Surgical management of chronic pancreatitis

Stavros Gourgiotis, Stylianos Germanos and Marco Pericoli Ridolfini

Rome, Italy

BACKGROUND: **Treatment of chronic pancreatitis (CP) is a challenging condition for surgeons. During the last decades, increasing knowledge about pathophysiology of CP, improved results of major pancreatic resections, and integration of sophisticated diagnostic methods in clinical practice have resulted in significant changes in surgery for CP.**

DATA SOURCES: **To detail the indications for CP surgery, the surgical procedures, and outcome, a Pubmed database search was performed. The abstracts of searched articles about surgical management of CP were reviewed. The articles could be identified and further scrutinized. Further references were extracted by cross-referencing.**

RESULTS: **Main indications of CP for surgery are intractable pain, suspicion of malignancy, and involvement of adjacent organs. The goal of surgical treatment is to improve the quality of life of patients. The surgical approach to CP should be individualized according to pancreatic anatomy, pain characteristics, baseline exocrine and endocrine function, and medical co-morbidity. The approach usually involves pancreatic duct drainage and resection including longitudinal pancreatojejunostomy, pancreatoduodenectomy (Whipple's procedure), pylorus-preserving pancreatoduodenectomy, distal pancreatectomy, total pancreatectomy, duodenum-preserving pancreatic head resection (Beger's procedure), and local resection of the pancreatic head with longitudinal pancreatojejunostomy (Frey's procedure). Non-pancreatic and endoscopic management of pain has also been advocated.**

CONCLUSIONS: **Surgical procedures provide long-term pain relief, a good postoperative quality of life with preservation of endocrine and exocrine pancreatic function, and are associated with low early and late mortality and morbidity. In addition to available results from randomized controlled trials, new studies are needed to determine which procedure is the most effective for the management of patients with CP.**

(***Hepatobiliary Pancreat Dis Int 2007; 6: 000-000***)

KEY WORDS: **chronic pancreatitis; surgery; pain; malignancy; pancreatic function**

Introduction

Chronic pancreatitis (CP), a chronic inflammatory disease of the pancreas, is often associated with complications that may require surgical intervention.[1-3] The incidence of CP is approximately 5-10 cases per 100 000 population[4, 5] and has nearly quadrupled in the past 30 years, although this likely represents increased recognition due to a broader definition and improvement in pancreatic imaging (with consequent inclusion of earlier-stage patients) rather than a true increase in occurrence.

Because of our limited understanding of disease pathogenesis, the unpredictability of the clinical course in a given individual and controversies in both diagnostic criteria and therapeutic options, management of patients with CP remains a difficult and challenging problem. The vast majority of them is managed conservatively and never requires operative intervention,[6] although about 20% of patients require frequent opioid analgesia. In general, patients are referred for surgery late in the course of disease, which means that the pathologic process can at most be halted or stabilized but not reversed. The usual technical complexities of pancreatic surgery are made even more imposing by the presence of inflammation in the pancreas and peripancreatic areas, which can obscure anatomic landmarks and planes. The choice of surgical procedure is rarely straightforward and other factors including disease location, prior

Author Affiliations: Department of Hepatobiliary and Pancreatic Surgery, Royal London Hospital, UK (Gourgiotis S); Upper GI and General Surgery, Leighton Hospital, Mid Cheshire NHS Trust, UK (Germanos S); Department of Surgical Sciences, Gemelli University Hospital, Catholic University of the Sacred Heart School of Medicine, Rome, Italy (Ridolfini MP)

Corresponding Author: Stavros Gourgiotis, MD, PhD, Royal London Hospital, Whitechapel, London E1 1BB, UK (Tel: +44(0) 207-377-7000ext2297; Fax: +44(0) 207-377-7439; Email: drsgourgiotis@tiscali.co.uk)

treatment, and suspicion of cancer may influence a surgeon's approach.

This review will detail the indications for surgery in CP patients, the surgical procedures, and the results, while determining the current role of surgical treatment in the management of this disease.

Pathogenesis, symptoms, and diagnosis of CP

The majority of cases are caused by alcohol abuse, although CP is about 30 times less common than alcoholic cirrhosis. In alcoholics, the disease typically manifests in middle age. Cigarette smoking plays an important role and constitutes a major risk factor for CP, statistically independent of alcohol intake.[7-9] There are now well-defined inherited germline mutations that can cause CP in families.[10] Clinically, the familiar form of CP is similar to alcoholic form, with the exception that the onset of symptoms is earlier in life, often in teenagers. Rarely is CP related to the biliary tract or gallstone disease. Other etiologies for CP include anatomical variants such as pancreas divisum or annular pancreas, metabolic (hypertriglyceridemia or hypercalcemia), and sphincter of Oddi dysfunction or trauma. Finally, some cases of CP are idiopathic.

CP is characterized by the progressive, unremitting nature of its symptoms; patients usually have long-term experience with abdominal or epigastric pain, which at times can be acutely exacerbated. Steatorrhea and postprandial abdominal discomfort may also be present, depending on the extent of gland destruction, often associated with anorexia, significant malabsorption, and weight loss. Diabetes mellitus due to progressive encasement and destruction of islets of Langerhans may develop over the course of the disease but is generally absent in its earliest stages unless coincident. As the pancreas response to repetitive inflammatory injury, parenchymal fibrosis develops to an extent that the organ's endocrine and exocrine functions are impaired.

The diagnosis of CP is generally made by detecting calcifications in the pancreas, which are stones in the pancreatic duct, on a computed tomography (CT). Pancreatic calcifications are pathognomonic of the disease and their presence indicates that the disease is advanced. The diagnosis of CP can also be made by endoscopic retrograde cholangiopancreatography (ERCP); the changes in the pancreatic duct system associated with CP and the criteria for a diagnosis by ERCP have been delineated.[11] Recently, endoscopic ultrasonography (EUS) has been used to diagnose CP by detecting textural abnormalities in the pancreatic parenchyma.[12] Magnetic resonance imaging (MRI) provides an excellent contrast image that evaluates the pancreatic parenchyma and magnetic resonance cholangiopancreatography (MRCP) provides great resolution of the biliary and pancreatic duct system.

Pain

The most common indication for surgery in patients with CP is pain. In general, daily pain associated with CP is managed initially by oral non-enteric-coated pancreatic enzymes and by non-narcotic analgesics, although the impact of these measures is modest.[13] Combinations of antioxidants including l-methionine, beta-carotene, vitamin C, vitamin E, and organic selenium have been used in small studies in patients with CP.[14] Many of these patients need frequent hospitalization for acute pain flare-ups, even if the background chronic pain can be adequately managed. An addition problem is that patients with alcoholic CP can develop narcotic dependence and not uncommonly exhibit psychiatric or psychosocial components of their pain syndromes.[15, 16]

The mechanism of pain in patients with CP remains poorly understood.[17] It is thought that significantly elevated pressure in the main pancreatic duct of patients with CP cause a compartment syndrome, which may be the source of the pain characteristic.[18-22] The fibrosis that envelops the chronically inflamed pancreas plays a central role in the evolution of this pressure by limiting the ability of the gland to expand during periods of exocrine secretion and to absorb the pressure created by the increased ductal volume.[18]

Another source of pain stimulation may be direct contact of sensory nerves with parenchymal neural irritants generated by the process of CP. The pancreas is a highly innervated, and visceral organ as well as its nerves (all autonomic) appear to be sensitive to both chemical and mechanical stimuli.[23] Major disturbances in and around the nerves occur as a consequence.[23, 24] Pain neurotransmitters (substance P and calcitonin gene-related peptide) are also increased in the pancreatic nerves of patients with CP, supporting the role of neural chronic inflammation in the pathogenesis of pain.[25]

Pancreatic duct drainage

Ductal decompression and drainage are the basis for

surgical treatment of a dilated and strictured main pancreatic duct, with or without additional calculi. After the report by Du Val[26] in 1954, who described caudal pancreatojejunostomy with pancreatic tail resection, the technique for surgical decompression of the pancreatic ductal system in patients with CP was modified by Puestow and Gillesby[27] in 1958. They described "retrograde" pancreatic ductal drainage involving a longitudinal anastomosis between the main pancreatic duct and a Roux-en-Y jejunal loop. Their original procedure also involved distal pancreatic tail resection and splenectomy to allow for long-segment pancreatojejunostomy. In 1960, Partington and Rochelle[28] proposed a modification which primarily advocated the direct anastomosis of the anterior surface of the pancreas to the jejunum. This simplification not only allows preservation of the spleen but also reduces the amount of pancreatic mobilization that is required, thereby decreasing operation time and blood loss. They also described that the ductal decompression should encompass the whole length of the ductal from the tail of the pancreas to the pancreatic head; the advantage of this extended decompression is that the removal of pancreatic duct calculi is greatly facilitated. This modified Puestow procedure, longitudinal pancreaticojejunostomy (LPJ), addresses the multiple obstructions typically seen in these patients and remains the preferred ductal decompression procedure for CP.[29]

LPJ should be considered for patients with CP and a dilated ($\geqslant$ 7 mm) main pancreatic duct of Wirsung.[30-32] Operative technique includes thorough abdominal exploration, wide exposure of the anterior aspect of the pancreas by opening the gastrocolic ligament, hepatic flexure mobilization, and a Kocher maneuver.[29] The dilated pancreatic duct can often be identified by palpation, and the location of the pancreatic duct is confirmed by a needle to aspirate ductal fluid. Intraoperative ultrasound may be useful when the duct is not readily palpable. The duct is incised longitudinally as extensively as required and all pancreatic ductal calculi are extracted.[29] A Roux-en-Y jejunal limb is constructed about 30 cm distal to the ligament of Treitz and a side-to-side Roux-en-Y retrocolic pancreatojejunostomy is then created.

The results of LPJ in patients with CP are summarized in Table 1.[30, 31, 33-39] A review of numerous series with this procedure reports that LPJ relieves chronic abdominal pain in 65%-93% of patients.[30, 31, 33-39] Morbidity and mortality rates are generally low, averaging 20% and 2%, respectively.[30, 31, 33-35, 40, 41] The largest series has been reported by Nealon and Matin[39] who reviewed the surgical treatment of 124 patients with CP who had undergone a modified LPJ. At a mean follow-up of 6.5 years, 106 of 124 patients experienced complete resolution of pain as defined by absence of narcotic use. Successful operation seems to be related to both technique and patient selection. Bradley[30] has reported that ductal decompression of less than 6 cm is associated with inadequate relief of pain compared with greater than 6 cm of decompression. Furthermore, duct size greater than 7 mm also correlated with success. Finally, Tantia et al[42] and Kurian and Gagner[43] have reported the technical feasibility of laparoscopic LPJ.

Table 1. Results of longitudinal pancreaticojejunostomy for chronic pancreatitis[30, 31, 33-39]

References	Year	No. of patients	Follow-up (years)	Pain relief (%)
Prinz and Greenlee[33]	1981	43	8	65
Sarles et al[34]	1982	69	5	85
Warshaw[35]	1984	33	4	88
Holmberg et al[36]	1985	51	8	72
Bradley[30]	1986	48	6	66
Nealon et al[31]	1988	41	1	93
Greenlee et al[37]	1990	50	8	82
Delcore et al[38]	1994	28	3.5	86
Nealon and Matin[39]	1999	124	6.5	86

Despite these encouraging results, long-term follow-up of patients after LPJ reveals that up to 50% of patients develop recurrent symptoms and 10%-35% fail to obtain pain relief.[41, 44]

Pancreatic resection

Longmire's hypothesis that the pancreatic head is the "pacemaker" for pancreatic pain in CP,[45] the hypothesis that neural inflammation is an important pathologic mechanism of pain, the intractable pain from head-dominant small-duct disease,[46] the high incidence of ductal alteration, and an inflammatory mass in the head of the pancreas[47-51] are the most common indications for pancreatic resection as the treatment of choice for patients with CP.

The results of pancreatic resection procedures in patients with CP, which are based on cohorts from high-volume pancreatic surgery centres, are summarized in Table 2.[2, 52-61] Unfortunately only a few randomized controlled trials have compared the different surgical approaches; they are summarized in Table 3.[62-66]

Table 2. Pancreatic resection procedures for CP2[52-61]

References	Procedure	No. of patients	Overall mortality (%)	Morbidity (%)	Postoperative EI (%)	Pain relief (%)
Heise et al[52] 2001	PPPD vs.	41	4.8	–	67	54
	DP	26			50	89
Jimenez et al[53] 2000	PPPD vs.	39	1.4	44	63	60
	Whipple's	33		45	77	70
Sakorafas et al[54] 2001	DP	40	0	15	47	81
Sakorafas et al[55] 2000	PPPD vs.	33	3.0	32	36	89
	Whipple's	72				
Vickers et al[56] 1999	PPPD vs.	18	0	31	–	71
	Whipple's	14				
Beger et al[57] 1999	Beger's	504	0.8	–	21	79
Traverso and Kozarek[58] 1997	Whipple's	47	0	36	22	100
Evans et al[2] 1997	Whipple's vs.	15	–	73	30	70
	Beger's	18	–	55	60	70
Martin et al[59] 1996	PPPD	45	2.1	54	46	92
Frey and Akimura[60] 1994	Frey's	50	0	22	11	87
Stone et al[61] 1988	Whipple's vs.	15	0	20	47	70
	TP	15			53	67

EI: endocrine insufficiency; PPPD: pylorus-preserving pancreatoduodenectomy; DP: distal pancreatectomy; TP: total pancreatectomy.

Table 3. Randomized controlled trials comparing surgical procedures for the treatment of CP[62-66]

References	Procedure	No. of patients	Follow-up (mon)	Results
Izbicki et al[62] 1998	PPPD vs. Frey's	61	24 (median)	Better quality of life and lower in-hospital complications in Frey's procedure; equal pain relief and pancreatic function
Izbicki et al[63] 1997	Beger's vs. Frey's	74	30 (median)	Lower morbidity in Frey's procedure; equal pain relief, pancreatic function and quality of life
Izbicki et al[64] 1995	DPPHR vs. Frey's	42	18 (median)	Equal pain relief, weight gain, pancreatic function and quality of life
Buchler et al[65] 1995	DPPHR vs. PPPD	40	6	Less pain, greater weight gain, better endocrine function and lower morbidity in DPPHR
Klempa et al[66] 1995	DPPHR vs. Whipple's	43	36-66	Pain relief higher and new onset of diabetes lower in DPPHR; equal mortality and morbidity

PPPD: pylorus-preserving pancreatoduodenectomy; DPPHR: duodenum-preserving pancreatic head resection.

Pancreatoduodenectomy (Whipple's procedure)

This procedure was originally described for resection of periampullary malignancies,[67] but it has also been used in the surgical management of patients with CP. It is a safe procedure with a hospital mortality of 0%-5%,[68] and a postoperative pain relief of 50%-75% at a long-term follow-up period.[34, 58, 61] It is associated with poor long-term results in patients with CP: poor postoperative digestive function including dumping, diarrhea, peptic ulcer, dyspeptic complaints, and diabetes mellitus which is responsible for the late postoperative morbidity and mortality in these patients.[62, 69] The long-term surgical results, especially regarding quality of life of patients, are disappointing in some studies.[62, 70, 71]

Pylorus-preserving pancreatoduodenectomy (PPPD)

This technique was described by Traverso and Longmire in 1978.[72] They tried to minimize the derangements in gastrointestinal physiology observed in patients who had undergone a Whipple resection, including weight loss, diarrhea, dumping, delayed gastric emptying, and marginal ulceration. A long-term follow-up has shown that there is a significantly reduced incidence of gastrointestinal

disturbances after PPPD when compared with the Whipple's procedure,[73] and a better quality of life after the PPPD.[74] One large retrospective study found comparable results in postoperative pancreatic function comparing these procedures,[53] while Berberat et al[75] reported that the maintenance of a near normal upper gastrointestinal tract was shown to reduce the incidence of postoperative steatorrhea and exocrine insufficiency when compared with the Whipple's procedure. However, Müller et al[76] reported three major drawbacks of PPPD in patients with CP: the increased incidence of postoperative sequalae of transient delayed gastric emptying (30% to 50% of patients), which often is associated with slower weight gain; the risk of cholangitis; and the long-term occurrence of exocrine and endocrine pancreatic insufficiency in more than 45% of patients.

Distal pancreatectomy (DP)

DP is a safe procedure, with a perioperative mortality of 0%-3.8% and a morbidity of 15%-31%, that may be performed with or without splenectomy.[52, 54] Sawyer and Frey[77] emphasized that DP should be utilized only in appropriate patients with CP (pancreatic duct <5 mm diameter, disease seen on CT and ERCP to be restricted to the pancreatic body, tail, or both) and they also found adequate pain relief in 90% of patients with distal disease at a mean follow-up of 4 years. Rattner et al[78] on the other hand, reported good pain relief in only 31% of patients undergoing DP for distal CP. In two recent studies, DP with splenic preservation controlled pain in 72%-82% of patients with CP.[79, 80]

Hutchins et al[81] reported on a series of 90 patients who had undergone a DP for CP. Eighty-eight of 84 patients available for follow-up had zero or minimal abdominal pain. 46% of these patients became diabetic at a median follow-up of 2 years. Similarly, Schoenberg et al[82] reported 74 patients undergoing DP for CP with a median follow-up of 58 months; 88% of patients had significantly less pain and 66% had an increase in median body weight, while diabetes mellitus occurred in 22% of patients.

Total pancreatectomy (TP)

TP with duodenum- and spleen-preserving was carried out for benign disease that required removal of the whole gland. It was also indicated for patients with CP and disabling pain for whom the partial resection had failed,[83] for those with total endocrine and exocrine pancreatic failure,[84] and for those with hereditary pancreatitis or familial pancreatic cancer, as prophylaxis against cancer.[85-88] The main contraindication for this procedure is the presence or suspicion of pancreatic malignancy. TP creates a significant postoperative morbidity in the form of insulin-dependent diabetes mellitus and exocrine insufficiency with malabsorption. However, the introduction of islet isolation and autotransplantation has led to renewed interest in TP as a treatment modality for end-stage CP. Many well documented cases of TP and islet autotransplantation (infusion of isolated islet cells into the portal vein following pancreatectomy) with good results in the control of the pancreatic endocrine insufficiency have been reported.[89-92] In some series, patients no longer need insulin,[92] while some patients may require exogenous insulin to treat hyperglycemia.[93]

A review of Whipple's procedure versus TP for CP[61] showed that TP resulted in complete pain relief in 27% of patients compared to 53% in the Whipple group, and 33% of patients who underwent TP continued to have significant pain after surgery. Finally, some authors reported a hospital mortality of 26%-47%, with complete a pain relief of 75%-83% in series with TP, with or without spleen and duodenum preservation.[71, 78, 83]

Duodenum-preserving pancreatic head resection (Beger's procedure)

Duodenum-sparing resection of the pancreatic head was first described by Beger et al.[47] Indications for this procedure include intractable abdominal pain, small duct CP, and head dominant disease. The Beger's procedure is contraindicated in circumstances in which pancreatic cancer is suspected.[57] Surgical technique consists of ventral transection of the pancreatic neck and subtotal head resection combined with Roux-en-Y loop of jejunum anastomosis to the distal pancreatic remnant and the rim of pancreatic tissue along the inner surface of the duodenum to restore gastrointestinal continuity.[94] The goal of this technique is to treat only the enlarged pancreatic head, where the disease is mainly present, and to preserve the duodenum, which has a crucial role in the regulation of digestion and glucose metabolism.

Beger et al[57] reported 26-year experience with this procedure in 504 patients with CP and pancreatic head inflammatory mass. A median follow-up of 5.7 years demonstrated that 91.3% of patients were pain-free following the Beger's procedure, and that the hospital mortality was 0.8% and the late death rate was 8.9%-12.6%, compared to 20.8%-35% for patients without surgery as reported. No data concerning the

There are total 84 cases. How come to 88?

effect of this procedure on steatorrhea or pancreatic enzyme requirements were provided. A randomized trial of 20 patients per procedure, Beger's procedure versus Whipple's procedure, showed that patients undergoing Beger's procedure had significantly less pain, increased postoperative weight gain, and better glucose tolerance at a 6-month follow-up.[65]

Local pancreatic head resection with longitudinal pancreatojejunostomy (Frey's procedure)

A modified Beger's procedure was described by Frey in 1987.[48] This procedure consists of a subtotal duodenum-sparing pancreatic head resection combined with LPJ. The resection in the head of the pancreas allows opening the main pancreatic duct as it courses posteriorly toward the duodenum and provides drainage of all pancreatic ducts by extending the Roux limb to the duodenum.[95] The operation is designed to avoid the more technically challenging aspects of the Beger's procedure, the division of the pancreatic neck, and the need for 2 separate pancreatic anastomosis.[95] It is also described for patients who have "head-predominant" disease on the assumption that the pancreatic head, with fibrotic and obstructed ducts, is not adequately addressed by simply decompression of the main pancreatic duct with the Puestow procedure.[95] It is also indicated for patients with small duct CP, and for patients with mild dilation and stricture of the proximal pancreatic duct.[48, 95] The inability to exclude pancreatic malignancy is a contraindication to the performance of Frey's procedure.[95]

Operative results indicate that Frey's procedure has an operative mortality of 0% and a perioperative morbidity of 22%.[60, 95] Excellent pain relief was achieved in 74.5% of patients in a mean follow-up of 37 months, while progression of endocrine (11%) and exocrine (11%) insufficiency was noted to be minimal and less than that for other procedures.[95] Frey's procedure was also compared with PPPD in a prospective randomized trial at the University of Hamburg.[62] The morbidity rate was 19.4% in the Frey group and 53.3% in the PPPD group; the pain score decreased after surgery by 94% and 95% respectively. A median follow-up of 2 years, showed that the global quality of life improved by 71% and 43%, respectively.

In a prospective randomized trial by Izbicki et al[64] the Frey's procedure was compared with the Beger's procedure. At a mean follow-up of 1.5 years postoperatively, patients undergoing the Frey's or Beger's procedure demonstrated decreased pain scores of 94% and 95% respectively. Both patients groups had an increase of 67% in their overall quality of life indices, and there were no significant differences in postoperative endocrine and exocrine function.

We believe that all types of pancreatic head resection are effective for the relief of pain from CP. We support the choice of pancreatoduodenectomy (Whipple's procedure or PPPD) if there is any possibility of malignancy. For patients with head predominant disease with a normal sized pancreatic duct that is devoid of stricture, Beger's procedure is preferable. For patients with chain-of-lakes-type anatomy, the Frey's procedure is the best choice because it addresses these abnormalities via the pancreatojejunostomy. Distal pancreatectomy is highly effective for patients with benign-appearing left-sided pancreatic duct stricture with upstream duct dilation, or duct disruption not amenable to pancreatojejunostomy and for those with complications of pancreatitis limited to the distal pancreas such as pseudocysts or associated splenic vein thrombosis.

Non-pancreatic and endoscopic pain control

Many attempts have been made to manage the pain in CP without submitting the patient to a major abdominal procedure and the associated potential complications. To modify transmission of pancreatic pain at the level of the celiac ganglia, several attempts have been made, including temporary blockade, permanent blockade (neurolysis), and surgical resection.[96] Celiac plexus blockage has successfully been used in the management of abdominal pain secondary to pancreatic carcinoma.[97] However, the long-term results of percutaneous or endoscopic celiac plexus blockage are far from encouraging, since no more than 50% of the patients even develop a significant short-lived pain relief.[98, 99]

A technique of neural ablation that may offer a higher success rate is splanchnicectomy. Currently, the main indication for splanchnicectomy is intractable abdominal pain caused by pancreatic and gastric carcinomas.[100] Thoracotomy is often perceived as too invasive for these debilitated patients. Thoracoscopic splanchnicectomy, which is less invasive than thoracotomy, is effective in pain control while minimizing the morbidity of the treatment.[101]

Reduction of intraductal pancreatic pressure in patients with CP presenting with ductal strictures or stones has been attempted by endoscopically inserted intraductal stents. This is an effective, relatively safe, and technically feasible method in a subgroup of

patients with symptomatic CP.[102-112] Stenting of the main pancreatic duct is the major problem that the stents tend to occlude rapidly; most are occluded by 8 weeks.[113] Pancreatic stents should not be used for definitive therapy but sparingly because stents induce morphologic alterations of the main pancreatic duct in 16% to 34% of the patients, which may resemble CP.[107, 114] The goal of dilation and stenting of pancreatic duct stricture is decompression that, if successful, is associated with pain relief in 60% of the patients with an average follow-up of 5 years.[110] However, the long-term results in large series are not so impressive.[110, 115]

Stone extraction can also be achieved by various techniques including balloon sweep, lithotripsy (mechanical, extracorporeal shock wave lithotripsy followed by balloon sweep, or electrohydraulic shock wave lithotripsy) or stone retrieval using a basket.[116-118]

Treatment of complications of CP

Biliary stricture and duodenal obstruction which are well-known complications of CP occur in 6% and 1.2% of the patients, respectively.[35, 119-121] For patients requiring an operation for CP, the incidence increases to 35% for biliary stricture and 12% for duodenal obstruction.[120] Most patients will present with an elevated alkaline phosphatase and/or bilirubin level, but the initial presentation with clinical jaundice, cholangitis, or biliary cirrhosis is rare. Surgery is indicated if patients develop jaundice which seems to be due to progressive chronic disease and fibrosis or have an episode of cholangitis.[3] The procedure of choice in pain-free patients with isolated biliary stricture is Roux-en-Y choledochojejunostomy to bypass the obstructed intra-pancreatic portion of the common bile duct.[119] Choledochoduodenostomy and cholecystoenterostomy must be avoided whenever possible because they are associated with the high incidence of cholangitis.[119, 120, 122]

For patients who are at high risk for operation or demonstrate portal vein thrombosis with associated varices, endobiliary stents provide acceptable short and medium-term resolution of common bile duct obstruction caused by CP,[123, 124] but they cannot be used as a definitive treatment because their long-term results are poorer than those of surgical management.[125,126] More recently, however, the use of self-expandable metal stents has demonstrated better results.[127]

Why "poorer"?

Duodenal obstruction is usually found in patients with "head-predominant" version of chronic pancreatitis, in which the head is significantly enlarged (⩾7 cm in diameter).[128] Isolated duodenal obstruction in patients with CP is much less common than obstruction of the common bile duct. For patients with isolated duodenal obstruction, the procedure of choice is gastrojejunostomy,[129] while combined duodenal and distal bile duct obstruction is effectively controlled by duodenal-preserving pancreatic head resection (DPPHR).[60, 130, 131]

Pseudocyst complicates CP in 30% to 40% of patients.[132] Over the last several decades, several series have documented the feasibility of conservative treatment of asymptomatic pseudocysts.[125-135] Based on these series, the current policy for patients with asymptomatic pseudocysts, regardless of size or duration, is nonoperative management. Treatment is reserved for patients with symptomatic pseudocysts, enlarging pseudocysts, or complications (infection, rupture, or pseudoaneurysm) related to the pseudocyst. Symptoms may include pain, early satiety, compression of the duodenum or stomach causing obstruction, and compression of the bile duct causing jaundice or abnormal liver function.

Septate pancreatic cysts and those containing fluid with elevated carcinoembryonic antigen (CEA) and CA 125 levels are generally treated by resection because of the possibility that they represent cystic neoplasm.[136] Unsurprisingly, pancreatic pseudocysts may show high CA 19-9 values because this marker may also be elevated in the serum of patients with pancreatitis.[136] If the pseudocyst is adherent to the posterior wall of the stomach, the preferred operation is a cyst-gastrostomy. If the pseudocyst is in the head of the pancreas, adherent to either the first or third portions of the duodenum, and away from the ampulla and common bile duct, Roux-en-Y cyst-jejunostomy is advisable. For smaller intra-pancreatic pseudocysts within the pancreatic head, a Whipple's procedure may be appropriate. If the pseudocyst is small and located in the tail of the pancreas, DP is recommended.

Is it right?

Rosso et al[137] reported the success rates of cyst-duodenostomy, cyst-gastrostomy, and cyst-jejunostomy were 100%, 90%, and 92%, respectively. The morbidity ranging from 9% to 36% included bleeding from anastomosis, infection of pseudocyst, erosion of pseudocyst wall, and rupture of pseudoaneurysms.

Endoscopic therapy includes transampullary and/or transgastric approaches. Transampullary drainage is not effective if the pseudocyst is not in communication with the main pancreas duct, while

endoscopic transgastric/duodenal drainage is not possible if the pseudocyst is not adherent to the gastric/duodenal wall, if the common wall is thicker than 1 cm, or if extensive intervening collateral blood vessels due to splenic vein thrombosis are present. When possible, endoscopic drainage has a technical success rate of 80% to 90% and is associated with a 75% incidence of pseudocyst resolution.[133, 138] The morbidity for these procedures ranges from 0% to 30%; bleeding and infectious complications may require emergency operation.[137]

An increasing number of patients with CP are diagnosed with splenic vein thrombosis and secondary left-sided portal hypertension.[139-144] Heider et al[145] reported 55 patients with a diagnosis of CP and splenic vein thrombosis; 77% of patients developed gastrosplenic varices, while only 2 patients had gastric variceal bleeding and required splenectomy. Splenectomy is the treatment of choice for symptomatic patients with left-sided portal hypertension caused by splenic vein thrombosis. Asymptomatic patients should be treated expectantly, as prophylactic splenectomy is indicated for those patients with splenic vein obstruction who are operated on for other complications of CP.

Finally, the last group of indications for surgery in patients with CP relates to complications of ruptured pancreatic duct or leaking pseudocysts and includes internal pancreatic fistula, and pancreatic ascites.[146-150] Patients with a leaking pseudocyst or a disrupted pancreatic duct will be best treated, respectively, by a cyst or a pancreatic duct internal drainage, whereas DP should be indicated for those patients with a narrow disrupted duct.[147] External pancreatic drainage may be complicated by a persistent percutaneous fistula in patients with a proximal pancreatic duct obstruction;[146] transpapillary pancreatic ductal stents have been used in patients who failed to respond to conservative measures.[150]

Concomitant pancreatic cancer

There is an association between CP and an increased incidence of pancreatic cancer, especially in smokers.[7, 151] The risk of pancreatic cancer in patients with CP varies from 2.3% to 26.7%,[151-153] whereas in patients with hereditary pancreatitis it approaches almost 75% for patients with a paternal inheritance pattern.[85] In addition, patients with intraductal papillary mucinous neoplasms (IPMN) may present with symptoms similar to those of CP. Therefore, it is important to rule out the presence of IPMN in patients referred for surgical treatment of CP, especially lesions located in the body or tail of the pancreas.

Many studies report deaths from pancreatic carcinoma in patients who had previously had pancreatic drainage.[33, 154-156] A high index of suspicion should be kept in mind, especially when there is an inflammatory mass in the pancreatic head associated with a dominant stricture of the pancreatic duct. Despite the adoption of sophisticated diagnostic tools (ERCP, CT, MRI, EUS, fine needle cytology)[157-161] in a high percentage of cases (up to 30%), it is impossible for the surgeon to say preoperatively whether a mass in the head of the pancreas is inflammatory or malignant.[162] This can be difficult even in the operating room using incisional biopsies,[163, 164] intra-operative ultrasonography,[165] or pancreatic ductoscopy.[166] Therefore, when there is a strong suspicion of an underlying malignancy, a Whipple's procedure or a PPPD should be considered.

Conclusion

Surgical management of CP remains controversial. Pancreatic duct drainage provides short-term pain relief, and presentation of endocrine and exocrine pancreatic function. Whipple's procedure and PPPD represent appropriate approaches for the adequate treatment of malignancy in suspected patients, both can be performed with low mortality rates, and they result in similar levels of endocrine and exocrine insufficiency. But PPPD seems to provide better postoperative results concerning quality of life and adequate relief of pain. Duodenum- and spleen-preserving TP has a role in selected patients with medically intractable pain and complications resulting from CP, which are usually reserved for the patients who have a failed previous resection. DP is more effective, however, when pathology is limited to the pancreatic body or tail. In recent years attempts have been made to develop organ-preserving operations, such as Beger's and Frey's procedures, which are safe and effective in providing long-term pain relief and in treating complications of CP with the preservation of pancreatic endocrine and exocrine function. But both are contraindicated when pancreatic cancer is suspected. Effort have also been devoted to pain control in CP by thoracoscopic splanchnicectomy or endoscopically inserted intraductal stents. Because of lack of data from randomized controlled trials, the surgical treatment of patients with CP remains

Please list the full name!

This sentence is vague. Please check!

a problem, and additional trials are needed to determine the most effective surgical procedure.

Funding: None.
Ethical approval: Not needed.
Contributors: SG is the corresponding author. SG and MPR are responsible for the literature research. All the authors contributed to the intellectual context and approved the final version. ?? is the guarantor.
Competing interest: No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Who is the guarantor?

References

Please give the PMID of each reference!

1 Lankisch PG, Lohr-Happe A, Otto J, Creutzfeldt W. Natural course in chronic pancreatitis: pain, exocrine and endocrine pancreatic insufficiency and prognosis of the disease. Digestion 1993;54:148-155.
2 Evans JD, Wilson PG, Carver C, Bramhall SR, Buckels JA, Mayer AD, et al. Outcome of surgery for chronic pancreatitis. Br J Surg 1997;84:624-629.
3 Bell RH Jr. Surgical options in the patient with chronic pancreatitis. Curr Gastroenterol Rep 2000;2:146-151.
4 Secknus R, Mossner J. Changes in incidence and prevalence of acute and chronic pancreatitis in Germany. Chirurg 2000;71:249-252.
5 Etemad B, Whitcomb DC. Chronic pancreatitis: diagnosis, classification, and new genetic developments. Gastroenterology 2001;120:682-707.
6 Buhler L, Schmidlin F, de Perrot M, Borst F, Mentha G, Morel P. Long-term results after surgical management of chronic pancreatitis. Hepatogastroenterology 1999;46:1986-1989.
7 Talamini G, Bassi C, Falconi M, Sartori N, Salvia R, Rigo L, et al. Alcohol and smoking as risk factors in chronic pancreatitis and pancreatic cancer. Dig Dis Sci 1999;84:1303-1311.
8 Talamini G, Bassi C, Falconi M, Frulloni L, Di Francesco V, Vaona B, et al. Cigarette smoking an independent risk factor in alcoholic pancreatitis. Pancreas 1996;12:131-137.
9 Maisonneuve P, Lowenfels AB, Mullhaupt B, Cavallini G, Lankisch PG, Andersen JR, et al. Cigarette smoking accelerates progression of alcoholic chronic pancreatitis. Gut 2005;54:510-514.
10 Whitcomb DC. Genetic predispositions to acute and chronic pancreatitis. Med Clin North Am 2000;84:531-547.
11 Sarner M, Cotton PB. Classification of pancreatitis. Gut 1984;25:756-759.
12 Kahl S, Glasbrenner B, Zimmermann S, Malfertheiner P. Endoscopic ultrasound in pancreatic diseases. Dig Dis 2002;20:120-126.
13 Singh VV, Toskes PP. Medical therapy for chronic pancreatitis pain. Curr Gastroenterol Rep 2003;5:110-116.
14 De las Heras Castano G, Garcia de la Paz A, Fernandez MD, Fernandez Forcelledo JL. Use of antioxidants to treat pain in chronic pancreatitis. Rev Esp Enferm Dig 2000;92:375-385.
15 Glasbrenner B, Adler G. Evaluating pain and the quality of life in chronic pancreatitis. Int J Pancreatol 1997;22:163-170.
16 Lankisch PG, Andren-Sandberg A. Standards for the diagnosis of chronic pancreatitis and for the evaluation of treatment. Int J Pancreatol 1993;14:205-212.
17 Andren-Sandberg A, Hoem D, Gislason H. Pain management in chronic pancreatitis. Eur J Gastroenterol Hepatol 2002;14:957-970.
18 Karanjia ND, Singh SM, Widdison AL, Lutrin FJ, Reber HA. Pancreatic ductal and interstitial pressure in cats with chronic pancreatitis. Dig Dis Sci 1992;37:268-273.
19 Karanjia ND, Widdison AL, Leung F, Alvarez C, Lutrin FJ, Reber HA. Compartment syndrome in experimental chronic obstructive pancreatitis: effect of decompressing the main pancreatic duct. Br J Surg 1994;81:259-264.
20 Bradley EL. Pancreatic duct pressure in chronic pancreatitis. Am J Surg 1982;144:313-316.
21 Madsen P, Winkler K. Intraductal pancreatic pressure in chronic obstructive pancreatitis. Scand J Gastroenterol 1982;17:553-554.
22 Ebbehoj N, Svendsen LB, Madsen P. Pancreatic tissue pressure: techniques and pathophysiologic aspects. Scand J Gastroenterol 1984;19:1066-1068.
23 Tsiotou AG, Sakorafas GH. Pathophysiology of pain in chronic pancreatitis. Clinical implications from a surgical respective. Int Surg 2000;85:291-296.
24 Bockman DE, Buchler M, Malfertheiner P, Beger HG. Analysis of nerves in chronic pancreatitis. Gastroenterology 1988;94:1459-1469.
25 Buchler M, Weihe E. Distribution of neurotransmitters in afferent human pancreatic nerves. Digestion 1988;38:8-14.
26 Du Val MK. Caudal pancreaticojejunostomy for chronic relapsing pancreatitis. Ann Surg 1954;140:775-785.
27 Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. AMA Arch Surg 1958;76:898-907.
28 Partington PF, Rochelle RE. Modified Puestow procedure for retrograde drainage of the pancreatic duct. Ann Surg 1960;152:1037-1043.
29 Harrison JL, Prinz RA. The surgical management of chronic pancreatitis: pancreatic duct drainage. Adv Surg 1999;32:1-21.
30 Bradley EL. Long-term results of pancreatojejunostomy in patients with chronic pancreatitis. Am J Surg 1987;153:207-213.
31 Nealon WH, Townsend CM Jr, Thompson JC. Progressive loss of pancreatic function in chronic pancreatitis is delayed by main pancreatic duct decompression. A longitudinal prospective analysis of the modified Puestow procedure. Ann Surg 1993;217:458-466.
32 Wilson TG, Hollands MJ, Little JM. Pancreatojejunostomy for chronic pancreatitis. ANZ J Surg 1992;62:111-115.
33 Prinz RA, Greenlee HB. Pancreatic duct drainage in 100 patients with chronic pancreatitis. Ann Surg 1981;194:313-320.
34 Sarles JC, Nacchiero M, Garani F, Salasc B. Surgical treatment of chronic pancreatitis: report of 134 cases treated by resection or drainage. Am J Surg 1982;144:317-321.
35 Warshaw AL. Conservation of pancreatic tissue by combined gastric, biliary, and pancreatic duct drainage for

pain from chronic pancreatitis. Am J Surg 1985;149:563-569.
36 Holmberg JT, Isaksson G, Ihse I. Long-term results of pancreaticojejunostomy in chronic pancreatitis. Surg Gynecol Obstet 1985;160:339-346.
37 Greenlee HB, Prinz RA, Aranha GV. Long-term results of side-to-side pancreaticojejunostomy. World J Surg 1990;14: 70-76.
38 Delcore R, Rodriguez FJ, Thomas JH, Forster J, Hermreck AS. The role of pancreatojejunostomy in patients without dilated pancreatic ducts. Am J Surg 1994;168:598-602.
39 Nealon WH, Matin S. Analysis of surgical success in preventing recurrent acute exacerbations in chronic pancreatitis. Ann Surg 2001;233:793-800.
40 Kalady MF, Broome AH, Meyers WC, Pappas TN. Immediate and long-term outcomes after lateral pancreaticojejunostomy for chronic pancreatitis. Am Surg 2001;67:478-483.
41 Rober HA. Chronic pancreatitis. In: Zinner MJ (ed). Maingot's abdominal operations, 10th edn. Stamford: Appleton & Lange; 1997:1941-1960.
42 Tantia O, Jindal MK, Khanna S, Sen B. Laparoscopic lateral pancreaticojejunostomy our experience of 17 cases. Surg Endosc 2004;18:1054-1057.
43 Kurian MS, Gagner M. Laparoscopic side-to-side pancreaticojejunostomy (Partington-Rochelle) for chronic pancreatitis. J Hepatobiliary Pancreat Surg 1999;6:382-386.
44 Prinz RA, Aranha GV, Greenlee HB. Redrainage of the pancreatic duct in chronic pancreatitis. Am J Surg 1986;151: 150-156.
45 Traverso LW. The surgical management of chronic pancreatitis: the Whipple procedure. Adv Surg 1999;32:23-39.
46 Sakorafas GH, Tsiotou AG. Proximal pancreatectomy in the surgical management of chronic pancreatitis. J Clin Gastroenterol 2002;34:72-76.
47 Beger HG, Krautzberger W, Bittner R, Buchler M, Limmer J. Duodenum-preserving resection of the head of the pancreas in patients with severe chronic pancreatitis. Surgery 1985; 97:467-473.
48 Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. Pancreas 1987;2:701-707.
49 Buchler MW, Friess H, Muller MW, Wheatley AM, Beger HG. Randomized trial of duodenum-preserving pancreatic head resection versus pylorus-preserving Whipple in chronic pancreatitis. Am J Surg 1995;169:65-69.
50 Jimenez RE, Fernadez-Del Castillo C, Rattner DW, Warshaw AL. Pylorus-preserving pancreaticoduodenectomy in the treatment of chronic pancreatitis. World J Surg 2003; 27:1211-1216.
51 Farkas G, Leindler L, Daroczi M, Farkas G Jr. Organ-preserving pancreatic head resection in chronic pancreatitis. Br J Surg 2003;90:29-32.
52 Heise JW, Katoh M, Luthen R, Roher HD. Long-term results following different extent of resection in chronic pancreatitis. Hepatogastroenterology 2001;48:864-868.
53 Jimenez RE, Fernadez-Del Castillo C, Rattner DW, Chang Y, Warshaw AL. Outcome of pancreaticoduodenectomy with pylorus preservation or with antrectomy in the treatment of chronic pancreatitis. Ann Surg 2000;231:293-300.
54 Sakorafas GH, Sarr MG, Rowland CM, Farnell MB. Postobstructive chronic pancreatitis: results with distal resection. Arch Surg 2001;136:643-648.
55 Sakorafas GH, Farnell MB, Nagorney DM, Sarr MG, Rowland CM. Pancreaticoduodenectomy for chronic pancreatitis. Arch Surg 2000;135:517-524.
56 Vickers SM, Chan C, Heslin MJ, Bartolucci A, Aldrete JS. The role of pancreaticoduodenectomy in the treatment of severe chronic pancreatitis. Am Surg 1999;65:1108-1112.
57 Beger HG, Schlosser W, Friess HM, Buchler MW. Duodenum-preserving head resection in chronic pancreatitis changes the natural course of the disease: a single-center 26-year experience. Ann Surg 1999;230:512-519.
58 Traverso LW, Kozarek RA. Pancreatoduodenectomy for chronic pancreatitis: anatomic selection criteria and subsequent long-term outcome analysis. Ann Surg 1997; 226:429-435.
59 Martin RF, Possi RL, Leslie KA. Long-term results of pylorus-preserving pancreatoduodenectomy for chronic pancreatitis. Arch Surg 1996;131:247-252.
60 Frey CF, Akimura K. Local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy in the management of patients with chronic pancreatitis. Ann Surg 1994;220:492-504.
61 Stone WM, Sarr MG, Nagorney DM, McIlrath DC. Chronic pancreatitis. Results of Whipple's resection and total pancreatectomy. Arch Surg 1988;123:815-819.
62 Izbicki JR, Bloechle C, Broering DC, Knoefel WT, Kuechler T, Broelsch CE. Extended drainage versus resection in surgery for chronic pancreatitis: a prospective randomized trial comparing the longitudinal pancreaticojejunostomy combined with local pancreatic head excision with the pylorus-preserving pancreatoduodenectomy. Ann Surg 1998;228:771-779.
63 Izbicki JR, Bloechle C, Knoefel WT, Kuechler T, Binmoeller KF, Soehendra N, et al. Drainage versus resection in surgical therapy of chronic pancreatitis of the head of the pancreas: a randomized study. Chirurg 1997;68:369-377.
64 Izbicki JR, Bloechle C, Knoefel WT, Kuechler T, Binmoeller KF, Broelsch CE. Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis: a prospective randomized trial. Ann Surg 1995;221:350-358.
65 Buchler MW, Friess H, Muller MW, Wheatley AM, Beger HG. Randomized trial of duodenum-preserving pancreatic head resection versus pylorus-preserving Whipple in chronic pancreatitis. Am J Surg 1995;169:65-69.
66 Klempa I, Spatny M, Menzel J, Baca I, Nustede R, Stockmann F, et al. Pancreatic function and quality of life after resection of the head of the pancreas in chronic pancreatitis: a prospective, randomized comparative study after duodenum preserving resection of the head of the pancreas versus Whipple's operation (in German). Chirurg 1995;66:350-359.
67 Whipple AO, Pearson WB, Mullius CR. Treatment of carcinoma of the ampulla of Vater. Ann Surg 1935;102: 763-779.
68 Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA, et al. Six hundred fifty consecutive pancreat icoduodenectomies in the 1990s: pathology, complications and outcomes. Ann Surg 1997;226:248-257.
69 Trede M, Schwall G, Saeger HD. Survival after pancreatoduodenectomy. One hundred and eighteen consecutive resections without an operative mortality. Ann Surg 1990;211:447-458.

70 Eckhauser FE, Knol JA, Mulholand MW, Colletti LM. Pancreatic surgery. Curr Opin Gastroenterol 1996;12:448-456.
71 Sakorafas GH, Farnell MB, Farley DR, Rowland CM, Sarr MG. Long-term results after surgery for chronic pancreatitis. Int J Pancreatol 2000;27:131-142.
72 Traverso LW, Longmire WP. Preservation of the pylorus in pancreaticoduodenectomy. Surg Gynecol Obstet 1978;146: 959-962.
73 Grace PA, Pitt HA, Longmire WP. Pylorus-preserving pancreatoduodenectomy: an overview. Br J Surg 1990;77: 968-974.
74 Wenger FA, Jacobi CA, Haubold K, Zieren HU, Muller JM. Gastrointestinal quality of life after duodenopancreatectomy in pancreatic carcinoma. Preliminary results of a prospective, randomized study: pancreatoduodenectomy or pylorus-preserving pancreatoduodenectomy. Chirurg 1999; 70:1454-1459.
75 Berberat PO, Friess H, Martignoni ME, Tempia A, Buchler MW. What should be the standard operation in chronic pancreatitis: Whipple or duodenum-preserving pancreatic head resection? Ann Ital Chir 2000;71:81-86.
76 Müller MW, Friess H, Beger HG, Kleeff J, Lauterburg B, Glasbrenner B, et al. Gastric emptying following pylorus-preserving Whipple and duodenum-preserving pancreatic head resection in patients with chronic pancreatitis. Am J Surg 1997;173:257-263
77 Sawyers R, Frey CF. Is there still a role for distal pancreatectomy in surgery for chronic pancreatitis? Am J Surg 1994;168:6-9.
78 Rattner DW, Fernadez-Del Castillo C, Warshaw AL. Pitfalls of distal pancreatectomy for relief of pain in chronic pancreatitis. Am J Surg 1996;171:142-146.
79 White SA, Sutton CD, Weymss-Holden S, Berry DP, Polland C, Rees Y, Dennison AR. The feasibility of spleen-preserving pancreatectomy for end-stage chronic pancreatitis. Am J Surg 2000;179:294-297.
80 Govil S, Imrie CW. Value of splenic preservation during distal pancreatectomy for chronic pancreatitis. Br J Surg 1999;86:895-898.
81 Hutchins RR, Hart RS, Pacifico M, Bradley NJ, Williamson RC. Long-term results of distal pancreatectomy for chronic pancreatitis in 90 patients. Ann Surg 2002;236:612-618.
82 Schoenberg MH, Schlosser W, Ruck W, Beger HG. Distal pancreatectomy in chronic pancreatitis. Dig Surg 1999;16:130-136.
83 Warshaw AL, Banks PA, Fernadez-Del Castillo C. AGA technical review: treatment of pain in chronic pancreatitis. Gastroenterology 1998;115:765-776.
84 Alexakis N, Ghaneh P, Connor S, Raraty M, Sutton R, Neoptolemos JP. Duodenum- and spleen-preserving total pancreatectomy for end-stage chronic pancreatitis. Br J Surg 2003;90:1401-1408.
85 Lowenfels AB, Maisonneuve P, DiMagno EP, Elistur Y, Gates LK Jr, Perrault J, et al. Hereditary pancreatitis and the risk of pancreatic cancer. International Hereditary Pancreatitis Study Group. J Natl Cancer Inst 1997;89: 442-446.
86 Rylyak SJ, Brentnall TA. Inherited pancreatic cancer: surveillance and treatment strategies for affected families. Pancreatology 2001;1:477-485.
87 Wong T, Howes N, Threadgold J, Smart HL, Lombard MG, Gilmore I, et al. Molecular diagnosis of early pancreatic ductal adenocarcinoma in high-risk patients. Pancreatology 2001;1:486-509.
88 Hahn SA, Greenhalf B, Ellis I, Sina-Frey M, Rieder H, Korte B, et al. BRCA2 gemline mutations in familial pancreatic carcinoma. J Natl Cancer Inst 2003;95:214-221.
89 Berney T, Rudisuhli T, Oberholzer J, Caulfield A, Morel P. Long-term metabolic results after pancreatic resection for severe chronic pancreatitis. Arch Surg 2000;135:1106-1111.
90 White SA, Davies JE, Pollard C, Swift SM, Clayton HA, Sutton CD, et al. Pancreas resection and islet autotransplantation for end-stage chronic pancreatitis. Ann Surg 2001;233:423-431.
91 Clayton HA, Davies JE, Pollard C, White SA, Musto PP, Dennison AR. Pancreatectomy with islet autotransplantation for the treatment of severe chronic pancreatitis: the first 40 patients at the Leicester General Hospital. Transplantation 2003;76:92-98.
92 Robertson RP. Insights into alloislets from successful autoislet transplantation in patients with chronic pancreatitis. J Investig Med 2001;49:563-565.
93 White SA, Pollard C, Davies JE, Sutton CD, Hales CN, Dennison AR. Temporal relationship of insulin, intact proinsulin and split proinsulin after islet autotransplantation. Transplant Proc 2001;33:680.
94 Beger HG, Schlosser W, Siech M, Poch B. The surgical management of chronic pancreatitis: duodenum preserving pancreatectomy. Adv Surg 1999;32:87-104.
95 Frey CF. The surgical management of chronic pancreatitis: the Frey procedure. Adv Surg 1999;32:41-85.
96 Bradley EL, Bem J. Nerve blocks and neuroablative surgery for chronic pancreatitis. World J Surg 2003;27:1241-1248.
97 Leung JW, Bowen-Wright M, Aveling W, Shorvon PJ, Cotton PB. Coeliac plexus block for pain in pancreatic cancer and chronic pancreatitis. Br J Surg 1983;70:730-732.
98 Ihse I, Borch K, Larsson J. Chronic pancreatitis: results of operations for relief of pain. World J Surg 1990;14:53-58.
99 Gress F, Schmitt C, Sherman S, Ciaccia D, Ikenberry S, Lehman G. Endoscopic ultrasound-guided celiac plexus block for managing abdominal pain associated with chronic pancreatitis: a prospective single center experience. Am J Gastroenterol 2001;96:409-416.
100 Flores R, Park B, Rusch V. Video-assisted thoracic surgery. In: Souba W, Fink M, Jurkovich G (eds). ACS surgery principles and practice 34, WebMD; 2005:1-33.
101 Glasbrenner B, Adler G. Evaluating pain and the quality of life in chronic pancreatitis. Eur J Gastroenterol Hepatol 2002;14:957-970.
102 McCarthy J, Geenen JE, Hogan WJ. Preliminary experience with endoscopic stent placement in benign pancreatic diseases. Gastrointest Endosc 1988;34:16-18.
103 Kozarek RA, Patterson DJ, Ball TJ, Traverso LW. Endoscopic placement of pancreatic stents and drains in the management of pancreatitis. Ann Surg 1989;209:261-266.
104 Cremer M, Deviere J, Delhaye M, Baize M, Vandermeeren A. Stenting in severe chronic pancreatitis: results of medium-term follow-up in seventy-six patients. Endoscopy 1991;23:171-176.
105 Geenen JE, Rolny P. Endoscopic therapy of acute and

chronic pancreatitis. Gastrointest Endosc 1991;37:377-382.
106 Binmoeller KF, Jue P, Seifert H, Nam WC, Izbicki J, Soehendra N. Endoscopic pancreatic stent drainage in chronic pancreatitis and a dominant stricture: long-term results. Endoscopy 1995;27:638-644.
107 Smits ME, Badiga SM, Rauws EA, Tytgat GN, Huibregtse K. Long-term results of pancreatic stents in chronic pancreatitis. Gastrointest Endosc 1995;42:461-467.
108 Ponchon T, Bory RM, Hedelius F, Roubein LD, Paliard P, Napoleon B, et al. Endoscopic stenting for pain relief in chronic pancreatitis results of a standardized protocol. Gastrointest Endosc 1995;42:452-456.
109 Hammarstrom LE, Stridbeck H, Ihse I. Endoscopic drainage in benign pancreatic disease immediate and medium term outcome. Eur J Surg 1997;163:577-589.
110 Rosch T, Daniel S, Scholz M, Huibregtse K, Smits M, Schneider T, et al. Endoscopic treatment of chronic pancreatitis a multicenter study of 1000 patients with long-term follow-up. European Society of Gastrointestinal Endoscopy Research Group. Endoscopy 2002;34:765-771.
111 Morgan DE, Smith JK, Hawkins K, Wilcox CM. Endoscopic stent therapy in advanced chronic pancreatitis: relationships between ductal changes, clinical response, and stent patency. Am J Gastroenterol 2003;98:821-826.
112 Gabbrielli A, Pandolfi M, Mutignani M, Spada C, Perri V, Petruzziello L, et al. Efficacy of main pancreatic-duct endoscopic drainage in patients with chronic pancreatitis, continuous pain, and dilated duct. Gastrointest Endosc 2005;61:576-581.
113 Ikenberry SO, Sherman S, Hawes RH, Smith M, Lehman GA. The occlusion rate of pancreatic stents. Gastrointest Endosc 1994;40:611-613.
114 Kozarek RA, Ball TJ, Patterson DJ, Brandabur JJ, Traverso LW, Raltz S. Endoscopic pancreatic duct sphincterotomy: indications, technique, and analysis of results. Gastrointest Endosc 1994;40:592-598.
115 Boerma D, van Gulik TM, Rauws EA, Obertop H, Gouma DJ. Outcome of pancreaticojejunostomy after previous endoscopic stenting in patients with chronic pancreatitis. Eur J Surg 2002;168:223-228.
116 Deviere J, Delhaye M, Cremer M. Pancreatic duct stones management. Gastrointest Endosc Clin N Am 1998;8:163-179.
117 Dumonceau JM, Deviere J, Le Moine O, Delhaye M, Vandermeeren A, Baize M, et al. Endoscopic pancreatic drainage in chronic pancreatitis associated with ductal stones: long-term results. Gastrointest Endosc 1996;43:547-555.
118 Farnbacher MJ, Schoen C, Rabenstein T, Benninger J, Hahn EG, Schneider HT. Pancreatic duct stones in chronic pancreatitis: criteria for treatment intensity and success. Gastrointest Endosc 2002;56:501-506.
119 Cunha JE, Bacchella T, Mott CB, Jukemura J, Abdo EE, Machado MC. Surgical treatment of biliary complications from calcifying chronic pancreatitis. Int Surg 1984;69:149-154.
120 Vijungco JD, Prinz RA. Management of biliary and duodenal complications of chronic pancreatitis. World J Surg 2003;27:1258-1270.
121 Frey CF, Suzuki M, Isaji S. Treatment of chronic pancreatitis complicated by obstruction of the common bile duct or duodenum. World J Surg 1990;14:59-69.
122 Aranha CV, Prinz RA, Greenlee HB. Biliary enteric bypass for benign and malignant disease. Am Surg 1987;53: 403-406.
123 Cunha JE, Penteado S, Jukemura J, Machado MC, Bacchella T. Surgical and interventional treatment of chronic pancreatitis. Pancreatology 2004;4:540-550.
124 Sezgin O, Oguz D, Altintas E, Saritas U, Sahin B. Endoscopic management of biliary obstruction caused by cavernous transformation of the portal vein. Gastrointest Endosc 2003;58:602-608.
125 Vitale GC, Reed DN Jr, Nguyen CT, Lawhon JC, Larson GM. Endoscopic treatment of distal bile duct stricture from chronic pancreatitis. Surg Endosc 2000;14:227-231.
126 Born P, Rosch T, Bruhl K, Ulm K, Sandschin W, Frimberger E, et al. Long-term results of endoscopic treatment of biliary duct obstruction due to pancreatic disease. Hepatogastroenterology 1998;45:833-839.
127 Kahl S, Zimmermann S, Glasbrenner B, Pross M, Schulz HU, McNamara D, et al. Treatment of benign biliary strictures in chronic pancreatitis by self-expandable metal stents. Dig Dis 2002;20:199-203.
128 Bell RH Jr. Current surgical management of chronic pancreatitis. J Gastrointest Surg 2005;9:144-154.
129 Uvaric M, Stimac D, Rubinic M, Kovac D, Zilli M, Petrosic N, et al. Duodenal obstruction from chronic pancreatitis. Minerva Chir 1997;52:885-889.
130 Beger HG, Buchler M. Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis with inflammatory mass in the head. World J Surg 1990;14: 83-87.
131 Izbicki JR, Bloechle C, Knoefel WT, Wilker DK, Dornschneider G, Seifert H, et al. Complications of adjacent organs in chronic pancreatitis managed by duodenum-preserving resection of the head of the pancreas. Br J Surg 1994;81:1351-1355.
132 Usatoff V, Brancatisano R, Williamson RC. Operative treatment of pseudocysts in patients with chronic pancreatitis. Br J Surg 2000;87:1494-1499.
133 Yeo CJ, Bastidas JA, Lynch-Nyhan A, Fishman EK, Zinner MJ, Cameron JL. The natural history of pancreatic pseudocysts documented by computed tomography. Surg Gynecol Obstet 1990;170:411-417.
134 Vitas GJ, Sarr MG. Selected management of pancreatic pseudocysts: operative versus expectant management. Surgery 1992;111:123-130.
135 Cheruvu CV, Clarke MG, Prentice M, Eyre-Brook IA. Conservative treatment as an option in the management of pancreatic pseudocyst. Ann R Coll Surg Engl 2003;85:313-316.
136 Lewandrowski KB, Southern JF, Pins MR, Compton CC, Warshaw AL. Cyst fluid analysis in the differential diagnosis of pancreatic cysts. A comparison of pseudocysts, serous cystadenomas, mucinous cystic neoplasms, and mucinous cystadenocarcinoma. Ann Surg 1993;217:41-47.
137 Rosso E, Alexakis N, Ghaneh P, Lombard M, Smart HL, Evans J, et al. Pancreatic pseudocyst in chronic pancreatitis endoscopic and surgical treatment. Dig Surg 2003;20:397-406.
138 Baron TH, Harewood GC, Morgan DE, Yates MR. Outcome differences after endoscopic drainage of

pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. Gastrointest Endosc 2002; 56:7-17.
139 Sakorafas GH, Sarr MG, Farley DR, Farnell MB. The significance of sinistral portal hypertension complicating chronic pancreatitis. Am J Surg 2000;179:129-133.
140 Broechle C, Busch C, Tesch C, Nicolas V, Binmoeller KF, Soehendra N, et al. Prospective randomized study of drainage and resection on non-occlusive segmental portal hypertension in chronic pancreatitis. Br J Surg 1997;84:477-482.
141 Izbicki JR, Yekebas EF, Strate T, Eisenberger CF, Hosch SB, Steffani K, et al. Extrahepatic portal hypertension in chronic pancreatitis: an old problem revisited. Ann Surg 2002;236:82-89.
142 Bradley EL. The natural history of splenic vein thrombosis due to chronic pancreatitis: indications for surgery. Int J Pancreatol 1987;2:87-92.
143 Bernades P, Baetz A, Levy P, Belghiti J, Menu Y, Fekete F. Splenic and portal vein obstruction in chronic pancreatitis: a prospective longitudinal study of a medical-surgical series of 266 patients. Dig Dis Sci 1992;37:340-346.
144 Adam U, Makowiec F, Riediger H, Keck T, Kroger JC, Uhrmeister P, et al. Pancreatic head resection for chronic pancreatitis in patients with extrahepatic generalized portal hypertension. Surgery 2004;135:411-418.
145 Heider TR, Azeem S, Galanko JA, Behrns KE. The natural history of pancreatitis-induced splenic vein thrombosis. Ann Surg 2004;239:876-882.
146 Cunha JE, Machado MC, Bacchella T, Penteado S, Mott CB, Jukemura J, et al. Surgical treatment of pancreatic ascites and pancreatic pleural effusions. Hepatogastroenterology 1995;42:748-751.
147 Kaman L, Behera A, Singh R, Katariya RN. Internal pancreatic fistulas with pancreatic ascites and pancreatic pleural effusions: recognition and management. ANZ J Surg 2001;71:221-225.
148 Parekh D, Segal I. Pancreatic ascites and effusion: risk factors for failure of conservative therapy and the role of octreotide. Arch Surg 1992;127:707-712.
149 Lipsett PA, Cameron JL. Internal pancreatic fistula. Am J Surg 1992;163:216-220.
150 Kozarek RA. Endoscopic therapy of complete and partial pancreatic duct disruptions. Gastrointest Endosc Clin N Am 1998;8:39-53.
151 Talamini G, Falconi M, Bassi C, Sartori N, Salvia R, Caldiron E, et al. Incidence of cancer in the course of chronic pancreatitis. Am J Gastroenterol 1999;94:1253-1260.
152 Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, Andersen JR, et al. Pancreatitis and the risk of pancreatic cancer. International Pancreatitis Study Group. N Engl J Med 1993;328:1433-1437.
153 Malka D, Hammel P, Maire F, Rufat P, Madeira I, Pessione F, et al. Risk of pancreatic adenocarcinoma in chronic pancreatitis. Gut 2002;51:849-852.
154 Jordan GL Jr, Strug BS, Crowder WE. Current status of pancreatojejunostomy in the management of chronic pancreatitis. Am J Surg 1977;133:46-51.
155 White TT, Slavotinek AH. Results of surgical treatment of chronic pancreatitis. Report of 142 cases. Ann Surg 1979;189:217-224.
156 Widdison AL, Alvarez C, Karanjia ND, Reber HA. Experimental evidence of beneficial effects of ductal decompression in chronic pancreatitis. Endoscopy 1991; 23:151-154.
157 Mullens JE. Endoscopic retrograde cholangiopancreatography in the diagnosis of chronic pancreatitis. Surgery 1978;84:308-312.
158 Lomanto D, Pavone P, Laghi A, Panebianco V, Mazzocchi P, Fiocca F, et al. Magnetic-resonance-cholangiopancreatography in the diagnosis of biliopancreatic diseases. Am J Surg 1997;174:33-38.
159 Thoeni RF, Blankenberg F. Pancreatic imaging: computed tomography and magnetic resonance imaging. Radiol Clin N Am 1993;31:1085-1113.
160 Suriyama K, Kimoto E, Nakazawa S. Endoscopic ultrasonography in pancreatic diseases. Gastroenterol Endosc 1984;26:649-662.
161 Parsons L Jr, Palmer CH. How accurate is fine-needle biopsy in malignant neoplasms of the pancreas? Arch Surg 1989;124:681-683
162 Smith CD, Behrns KE, van Heerden JA, Sarr MG. Radical pancreatoduodenectomy for misdiagnosed pancreatic mass. Br J Surg 1994;81:585-589.
163 Witz M, Shkolnik Z, Dinbar A. Intraoperative pancreatic biopsy: a diagnostic dilemma. J Surg Oncol 1989;42:117-119.
164 Ihse I, Toregard BM, Akerman M. Intraoperative fine needle aspiration cytology in pancreatic lesions. Ann Surg 1979;190:732-734.
165 Printz H, Klotter HJ, Nies C, Hasse C, Neurath M, Sitter H, et al. Intraoperative ultrasonography in surgery for chronic pancreatitis. Int J Pancreatol 1992;12:233-237.
166 Branum GD, Pappas TN, Meyers WC. The use of pancreatic ductoscopy in the operative management of benign and malignant pancreatic disorders. Surg Endosc 1995;9:53-55.

Received October 5, 2006
Accepted after revision November 19, 2006