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## In Brief



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In the United States, chronic pancreatitis is diagnosed with increasing frequency and costs more than \$150 million annually to provide care. Regardless of the etiology, chronic inflammation results in irreversible fibrotic replacement of the pancreatic parenchyma. The pathophysiology of chronic pancreatitis is not well understood and is multifactorial. The most significant risk factors for chronic pancreatitis include alcohol and tobacco; however, there is increasing recognition of a hereditary component. The combination of alcohol and tobacco has a synergistic effect, resulting in an increased risk and earlier development of chronic pancreatitis. The best current understanding of the disease suggests that an underlying genetic susceptibility is combined with environmental risk factors to result in the development of chronic pancreatitis.

The hallmark symptom of chronic pancreatitis is debilitating abdominal pain that significantly impairs daily activity. Endocrine and exocrine failure is often present and develops slowly and progressively. Incapacitating abdominal pain is the most common indication for intervention. Abdominal pain, pancreatic insufficiency, and sociopsychological factors contribute to the malnutrition that is commonly associated with chronic pancreatitis. Complications of chronic pancreatitis include pseudocyst, biliary stricture, duodenal stricture, mesenteric vein thrombosis, visceral artery pseudoaneurysm, and pancreatic ductal adenocarcinoma. In addition to pain, these local complications of chronic pancreatitis and concern for malignancy are indications for operation. A critically important point for any caregiver treating patients with chronic pancreatitis is the relationship of chronic pancreatitis and pancreatic cancer, as more than 5% of patients with chronic pancreatitis will develop pancreatic cancer during the course of this disease. Epidemiological data show increasing risk of pancreatic cancer development over long-term follow-up: approximately 2% after 10 years and 4% after 20 years of disease. Intriguing population-based data suggest that effective drainage or resection may attenuate the development of pancreatic cancer.

Diagnosis of chronic pancreatitis can be made via computed tomography, magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography, or endoscopic ultrasound. Non-invasive imaging modalities, such as computed tomography and MRCP,

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are frequently utilized as the first step in diagnostic evaluation; however, these non-invasive techniques can result in false negatives in early chronic pancreatitis, before significant ductal and parenchymal changes become obvious. Secretin-enhanced MRCP provides improved evaluation of the pancreatic ductal anatomy compared to traditional MRCP, enhancing its diagnostic utility. Endoscopic methods (eg, endoscopic retrograde cholangiopancreatography, endoscopic ultrasound) are most sensitive in diagnosing chronic pancreatitis and offer therapeutic benefit.

Medical management and endoscopic intervention are first line therapies to treat chronic pancreatitis symptoms. Abdominal pain is initially treated with non-opioid medications and lifestyle modifications including alcohol and tobacco cessation and dietary changes. Progression of chronic pancreatitis often results in the requirement of prescription opioids. Pancreatic endocrine and exocrine insufficiency are present in up to 80% of patients with chronic pancreatitis. Chronic pancreatitis is the leading cause of pancreatogenic (type 3c) diabetes mellitus and is associated with hepatic and peripheral insulin resistance, impaired insulin secretion/production, and an altered hormonal response to meals.

Evidence supports early surgical intervention in chronic pancreatitis as outcomes in select patients may be superior to endoscopic intervention. Proper selection of the appropriate patient and operation in chronic pancreatitis is paramount to achieving successful outcomes. The goals of surgery are to preserve pancreatic parenchyma, minimize morbidity, and provide durable symptom relief. Individual patient pancreatic parenchyma and duct anatomy, peripancreatic anatomy, quality of life, and genetic profile must be considered. In general, pancreatic duct anatomy guides operative decision making. Patients with a dilated pancreatic duct (>7 mm) benefit from drainage, whereas patients with small duct disease benefit from resection. All therapeutic decisions should be made in the setting of multidisciplinary evaluation, including experienced advanced pancreatic endoscopists and pancreatic surgeons.

Lateral pancreaticojejunostomy (LPJ) is the classic drainage procedure for patients with a diffusely dilated pancreatic duct (>7 mm). The pancreatic duct is opened along its length, pancreatic duct lithiasis is cleared, and LPJ is performed using a Roux-en-Y (R-Y) limb of jejunum. Perioperative morbidity and mortality are acceptable and long-term pain relief is seen in up to 90% of carefully selected patients. The parenchyma-sparing technique and relief of ductal obstruction may delay progression of pancreatic endocrine and exocrine insufficiency.

Directed pancreatic resection, either distal pancreatectomy (DP) or pancreatoduodenectomy (PD), is useful in disease isolated to a segment of the pancreas. When disease is isolated to the body and tail, DP is performed using intraoperative ultrasound to guide the extent of pancreatic resection. Splenic preservation is possible but challenging; and patients should receive preoperative vaccinations against encapsulated organisms. Durable improvements in pain are seen in 80%-90% of patients after DP. Given resection of a sizable portion of pancreatic parenchyma, new-onset diabetes develops in 20%-51% of patients after DP; however, pancreatic exocrine function typically remains stable compared to the preoperative baseline. PD is warranted when biliary or duodenal stricture is present or in cases in which there is concern for malignancy. The diagnosis of malignancy in patients with chronic pancreatitis is extremely challenging because of distorted pancreatic anatomy, inflammation, and calcium deposition. Additionally, the tumor marker carbohydrate antigen 19-9 may be elevated spuriously simply from pancreatic inflammation or biliary obstruction. Compared to other operations, perioperative morbidity and mortality are highest in patients undergoing PD. However, long-term quality of life, pain relief, and pancreatic function are similar to that seen after other operations for chronic pancreatitis.

Duodenal-preserving pancreatic head resection (DPPHR) combines drainage with resection and spares peripancreatic structures. Multiple variations exist on this theme (Beger, Berne, Frey, Izbicki), with each individual procedure applied based on an individual patient's pancreatic anatomy. Chronic pancreatitis patients with bulky disease in the pancreatic head with or without dilation of the pancreatic duct are suitable for Beger's DPPHR. This procedure involves transection of the pancreatic neck over the portal vein, deep coring of the pancreatic head, and 2 pancreatic anastomoses into a shared R-Y limb of jejunum. The Berne modification of DPPHR leaves the neck of the pancreas intact, averting the potential for portal vein injury by avoiding dissection behind the pancreatic neck. After coring out the pancreatic head a single pancreatic

anastomosis to a jejunal R-Y is performed. Frey's iteration of DPPHR is widely applied and useful in patients with pancreatic head involvement and a dilated pancreatic duct throughout the neck, body, and tail of the pancreas. This operation combines LPJ with localized pancreatic head resection, thereby mitigating the risk of recurrent symptoms due to untreated disease in the head of the pancreas. The Izbicki modification is less frequently required but is applicable in patients with head dominant disease and a small pancreatic duct. The pancreatic head is excavated, a "V-shaped" coring of the pancreatic duct along its length is performed, and R-Y limb of jejunum is anastomosed along the length of the remaining pancreatic parenchyma. Many variations of DPPHR have been compared and found to have generally equivalent chronic pancreatitis specific outcomes, morbidity, and mortality.

Total pancreatectomy with islet autotransplantation (TP-IAT) is applied to patients with diffuse small duct chronic pancreatitis, particularly those patients with specific genetic changes. In this challenging group of patients, total pancreatectomy is performed, the islet cells are isolated from the pancreatectomy specimen, and the isolated islet cells are infused via the portal vein into the liver in the early postoperative period (<24 hours). In patients with prior chronic pancreatitis surgery, TP-IAT may be performed but with lower islet yield. Outcomes in TP-IAT are improving with increasing experience.

Chronic pancreatitis is a life-altering disease. Appropriate treatment requires an approach tailored to the individual patient, with clinical decisions made in the setting of a multidisciplinary team. Many different operations are available; the appropriate operation is guided by the patient's anatomy and clinical picture. Improvements in perioperative morbidity and mortality, and importantly improvements in long-term outcomes of chronic pancreatitis, are realized with proper patient and operation selection, and durable symptom relief is attainable. Ongoing study into basic disease mechanisms is particularly important, as all current chronic pancreatitis therapy treats complications of the disease, and not the pathophysiologic underpinning.