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Review

Operative management of chronic pancreatitis: A review

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ABSTRACT

Background: Pain secondary to chronic pancreatitis is a difficult clinical problem to manage. Many patients are treated medically or undergo endoscopic therapy and surgical intervention is often reserved for those who have failed to gain adequate pain relief from a more conservative approach.
Results: There have been a number of advances in the operative management of chronic pancreatitis over the last few decades and current therapies include drainage procedures (pancreaticojejunostomy, etc.), resection (pancreticoduodenectomy, etc.) and combined drainage/resection procedures (Frey procedure, etc.). Additionally, many centers currently perform total pancreatectomy with islet autotransplantation, in addition to minimally invasive options that are intended to tailor therapy to individual patients.
Discussion: Operative management of chronic pancreatitis often improves quality of life, and is associated with low rates of morbidity and mortality. The decision as to which procedure is optimal for each patient should be based on a combination of pathologic changes, prior interventions, and individual surgeon and center experience.

1. Introduction

Chronic pancreatitis (CP) places an immense burden on patients and physicians alike, costing the United States healthcare system an estimated $2.6 billion annually.[1] As the disease progresses, the gland undergoes irreversible destruction of its architecture; worsening small and large ductal disease, calcification, and fibrosis, ultimately lead to a loss of functional parenchyma and subsequent chronic pain, endocrine and/or exocrine insufficiency and increased susceptibility for developing pancreatic ductal adenocarcinoma.

Repeated bouts of acute pancreatitis, chronic abdominal pain and glandular dysfunction are the primary targets for initial medical, many of which are associated with only short-term improvements and high rates of recurrence. Non-operative strategies for managing pain, such as lifestyle modifications (dietary modification, cessation of smoking and alcohol), pancreatic enzyme replacement and various methods of analgesia, are typically employed before considering more invasive therapies such as splanchnic nerve ablations, endoscopic interventions, or surgery.[2] However, these less invasive methods are often ineffective or unsatisfactory and many patients eventually undergo more invasive procedures.[3] In recent years, a number of randomized trials comparing the various surgical approaches available to those who have failed conservative techniques have been reported, but there is still a clear need for further study. In this article we aim to give an overview of the etiology, pathophysiology, clinical presentation, diagnosis and surgical management of CP.

2. Epidemiology, etiology and pathophysiology

The incidence of CP is estimated to be between 2 and 200/100,000 individuals per year worldwide, depending on the population, and rising.[4–6] The most common etiological risk factors for the development of CP can be grouped according to the TIGAR-O classification system as reviewed in Table 1.[5,7,8]

While the exact pathophysiological mechanism(s) of CP is unknown, a number of hypotheses have been presented to account for the observed features commonly encountered. Many of the causes in the TIGAR-O scheme are likely unified by a similar process of

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Table 1
TIGAR-O classification of chronic pancreatitis.

Classification	Example
Toxic-metabolic	Alcohol Induced (up to 70% of cases in developed countries)
Idiopathic	Tropical pancreatitis
Genetic	SPINK1, PRSS1, CASR, or CFTR polymorphisms
Autoimmune	
Recurrent severe acute pancreatitis	Necrosis-fibrosis model
Obstructive	Stones, plugs, strictures and pseudocysts

pancreatic auto-digestion in the setting of pancreatic ductal system obstruction.[9–12] An often cited theory is the necrosis-fibrosis model which postulates that CP is simply the end result of numerous episodes of severe acute pancreatitis, whatever the cause, with repeated episodes of necrosis eventually leading to fibrosis of the gland.[13–15] The most complete and commonly accepted model for the development of CP is the so-called Sentinel Acute Pancreatitis Event (SAPE) hypothesis by Whitcomb et al..[16] This model attempts to provide a unifying theory for the etiology of CP by suggesting that a "sentinel event" (e.g. alcohol induced stress) leads to the initiation of an inflammatory response. This event may resolve completely; however, persistence of this inflammatory response leads to recruitment, activation and proliferation of pancreatic stellate cells and macrophages. Unchecked, this sensitizes the pancreas to further injurious events leading to stellate cell stimulation, progressive fibrosis, and parenchymal destruction. Fig. 1 depicts the SAPE model as described above.[11,16,17]

3. Clinical presentation and diagnosis

While chronic abdominal pain is the most common, and most consternating, presenting symptom of chronic pancreatitis, manifestations of glandular dysfunction, such as steatorrhea, diarrhea, weight loss and the onset of brittle diabetes mellitus due to the loss of α, β and γ islet cells may also be present.[5,9,17,18] Chronic pain is certainly the most debilitating symptom associated with CP and is experienced by 85% or more of individuals at some point.[19] Chronic pain is also the most important and common reason for patients to seek medical care. The exact origins of pancreatitis related pain are not completely understood but are thought to be multi-factorial in nature, attributable to either intrapancreatic processes, including inflammation, increased ductal/interstitial pressures or neural signaling changes, or extrapancreatic processes such as biliary stricture or duodenal obstruction.[20–28]

Some authors suggest that, in the majority of patients, CP "burns out" with time regardless of intervention, resulting in partial to complete pain relief around four to five years after initial pain onset.[29,30] Others report that fewer than 50% of patients become pain-free over a ten year time frame.[31,32] Whether or not this "burn out" phenomenon occurs in conjunction with the loss of endocrine and exocrine function remains controversial.[33]

Pancreatic pseudocysts, a consequence of acute pancreatitis and ductal injury, may be present in 20–40% of patients with CP and when symptomatic may be managed via percutaneous, surgical or, preferably, endoscopic drainage.[34] Some pseudocysts regress spontaneously, only requiring supportive medical care while others, particularly those associated with alcohol, can reoccur in up to 50% of cases.[35–38] Additional complications associated with chronic pancreatitis include duodenal obstruction, biliary tree strictures, pancreatic ascites or pleural effusion from disruption of pancreatic ducts or pseudocysts.[21,39]

The diagnosis of chronic pancreatitis is typically made clinically based on the classic symptoms of epigastric pain often radiating to the mid/upper back, nausea with inability to tolerate PO intake, weight loss, and endocrine/exocrine dysfunction. In contrast to acute pancreatitis, the elevation of amylase and lipase levels is uncommon and measuring c-reactive protein, procalcitonin levels and leukocytosis are unhelpful. However, other syndromes may present with a similar clinical picture, complicating diagnosis. Of note is Disconnected Pancreatic Duct Syndrome (DPDS) in which a viable left side of the pancreas cannot drain due to separation of the pancreatic duct, usually in the neck of the pancreas. Most often associated with acute necrotizing pancreatitis, this syndrome can also occur in chronic pancreatitis due to a longstanding stone impaction or stricture impeding drainage. DPDS typically presents as abdominal pain and exocrine dysfunction and is very resistant to medical management. Left unchecked, the uncontrolled drainage ultimately leads to fistula and pseudocyst formation. As such, it requires careful consideration as the syndrome can masquerade as CP, particularly if medical management is attempted first, prolonging the course.[40] When the diagnosis of CP is in question, or if there is concern for other pathology such as a pseudocyst or mass, then cross-sectional imaging of the gland is often obtained.

4. Endoscopic diagnosis and management

Endoscopic ultrasonography (EUS) and endoscopic retrograde cholangiopacreatography (ERCP) have well defined roles in the diagnosis and management of chronic pancreatitis.[11] While CT and MRI do offer noninvasive means of assessing the pancreas, EUS offers a minimally-invasive approach able to better visualize the pancreatic parenchyma and ductal system, and EUS-guided fine-needle aspiration or core biopsy enables the sampling of solid and cystic lesions, which can affect the surgical approach in cases where solid neoplasms or intrapapillary mucinous neoplasms are found that can be the cause of acute pancreatitis and masquerade as chronic pancreatitis. Additionally, ERCP offers the potential of accessing both the major and minor papillae, and offers both diagnostic and therapeutic capabilities as well, such as brushing of strictures for cytopathology, pancreatoscopy, papillotomy, and pancreatic duct stenting. However, this approach must be used with caution given the risk of post-procedural pancreatitis associated with its use, as well as risk of pancreatic infection, bleeding and duodenal perforation.[41]

ERCP is provides an effective therapy for proximal pancreatic and distal biliary strictures that arise from chronic pancreatitis, and it can be effective in treating patients with dilated pancreatic ducts due to strictures or stone disease. Strictures are a common occurrence in CP, with biliary strictures complicating a quarter of patients.[42] Balloon dilation or stent placement has a success rate ranging from 75 to 94% with regard to acute pain relief. Likewise, stenting provides an effective treatment in cases of ductal leakage.[41] Stent occlusion and migration have been longstanding problems stymying the effectiveness of these techniques. However, fully covered self-expandable metal stents have been develop to prolong patency, addressing the former concern and increasing