Chronic Pancreatitis
What the Clinician Wants to Know from MR Imaging

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KEYWORDS

• Pancreas • Chronic pancreatitis • MR imaging • Magnetic resonance cholangiopancreatography • Computerized tomography

KEY POINTS

- MR imaging, 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 MR imaging/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.

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, Minnesota,[3] translating to a total of 150,000 to 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 United States[5–11] conducted during the 1960s to 1990s and consisted primarily of men with alcoholic CP. Only one large retrospective longitudinal cohort study has been conducted in the United States for patients seen at the Mayo Clinic from 1976 to 1982.[12] Although 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 morphologic features of CP are not evident. There are no longitudinal prospective cohort studies of CP in the United States.

In the past two decades, new knowledge has broadened the etiologic profile of CP to highlight

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contributions from genetic,[13] autoimmune,[14] and environmental (smoking)[15] factors. Improvement in imaging techniques has enabled better recognition of morphologic and functional changes in the pancreas.[16] The clinical significance of type 3c diabetes mellitus in patients with diagnosed or undiagnosed pancreatic disease is increasingly recognized.[17,18] The impact of these developments on the natural history of CP is unknown.

The evaluation of chronic abdominal pain costs an estimated $30 billion in health care and lost wages annually.[19] Patients with suspected or definite CP comprise a significant fraction of these patients. Although diagnosing moderate-severe CP is often straightforward, detection of early stage CP remains difficult because of the absence of reliable morphologic and functional diagnostic methods. Biopsy of the pancreas is not usually performed because 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 suggest 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 United States).

Because treatment options for definite CP are limited, patients with early stage CP or at high-risk of developing CP are ideally suited for interventions (eg, anti-inflammatory or antifibrotic medications) to prevent the development of definite CP and its associated morbidity. It is desirable to have a practical, fast, and cost-efficient test 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 (eg, medication, surgery), and to monitor their effects to slow or reverse disease progression.

ETIOLOGY

The cause of CP is determined after a thorough patient investigation considering all known risk factors, including alcohol consumption and smoking, laboratory values (triglyceride levels, Ca^{2+} levels for ruling out elevated primary hyperparathyroidism, carbohydrate-deficient transferrin/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/d for at least 6 years is a threshold for developing CP. Smoking is probably an independent risk factor, and smoking cessation is advisable for patients with CP.[25]

Autoimmune pancreatitis should be ruled out following current consensus guidelines and when no other cause is found in patients (See Nima Hafezi-Nejad and colleagues' article, "Magnetic Resonance Imaging of Autoimmune Pancreatitis," in this issue for information on typical imaging and clinical findings of autoimmune pancreatitis.)

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 a matter of debate; however, with additional risk factors, pancreas divisum might lead to CP development. If no etiologic factor is identified, genetic screening for predisposing variants is 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. Further genetic susceptibility genes are cystic fibrosis transmembrane conductance regulator (CFTR), chymotrypsinogen C, and carboxyesterlipase.[13]

CLINICAL FEATURES

Abdominal pain is a dominant feature of CP. 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 CP, the pain may occur in discreet attacks; as the condition progresses, the pain tends to become more continuous.

The pain in CP 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 10 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 CP, it may be absent in some cases.