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CHRONIC PANCREATITIS: WHAT THE CLINICIAN WANT TO KNOW FROM MRI

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INTRODUCTION

Chronic pancreatitis (CP) is a low prevalence disease.[1–3] In 2006, there were approximately 50 cases of definite CP per 100,000 population in Olmsted County, MN [3], translating to a total of 150,000–200,000 cases in the US population. Clinical features of CP are highly variable and include minimal, or no symptoms of debilitating pain repeated episodes of acute pancreatitis, pancreatic exocrine and endocrine insufficiency and pancreatic cancer. CP profoundly affects the quality of life, which can be worse than other chronic conditions and cancers.[4]

Natural history studies for CP originated mainly from centers outside the U.S.[5–9,10,11] conducted during the 1960–1990's and consisted primarily of males with alcoholic CP. Only one large retrospective longitudinal cohort study has been conducted in the US for patients seen at the Mayo Clinic from 1976–1982.[12] While these data provide general insights into disease evolution, it is difficult to predict the probability of outcomes or disease progression in individual patients. Few data exist on the risk of progression in patients with recurrent acute pancreatitis, or in the early-stage disease when definitive morphological features of CP are not evident. There are no longitudinal prospective cohort studies of CP in the US.

In the past two decades, new knowledge has broadened the etiologic profile of CP to highlight contributions from genetic[13], autoimmune[14] and environmental (smoking)[15]

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factors. Improvement in imaging techniques has enabled better recognition of morphological and functional changes in the pancreas[16]. The clinical significance of Type 3c diabetes (Type 3c DM) in patients with diagnosed or undiagnosed pancreatic disease is increasingly recognized.[17,18] The impact of these developments on the natural history of CP are unknown.

The evaluation of chronic abdominal pain costs an estimated $30 billion in healthcare and lost wages annually[19]. Patients with suspected or definite CP comprise a significant fraction of these patients. While diagnosing moderate-severe CP is often straightforward, detection of early-stage CP remains difficult due to the absence of reliable morphologic and functional diagnostic methods. Biopsy of the pancreas is not usually performed as it may not provide a definite diagnosis and entails a risk of biopsy-related pancreatitis. Patients often undergo an exhaustive array of costly studies (endoscopic, radiologic) with their attendant risks. Pancreatic function testing (PFT) is usually performed as a clinical test in patients with chronic abdominal pain or suspected CP to assess for the presence of early-stage disease, but this practice varies between centers[20–22], and limited data suggests a high negative predictive value of PFT, however, it is cumbersome to perform, has low positive predictive value (~50%)[23], and has not gained widespread use (<20 centers in the US).

Since treatment options for definite CP are limited, patients with early-stage CP or at high-risk of developing CP are ideally suited for interventions (e.g., anti-inflammatory or anti-fibrotic medications) to prevent the development of definite CP and its associated morbidity. It will be desirable to have a pract, fast and cost-efficient test(s) to exclude CP with high certainty, to reliably rule-in early-stage CP or help predict disease progression in these patients, to identify patients suitable for intervention (medication, surgery, etc.) and to monitor their effects to slow or reverse disease progression.

ETIOLOGY

The etiology of CP is determined after a thorough patient investigation considering all known risk factors, including alcohol consumption and smoking, as well as laboratory values (triglyceride levels; Ca^{2+} levels for ruling out elevated primary hyperparathyroidism (PHPT); carbohydrate-deficient transferrin (CDT)/phosphatidylethanol levels, and family medical history.

The most common risk factor for CP is alcohol abuse, with a logarithmic risk increase, although the type of alcohol consumed is irrelevant.[24] The amount and duration of alcohol consumption required to develop CP have not been unequivocally defined. Some authors suggest at least 80 g/day for at least six years would be a threshold for developing chronic pancreatitis. Smoking is probably an independent risk factor, and smoking cessation is advisable for CP patients [25]

Autoimmune pancreatitis (AIP) should be ruled out following current consensus guidelines and when no other etiology can be found in patients. Please see Nima Hafezi-Nejad, Vikesh K. Singh, Christopher Fung, et al. article “Magnetic Resonance Imaging of Autoimmune Pancreatitis,” in this issue for information on typical imaging and clinical findings of AIP.

Cholecystolithiasis and choledocholithiasis are not considered independent risk factors for the development of CP. Whether anatomic anomalies such as pancreas divisum increase the CP risk is still a matter of debate; however, with additional risk factors, pancreas divisum might lead to CP development. If no etiological factor can be identified, genetic screening for predisposing variants can be offered.

Genetic factors also contribute to CP development. The most important genetic risk factors are variants in cationic trypsinogen (PRSS1), serine protease inhibitor Kazal-type 1 (SPINK1) and carboxypeptidase A1 (CPA1). Further genetic susceptibility genes are cystic fibrosis transmembrane conductance regulator (CFTR), chymotrypsinogen C (CTRC) and carboxyesterlipase (CEL).[13]

CLINICAL FEATURES

Abdominal pain is a dominant feature of chronic pancreatitis. The pain is typically epigastric, often radiates to the back, is occasionally associated with nausea and vomiting, and may be partially relieved by sitting upright or leaning forward. The pain is usually worse 15 to 30 minutes after eating. Early in the course of chronic pancreatitis, the pain may occur in discrete attacks; as the condition progresses, the pain tends to become more continuous.

The pain in chronic pancreatitis varies among patients. This pattern was illustrated in a prospective cohort of 207 patients with alcoholic CP in which two typical pain patterns were observed.[26] The first was characterized by episodes of pain (usually lasting less than ten days) with pain-free intervals lasting from months to more than a year. The second pattern was characterized by prolonged periods of daily pain or clusters of severe pain exacerbations often requiring repeated hospitalizations. Also, although abdominal pain is the most consistent finding in patients with chronic pancreatitis, it may be absent in some cases. In one series, for example, 20 percent of patients with chronic pancreatitis presented with evidence of pancreatic exocrine or endocrine dysfunction in the absence of pain.[12]

Patients with severe pancreatic exocrine dysfunction cannot correctly digest complex foods or absorb partially digested breakdown products. Nevertheless, clinically significant protein and fat deficiencies do not occur until over 90 percent of pancreatic function is lost.[27]

Steatorrhea usually occurs before protein deficiencies since lipolytic activity decreases faster than proteolysis.[28] The clinical manifestations of fat malabsorption include loose, greasy, foul-smelling stools that are difficult to flush. Malabsorption of the fat-soluble vitamins (A, D, E, and K) and vitamin B12 may also occur, although clinically symptomatic vitamin deficiency is rare.[29]

Glucose intolerance occurs with some frequency in chronic pancreatitis, but overt diabetes mellitus usually occurs late in the course of the disease. Patients with the calcifying CP, particularly those who develop them early, may develop diabetes more frequently than those with the non-calcifying CP.[30] Diabetes is also more likely to occur in patients with a family history of type 1 or type 2 diabetes; this observation suggests a role for an underlying decrease in pancreatic reserve or insulin responsiveness. Pancreatic surgery (including drainage or pancreaticoduodenectomy) does not appear to increase the risk of diabetes.

Exceptions include distal pancreatectomy and significant pancreatic resection in the setting of extensive pancreatic fibrosis.[30] Diabetes which develops in patients with CP is usually insulin-requiring. However, it is different from typical type 1 diabetes in that the pancreatic alpha cells, which produce glucagon, are also affected; as a result, there is an increased risk of hypoglycemia, both treatment-related and spontaneous. Diabetic ketoacidosis and nephropathy are rare; neuropathy and retinopathy occur more frequently.[28]

HISTOPATHOLOGY

Histologically, the two most common features of CP are the loss of acinar tissue (atrophy) and fibrosis. The fibrosis may surround the lobules (perilobular or interlobular fibrosis) or extend into the lobules of acinar tissue (intralobular fibrosis).[31] Chronic inflammatory infiltrate may be present, but this feature is highly variable and disappears late in the course of CP. A diagnosis of CP may be made by atrophy and fibrosis in the absence of other changes. Chronic pancreatitis can be a patchy or localized process with regional involvement. This feature is best understood by considering the mechanisms of pathogenesis, in particular, the necrosis-fibrosis hypothesis, which posits that CP develops as a result of multiple episodes of AP with necrosis and scarring. This process may be patchy at first, progressing to a diffuse pattern after multiple episodes. This is commonly considered to be the mechanism in alcoholic CP, paraduodenal CP, and likely hereditary pancreatitis. On the other hand, duct obstruction can lead to progressive fibrosis and loss of acinar tissue that may be localized or segmental, as in the presence of an obstructing neoplasm, or may be diffuse as is characteristic of cystic fibrosis.

IMAGING STUDIES

Imaging studies that may be useful in chronic pancreatitis include plain abdominal films, transabdominal ultrasound (US), CT scan, magnetic resonance imaging (MRI) combined with MR Cholangiopancreatography (MRCP), Endoscopic Retrograde Cholangiopancreatography (ERCP), and endoscopic ultrasound (EUS).

Calcifications within the pancreatic duct are present on plain film in approximately 30 percent of patients with chronic pancreatitis. Calcium deposition is most common with alcoholic pancreatitis, but can also be seen in the hereditary and tropical forms of the disorder; it is rare in idiopathic pancreatitis.

Transabdominal ultrasonography, CT scan, and MRI/MRCP may show ductal dilatation, enlargement of the pancreas, calcifications, and post-inflammatory fluid collections adjacent to the gland. The sensitivity and specificity of US for the diagnosis of chronic pancreatitis are 60 to 70 percent and 80 to 90 percent, respectively.[32] The corresponding values for CT scanning are 75 to 90 and 85 percent, respectively.[33] Most common CT imaging features of CP are listed in Table 1. [33]

MRCP is becoming the diagnostic test of choice since MRI/MRCP is a more sensitive imaging tool for the diagnosis of CP by evaluating both parenchymal and ductal changes. Most common findings of CP seen by MRI and MRCP are listed in Table 2. Ductal abnormalities are very specific and reliable MRI signs of CP, however, signal intensity

changes either by T1-weighted gradient echo or T1 mapping may precede ductal abnormalities and detect early CP.[34–38]} One study investigated the association between the bicarbonate level of the pancreatic juice and the T1-weighted gradient echo signal and reported a significant direct correlation. The signal intensity ratio of 1.2 yielded sensitivity of 77% and specificity of 83% for detection of pancreatic exocrine dysfunction (AUC 0.89). [34] This imaging finding can be very helpful information to the clinician who is evaluating a patient whose symptoms are suspected of CP but has normal ductal findings.

MRCP can also be performed by utilizing the hormone secretin, which stimulates a normal pancreas to secrete a significant amount of fluid while transiently increasing the tone of the sphincter of Oddi. Transient increase in the diameter of the duct improves the depiction of the anatomy, which can be useful in cases where detailed evaluation of the pancreatic duct is most desired in patients with the suspected pancreatic disease. [39,40] Improved visualization of the ductal anatomy can be important in differentiating side-branch IPMNs from other cystic neoplasms, diagnosis and classification of chronic pancreatitis, disconnected pancreatic duct syndrome and ductal anomalies such as anomalous pancreaticobiliary junction and pancreas divisum. In the post-pancreatectomy patients, stimulation by secretin can give information about the patency of the pancreatico-enteric anastomosis. Duodenal filling during the post-secretin phase of the MRCP can estimate the excretory reserve of the pancreas.[41] It is expected that with increasing severity of CP there will be a decrease in the number of acinar cells and the fluid output, which can be detected with S-MRCP. Current consensus is that duodenal filling during secretin MRCP does not help to evaluate the grade of severity of CP, because a substantial number of patients with severe CP may still have a normal duodenal filling.

Diffusion-weighted MRI measures the restriction of free water molecules in the gland. The more fibrosis there is, the more likely there will be less diffusion of water molecules (which is measured as apparent diffusion coefficient). The apparent diffusion coefficient value is expected to be lower in patients with pancreatic fibrosis than in normal patients. Exploiting this idea, one can evaluate the gland using diffusion MRI after IV secretin stimulation and enhance the sensitivity to depict subtle abnormalities in diffusion restriction and separate normal patients from those with early CP.[42]

MR Elastography (MRE) has been shown to be a reliable marker of hepatic fibrosis in patients with the chronic liver disease. While there are no controlled data evaluating this technique in patients with CP, there is room for optimism as recent data demonstrated the feasibility of using MRE to determine pancreatic stiffness in healthy volunteers. Reproducible stiffness measurements were noted throughout the pancreas, with imaging parameters and equipment different than that used for liver imaging. Preliminary data suggest that pancreatic MRE can provide promising and reproducible stiffness measurements throughout the pancreas, potentially allowing for assessment of pancreatic fibrosis. [43]

ERCP had been utilized to identify ductal abnormalities or obstructions, to clarify ductal anatomy before surgical intervention, and to confirm the patency of postsurgical anastomoses, including pancreatico-jejunostomies.[44] Guidelines published by the American

Society for Gastrointestinal Endoscopy (ASGE) in 2006, recommend that ERCP should be reserved for patients in whom the diagnosis remains unclear after pancreatic function testing (PFT) or other non-invasive (CT or MRI) or less invasive imaging studies (EUS) have been performed.[45] Characteristic beading of the main pancreatic duct and ectatic side branches is diagnostic of chronic pancreatitis. The Cambridge classification has divided patients into normal, equivocal, mild, moderate and severe CP categories based upon ductal changes on ERCP.[46,47] Today, ERCP is rarely used for diagnostic purposes.

Endoscopic ultrasonography may be as sensitive as ERCP or pancreatic function testing, but requires a highly skilled gastroenterologist to perform[48] and multicenter studies showed the inter-observer agreement to be less than optimal for the diagnosis of CP.[49] The most predictive endosonographic feature is the presence of stones. Other suggestive features include visible side branches, cysts, lobularity, an irregular main pancreatic duct, hyperechoic foci and strands, dilation of the main pancreatic duct, and hyperechoic margins of the main pancreatic duct. Many endosonographers consider the presence of four or more of these features to be highly suggestive of chronic pancreatitis.[48]

Several invasive and noninvasive pancreatic function tests are available for the diagnosis of pancreatic insufficiency, which can be classified as direct or indirect. Direct tests involve the stimulation of the pancreas through the administration of a meal or hormonal secretagogues, after which duodenal fluid is collected and analyzed to quantify normal pancreatic secretory content (i.e., enzymes, and bicarbonate). Only a few specialized centers perform these tests. Their main role is in the diagnosis of early chronic pancreatitis in patients with compatible clinical features but without characteristic radiographic findings. The estimated sensitivity and specificity of secretin pancreatic function testing in diagnosing chronic pancreatitis are 82% and 86%, respectively.[23] Indirect tests measure the consequences of pancreatic insufficiency and are more widely available. However, they depend upon the consequences of pancreatic maldigestion, which are not apparent until normal enzyme secretory output has declined by more than 90 percent. Thus, they are insensitive to early pancreatic insufficiency.

LABORATORY

Serum concentrations of amylase and lipase may be slightly elevated in patients with chronic pancreatitis. However, but these enzymes are more commonly normal for the following reasons: CP is a patchy, focal disease, leading to a minimal increase in pancreatic enzymes within the blood and there is frequently significant fibrosis, resulting in a decreased abundance of these enzymes within the pancreas. Thus, serum measurements of amylase or lipase should be reserved only for the diagnosis of acute pancreatitis and not chronic pancreatitis where they are neither diagnostic nor prognostic. It is not unusual that a patient with elevated amylase or lipase values <3 times the upper limit of normal is labeled as having chronic pancreatitis when, in fact, these are non-diagnostic.

The complete blood count, electrolytes, and liver function tests are typically normal. Elevations of serum bilirubin and alkaline phosphatase suggest compression of the intrapancreatic portion of the bile duct by edema, fibrosis, or pancreatic cancer. Markers of

chronic autoimmune pancreatitis include an elevated ESR, IgG4, rheumatoid factor, ANA, and anti-smooth muscle antibody titer.

Steatorrhea should no longer be diagnosed qualitatively by Sudan staining of feces since it is nonspecific. A 72-hour quantitative fecal fat determination is the gold standard. The quantitative test is usually performed over 72 hours; excretion of more than 7 g of fat per day is diagnostic of malabsorption, although patients with steatorrhea often have values greater than 10 g/day. In the proper clinical setting (e.g., in a patient with typical symptoms of abdominal pain), confirmation of increased fecal fat excretion may be sufficient to diagnose chronic pancreatitis.

Given the cumbersome nature of the 72-hour fecal fat test, measurement of fecal elastase can be helpful for evaluating pancreatic exocrine dysfunction, and it is considered the test of choice. Among pancreatic function tests, fecal elastase measurement is the most sensitive and specific, especially in the early phases of pancreatic insufficiency. Also, its values are independent of pancreatic enzyme replacement therapy and require only a single random stool sample. According to unpublished data from the manufacturer, values less than 200 mcg/g are suggestive of pancreatic insufficiency (sensitivity and specificity of 93 percent).[50]

GENETIC TESTING

In the past few years, genetic mutations have been associated with chronic pancreatitis. These genes include the CFTR gene responsible for cystic fibrosis, SPINK-1, which encodes for trypsin inhibitor, and the PRSS-1 gene linked to hereditary pancreatitis. In a study where extensive sequencing of the CFTR gene was performed in conjunction with functional analyses, 44 percent of patients with idiopathic chronic pancreatitis were found to have at least one variant in the CFTR gene which was associated with CFTR dysfunction.[51] The fact that 22 percent of healthy controls had at least one variant in that study combined with the data that over 2000 variants (i.e., not disease proven mutations and thus of unknown significance) have been detected in the CFTR gene by extensive sequencing, indicates that CF genotyping should not be performed routinely to diagnose a patient with chronic pancreatitis. Alternatively, sweat chloride testing may be of benefit since it assesses CFTR function and does not rely on full gene sequencing.[52] Up to 10 percent of patients will have abnormal results, which should prompt further investigation of occult male infertility or lung disease and may warrant professional genetic counseling. SPINK-1 mutations are present in 23 percent of patients with chronic pancreatitis but are seen in 2 percent of healthy individuals.[53] In conjunction with the finding that homozygous mutations can be found in healthy individuals, testing for this gene is presently not of diagnostic or therapeutic benefit and hence not recommended. PRSS-1 mutations can be diagnostic of hereditary pancreatitis which can present with recurrent acute episodes of pancreatitis and progress to the chronic form.

CLASSIFICATION

CP has been classified into different forms (calcifying, obstructive, autoimmune and groove). These classifications are based on clinical features, morphological characteristics

and response to treatment. In calcifying CP, for example, perilobular fibrosis and acinar destruction with infiltration of acute and chronic inflammatory cells are present. Obstructive CP develops as a secondary complication due to an area of obstruction with dilatation of the pancreatic duct proximal to the stenosis, atrophy of acinar cells and fibrosis. Finally, groove pancreatitis affects the groove between the pancreatic head, duodenum and the bile duct.

Classification systems are of great importance for guiding management strategies, since treatment strategies cannot rely solely on the type and degree of morphological changes in the pancreas, but need to include clinical, functional and imaging findings. So far no globally accepted classification system has been established. Classification systems for CP are:

1. Cambridge Classification
2. Manchester classification
3. ABC classification
4. M-ANNHEIM
5. TIGAR-O
6. Rosemont classification

There is no MRI/MRCP, CT or US-specific classification criteria for CP. Radiologists are interpreting MRCP often time use Cambridge classification which was designed for ERCP more than three decades ago. [46] There is a need for a new staging system for CP, specifically designed for CT, MRI, and MRCP combining the ductal and the parenchymal changes secondary to pancreatic fibrosis. American Pancreatic Association released a morphology characterization imaging guide for the current imaging modalities (Table 3). [47]

The Manchester classification system uses imaging modalities and clinical signs of CP.[54] The degree of severity is mostly influenced by the presence of exocrine and endocrine insufficiency or the presence of complications, while imaging findings are of minor importance. The ABC classification recommends similar findings to the Manchester classification system. [55,56] The Rosemont classification was developed to diagnose CP using EUS.[57]

Two major classification systems have been established to help assess risk factors in the development of CP: TIGAR-O and M-ANNHEIM and are helpful in guiding providers as to when to initiate testing for CP. Etiological factors in the M-ANNHEIM system are; alcohol consumption; nutrition; hereditary factors; ductal factors; immunology; miscellaneous and rare metabolic disorders (e.g., hypercalcemia, hyperparathyroidism, chronic renal failure, drugs, toxins.[58] The M-ANNHEIM system includes the stage, severity and clinical findings of CP and offers a severity index. Different guidelines recommend using the TIGAR-O classification. This system comprises six etiologic groups: toxic/metabolic, idiopathic, genetic, autoimmune, recurrent acute pancreatitis, and obstructive groups. [59]

DIFFERENTIAL DIAGNOSIS

Pancreatic cancer is the primary diagnosis that must be considered in patients suspected of having chronic pancreatitis. An endoscopic sampling of the pancreatic juice might be necessary to differentiate CP from the main or mixed-type intra-ductal papillary mucinous neoplasm. Acute pancreatitis may also be difficult to distinguish from chronic pancreatitis in some patients.

There are data to suggest that chronic pancreatitis is associated with an increased risk of developing pancreatic carcinoma.[60,61] In a report from the International Pancreatitis Study Group, 2015 patients with chronic pancreatitis were followed for a mean of 7.4 years.[60] A total of 56 pancreatic cancers were identified. The expected number of cases of cancer calculated from country-specific incidence data and adjusted for age and sex was 2.13, yielding a standardized incidence ratio (the ratio of observed to expected cases) of 26.3.

Findings suggestive of possible pancreatic cancer in a patient thought or known to have chronic pancreatitis include older age, the absence of a history of alcohol use, weight loss, a protracted flare of symptoms, and the onset of significant constitutional symptoms. Supporting data for malignancy include a pancreatic duct stricture greater than 10 mm in length on ERCP.[62] Markers such as CA 19–9, and carcinoembryonic antigen (CEA) is helpful if abnormal, but normal values do not rule out pancreatic cancer.

Radiologists sometimes encounter lesions that show focal enlargement or distortion of the normal contour of the pancreas while still lacking pathognomonic features of pancreatic carcinomas. In such cases, a small percentage of patients with such focal enlargements of the pancreas will have a conventional pancreatic carcinoma, while a small percentage of the patients may have an inflammatory pancreatic mass (IPM). Despite these histories that suggest the presence of chronic pancreatitis, one may not usually be certain whether a mass appearing at the pancreas is related to IPM or cancer. The duct-penetrating sign on MRCP images (a smoothly stenotic or normal main pancreatic duct penetrating a mass) was seen more frequently in IPM than in pancreatic cancer (Figure 1).[63]

Paraduodenal pancreatitis, also known as groove pancreatitis, is a rare form of chronic pancreatitis that masquerades as pancreatic adenocarcinoma affecting the pancreaticoduodenal groove, a potential space between the head of the pancreas, duodenum, and common bile duct (Figure 2). Imaging findings of groove pancreatitis often overlap with primary duodenal, ampullary, or pancreatic neoplasms, which often results in a diagnostic challenge.[64] Also, paraduodenal pancreatitis can be mistaken for cystic pancreatic lesions, especially when there is involvement of the duodenal wall. Preoperative recognition of this entity is essential to avoid unnecessary procedures, although surgery, such as pancreaticoduodenectomy, may still be required to relieve obstructive symptoms.

COMPLICATIONS

There are several potential complications of chronic pancreatitis which require active surveillance by clinicians, including diabetes, exocrine pancreatic insufficiency, metabolic bone disease, and pancreatic cancer (Table 4). [65] Most common complications of CP are

endocrine/exocrine insufficiencies, and metabolic bone disorder are not diagnosed by imaging studies. Those seen by the cross-sectional imaging include but not limited to; post-inflammatory cyst formation, bile duct or duodenal obstruction, pancreatic ascites or pleural effusion, splenic vein thrombosis, and pancreatic cancer.[5] Patients may also develop acute attacks of pancreatitis, particularly alcoholics who continue drinking.

CONCLUSION

The diagnosis of CP can be challenging since biopsy of the pancreas is not performed, and laboratory studies and imaging procedures may be normal during the early stage of the disease. The diagnosis of the advanced CP is confirmed if there are calcifications within the pancreas on plain abdominal films or computed tomography (CT) scan, an abnormal pancreatogram or an abnormal secretin pancreatic function test in subtle cases of early pancreatitis. Identification of early stage CP and its treatment may delay or prevent morbidity secondary to CP. In settings where MRI/MRCP is available and of high quality, it may be the imaging test of choice, allowing for assessment of ductal changes and potentially obviating the need for an invasive procedure. Stimulation of the pancreas using intravenous secretin may improve the diagnostic accuracy in the detection of ductal and parenchymal abnormalities seen in CP. T1 signal intensity changes in the pancreatic parenchyma may precede ductal abnormalities and may detect early CP. Ultrasound and CT are best for the late findings of CP but are limited in the diagnosis of early or mild pancreatitis. Contrast-enhanced CT scan can rule out other causes of pain that mimic CP and is helpful for the diagnosis and complications of CP. There is a need for an EUS-like MRI staging system for CP, combining the ductal findings with the parenchymal changes.

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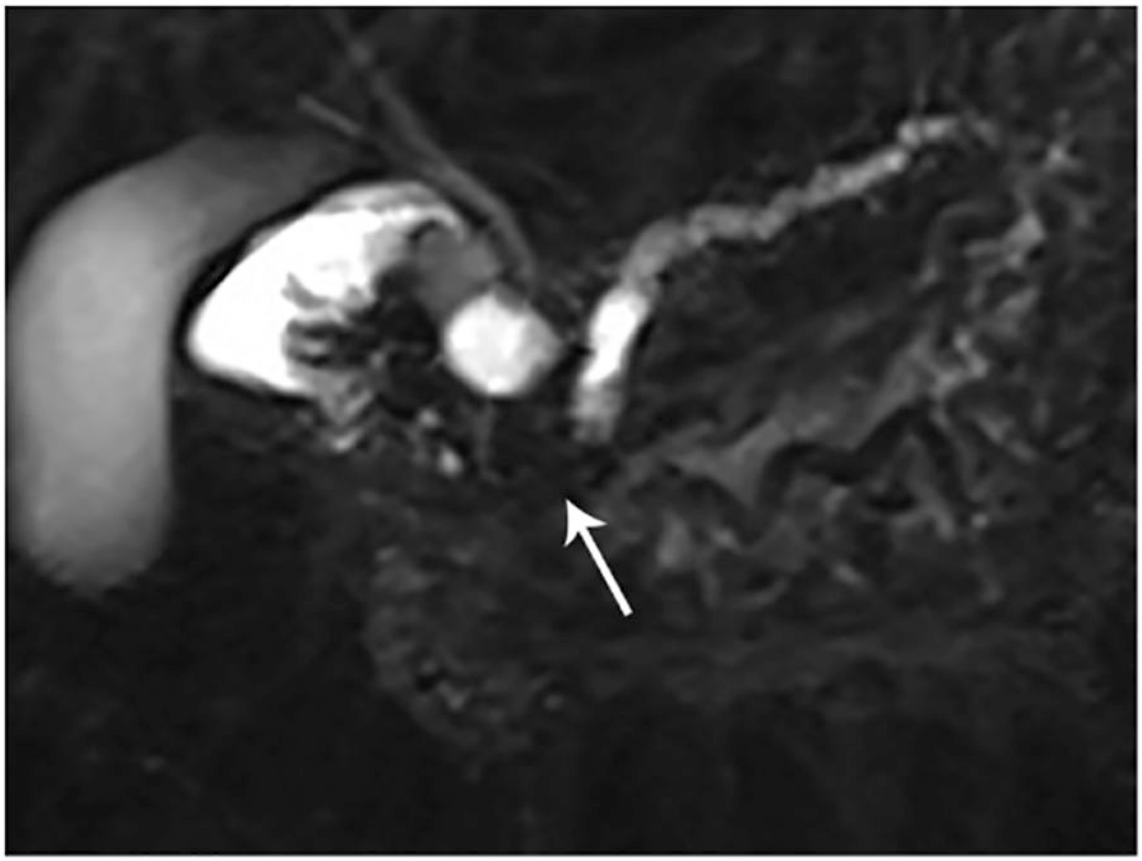
Key Points

- MRI, CT, and EUS are the best imaging methods for establishing a diagnosis of CP. ERCP is reserved for therapeutic purposes.
- The diagnosis of chronic pancreatitis remains challenging in early stages of the disease. T1 signal intensity changes of the parenchyma may precede ductal abnormalities and detect early CP.
- The use of secretin increases the diagnostic potential of MRCP in the evaluation of patients with known or suspected CP.
- There is a need for an MRI/MRCP based diagnostic criteria for CP, combining the ductal findings with the parenchymal changes secondary to fibrosis.
- Genetic discoveries are rapidly uncovering new susceptibility factors. Knowledge of gene and gene-environment interactions may translate into new diagnostic and treatment paradigms.

Synopsis

Diagnosis of CP requires a complete medical history and clinical investigations, including imaging technologies and function tests. MRI/MRCP is the preferred diagnostic tool for detection of ductal and parenchymal changes in CP patients. Ductal changes may not be present in the initial phase of the CP therefore early diagnosis remains challenging.



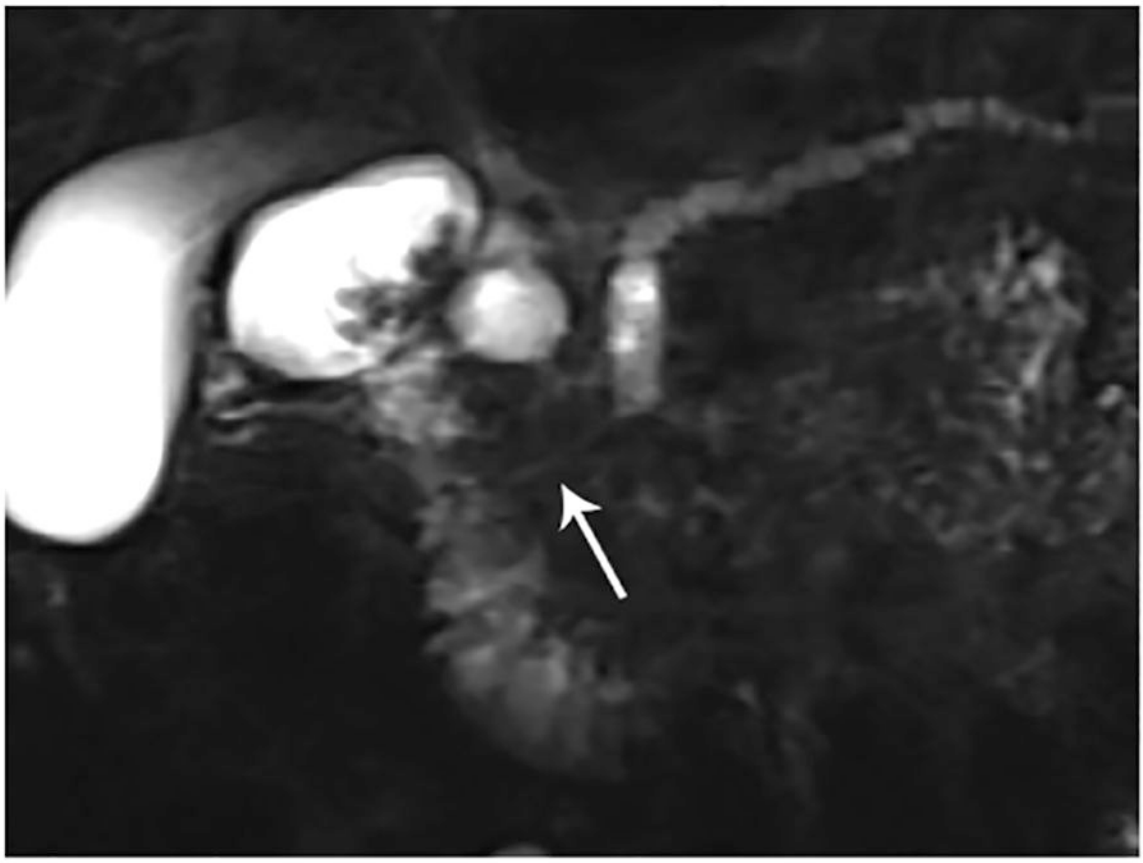
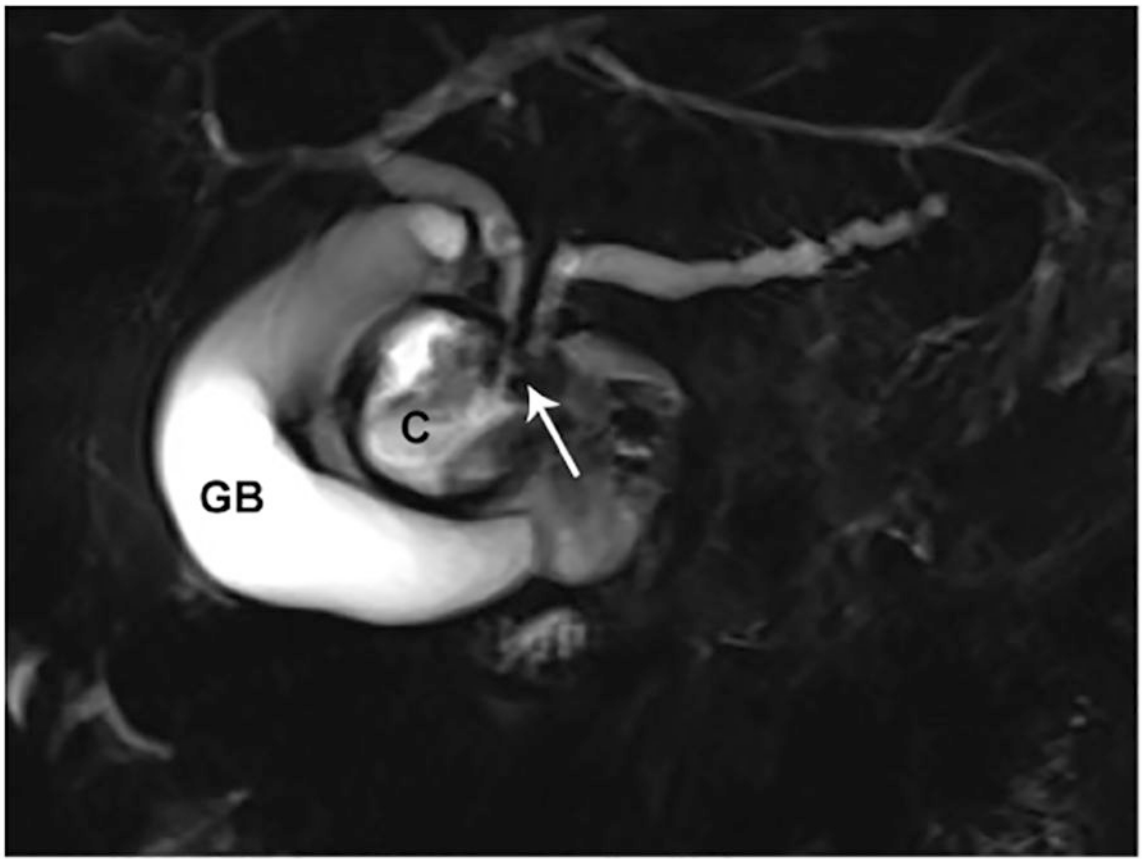
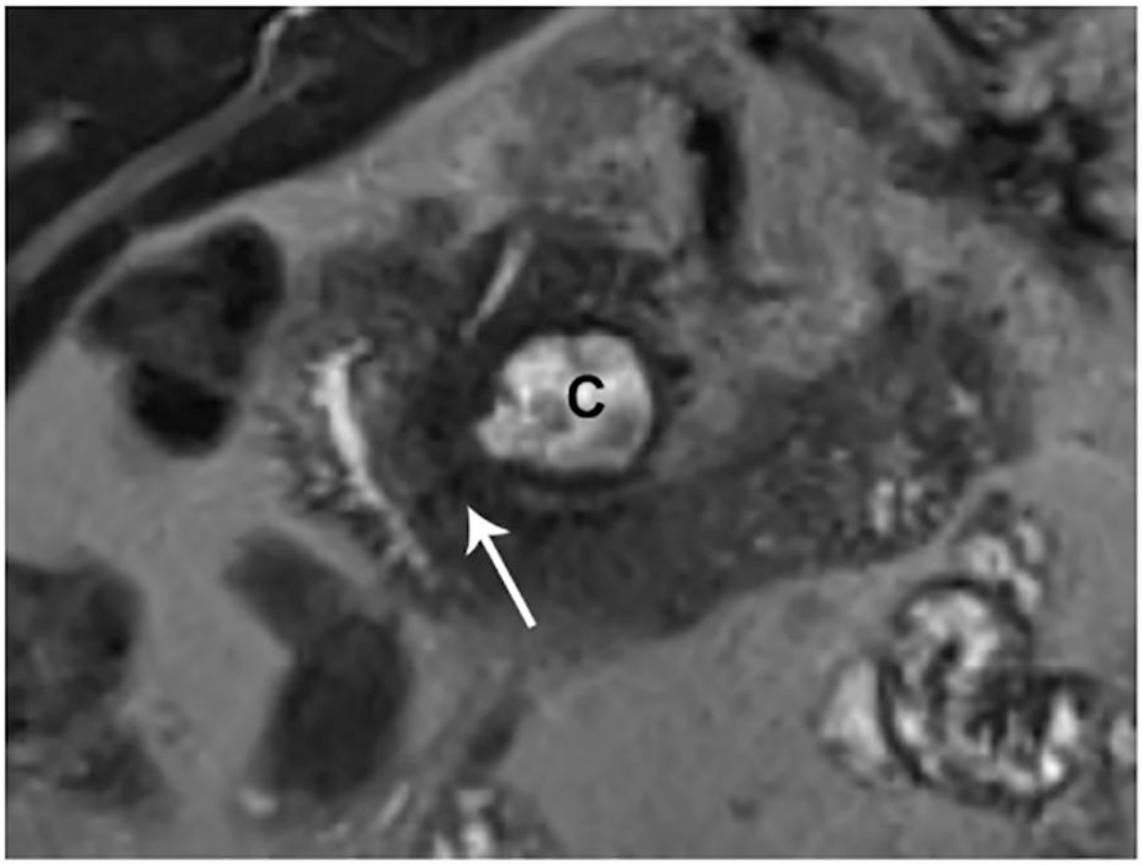


Figure 1.

Penetrating duct sign. **(A)** Coronal MRCP image in a 49-year-old patient with abdominal pain. There is obstruction of the pancreatic duct in the pancreatic head (arrow). Differential diagnosis includes CP given the history, however, also concerning for pancreatic cancer. **(B)** Coronal MRCP image obtained after administration of the secretin. The PD became visible (arrow) following stimulation of the pancreas with secretin. There is a smoothly narrowed PD from the level of obstruction to the sphincter compatible with penetrating duct sign. This finding favors a benign etiology of obstruction rather than malignancy.





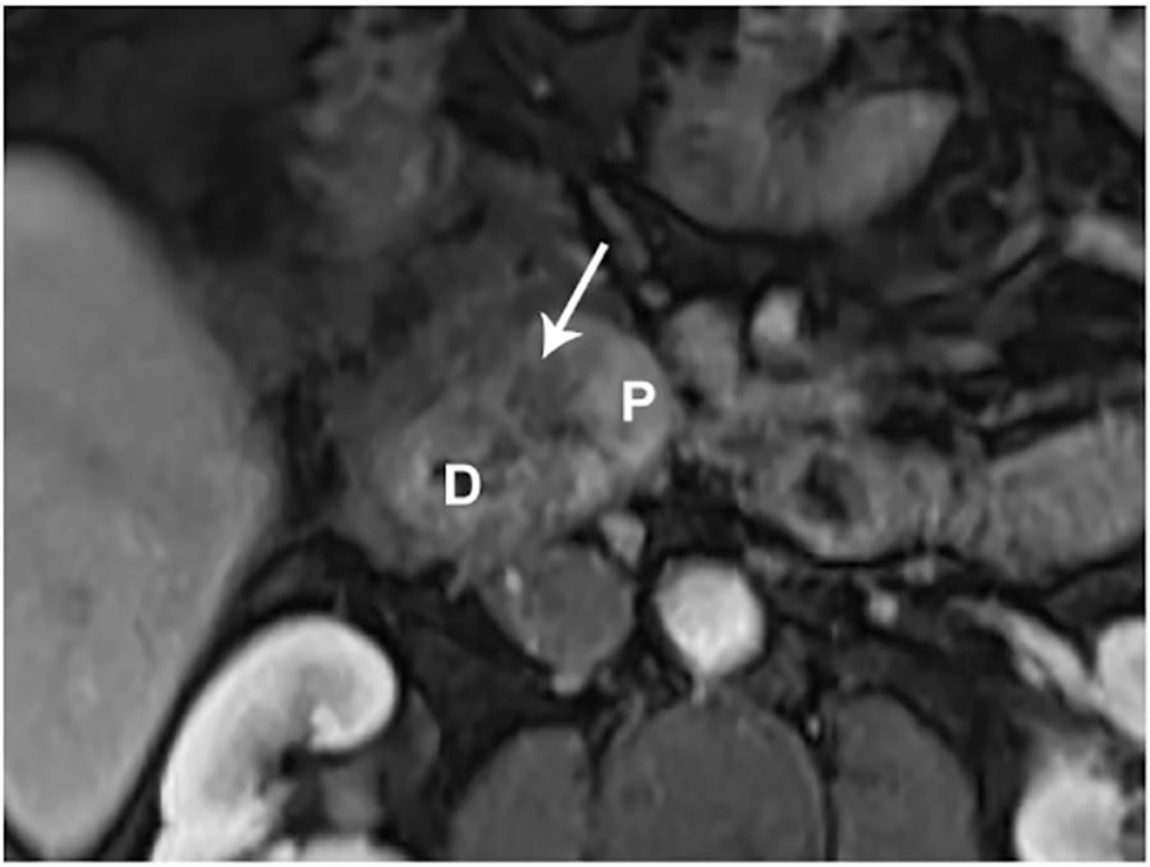


Figure 2.

Paraduodenal/groove pancreatitis. **(A)** Coronal MRCP image in a 36-year-old male with a history of alcohol abuse. There is obstruction of both the PD and the biliary tree in the region of the pancreaticoduodenal junction (arrow). The patient presented with acute pancreatitis and developed a post-inflammatory cyst (C). **(B)** A coronal T2-weighted image shows a relatively T2 hypointense tissue (arrow) causing stricture of the PD. **(C)** Axial T1-weighted image after contrast administration is shown. There is a hypoenhancing lesion (arrow) corresponding to T2 hypointense soft tissue in the pancreaticoduodenal junction concerning for necrotizing pancreatitis and possibly a malignancy. There are acute inflammatory changes in and around the duodenum and pancreatic head in addition to the history of acute on CP. Combination of the clinical and imaging findings favor a non-malignant etiology such as paraduodenal, also called groove CP. (G= gallbladder; C= post-inflammatory cyst; D=duodenum; P=pancreas)

Table 1.

Imaging features of CP observed by CT.

CT Features of CP	Incidence
Ectatic pancreatic duct	68%
Atrophy	54%
Calcifications	50%
Fluid collections	30%
Focal pancreatic enlargement	30%
Biliary ductal dilatation	29%
Alterations in peri-pancreatic fat	16%
Others	Contiguous organ invasion, large cavities, focal acute pancreatitis, intraductal filling defects, disconnected/ disrupted pancreatic duct.

Table 2.

Features of CP seen by MRI/MRCP with or without secretin.

MRI and MRCP Features of CP	
Main pancreatic duct and side branches	Strictures Ductal filling defects Ectatic side branches Ductal contour irregularity Disconnected/disrupted main pancreatic duct Congenital anomalies (e.g., pancreas divisum)
Parenchyma	Atrophy Steatosis
Fluid collections	Walled off necrosis vs pseudocyst
Secretin MRCP specific findings	Increase in diameter of main pancreatic duct Decreased duodenal filling by the pancreatic juice
T1 signal change	Decrease T1 signal in pre-contrast phase
Biliary system	Dilatation/strictures
Duodenum	Obstruction/stricture

Table 3.

Cambridge classification adapted for findings seen on MRCP, CT, and US. American Pancreatic Association Practice Guidelines, 2014. [47]

Cambridge Classification	MRCP/ERCP findings	US/CT/MR findings
0 Normal	no abnormal signs	no abnormal signs
I Equivocal	<3 abnormal branches	one of the following: - dilated main pancreatic duct (2 – 4mm) - slight gland enlargement - heterogeneous parenchyma - small cavities (<10 mm) - irregular ducts - focal pancreatitis - increased echogenicity of main duct wall - irregular head/body contour
II Mild	3 or more abnormal branches	≥ 2 of the following: - dilated main duct (2–4 mm) - gland enlargement - heterogeneous parenchyma - small cavities (<10 mm) - irregular ducts - focal AP - increased echogenicity of main duct wall - irregular head/body contour
III Moderate	>3 abnormal side branches and abnormal main duct	Same as above
IV Severe	all above and 1 or more of - large cavity >10mm - intraductal filling defects - duct obstruction (stricture) - duct dilatation or irregularity	Above changes and 1 or more of: - large cavity >10mm - gland enlargement - intraductal filling defects/calculi - duct obstruction/stricture/ or gross irregularity

Table 4.

Common complications of CP.

Complications of Chronic Pancreatitis	
Endocrine insufficiency (T3cDM)	Up to 80%
Exocrine insufficiency	30–80%
Metabolic bone disease	66%
Splenic vein thrombosis	10–20%
Biliary obstruction	Up to 25%
Pancreatic cancer	4%
Duodenal stricture	1%