International Journal of Surgery 7 (2009) 305–312

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.theijs.com

Review

Surgical therapy of chronic pancreatitis: Indications, techniques and results

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ARTICLE INFO

Article history:
Received 18 May 2009
Accepted 24 May 2009
Available online 6 June 2009

Keywords:
Chronic pancreatitis
Inflammatory mass
Ductal obstruction
Ductal hypertension
Pain
Neuropathy
Surgical therapy
Drainage
Resection
Duodenum-preserving pancreatic head resection

ABSTRACT

In chronic pancreatitis (CP) a benign inflammatory process in the pancreas results in progressive structural changes with replacement of functional exocrine and endocrine parenchyma by a fibrotic and inflammatory tissue, often evident as an inflammatory mass. The consequences are diabetes mellitus, exocrine insufficiency, and severe recurrent upper abdominal pain, often resulting in a significant reduction in the quality of life. The inflammatory process or the formation of pseudocysts can cause local complications such as obstruction of the pancreatic duct, bile duct or the duodenum. In spite of intensive research there is still no specific therapy for CP. Medical pharmacologic treatment is the basis of therapy in CP and aims at pain relief and treatment of exocrine and endocrine insufficiency. However, many patients require additional therapy for effective pain relief or treatment of local complications. Whereas a lot of these patients undergo repetitive endoscopic interventions, surgical drainage results in better long-term outcome. In patients with an inflammatory mass of the pancreatic head, surgical resection procedures provide good short and long-term results, especially in terms of pain relief. This article summarizes indications and potential of endoscopic/interventional and surgical therapy and gives an overview of surgical techniques with special focus on organ-sparing procedures such as the duodenum-preserving pancreatic head resection and its variants. Whereas exocrine and endocrine insufficiency may progress, adequate surgical therapy can provide effective long-term pain relieve and improvement in the quality of life in patients with CP.

1. Definition, epidemiology and etiology of chronic pancreatitis

Chronic pancreatitis (CP) is a benign, inflammatory process of the pancreas which leads to progressive and irreversible loss of functional parenchyma and replacement with fibrotic tissue and ductal metaplasia.[1] The ductal system displays stenoses and dilatations. CP can result in either an atrophy of the gland or in the formation of an inflammatory mass, as often observed in European series.[2,3] Furthermore, CP can result in intraductal and/or parenchymal calcifications. Clinically, the disease is characterized by recurrent episodes of severe and uncontrollable upper abdominal pain and by a loss of exocrine function (diarrhea, steatorrhea) and endocrine function (diabetes mellitus). Histologically, CP is characterized by inflammatory infiltration, acinar atrophy, formation of metaplastic ductal lesions (Tubular complexes and Pancreatic Intraepithelial Neoplasia), extended fibrosis, and in some cases by focal necrosis and cysts.[4] Further neural hypertrophy and perineural inflammation can frequently be observed and are the correlate of neuropathic pain as discussed below.[5]

Incidence and prevalence of CP vary between continents and countries. Most European studies show comparable incidence and prevalence rates around 7 per 100,000 and 28 per 100,000, respectively.[6–8] The numbers reported from Asia are markedly higher with a rapidly rising incidence up to 14 per 100,000.[9,10] The etiologic factors associated with CP are commonly summarized using the TIGAR-O classification: Toxic–metabolic (alcohol and tobacco are the main reasons is Western countries associated with up to 80–90% of cases), Idiopathic, Genetic (e.g. PRSS1, CFTR, or SPINK1 gene mutations), Autoimmune, Recurrent and severe acute pancreatitis or Obstructive (e.g. pancreas divisum, sphincter oddi dysfunctions or neoplasms).[11] The tropical CP is a common entity in India, southern Africa and parts of South America and typically affects younger patients; tropical CP is often classified as idiopathic but may in fact have a mixed etiology, including nutritional, metabolic and genetic factors.[12]

2. Pathophysiology and clinical presentation

The pathophysiology of CP remains a matter of debate. Over the last decades several theories focusing on different etiologic and pathomorphological aspects have been proposed (primary ductal inflammation, ductal obstruction, oxidative stress, toxic–metabolic,

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doi:10.1016/j.ijsu.2009.05.011

necrosis-fibrosis). The SAPE (sentinel acute pancreatitis event) hypothesis proposes a sentinel event of acute pancreatitis initiating the inflammatory process which is then sustained by a combination of the mechanisms mentioned above.[13,14]

Clinically the course of chronic pancreatitis is characterized by recurrent episodes of upper abdominal pain, which represents the most common indication for endoscopic and surgical intervention. Additionally, patients may present with symptoms of endocrine insufficiency (diabetes mellitus) and exocrine insufficiency (diarrhea, steatorrhea, malnutrition and weight loss). In the natural course of CP, as the gland "burns out", episodes of pain may occur less frequently and be less severe whereas endocrine and exocrine insufficiency frequently increase.[15]

2.1. Local complications

Depending of the morphologic changes of the pancreas, patients often have symptoms due to local complications (Fig. 1). The inflammatory ductal changes and intraductal calculi (pancreatolithiasis) result in obstruction of the pancreatic duct itself, which can result in multiple ductal stenoses and dilatations and aggravate the process in the distal part of the gland. Additionally, the intrapancreatic portion of the bile duct can be obstructed. An inflammatory mass of the pancreatic head, as it is regularly observed in European series,[2] frequently results in obstruction of the duodenum and compression and subsequent thrombosis of the splenic, superior mesenteric or portal veins. Development of pancreatic pseudocysts represents another local complication which results in obstruction, abscess formation or in ascites/pleural effusions in case of rupture. A rare but severe local complication of chronic pancreatitis is vascular erosion presenting as gastrointestinal hemorrhage or less frequently as intraabdominal bleeding. Finally, CP is a risk factor for the development of pancreatic cancer; Patients with CP have a 4-fold higher risk of cancer than individuals without CP.[16,17] Especially in the management of patients with an "inflammatory mass" this risk has to be taken in account.

2.2. Pancreatic pain

Whereas all these local complications can per se cause upper abdominal pain, the main mechanism of pain in CP is thought to be a "parenchymal hypertension" due to ductal obstruction. This mechanism is the rationale for endoscopic treatment as well as surgical drainage procedures. However, recent studies demonstrate that to a large extent the pain in patients with chronic pancreatitis is the consequence of neural alterations, namely a hypertrophy and an inflammatory infiltration of peripheral intra- and peripancreatic nerves.[5] Thus, pancreatic neuropathic pain is the consequence of pancreatic neuritis, which represents a common clinical feature of CP and pancreatic cancer and appears to be associated with upregulation of specific proteins.[18,19] This pancreatic pain is frequently observed in patients with an inflammatory mass in the pancreatic head and can be effectively relieved by pancreatic head resection (see Table 5).

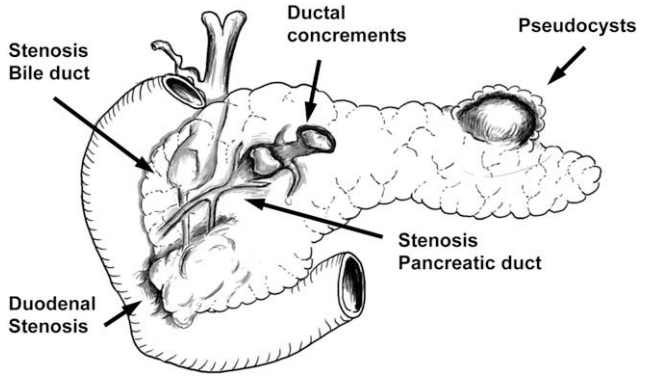

Fig. 1. Local complications of chronic pancreatitis. Fibrosis and the inflammatory mass can result in stenosis and prestenotic dilatation of the pancreatic duct, the common bile duct and the duodenum. Intraductal concrements result in ductal obstruction. Formation of pseudocysts result in local compression of neighboring structures. Not shown: Parenchymal calcifications and portal vein thrombosis.

3. Diagnostic work-up for chronic pancreatitis

A thorough medical history and physical examination is pivotal for the diagnosis and adequate therapy of patients with CP (Table 1). In the medical history, evaluation of etiologic factors (especially alcohol) and of pancreatic pain is crucial to select patients for the different therapeutic options as discussed below. Besides routine parameters, laboratory data should include cholestasis parameters, and tumor markers for pancreatic adenocarcinoma. In order to adequately inform patients about the course of their disease and possible consequences of surgery (e.g. need of insulin), the endocrine and exocrine function have to be evaluated. Exocrine function test are often provided by gastroenterologists but not required for surgical decision-making, except for patients with uncertain diagnosis due to atypical clinical presentation.

For tailored therapy and especially for planning of surgical therapy, imaging studies play a central role in the diagnostic work-up of patients with CP. Most patients with CP first consult general practitioners and gastroenterologists. For the general practitioner abdominal ultrasound is an effective screening method, which may help to establish the diagnosis in patients with a thickened pancreas or head mass, a dilated duct, or pseudocysts. Gastroenterologists frequently use endoscopic ultrasound, which is more sensitive and specific than transabdominal ultrasound. Many patients undergo multiple endoscopic retrograde cholangio-pancreatographies (ERCP) for diagnosis and therapeutic intervention. The gold standard of imaging for diagnosing CP and for the design of surgical therapy is cross section imaging by contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI). The superiority of CT or MRI is still a matter of debate, but either imaging study is adequate if

Table 1
Preoperative diagnostic work-up in chronic pancreatitis.

Thorough medical history: & Physical exam	- Etiologic factors: especially alcohol, smoking - Symptoms: pain, signs of exocrine and endocrine insufficiency, weight loss - Previous treatment: analgesics, endoscopy
Laboratory work-up:	- Routine laboratory parameters including liver and cholestasis parameters - Tumor markers (CEA, CA19-9)
Helpful but not mandatory:	- Endocrine and exocrine function test (oral glucose tolerance, fecal elastase etc.)
Imaging procedures: mandatory:	- computed tomography (CT) or magnetic resonance imaging (MRI)
Often provided by referring gastroenterologist and helpful, but not mandatory:	- Endoscopic retrograde cholangio-pancreaticography (ERCP)[a] Endoscopic ultrasound (EUS)
Not needed:	- Preoperative tissue diagnosis

[a] Either ERCP or MRI with MRCP have to be performed for reliable evaluation of the pancreatic duct.