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REVIEW ARTICLE

Imaging of inflammatory disease of the pancreas

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ABSTRACT

Increasingly acute and chronic pancreatitis (AP and CP) are considered a continuum of a single entity. Nonetheless, if, after flare-up, the pancreas shows no residual inflammation, it is classified as AP. CP is characterised by a long cycle of worsening and waning glandular inflammation without the pancreas ever returning to its baseline structure or function. According to the International Consensus Guidelines on Early Chronic Pancreatitis, pancreatic inflammation must last at least 6 months before it can be labelled CP. The distinction is important because, unlike AP, CP can destroy endocrine and exocrine pancreatic function, emphasising the importance of early diagnosis. As typical AP can be diagnosed by clinical symptoms plus laboratory tests, imaging is usually reserved for those with recurrent, complicated or CP. Imaging typically starts with ultrasound and more frequently with contrast-enhanced computed tomography (CECT). MRI and/or MR cholangiopancreatography can be used as a problem-solving tool to confirm indirect signs of pancreatic mass, differentiate between solid and cystic lesions, and to exclude pancreatic duct anomalies, as may occur with recurrent AP, or to visualise early signs of CP. MR cholangiopancreatography has replaced diagnostic endoscopic retrograde cholangiopancreatography (ERCP). However, ERCP, and/or endoscopic ultrasound (EUS) remain necessary for transpapillary biliary or pancreatic duct stenting and transgastric cystic fluid drainage or pancreatic tissue sampling, respectively. Finally, positron emission tomography-MRI or positron emission tomography-CT are usually reserved for complicated cases and/or to search for extra pancreatic systemic manifestations. In this article, we discuss a broad spectrum of inflammatory pancreatic disorders and the utility of various modalities in diagnosing acute and chronic pancreatitis.

INTRODUCTION

Despite the continuum of acute and chronic pancreatitis (AP and CP), we will discuss both entities separately.[1] AP is nearly three times as common as pancreatic cancer,[2] and is triggered by alcohol abuse, particularly binge-drinking, or obstructing gallstones in 80% of cases.[3] Moreover, its incidence has more than doubled in the past 10 years. Whether this is due to the increasing prevalence of obesity or simply higher detection rates is unclear.[4] AP occurred in 1.04% patients following bariatric surgery, *e.g.* a rate significantly higher than in the general population.[5]

Although pancreatic and periglandular inflammation, as well as systemic inflammatory response (SIR) are the predominant sequelae of AP, the underlying aetiology of inflammation includes mechanical obstacles,[4] such as biliary or pancreatic duct (PD) stones, strictures, or tumour masses, such as cystadenomas or early pancreatic adenocarcinoma (PCa).[6]

Intermittent mechanical obstruction, such as Sphincter of Oddi dysfunction, where the duodenal sphincter fails to relax normally, along with anatomic variations in the union of the PD and common bile duct (CBD), are rare causes of recurrent AP.[7] Up to 10% of AP is due to infection, *e.g.* mumps[8] or salmonella.[9] AP may follow surgery or endoscopic retrograde cholangiopancreatography (ERCP).[10,11] Trauma-induced AP, after penetrating or blunt injury, is far more frequent than recognised.[12]

According to the International Consensus Guidelines on Early Chronic Pancreatitis, pancreatic inflammation must last at least 6 months before it can be labelled CP.[13] Several factors, including alcohol, bile stones, and infection, can induce either acute or chronic inflammation of the pancreas. AP means, after flare-up, the pancreas shows no residual inflammation. In contrast, CP is characterised by a cycle of progressing and relenting glandular inflammation without the pancreas ever returning to its baseline state.

Table 1. Overview of known risk factors of acute and chronic pancreatitis, age-dependent and age-independent

Age of onset	Acute pancreatitis	Chronic pancreatitis
Youth		Cystic fibrosis
	Pancreas divisum	Hereditary pancreatitis
	Mumps	Tropical pancreatitis
Middle-Aged	Stones* (GB, PD, CBD, Cystic duct)	Chronic alcoholism
	Obesity	Hyperlipidaemia
	S/P bariatric surgery	Groove pancreatitis
	Ectopic pancreatic tissue	Autoimmune pancreatitis
	Sphincter of Oddi dysfunction	Pancreatic or duodenal neoplasm
	Ascaris lumbrocoides (parasitic)	
Older	Pancreatic or duodenal neoplasm	
Age-independent	Binge-drinking Polytrauma involving pancreas	
	Salmonella	
	Drug-induced	
	Iatrogenic, *e.g.* ERCP	

Nonetheless, nowadays, pancreatitis is considered a spectrum of disease spanning from acute to recurrent to chronic pancreatitis[1,14] (Table 1).

In Western societies, chronic alcoholism accounts for 80% of CP in adults.[15] Nicotine consumption also increases the risk of CP and malignancy, mainly PCa.[16] Otherwise, patient demographics, family history, and geography can help in determining the aetiology of CP, *e.g.,* hereditary CP or cystic fibrosis. In young to middle-aged adults, autoimmune pancreatitis (AIP), pancreas divisum, and hyperlipidaemia should be leading considerations. Obstructive pancreatitis, due to pancreatic or duodenal neoplasms, or groove pancreatitis should be considered in middle-aged to elderly patients, especially if there is a history of weight loss.[17] CP, like recurrent AP, may also occur as a sequelae of AP.[1,18]

Diagnosis of acute pancreatitis

The 2012 Revised Atlanta Criteria provide a standardised framework for classifying AP. Clinically, these criteria divide AP into mild, moderate, and severe forms, depending on the absence or presence of additional organ involvement. Morphologically, AP is classified as either interstitial oedematous (IEP) or necrotising acute pancreatitis (NAP). Because the pancreas synthesises digestive enzymes, in AP, pathophysiologically, the parenchyma "self-digests" due to the release of prematurely-activated pancreatic enzymes.[11]

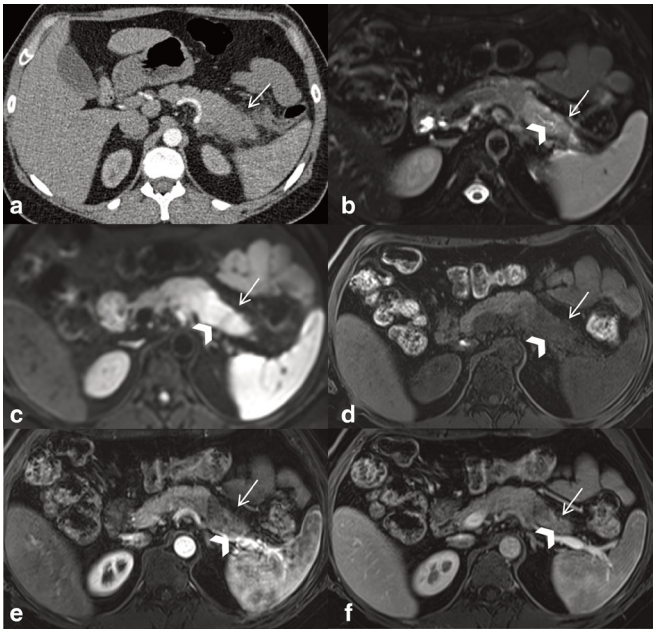
Clinically, early-phase AP, usually lasting 1 week, is accompanied by a systemic inflammatory response (SIR)[4] indicated by elevated serum C-reactive protein (CRP), leukocyte count,[10] and fibrinogen.[19] The late phase begins in the second week and can last months, in moderate or severe pancreatitis,[4] as local complications arise or systemic inflammation persists.[20] Periumbilical or flank ecchymoses, referred to as the Cullen and Grey Turner signs, respectively, suggest NAP,[21] which, on cross-sectional imaging, appear as inflammation along the gastrohepatic and/or falciform ligaments and other peritoneal reflections, respectively.[22,23] These signs are neither sensitive nor specific for necrotising pancreatitis. However, they indicate life-threatening disease, the extent of which can be seen on cross-sectional imaging, with mortality approaching 40%.[24]

The 2012 Revised Atlanta Criteria require two of three criteria to establish the diagnosis of AP: (1) characteristic epigastric pain; (2) ≥threefold increase in lipase and/or amylase concentration in the blood serum; and/or (3) pathognomonic CT or MRI features of AP.[20] Although imaging is not a prerequisite for diagnosis, portal venous phase imaging on contrast-enhanced CT (CECT) especially, may diagnose when labs lag or identify complications precluding clinical improvement after 48–72 h of therapy, *e.g.*[20,25] splenic and/or portal venous thrombosis or pseudoaneurysm of the splenic or less commonly gastroduodenal artery.[26]

Because AP is of biliary origin in approximately 40% of cases,[27] ultrasound is an ideal radiation-free starting point to search for stones within the gallbladder, cystic duct or PD. However, ultrasound is unsatisfactory for assessing the pancreas due to anatomic and echotexture variations in the healthy pancreas. Furthermore, because the pancreas lacks a capsule, extrapancreatic structures, such as bowel, lymph nodes or vessels, may be mistaken for pancreatic lesions.[28]

Should there be a suspicion of glandular and/or peripancreatic fluid collections, cross-sectional imaging is indicated to determine management.[4,25] CT is usually the modality of choice in AP, principally because it enables a rapid examination of the entire abdomen/pelvis, exclusion of symptom-mimickers of AP, such as aortic dissection, shedding light on other causes of an acute abdomen or the aetiology and/or extent of pancreatic

Figure 1. Acute interstitial oedematous pancreatitis in a 37-year-old female a, Axial CE-CT; b, axial turbo spin-echo *T2* weighted (HASTE) image with fat-suppression; c, axial DWI, b-value = 50; d, pre-; and e, f, post-contrast arterial and portal venous 3D-GRE *T1* weighted images with fat-suppression. The pancreatic tail and a part of the body are swollen and the lobules diminished compared to the rest of the pancreas. Mild peripancreatic stranding (arrow) is present. On the HASTE image, the pancreatic duct is minimally dilated. Increased signal (arrowheads) is seen in the pancreatic tail and the affected part of the body on T2 and DWI. Low signal intensity on T1 and inhomogeneous but preserved enhancement in the pancreatic tail and body represent oedema and no necrosis (arrowheads). DWI, diffusion-weighted image.



disease.[25,29] Of the various scoring systems for AP, the 10-point Balthazar CT Severity Index (CTSI) correlates most closely with clinical prognosis.[26]

Should radiation exposure (in pregnancy or females of childbearing age) be paramount, then MRI is preferable.[11] In addition, the risk of iodine-induced nephrotoxicity should be considered. If CT is negative despite a strong suspicion of AP, fat-saturated turbo spin echo (TSE) T_2 weighted or diffusion-weighted image (DWI) sequences may show subtle pancreatic and/or peripancreatic inflammation, *i.e.* high signal intensity.[30–32] Furthermore, it can precisely localize pancreatic cancer with associated pancreatitis.[33] Due to the higher signal intensity of the pancreas on T_1 weighted images, this is the ideal sequence for excluding a solid mass presenting as AP.[29,34,35] Nonetheless, CT remains the workhorse for acute abdominal pain.[11,36] Compared to MRI, CT is faster, better tolerated by an acutely ill patient, more accessible, and better for both temporal resolution and pancreatic calcification detection.[37]

In the trauma setting, even with state-of-the-art CT, 20–40% of CTs done within 12 h of presentation will appear normal. Follow-up CT should be done at 12 to 24 h. If "hard" signs of pancreatic trauma, *i.e.* laceration, contusion or hematoma are found, therapy can begin. But if fluid is present between the pancreas and splenic vein or there is an abrupt cut-off of the superior mesenteric vein, *i.e.* "soft" signs, further CT or MRI is warranted, especially if serial amylase/lipase levels, which are not specific for pancreatitis, are trending higher.[12,38] A high index of suspicion is necessary to prevent the high morbidity and mortality associated with delayed or missed diagnosis of main pancreatic duct (MPD) injury especially, most common at the body–tail junction.[39] MRI, and if necessary and available, secretin-enhanced MR cholangiopancreatography (MRCP), can reliably exclude MPD rupture.[40]

Clinical categorisation using the Revised Atlanta Criteria

These criteria define three stages: (a) mild AP, most common, where involvement is limited to the pancreas. There are no complications. Most patients are discharged after 1 week[4]; (b) moderate pancreatitis applies to those who experience transient organ involvement ≤48 h after onset of AP. Local or systemic complications may also occur; and (c) severe AP where organ involvement occurs >48 h after the onset. Usually the cardiovascular, respiratory, and renal systems are involved.[4,20]

Morphological categorisation using imaging findings

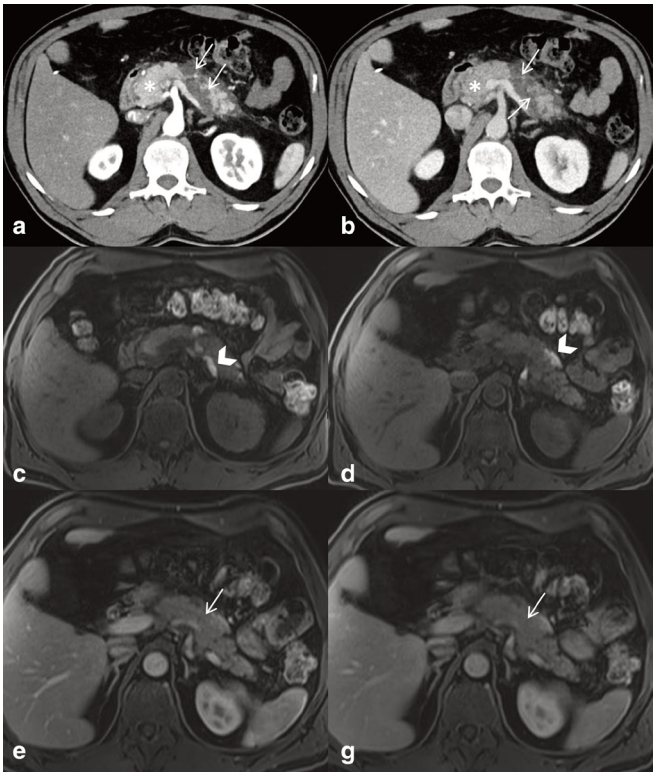
The Revised Atlanta Criteria separate AP, histologically, into IEP and NAP, which correspond to the mild and severe clinical forms defined above, respectively.[4] On cross-sectional imaging, IEP, accounting for 85% of all hospitalised AP cases,[41] appears as diffuse or focal parenchymal swelling, with fluid-like density/signal intensity on CT/MRI, respectively, within the pancreas (Figure 1).[4] On CE-CT, pancreatic lobules may be less distinct and contrast uptake is heterogeneous. If contrast uptake in the pancreas is preserved, by definition, there is no necrosis. The absence of contrast uptake raises the possibility of NAP.[4,20] IEP usually subsides within a week,[20] and its mortality is only 3%[41] rather than the four- and more than 10-fold greater mortality as with NAP and NAP complicated by infection, respectively.[42,43] NAP can affect parenchymal and/or peripancreatic tissue and accounts for 5–10% of all AP cases.[20] On CT, three distinct patterns have been identified: (a) necrosis of pancreas and peri-pancreatic tissues (75%); (b) necrosis limited to the peri-pancreatic tissues (20%); and (c) necrosis involving only the pancreas (5%) (Figure 2).[4] Since necrosis requires several days to occur, CECT done during the first week may be inconclusive. Follow-up CECT is recommended, if suspected.[4]

Pancreatic and peripancreatic fluid collections

The Revised Atlanta Criteria further subdivides IEP and NAP fluid collections according to their age, and content, *i.e.* purely liquid or partly solid/necrotising[20] into four types (Table 2).

(1) Acute peripancreatic fluid collection (APFC) occurs before 4 weeks of IEP, appearing as a homogeneous, extra pancreatic fluid accumulation without a wall (Figure 3). Over half of APFC regress spontaneously. Rarely, APFC evolves into a pseudocyst.[4,20]

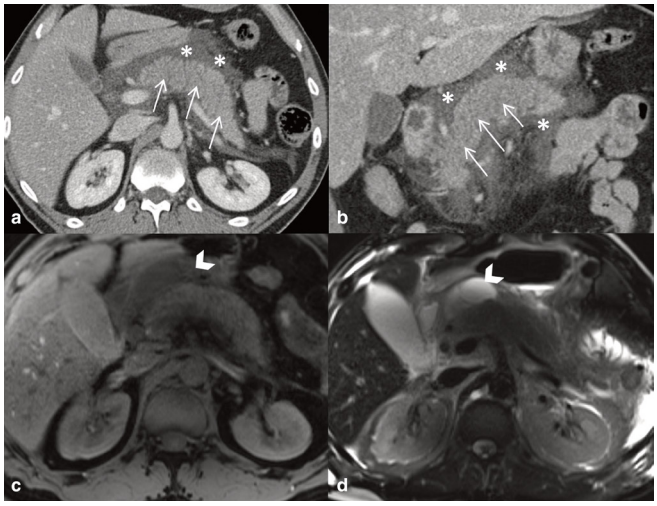
Figure 2. Acute necrotising pancreatitis in a 57-year-old male a and b, Axial CECT, arterial and portal-venous phases. c and d, Pre-contrast; and e and f, post-contrast arterial and portal venous axial 3D-GRE *T1* weighted images with fat-suppression. On CECT, negligible pancreatic body and tail enhancement (arrows) compared to that of the head and neck (asterisk) indicates partial glandular necrosis (arrows). The tubular hyperintense structures along the periphery of the gland on pre-contrast MR images represent haemorrhagic areas (arrowheads). MR images post-contrast show little or no enhancement of the pancreatic body and tail which had decreased signal intensity pre-contrast (arrows).



(2) Pancreatic pseudocyst, a late complication of IEP, is an encapsulated, non-enhancing, purely liquid collection (Figure 4). It appears homogeneously hypodense on CE-CT and hyperintense on T_2 weighted MRI. Occasionally, these cysts may be connected to the PD and are easily identified on MRCP.[4,20]

(3) Acute necrotising collection (ANC), like APFC, appears before 4 weeks of NAP. ANCs contain solid or fatty tissue surrounded by fluid, pancreatic and/or peripancreatic. Often, ANC spreads to the omental bursa and perirenal space (Figure 5). Cross-sectional imaging after the first week distinguishes ANC from APFC.[4,20]

Figure 3. Acute interstitial oedematous pancreatitis with peripancreatic fluid in a 54-year-old male a, Axial; and b, coronal CE-CT scan images, portal venous phase. The sausage-shaped pancreas has nearly homogeneous attenuation though much-diminished contrast enhancement (arrows). Free fluid surrounds the gland (asterisk). The absence of a capsule excludes a pseudocyst. c, Axial *T1* weighted fast low-angle shot (FLASH) image with fat-suppression shows mild diffuse swelling and decreased signal intensity of the pancreas which makes the peripancreatic fluid barely visible. d, Axial turbo spin-echo *T2* weighted (HASTE) image with fat-suppression shows the homogeneously increased T2 signal of the peripancreatic fluid much better. The fluid extends into the lesser sac (arrowheads) between the gallbladder and the pancreatic head.



(4) Walled-off necrosis (WON) is a late consequence of NAP, since the thick enhancing rim takes time to organise. But, unlike the pseudocyst, it contains necrotising/solid tissue (Figure 6). WON is frequently localised peripancreatically rather than in the organ.[4] MRI is superior to CT in that it characterises lesions as solid, semi-solid or liquid, identifying targets for drainage. PD interruption, which may cause parenchymal necrosis, is usually better discerned by MRI,[44] especially secretin-enhanced MRCP (S-MRCP).[45]

Local and systemic complications

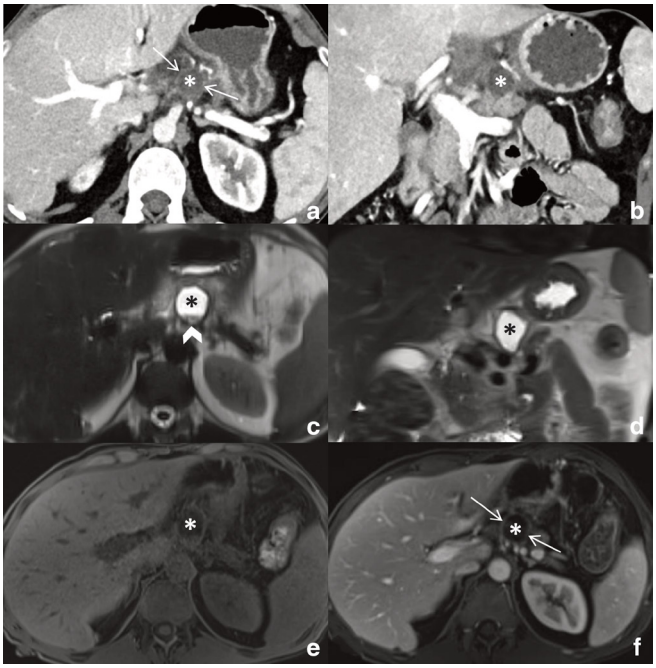
These include retroperitoneal bleeding, pseudoaneurysm, pancreatic fistula formation, extrahepatic portal hypertension, gastric/bowel perforation, renal obstruction, and "gastric-outlet syndrome" due to extrinsic luminal compression. Additional CT (or MRI) findings predictive of multiorgan failure, including pleural effusions, ascites, pulmonary oedema, renal, and perinephric oedema, were integrated into Balthazar's modified CTSI,

Table 2. Types of fluid collections in AP

	Interstitial edematous pancreatitis		Necrotising acute pancreatitis	
<4 weeks	1)	APFC	3)	ANC
>4 weeks	2)	Pseudocyst	4)	WON

ANC, Acute Necrotizing Collection; AP, acute pancreatitis; APFC, Acute Peripancreatic Fluid Collection; WON, Walled Off Necrosis.

Figure 4. Small pancreatic pseudocyst in a 43-year-old male more than 4 weeks after the onset of acute pancreatitis a, Axial; and b, coronal CECT, arterial phase images, show a 3 cm, thin-walled ovoid collection (asterisks) with attenuation identical to that of the stomach, indicating it is a cyst. Note the mild rim enhancement typical of pancreatic pseudocysts (arrows). c, Axial; and d, coronal turbo spin-echo *T2* weighted (HASTE) images with fat-suppression. e, Axial pre-contrast; and f, post-contrast portal venous-phase 3D-GRE *T1* weighted image with fat-suppression. The small ovoid lesser sac cyst (asterisks) is bright on *T2* weighted images, with slight non-enhancing layering material dark on *T2* weighted images, typical of fluid (arrowhead). Rim enhancement helps demarcate the pseudocyst from the more ventral stomach (arrows).



which is occasionally used by radiologists.[21,46] When gas is seen within the pancreatic or peripancreatic tissues, a fistula with bowel should be ruled out. Rarely, gas is seen within a walled-off retroperitoneal collection implying super-infection with a gas-forming organism. This complication of NAP is associated with very high mortality, especially in the setting of extra pancreatic

Figure 5. Severe necrotising pancreatitis with fluid collection in a 39-year-old male a, Axial; and b, coronal CECT, arterial phase images, show a huge well-defined multi loculated inhomogeneous fluid collection partially containing solid tissue (arrows), which replaces most of the pancreas. The absence of any appreciable enhancement of the remaining pancreatic gland (asterisks) is consistent with necrotising pancreatitis.

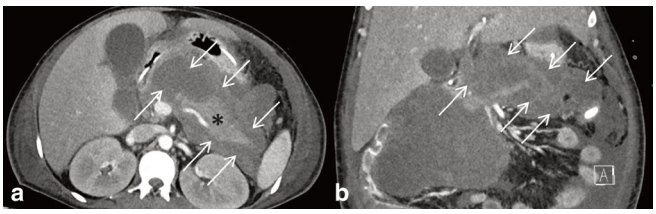


Figure 6. Walled-off necrosis in 63-year-old male 8 weeks after the onset of severe necrotising pancreatitis a, Axial; and b, coronal CT, non-contrast; c, coronal turbo spin-echo *T2* weighted (HASTE) image. d, Axial pre-; and e, post-contrast arterial phase; and f, portal venous-phase 3D-GRE *T1* weighted images with fat-suppression. There is a sausage-shaped encapsulated mass (arrows) in the pancreatic body and tail. On CT, the collection appears partially fatty and is inhomogeneous consistent with walled-off necrosis (asterisks). There is a patchy, lace-like hypointense area on T2 which is hyperintense on T1 images and does not enhance, consistent with necrotic tissue or haemorrhagic areas (asterisks). The head and neck of the pancreas have been auto-digested and are no longer visible.

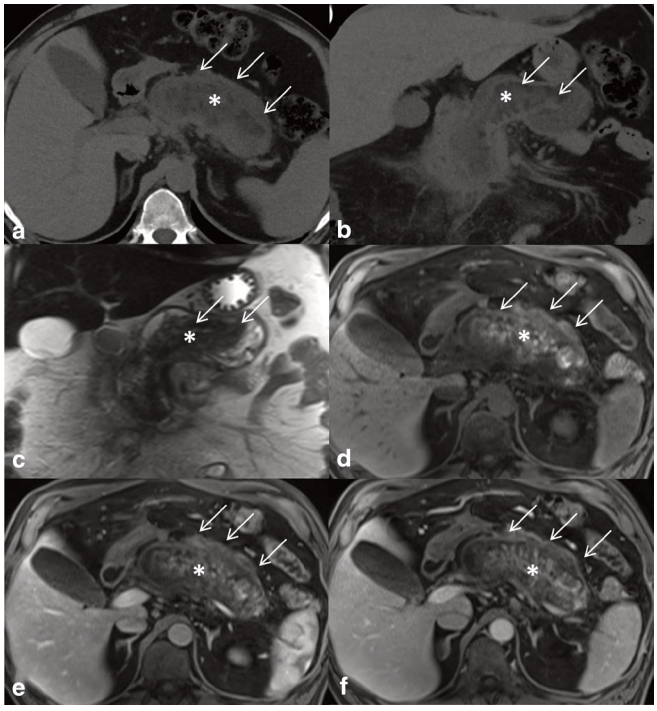


Figure 7. A 63-year-old male who developed infected necrosis following acute pancreatitis a, Axial CECT, arterial phase images; and b, coronal CE-CT, portal venous phase images, show a large, thick-walled, rim-enhancing collection in the pancreatic bed (arrows). Several air bubbles within the fluid collection and a large air-fluid level (arrowhead) are suspicious for an infected necrosis replacing the entire pancreatic gland. Fine-needle aspiration confirmed the diagnosis. Minimal peri-pancreatic stranding is present. Note the stomach ventral to the infected necrosis (asterisk).

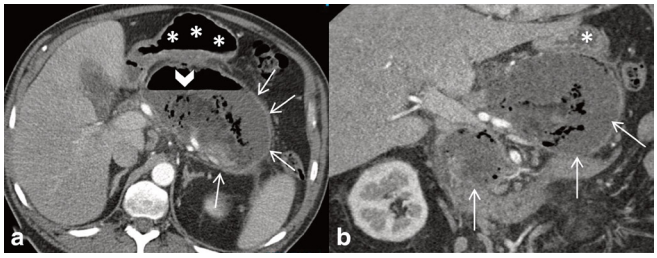
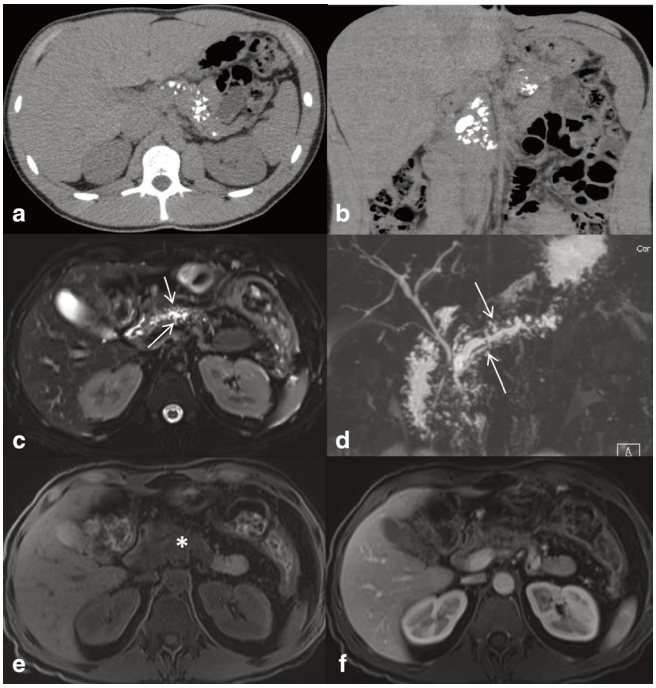


Figure 8. Signs of advanced chronic pancreatitis in two different patients a, Axial; and b, coronal non-enhanced CT in a 17-year-old male. Diffuse parenchymal atrophy and calcification consistent with severe chronic pancreatitis. MRI of a 35-year-old male patient with advanced chronic pancreatitis. c, Axial turbo spin-echo *T2* weighted (HASTE) image with fat-suppression shows moderate dilatation and diffuse irregularity of the MPD with a few visible side-ducts (arrows) and atrophy of the pancreatic gland. d, Coronal oblique maximal intensity projection image of a 3D MR cholangiopancreatogram shows generalised irregularity and marked dilatation of the MPD with multiple massively dilated side-branches (arrows), classified as Cambridge 4. e, Pre-contrast axial 3D- GRE *T1*-weighted image with fat-suppression shows markedly decreased signal intensity of the pancreatic body compared to that of the tail (asterisk). f, Contrast-enhanced, portal venous phase, axial, *T1*- weighted images show the atrophied pancreas with lobular disappearance and mild MPD dilation, as well as diminished contrast enhancement of the body more than the tail.



organ failure[47] (Figure 7). A positive bacterial culture on fine needle aspiration confirms the diagnosis prior to antibiotics.[20] Furthermore, sterile NAP must be distinguished from superinfected NAP since the latter often requires drainage, while necrosis can be managed expectantly and rarely requires endoscopic or surgical necrosectomy.[3,48,49]

Diagnosis of chronic pancreatitis

CP will develop in 4–24% of patients with recurrent AP. CP refers to episodic flareups of acute inflammation that result in irreversible fibrosis of the pancreatic gland, which causes first exocrine, and, ultimately, endocrine insufficiency.[50] End-stage CP is a straightforward imaging diagnosis, typically characterised by atrophy,[51] calcifications (parenchymal much more frequent than intraductal), calibre, and/or contour alterations of the main and side-branch PD (Figure 8).[3] Because the degree of fibrosis seen on conventional imaging does not directly correlate with the severity of glandular dysfunction, imaging does not help determine CP severity. It only excludes end-stage disease.[52]

The diagnosis of early CP is very challenging because the symptoms are nonspecific. Ninety percent reduction of pancreatic lipase, the first enzyme impaired in pancreatic insufficiency, must occur before malabsorption occurs. S-MRCP is by far the best test to estimate exocrine function, with 75% sensitivity for early- and up to 97% sensitivity for late-stage CP.[53] However, Secretin (Secrelux®) is no longer commercially available in the EU. Although it may be purchased in the US under the generic name human secretin (trade name ChiRhoStim®), it is rather expensive.

Alternatively, indirect tests, such as foecal elastase is better than fecal chymotrypsin since the foecal concentration of elastase is directly proportional to that excreted by the pancreas. Furthermore, if the patient is on exogenous enzyme, the foecal elastase test can be done without stopping the oral preparation. However, it has very low sensitivity in mild CP and circa 75% in moderate and severe CP.[54] Therefore, MRCP has become the diagnostic exam for CP in many radiology centres with a sensitivity of 75% for advanced disease and 25% for small-duct, *i.e.,* early CP.[53]

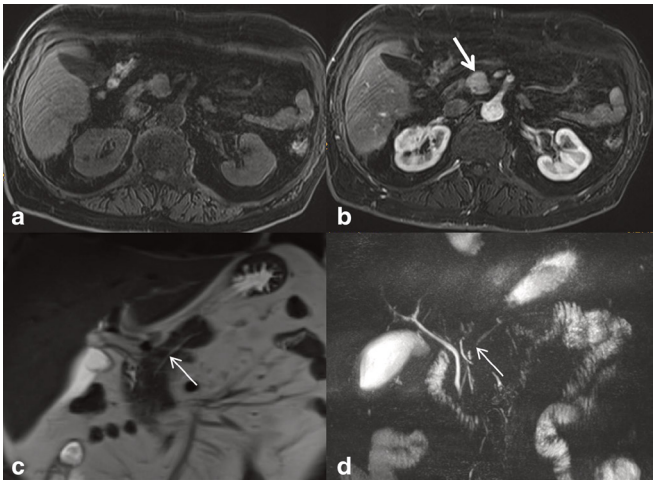
Because debilitating pain, malabsorption and malnutrition impair quality of life in end-stage CP and predispose to PCa,[17] the goal of imaging is to identify CP as early as possible. This usually means assessing for anatomical variations, early changes along the main and side-branch PDs that might progress to strictures/stenosis, and morphologic pancreatic changes. With early diagnosis, using S-MRCP[45] oral pancreas lipase (Creon) can be started, and if necessary insulin, to replace exocrine and endocrine pancreatic enzymes, respectively. Additionally, chronic epigastric pain can be managed by alcohol cessation, analgesics or narcotic drugs, endoscopic drainage, stenting or stone removal from the PD, extracorporeal shock-wave lithotripsy for PD calculi, surgical PD drainage or resection of pancreatic tissue and/ neuroablation.[55] For early detection of PCa, the Cancer of the Pancreas Screening consortium recommends periodic EUS or MRI in these high-risk individuals.[56]

Although CP is more likely to present as atrophy, due to fibrosis in advanced cases, the gland may also be enlarged early on and/ or exhibit focal inflammation.[51] This mass-forming appearance of AP or CP can be very difficult to distinguish from PCa on cross-sectional imaging. Both are hypo- or isodense on CE-CT, have a predilection for the pancreatic head, and can dilate the PD. Biopsy can be equivocal and may not help as atrophy, fibrosis, and leukocytic infiltration may occur in both entities.[50] S-MRCP can demonstrate the duct penetrating sign which can be helpful in such cases (Figure 9).[45]

Classification of chronic pancreatitis

In 1988, the Marseilles-Rome Classification[57] was redefined, based upon aetiology of CP, and pancreatic morphology and function.[58] With ERCP, the 1984 Cambridge Classification[59]

Figure 9. Focal chronic pancreatitis in a 56 year old male mimicking pancreatic cancer. a, Axial non-contrast; and b, axial contrast-enhanced arterial-phase 3D- GRE T_1 weighted images with fat-suppression show a well-circumscribed, 3 cm pancreatic head mass of decreased signal intensity with strong early enhancement (thick arrow). c, Coronal T_2 weighted HASTE image shows the non-obstructed MPD in the pancreatic neck and body (arrow). d, Coronal oblique maximal intensity projection image of a 3D MR cholangiopancreatogram shows that the pancreatic duct is narrowed in the head, but neither obstructed nor dilated. The duct passes through the mass, joining the CBD in the major papilla, the so-called duct penetrating sign (arrow).



was devised to clinically quantify CP according to the extent and severity of main and side branch PD involvement.[60]

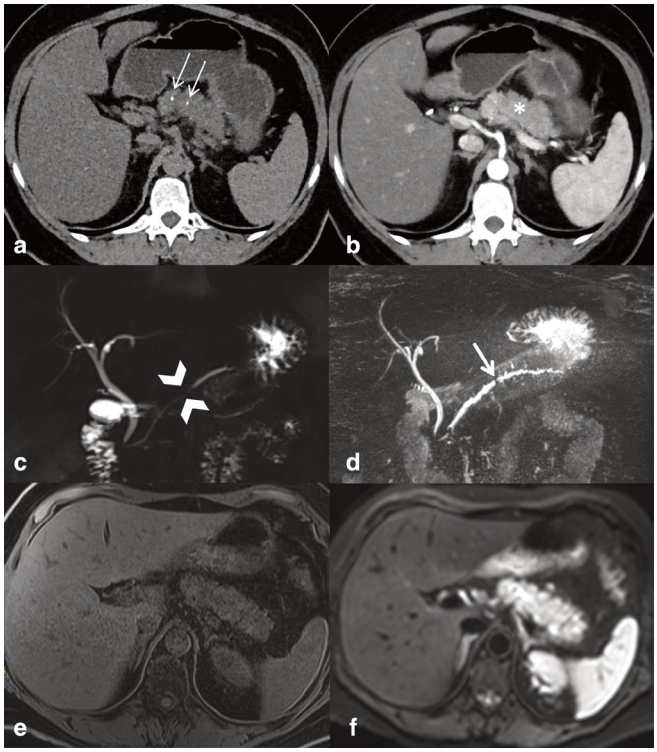
PD pathologies include strictures, dilatations, and cysts. Side-branch pathologies additionally include a reduction in the number or length of side branches. However, with the advent of non-invasive S-MRCP, ERCP has largely been relegated to therapeutic interventions, thus reducing the risk for ERCP-related AP.[61] The American Pancreatic Association recommends adapting the Cambridge Classification to coronal-oblique MRCP images. Since only PD morphology is quantified, the pancreatic exocrine functional reserve cannot be estimated by this method.[45]

In contrast, S-MRCP can detect an obstruction and estimate pancreatic exocrine function, respectively, in response to secretin provocation. The healthy MPD distends about 66% after secretin, returning to its original calibre within 10 min.[45] Signs of PD pathology include loss of MPD tapering within the pancreatic tail, rigid MPD post secretin (Figure 10); visualisation of ≥3 side-branch ducts, strictures, and/or sacculations of the MPD, and reduced and/or delayed duodenal filling (Table 3). Pancreatic exocrine function, is considered impaired if <Grade 3[45] according to the Matos classification (Table 3). But, it is limited because it cannot distinguish between patients with early *versus* more advanced CP.[45]

Complications of CP

The foremost complication of CP is PCa, which is 15 to 25 times more likely to occur in this group than in the general population.

Figure 10. A 46-year-old female with signs of acute pancreatitis exacerbating underlying early-stage chronic pancreatitis a, Non-contrast CT axial shows punctate calcifications within the pancreatic body (arrows). b, CECT, arterial phase, axial shows mild swelling of the gland with a residual lobular pattern and inhomogeneous diminished enhancement (asterisk). c, Coronal oblique thick-slab MR cholangiopancreatogram image eight minutes after administration of secretin (S-MRCP). Mild dilatation of the PD in the tail suggests stenosis or obstruction (arrowheads). d, MRCP repeated four months after ERCP. There is a recurrent short-segment stenosis in the main PD (thick arrow) and mild irregularity along the entire MPD with multiple dilated side-branches, classified as Cambridge 3. e, Pre-contrast axial 3D- GRE T_1 weighted image with fat-suppression shows mild signal intensity decrease with incipient atrophy and early loss of lobulation. f, DWI, b 50, shows increased signal intensity of the pancreas, indicating diffuse oedema from the bout of acute on chronic pancreatitis. DWI, diffusion-weightedimage



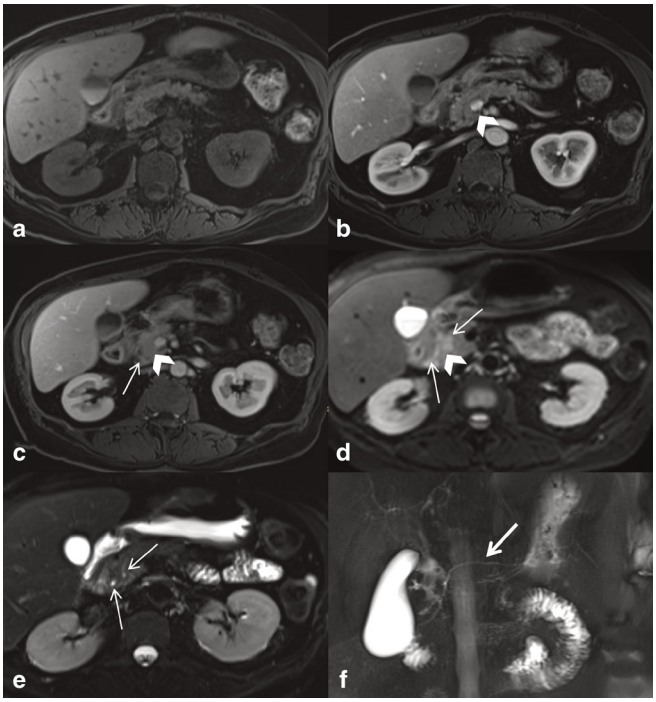
Two types of CP deserve special mention in this regard: tropical pancreatitis, where PCa favours the body or tail rather than the pancreatic head; and hereditary pancreatitis in which not only

Table 3. The Matos classification for the diagnosis of CP on S-MRCP

Grade 0	No fluid is observed.
Grade 1	Fluid is limited to the duodenal bulb.
Grade 2	Fluid partially fills the duodenum up to the horizontal portion of the duodenum genu.
Grade 3	Fluid fills beyond the genu.

MRCP, MR cholangiopancreatography.

Figure 11. Biopsy-proven groove pancreatitis in a 44-year-old female a, Axial non-contrast; and b, axial contrast-enhanced arterial-phase; and c, portal venous-phase 3D- GRE *T1* weighted images with fat-suppression; and d, axial DWI, b-value = 50; and E, axial turbo spin-echo *T2* weighted (HASTE) image with fat-suppression. There is mild duodenal thickening and oedema associated with a sheet-like mass in the pancreaticoduodenal groove that extends to the pancreatic head (arrowheads), plus multiple tiny bright cystic lesions in the pancreatico-duodenal groove (arrows) (a). Decreased pancreatic parenchymal T1 signal and diminished enhancement on post-contrast images (d). f, Coronal, oblique, thick-slab MR cholangiopancreatogram image after administration of secretin (S-MRCP) shows normal calibre of the entire MPD (thick arrow) as it goes through the mass (duct penetrating sign), excluding malignancy. MRCP, MRcholangiopancreatography.



is the risk of PCa still greater (50- to 70-fold above the general population), but it can occur within 7 years from diagnosis of CP.[62]

Other complications include those seen with AP, namely pseudocysts, bile duct compression due to pseudocysts, pseudoaneurysms, and splenic vein thrombosis with variceal collaterals. Gastrointestinal complications, such as intestinal ischaemia or gastric outlet stenosis due to pancreatic head enlargement may also occur.[63]

Specific cross-sectional imaging patterns of chronic pancreatitis

Typical CP

This is most frequently assessed with CT rather than MRI. Transabdominal ultrasound is not recommended.[61] Although calcifications and atrophy, *i.e.,* end-stage features, are more easily detected on CT (Figure 8), MRI is superior for detecting the subtle findings of early CP, including subtle duct irregularities, signal intensity alterations, and loss of lobulations (Figure 10).[61] Furthermore, both *T1* weighted sequences and T1-mapping techniques have shown promise. Tirkes et al[64,65] found a positive correlation between T1 relaxometry and exocrine dysfunction, even in persons without ductal changes. Also, MR elastography (MRE) has been reported to be diagnostically helpful.[66] Therefore, MRI and, in particular, S-MRCP, is particularly very helpful in diagnosing early CP (Figure 10).[45] However, CT remains the first-line exam because of its wide field of view that can help exclude other entities that mimic CP, as well as detect the above-mentioned complications of end-stage disease easily.[61]

Groove pancreatitis

Also known as paraduodenal pancreatitis or cystic duodenal dystrophy, groove pancreatitis is a focal form of CP, between the duodenum, pancreatic head, and CBD, mainly found in alcoholics. The CBD may also become fibrosed.[67] If fibrosis spreads to the pancreatic head, it can mimic carcinoma.[68] Anatomic variants, such as pancreas divisum or stenosis of the papilla duodeni minor, are believed to cause the inflammatory changes.[67] Excess alcohol or nicotine use, by changing pancreatic secretion viscosity, causes PD calcification, enzyme flow impairment, and Brunner gland hyperplasia and duodenal wall cysts, which can be seen at histology.[69]

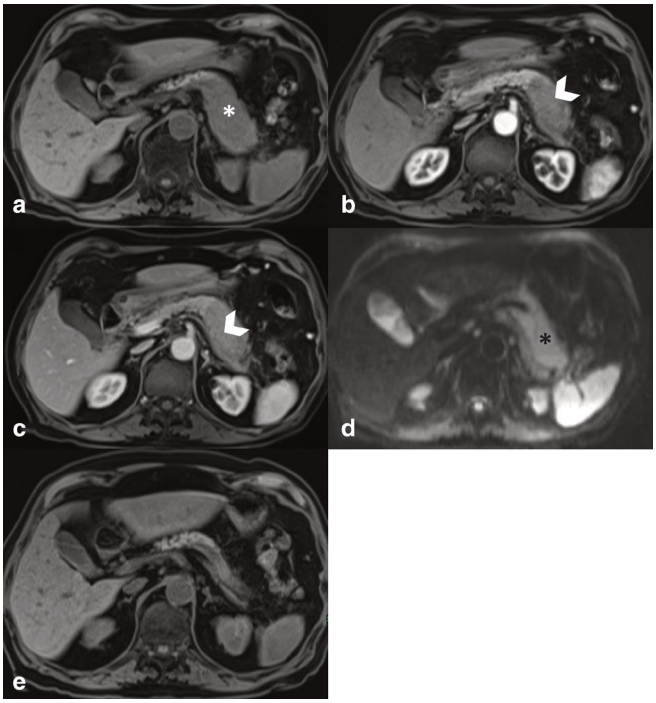
Small duodenal cysts seen on endoscopic ultrasound (EUS) suggest the diagnosis. Low attenuation in the pancreatic head on late-phase CE-MR images, and/or CBD or gastroduodenal artery displacement without invasion or encasement, as can be seen with groove pancreatitis, may be helpful to avoid the misdiagnosis of PCa.

Unlike the moderately hyperintense, non-pathologic pancreas seen on fat-saturated *T1* weighted MRI, paraduodenal pancreatitis, like any pancreatitis, appears iso- to hypointense. On *T2* weighted images, it is iso- to hyperintense. The "double duct sign," thought to be pathognomonic for rigid malignancy, *e.g.* PCa, compressing the ampullary PD and CBD, and causing upstream dilatation of the CBD and PD, can be seen with duodenal wall fibrosis.[68] S-MRCP can also display the "duct-penetrating sign," indicating that the main PD can pass unhindered through non-carcinomatous tissue (Figure 11).[45]

Autoimmune pancreatitis

AIP, accounting for 2–10% of all CP,[70] frequently affects males.[71] Although incompletely understood, immunological and genetic factors are suspected as its cause.[72] Unlike alcohol-induced or biliary-associated pancreatitis, AIP is characterised by the expression of various autoantibodies, as with autoimmune hepatitis (AIH) or primary biliary cholangitis (PBC).[73] Although AIP has two distinct subgroups, expressing different pathological and clinical features,[74] a common denominator is that many lack increased inflammatory parameters[75] or fever[71] and all respond well to corticosteroids, which can be used both therapeutically and diagnostically.[76] On CT and MR imaging, a capsule-like rim, which is thought to correspond to an inflammatory process

Figure 12. Autoimmune pancreatitis of the pancreatic body and tail in an 83-year-old male. The diagnosis was made at follow-up, by good response to steroid therapy, since repeated biopsies were equivocal. a, Axial non-contrast; and b, axial post-contrast, arterial-phase; and c, portal venous-phase 3D-GRE T_1 weighted images with fat-suppression show marked swelling and loss of lobules and signal intensity in the pancreatic body and tail (asterisk). Moderate enhancement seen with contrast (arrowheads). d, Axial DWI, b 300, with fat-suppression, shows high signal intensity limited to the swollen distal gland (black asterisk). e, Axial non-contrast 3D-GRE T_1 weighted image six weeks after steroid therapy confirms the diagnosis of AIP. There is near-complete resolution of distal pancreatic swelling, with only mild residual decreased signal intensity. DWI, diffusion-weightedimage



involving peripancreatic tissues, appears to be a characteristic finding of AIP.[77]

The Type 1 AIP IgG4-positive patients have systemic manifestations of autoimmune diseases, which can pre-or post-date AIP.[71] In some cases, multiple organ involvement occurs, sparing the pancreas.[78] Histology shows lymphoplasmocytic infiltration and fibrosis.In contrast, Type 2 AIP has neutrophil infiltrates and epithelioid cell granulomas on histology and no increase in serum IgG4.[79] Unlike Type 1, which predominates in Asian countries, Type 2 AIP occurs mainly in Europe and America.[80]

On cross-sectional imaging, any of the three patterns can be seen: diffuse "sausage-like" (Figure 12); focal swelling (30–40%) usually limited to the pancreatic head; and multifocal pancreatic involvement. PD dilatation, as well as pancreatic atrophy, are absent.[72,81,82] In challenging cases, DWI may help, showing significantly lower apparent diffusion coefficient (ADC) values in a pseudotumour than PCa.[83] F-18 fludeoxyglucose (FDG) positron emission tomography (PET) may help diagnose AIP, showing uptake beyond the pancreas.[71] Conversely, FDG-PET/CT may exclude a pseudotumour when the standard uptake value (SUV) is raised.[84]

It is estimated that 3–9% of all patients with AIP undergo unnecessary pancreatic resection for suspected carcinoma,[71] particularly if repeated biopsy remains equivocal. Serology, *i.e.* IgG4, and CA 19–9 levels, as well as a trial of steroids, should be recommended under such circumstances. Because the CA 19–9 tumour marker is not specific to pancreatic cancer and can even be found with some benign entities, performing all three of these recommendations yields higher certainty than any single one.[82,85] Imaging findings that support PCa over focal AIP include persistent hypodensity/hypointensity of a cancer on the late phase of CECT and CE-MR relative to a non-pathologic pancreas.[76] The presence of intralesional enhancement of the MPD wall ("enhanced duct sign") on CECT indicates pancreatitis.[86]

And, finally, the degree of MPD dilatation suggests the aetiology. While in focal AIP the MPD is only slightly dilated (≤4 mm), more pronounced PD dilatation indicates malignant obstruction. In addition, as with colon cancer versus diverticulitis,[87] long-segment PD narrowing argues for AIP rather than the abrupt calibre changes in cancer. Likewise, multiple, segmental stenosis along the MPD favours AIP.[82] The key is that confirmed AIP does not exclude synchronous PCa, which was found at histology in nearly 5% of Type 1 AIP patients.[88]

In summary, the spectrum of pancreatitis includes acute, recurrent and chronic pancreatitis. The aetiologies are multifactorial. However, two of the leading causes remain alcohol abuse and gallstones. Clinical and lab findings are often adequate for diagnosing AP. Cross-sectional imaging is warranted when the clinical course is severe or atypical. Generally, CE-CT is preferable to MRI because it allows coverage of an extended area. But, MRCP is the preferred technique for the diagnosis of early CP, and the estimation of exocrine pancreatic function. In the near future, DWI, T1 mapping, and MRE may become routine imaging adjuncts.

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