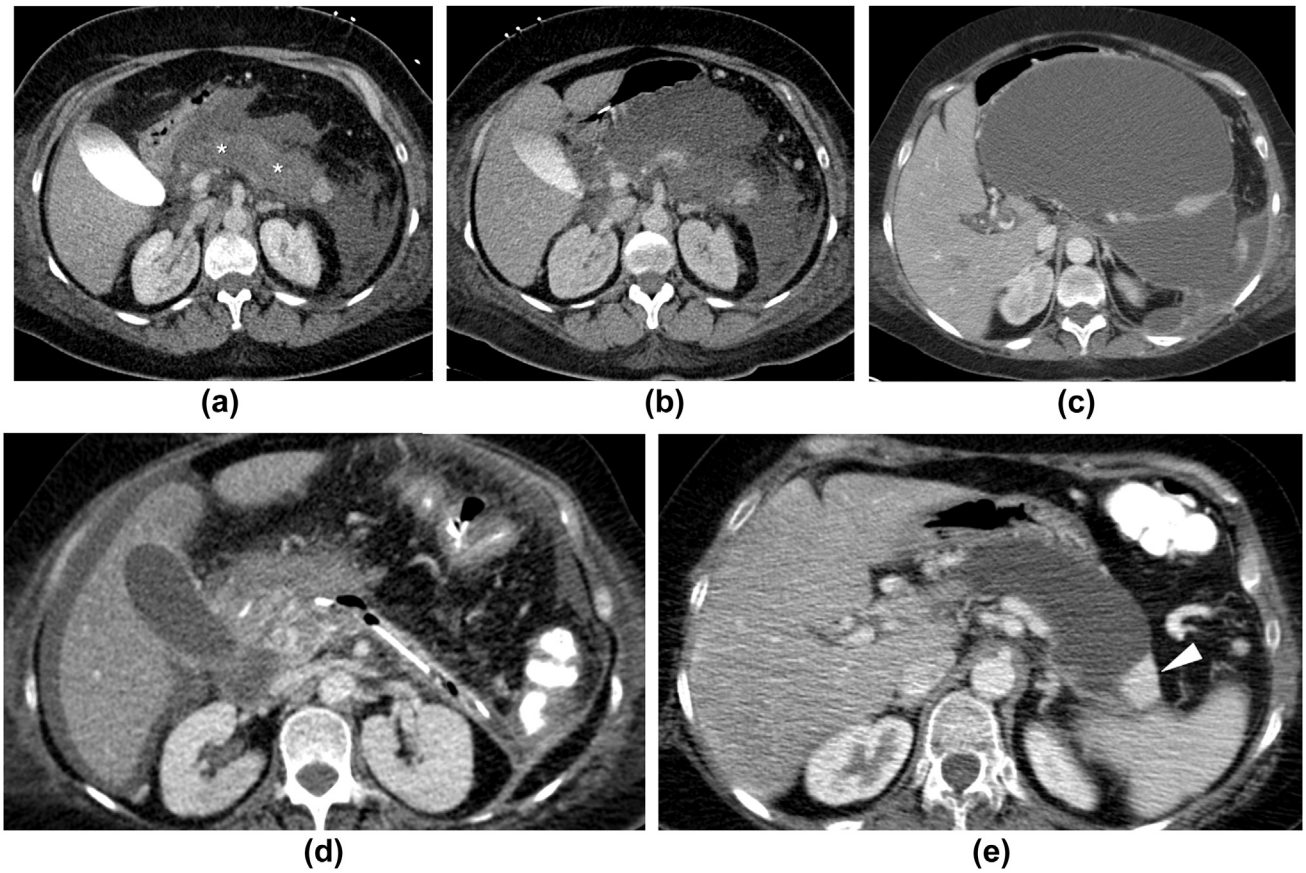

Figure 7 Post-necrosectomy pseudocyst developing in a 42-year-old woman with necrotising pancreatitis of the central gland after surgical retroperitoneal debridement. (a) Five days after symptom onset, contrast-enhanced CT depicts necrosis of the pancreatic neck, body, and part of the tail (asterisks) with sparing of the distal tail. Note the presence of ANCs adjacent to the pancreas. Serial CT images at day 13 (b) and day 35 (c) show enlarging collections. The patient underwent surgical debridement via the left retroperitoneum (d) with resolution of collections. (e) One year after debridement, follow-up CT reveals a recurrent homogeneous encapsulated collection in the pancreatic area consistent with a post-necrosectomy pseudocyst. Arrowhead points to the viable remnant tail.

collections, and the balance between the extravasation of pancreatic juice and the absorbing capacity of the (retro-) peritoneal membranes. Clinical manifestations of pancreatic collections are related to local mass effect (depending on their size and site), bleeding (when located in proximity to vessels), and signs of infection (by seeding from nearby bowel). Most abdominal complications in AP occur in patients with necrosis of (peri-)pancreatic tissues and

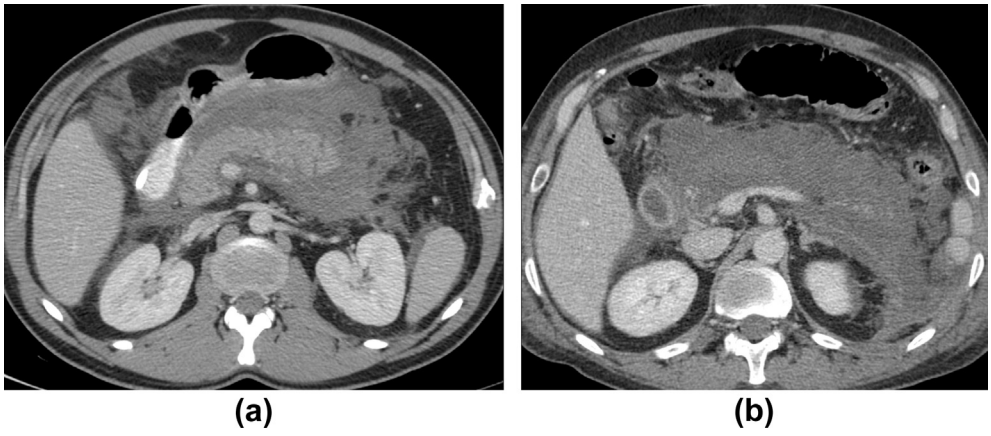

Figure 8 Acute necrotic collections in two different patients with necrotising pancreatitis: isolated extrapancreatic fat necrosis in (a) and combined necrosis in (b). Note the heterogeneity of pancreatic collections with various densities and absence of a surrounding wall.

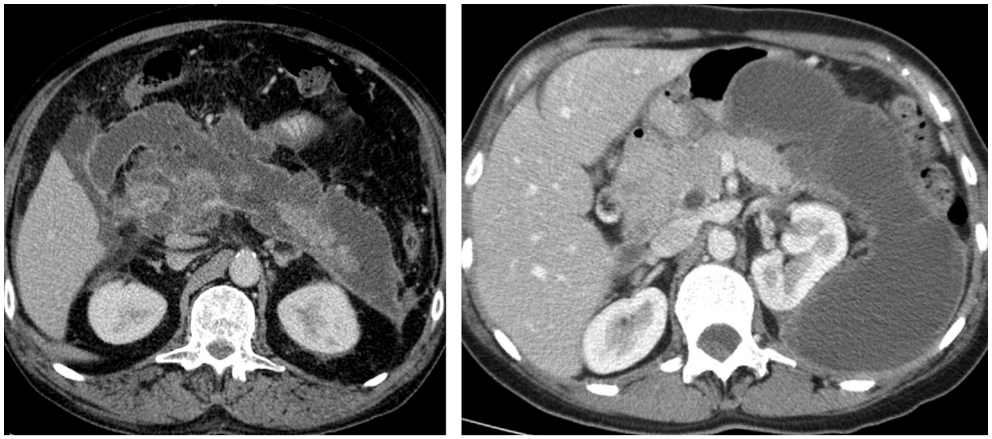

Figure 9 WON in two different patients with necrotising pancreatitis: combined necrosis in (a) and isolated extrapancreatic fat necrosis in (b). In both cases, the collection is slightly heterogeneous and fully encapsulated.

associated pancreatic collections.[30,31] Some of these complications have equivocal symptomatology and are detected on cross-sectional imaging only.

Pancreatic collections resolving spontaneously

Currently, it is poorly understood why some pancreatic collections remain stable or resolve whereas others remain or progress and cause significant morbidity. Even in the individual patient, the evolution of pancreatic collections may differ per site. Small-sized pancreatic collections that are not associated with a disrupted pancreatic duct and contain no or little necrotic material are readily absorbed by the (retro-)peritoneal membranes. Depending on the population studied, it is estimated that 40–50% of pancreatic collections resolve spontaneously.[16,32]

Pancreatic collections remaining stable and sterile

Pancreatic collections that are not readily absorbed but decrease in size during the course of disease are generally more extensive in magnitude than those spontaneously resolving (Fig 11). Typically, they have no connection with the pancreatic duct and most likely contain significant amount of necrotic material not easily absorbed by the (retro-)peritoneal surfaces. Absorption of necrosis is size-dependent; up to 2 cm of necrotic tissue gets absorbed or liquefied, but necrotic material exceeding 5 cm rarely completely disappears.[33] In the long term, residual remnants of pancreatic collections may be mistaken for enlarged lymph nodes or tumour.[34] Comparison with prior imaging is advised to avoid unnecessary invasive diagnostic procedures.

Pancreatic collections causing mass effect

Pancreatic collections causing mass effect are typically large, may be connected with the pancreatic duct, and generally increase in size compared with baseline study as established on serial imaging (Fig 12). Depending on their site, these collections may displace and compress adjacent organs resulting in bowel obstruction (gastric outlet obstruction with distended stomach), biliary obstruction or strictures (inflammatory narrowing of common bile duct from exposure to pancreatic proteolytic enzymes), hydronephrosis (obstruction of ureter), and venous collaterals (by compressing the portal venous system with gastric variceal formation, potentially leading to sinistral portal hypertension).[6,23,31] Increasing pancreatic collections are likely the result of continuing extravasations of pancreatic enzymes or secretions (possibly from a disrupted duct) outweighing the absorbing capacity of the (retro-)peritoneal surfaces.

Pancreatic collections with infection

Pancreatic collections located in close proximity to bowel structures that persist and contain necrotic material (ANC or WON) are prone to develop infection from translocation of gut-derived organisms (i.e., infected necrosis).[35–37] Patients with pancreatic necrosis are at highest risk of developing infected necrosis, occurring in about one-third of patients.[3,20] Infection of pancreatic collections can occur at any time, but is most common between week 2–4 after symptom onset.[38] On CECT, the presence of gas identified in areas of previously demonstrated necrosis in a patient with a septic profile signifies infection (Fig 13). This finding is present in about 20–40% of cases.[39] The remainder is diagnosed either by high clinical suspicion or by positive culture from fine-needle aspiration.[39] When infected necrosis is suspected or confirmed, some form of (invasive) intervention is usually indicated. Most cases of infected necrosis are now treated conservatively initially (i.e. empiric antibiotics); the decision on when and how to intervene is dictated by additional clinical and morphological criteria (i.e., organ failure and degree of encapsulation).[40]

Pancreatic collections with miscellaneous complications

The extravasation of proteolytic pancreatic enzymes may cause various other complications, including damage to the

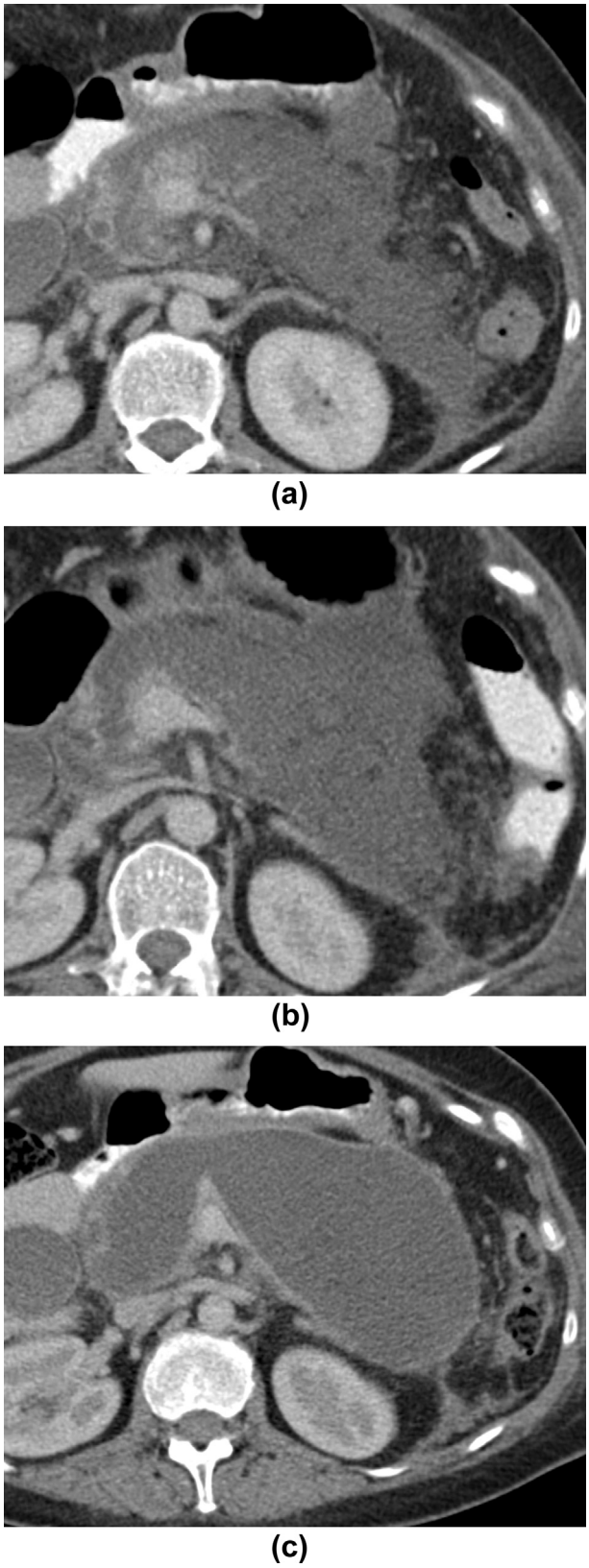

Figure 10 Evolution of a pancreatic collection from an ANC to WON. Contrast-enhanced CT images on day 4 (a) and day 12 (b) show non-enhancement of the pancreatic body and tail with an associated ANC in the left retroperitoneum. Note the absence of a fully encapsulating wall. (c) Follow-up CT 30 days after symptom onset reveals a fully encapsulated collection in the pancreatic and peripancreatic region consistent with WON. The collection replaces portions of the pancreas, which is not compatible with a pseudocyst.

vascular system. Arterial complications associated with AP occur typically late in the disease course, are potentially fatal, and include pseudoaneurysm formation and haemorrhage within established pancreatic collections.[41] Pseudoaneurysms develop by weakening of the arterial wall by the pancreatic enzymes and are typically solitary, usually involving the splenic, gastroduodenal, or small pancreatic arteries (Fig 14). Haemorrhage occurs from erosion of small peripanceatic vessels or rupture of a pseudoaneurysm. At CT, haemorrhage is depicted as areas of high attenuation, typically in a region of necrosis.[41] The peripancreatic inflammation may also lead to thrombosis of the portal, splenic, or mesenteric veins in up to 40% of patients with severe AP (Fig 14).[42,43] Extravasated pancreatic enzymes can spread to the mesenteries of the colon causing local inflammation and vascular thrombosis. Third-spacing of fluid and splanchnic hypotension may contribute to varying degrees of bowel ischaemia, ultimately culminating in bowel infarction, necrosis, and perforation. Areas most commonly involved are the transverse mesocolon and splenic flexure, generally regarded as watershed areas.[44] Patients with necrotising pancreatitis with sudden increase of abdominal pain or signs or peritonitis should receive an urgent CT to rule out this potential lethal complication. Other complications associated with pancreatic collections are rupture into the greater peritoneal cavity or, rarely, the pleural space.

Remaining issues in the nomenclature

Lack of histopathological evidence

Much of our current understanding of the dynamic process of AP stems from serial cross-sectional imaging, primarily in those with severe disease. In the RAC, the pathogenesis of pancreatic collections is based on several assumptions with lack of histopathological proof. It is assumed that in AP pancreatic collections develop from rupture of the pancreatic duct or its side-branches or from oedema. In the RAC, a divergent pathogenesis of pseudocyst and WON is presumed; however, the reverse may also be true; both may develop from damage of pancreatic tissue with leakage of pancreatic juice in damaged areas and formation of a fibrous capsule around such collections. Furthermore, the natural evolution and exact composition of pancreatic collections may vary for different patients in different anatomical locations at different stages of disease. Unfortunately, there is lack of data on the exact composition of these collections in the early and late phases. In addition, the process and rate of liquefaction of (peri-)pancreatic tissues remains an area of enigma. Finally, it is not clearly understood why some collections resolve or regress and some persist. Notwithstanding these gaps in knowledge of the pathophysiology of pancreatic collections, the following

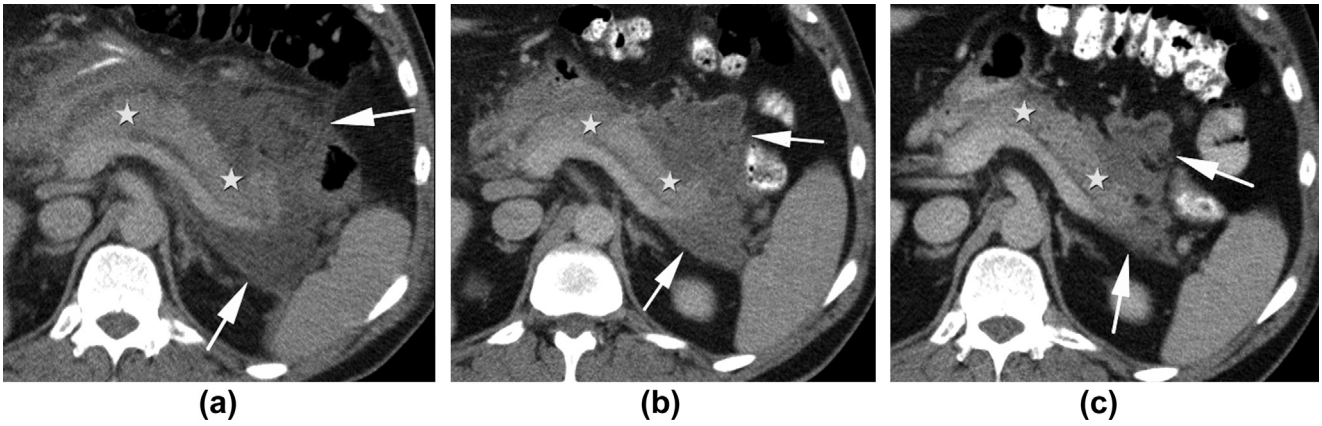

Figure 11 Pancreatic collections remaining. A 52-year-old woman with necrotising pancreatitis (subtype: isolated extrapancreatic fat necrosis) with a normal enhancing pancreas (asterisks) surrounded by pancreatic collections (arrows point to the borders) at day 6 (a), day 21 (b), and day 115 (c). The patient did not develop signs of infection in keeping with sterile necrosis.

observations can be made: (a) after an episode of mild to moderate AP no or little residual findings remain when imaged several weeks to months later;[32] (b) patients with severe AP and signs of infected necrosis invariably show evidence of peripancreatic fat necrosis within pancreatic collections during surgery;[27] (c) in patients operated upon months to years after an episode of necrotising pancreatitis, surgeons may still encounter pancreatic collections composed of necrotic material with varying degrees of liquefaction.[45]

Differentiating fat stranding from collection

Pancreatic collections may range from discrete to extensive in size and extension. The distinction between "extensive fat stranding" and a "collection" is subjective and arbitrarily. In the RAC, the term "collection" is used for any peripancreatic abnormality, which is more than simple fat stranding (comparable to conditions such as uncomplicated appendicitis or diverticulitis). If fluid is acquired when punctured by a large-bore needle, a pancreatic collection is deemed to be present, even when no well-defined wall is seen. In the author's experience, radiologists intuitively tend to use the term "collection" only when some degree of encapsulation has taken place (Fig 15).

Differentiating liquid from necrotic collections

The RAC heavily relies on CT criteria for defining the four subsets of pancreatic collections based on content and maturation. Although, CT elegantly depicts the extent of pancreatic collections and degree of encapsulation, it is limited in the accurate assessment of internal contents of pancreatic collections.[15] Indeed, a collection may display

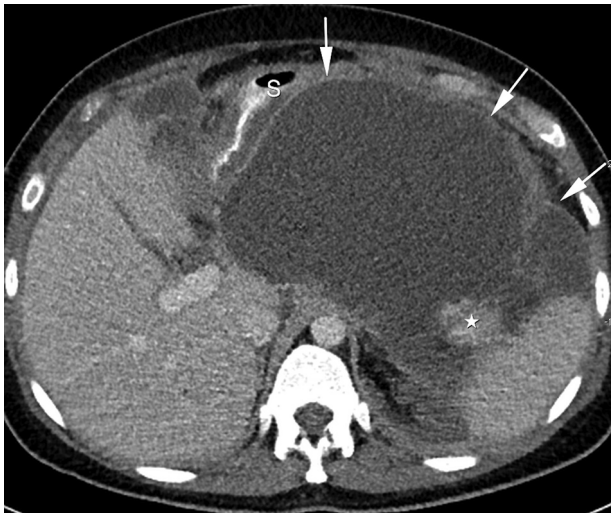

Figure 12 Pancreatic collection with mass effect. A 38-year-old man with necrotising pancreatitis with necrosis of the pancreatic neck, body, and tail with little remaining viable tail (asterisk) and a large collection (arrows point to the borders) exerting mass effect on the stomach (s).

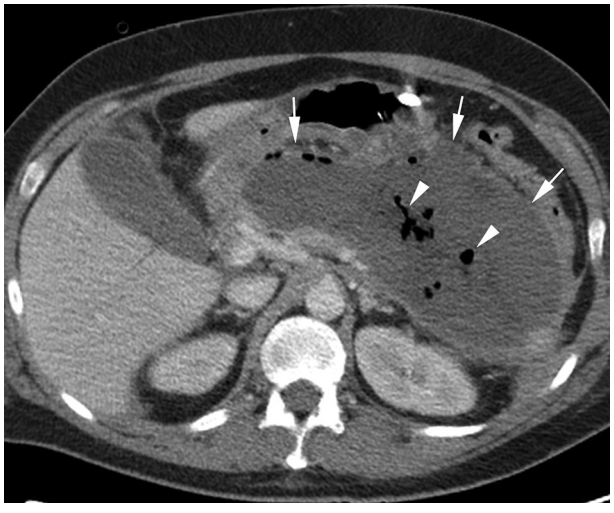

Figure 13 Pancreatic collection with infection (infected necrosis). A 44-year-old woman with necrotising pancreatitis and sepsis 29 days after symptom onset. Contrast-enhanced CT demonstrates gas bubbles (arrowheads) within the WON (arrows point to the borders) consistent with infected necrosis.

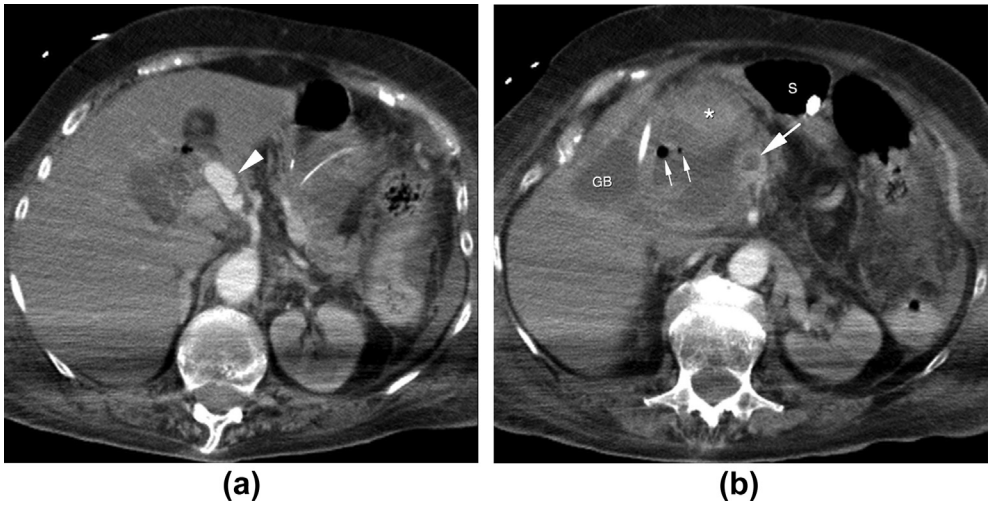

Figure 14 Pancreatic collection with vascular complications. (a) During the course of necrotising pancreatitis this 67-year-old woman developed an arterial pseudoaneurysm originating from the common hepatic artery (arrowhead). (b) At a lower level, the same patient has a thrombus in the portal vein (large arrow), haematoma (asterisk), and gas bubbles (small arrows) within the pancreatic collection. GB, gallbladder; S, stomach.

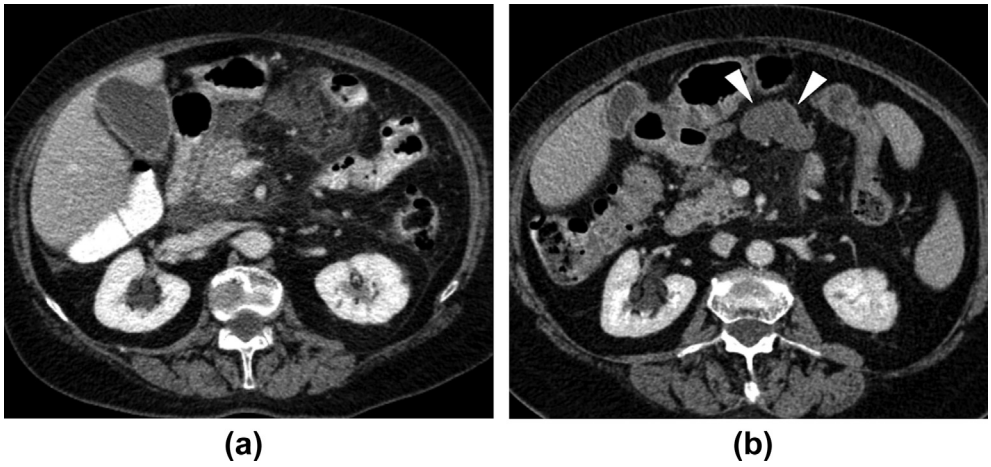

Figure 15 Differentiating fat stranding from a collection. A 48-year-old woman with AP and peripancreatic abnormalities around the pancreatic head and transverse mesocolon on day 4 (a) and day 43 (b). The abnormality in the transverse mesocolon in (a) could be regarded as extensive fat stranding, whereas in (b) a definite small WON (arrowheads) is observed. Note resolution of fluid dorsal of pancreatic head.

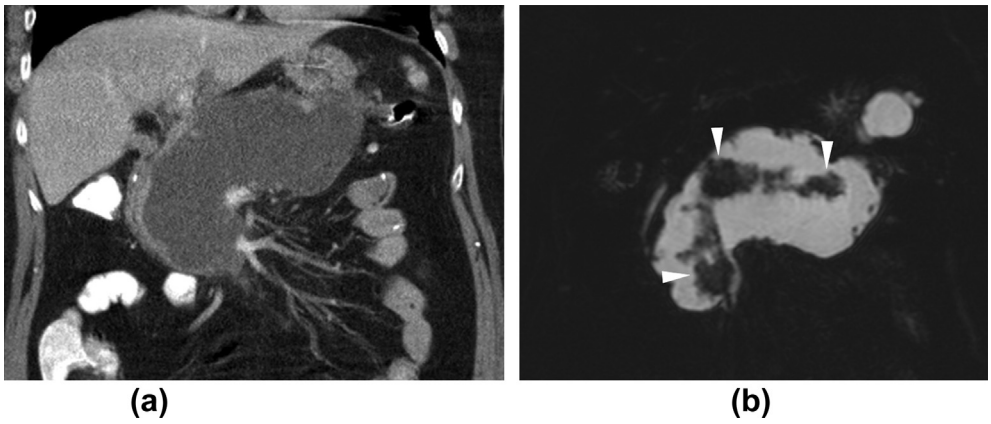

Figure 16 Differentiating liquid from a necrotic collection. (a) Coronal reformatted contrast-enhanced CT image shows a homogeneous pancreatic collection. The corresponding heavily T2-weighted sequence nicely depicts the exact composition of the collection: a necrotic pancreas (arrowheads) surrounded by clear fluid (WON).

attenuation values approaching water densities on CT; the actual fluid content of such a collection may be minimal. In particular, collections developing in the first week of AP may have an equivocal appearance on CT (i.e., homogeneous fluid attenuation) where it is impossible to distinguish an APFC from an ANC, and thus, in determining the type of pancreatitis (interstitial or necrotising pancreatitis). These should then be called "(indeterminate) pancreatic collections".[28] Beyond the first week, better definition of inflamed and adjacent normal fat with heterogeneous appearance of collections (i.e., collection with divergent densities) facilitates the diagnosis of necrotic collections (ANC and WON). Importantly, when pancreatic necrosis is present, all associated collections are considered necrotic collections, regardless of their appearance.[12] In equivocal cases, an MRI examination may be helpful to differentiate liquid and non-liquid collections (Fig 16) and decisive in the type of intervention employed (simple drainage versus necrosectomy).

Diagnosis of isolated EXPN

Activated pancreatic enzymes (such as lipase) that intersperse with anatomical areas containing fat (primarily in retroperitoneum and mesenteries) may lead to lypolysis of extrapancreatic fat with the development of EXPN. It is a difficult diagnosis to make at cross-sectional imaging as current imaging techniques are not able to demonstrate fat perfusion or lack thereof. Moreover, CT cannot reliably distinguish peripancreatic fat necrosis (EXPN) from other causes of peripancreatic fluid (interstitial pancreatitis). At early baseline CT, the diagnosis of EXPN is suggested by the presence of collections that show increased attenuation and fluid densities interspersed among fat present in the retroperitoneum and mesenteries. At follow-up CT, EXPN becomes more apparent when pancreatic collections have a more heterogeneous appearance with varying densities (i.e., ANCs; Fig 11)[12,28,30]; however, the morphological type of AP may remain indeterminate in those patients who have only one early CT examination available for severity evaluation showing equivocal findings.

Conclusion

AP remains a perplexing clinical and morphological entity with a myriad of clinical presentations and variable imaging characteristics. Imaging has an important role in diagnosis, assessment of morphological severity, and identification of complications associated with AP. The RAC redefines the morphological types of AP and introduces new nomenclature of pancreatic collections to better characterise morphological and imaging features of AP. Adoption of the RAC definitions by radiologists should standardise and facilitate the reporting of cross-sectional imaging findings of AP to referring clinicians. In the end, accurate and consistent conveyance of all imaging findings, including the many possible complications associated with AP, is pivotal for guiding individual patient management.

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