J Gastrointest Surg (2012) 16:1362–1369
DOI 10.1007/s11605-012-1904-8

ORIGINAL ARTICLE

Frey Procedure in Patients with Chronic Pancreatitis: Short and Long-term Outcome from a Prospective Study

Alexandra M. D. Roch · Dorothée Brachet · Emilie Lermite · Patrick Pessaux · Jean-Pierre Arnaud

Received: 31 January 2012 / Accepted: 30 April 2012 / Published online: 12 May 2012
© 2012 The Society for Surgery of the Alimentary Tract

Abstract
Background The aim of this prospective study was to determine the short- and long-term results of the Frey procedure in the treatment of chronic pancreatitis.
Methods From September 2000 to November 2009, 44 consecutive patients underwent the Frey procedure. Patients were included in the study before surgery and followed prospectively with assessment of pain relief, weight gain and exocrine/endocrine insufficiency. Twenty-one patients (47.7 %) were followed for more than 5 years.
Results This study included 40 men (91 %) and four women (9 %) (mean age: 49 years) with a mean follow-up of 51.5 months. The primary etiology of chronic pancreatitis was chronic alcohol abuse in 38 patients (86.4 %). The major indication for surgery was disabling pain (95.5 %). There was no postoperative mortality. Postoperative morbidity occurred in 15 patients (34.1 %), with specific surgical complications in 11 patients (25 %). The percentage of pain-free patients after surgery was 68.3 %. Eight patients (18.1 %) and seven patients (16 %) developed diabetes de novo and exocrine insufficiency, respectively. The Body Mass Index showed statistically significant improvement during follow-up. Similar beneficial results concerning pain relief and weight gain persisted after the initial 5-year follow-up.
Conclusions The Frey procedure is an appropriate, safe and effective technique for management of patients with chronic pancreatitis in the absence of neoplasia, based on long-term follow-up.

Keywords Surgery · Frey · Chronic Pancreatitis · Long-term follow-up · Pain

Introduction

Patients with chronic pancreatitis suffering from severe and disabling pain present a therapeutically challenging problem. Based on a previous review of the pathophysiological origins of pain in chronic pancreatitis[1] (perineural inflammation, increased parenchymal pressure and ductal hypertension), two procedures have been introduced to surgery: drainage and (organ-preserving) resection. The choice of operative procedure has been determined by the pancreatic duct dilatation and gland morphology.[2]

An inflammatory mass in the pancreatic head has long been considered a classic indication for radical resection (pancreaticoduodenectomy). This procedure has been for a long time associated with high mortality and morbidity rates, which are consequences of the sacrifice of a great amount of pancreatic parenchyma. On the other hand, the extent of drainage appears to be directly proportional to the degree of pain relief. In 1909, Coffey[3] first described the technical aspects of partial pancreatectomy with pancreatoenterostomy in a canine model. Modern surgical management[4] of painful chronic pancreatitis dates back to the 1950s, when Puestow and Gillesby[5] performed their

This article was presented at the 113th Congress of the French Surgical Association (2011, Paris, France).

A. M. D. Roch (✉) · D. Brachet · E. Lermite · J.-P. Arnaud
Department of Digestive Surgery, University Hospital,
4 rue Larrey,
49933 Angers, France
e-mail: maxandra25@hotmail.com

P. Pessaux
Department of General Surgery, Hôpital de Hautepierre,
Avenue Molière,
67098 Strasbourg, France

lateral pancreaticojejunostomy. This procedure has stimulated ongoing efforts to design newer approaches[6] that could provide permanent benefits to patients with low short and long-term morbidity compared to pancreaticoduodenectomy, which was previously considered to be the "gold" standard for surgical treatment.

In 1987, Frey and Smith[7] described the local resection of the pancreatic head using lateral pancreaticojejunostomy that combined the options of resection and drainage of the entire duct.[8] There are many reports in the literature on the short-term results of the Frey procedure[9] but very few on the long-term results.[10] The literature reported retrospective results longer than 5 years[11–13] and very few prospective results.[14] The aim of this study was to prospectively analyze the short and long-term outcome in a series of patients with chronic pancreatitis who underwent the Frey procedure and to determine if the results were persistent after 5 years.

Materials and Methods

Protocol

All consecutive patients scheduled to undergo the Frey procedure for chronic pancreatitis from September 2000 to November 2009 were considered for inclusion in this study. The diagnosis[15] of chronic pancreatitis was based on clinical (clinical history, physical examination) and imaging (calcifications in the pancreas or pancreatic duct on computed topographic scan, ultrasonography, magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography) findings. Pain rating and visual analog scales were used to assess the intensity of pain (0 corresponding to “no pain” and 10 to “maximum pain”), its relief and the impact of the residual pain on daily activities. Each patient was then referred to a pain management clinic where a specialist initiated the appropriate analgesic treatment. The indication for the Frey procedure was decided in our institution by a multidisciplinary committee including gastroenterologists, radiologists and surgeons. There were no strict selection criteria, but the indication was gladly given in cases of large cephalic mass and/or a small pancreatic duct dilatation. The main indication for surgery was intractable chronic pain resistant to appropriate painkillers in 42 patients (95.5 %). Asthenia was diagnosed in 18 patients (40.9 %), endoscopic interventional therapy failure or technical impossibility was observed in 14 patients (31.8 %) and pain reappeared after previous endoscopic treatment in 11 patients (25 %). The mean interval between the first onset of symptoms of pancreatitis and surgery was 70.4±64.9 months (range: 12–300 months). Written informed consent was obtained preoperatively for all patients included in the study who were then prospectively followed at regular intervals. The protocol was approved by the local ethics committee.

Patient Demographics

This study included 44 patients, of whom 40 were men (91 %) and four were women (9 %) with a mean age of 49±6.8 years (range: 32–65). One patient (2.3 %) was suffering from high blood pressure and one other patient (2.3 %) from cardiac arrhythmia. No patient was known to suffer from chronic obstructive pulmonary disease or coronary trouble.

The primary etiology of chronic pancreatitis was chronic alcohol abuse in 38 patients (86.4 %). Preoperatively, 28 of the 38 patients with alcohol-related chronic pancreatitis had abstained from alcohol (73.7 %) with a mean duration of 17.2±41 months (range: 5–192 months). Only four of these 38 patients (10.5 %) were still abusing alcohol before surgery. The same indications were used for surgery, i.e., intractable pain resistant to painkillers and therapeutical problem in a head dominant chronic pancreatitis. Alcohol withdrawal was preferred but not mandatory. Indeed, Schnelldorfer’s team[16] in California demonstrated that surgery for chronic pancreatitis could be performed with similar mortality and morbidity even without alcohol abstinence and that alcohol abuse after operation did not affect success for pain control at follow-up. Hereditary chronic pancreatitis was found in two patients (4.5 %) and other etiologies were found in four patients (9.1 %) including two with obstructive gallstones, one with pancreas divisum and one with an idiopathic cause.

Preoperative Imaging and Biological Findings

An inflammatory mass in the head of the pancreas was visualized by computed tomography scan in 43 patients (97.7 %), by magnetic resonance cholangiopancreatography in 25 patients (56.8 %) and by endosonography in 21 patients (47.7 %). Preoperative imaging also revealed gastrointestinal tract abnormalities (two duodenal stenoses, one choledochal cyst), biliary dilatation or stenosis (15 intra- and extrahepatic biliary ducts dilatation, one common bile duct narrowing due to chronic pancreatitis lesions) and vascular thromboses (one splenic vein thrombosis and two superior mesenteric vein thromboses). Neither of these findings was considered contraindications to surgery.

The average size of the most dilated part of the main pancreatic duct, excluding a pseudocyst, was 7.8±2.2 mm (range: 3–12 mm). Nine patients (20.5 %) had an associated pseudocyst localized primarily at the pancreatic head, which did not modify the surgical strategy.

A biological cholestasis was present in 20 patients (45.5 %) at presentation, among which only seven (15.9 %) were also

clinically jaundiced. Three patients (6.8 %) were still clinically and biologically jaundiced preoperatively (bilirubin range: 71–231 μmol/l). The other four patients were previously treated by endoscopic biliary stent. The indications for a biliary drainage procedure are similar to those described by Frey et al. in 1990[17] with clinical criteria (jaundice, cholangitis evidenced by symptoms or infected bile), radiological findings (progression of the common duct stricture based on radiologic assessment of increased dilatation of the common and intrahepatic or presence of associated common bile duct stones), histological findings (biopsy evidence of biliary cirrhosis), or biological findings (elevation of serum bilirubin exceeding 300 for more than a month or elevation of alkaline phosphatase, three times normal levels or more, for more than a month). All patients filling one of these criteria underwent a biliary drainage procedure.

Three patients (6.8 %) had alcoholic cirrhosis confirmed by pathology at the time of diagnosis. Tumor markers (Ca19.9 and carcinoembryonic antigen [CEA]) were measured in only seven patients (15.9 %) with a clinical or radiological suspicion of malignancy. In the 37 other patients (84 %) with no suspicion of malignant process, tumor markers were not controlled routinely.

Surgical Technique

The operative procedure was performed as described by Frey and Smith in 1987:[18] excavation of the pancreatic head including the ductal structures in continuity with a long dichotomy of the Wirsung duct followed by a two-layer pancreaticojejunostomy. Continuity was reestablished by a Roux-en-Y loop. The cored tissue was routinely sent for anatomopathological analysis. The confirmation by frozen section analysis of normal ductal epithelial findings at the local head resection and main pancreatic duct incision was a requirement for each procedure. A failure to obtain confirmation of satisfactorily benign duct margins intra operatively was considered an indication to abandon this technique and convert to an oncological procedure (pancreaticoduodenectomy).

Perioperative Management

Patients were reviewed by an independent physician daily until discharge from the hospital. Blood tests including serum amylase level, hemoglobin level, white cell count, platelet count, and liver function test (including aminotransferase, γ-glutamyl transpeptidase, alkaline phosphatase and bilirubin level) were carried out before the operation and postoperatively on days 1, 3, 5 and 7. The peripancreatic drainage fluid was collected and measured and the amylase level monitored on days 1, 3, 5 and 7 postoperatively. Chest radiography was performed routinely on days 3 and 7 postoperatively. Oral diet was initiated 3–5 days postoperatively if there were no pancreatic fistulas (PF) or other intra-abdominal complications. All patients were reviewed at 6 weeks, 3 and 6 months and then at yearly intervals to complete the follow-up.

Definitions

Exocrine pancreatic function was assessed on clinical steatorrhea and the need to take oral pancreatic enzyme supplementation. Diabetes was defined, according to the American Diabetes Association, as a fasting blood glucose concentration greater than 7 mmol/l.[19] Endocrine pancreatic function was assessed on the glycosylated hemoglobin, the need to treat diabetes mellitus with diet, oral hypoglycemic agents or insulin.

Prescribed analgesics were classified using the World Health Organization analgesic ladder:[20] class 1 for acetaminophen, class 2 for acetaminophen and weak opioid combinations, and class 3 for opiates.

Mortality and morbidity were defined respectively as death or complication occurring either within 30 days following surgery or during the hospital stay. Complications were classified in accordance with Clavien's classification.[21]

PF was defined, according to the International Study Group of Pancreatic Fistula,[22] as amylase-rich fluid (amylase concentration more than three times the serum concentration) collected from day 3 using the drainage placed intraoperatively or by needle aspiration for intra-abdominal collection. PFs were graded according to the clinical impact on the patients' hospital course (grades A, B, and C).

Delayed gastric emptying was defined as the inability to return to a standard diet by the end of the first postoperative week and included prolonged nasogastric intubation of the patient.[23] Pulmonary infection was defined as a suggestive radiographic study with fever and requirement for antibiotics. Septicemia was defined as positive peripheral blood culture or positive blood culture from the central venous catheter. Infectious complications were proved bacteriologically by positive culture, and the types of microorganisms isolated were compared with those from operative bile samples (when available).

Data Collection

Demographic data, pathological variables, co-morbid conditions, preoperative risk factors, details of surgical procedure, pathological diagnosis, and postoperative complications were recorded prospectively. The surgeon or gastroenterologist collected data at each follow-up visit using a standardized questionnaire. The examiner weighed the patients, judged their exocrine/endocrine pancreatic function and determined the completeness of their pain relief.

Statistical Analysis

No patient was considered lost to follow-up or excluded from this analysis. Quantitative data were expressed as means ± standard deviations and ranges. Statistical analysis was performed using Epi Info software Version 3.5.1, Centers for Disease Control and Prevention (Atlanta, GA, USA).[24] Preoperative and postoperative categorical variables were compared using the Fischer's exact test. Student's *t*-test was performed for numerical variables and two-tailed distributions. Statistical significance was assumed for values $p<0.05$.

Results

Preoperative Data

Forty-one patients (93.2 %) were using painkillers regularly for chronic abdominal pain. Pain control required class 3 analgesics in 27 patients (61.4 %): one patient used class 3 analgesics only, one used both class 1 and class 3 and 25 used an association of the three classes. Exocrine insufficiency was present preoperatively in 28 patients (63.6 %) who all used pancreatic enzyme substitution. Diabetes mellitus was present in seven patients (15.9 %).

At the time of surgery, the mean body weight was 59.8 kg (range: 37–84 kg) and the mean body mass index (BMI = weight [kg] divided by height [m^2]) was 20.1±2.9 kg/m^2 (range: 14.7–27.1). Weight loss occurred in 38 patients (86.4 %) with a mean loss of 10.2±7.8 % of the usual weight (range: 1.9–24.3 %).

Perioperative Data

The mean operative time was 266±99 min (range: 120–520 min). No patient was converted to a pancreatoduodenectomy. Additional surgical procedures were performed in 26 patients (59.1 %), including 24 biliodigestive anastomoses (12 choledocoduodenostomies, tenhepaticojejunostomies, two choledocojejunostomies) and three gastroenterostomies (one patient benefited from one biliodigestive and one digestive anastomoses). Gastrojejunostomies were performed for duodenal stenosis in two patients and choledochal cyst in one patient. Bilio-digestive anastomoses were performed in 15 cases for both intra- and extrahepatic biliary ducts dilatation, in eight cases for extrahepatic only biliary duct dilatation incidentally found during the procedure and in one case for common bile duct narrowing. One umbilical hernia repair was also performed in the same operative time. The mean blood loss was 307±227 ml (range: 50–1,000 ml). Two patients (4.5 %) needed perioperative blood transfusions (1 and 3 units of blood). Final histological analysis of all resected specimens confirmed chronic pancreatitis. No adenocarcinoma was found. The median hospital stay was 14 days (range: 9–40 days). There was no mortality.

The postoperative surgical and medical complications are summarized in Table 1. Fifteen patients (34.1 %) had postoperative complications including 11 surgical (25 %) and seven medical (15.9 %). Three patients had two surgical complications. Intra-abdominal abscess was the most frequent septic complication. It occurred in two patients due to one PF and one biliary fistula (treated medically). PF occurred in four patients (9.1 %). We reported two grade A fistulas. The one grade B fistula led to a deep abdominal abscess and was treated by conservative management (i.e., total parenteral nutrition, antibiotics and octreotide [Sandostatin®]). One patient with a grade C PF developed massive intra-abdominal bleeding at day 8 requiring another intervention for ligation of the gastroduodenal artery.

Postoperative Data

The mean follow-up time was 51.5±25.7 months (range: 12–97.1 months).

The early postoperative re-operations ($n=4$, 9 %) resulted all from hemorrhagic complications (Table 2). During the follow-up period, two patients were admitted with surgical complications requiring a delayed procedure. The delayed re-operations were consequential to general surgical complications: incisional hernia on the 11th month surgically requiring the use of a mesh

Table 1 Postoperative morbidity according to the Dindo Clavien classification

Postoperative outcomes	Number of patients (percentage)
Perioperative mortality	0
Complications	15 (34.5 %)
Surgical complications	11 (25 %)
Medical complications	7 (16 %)
Dindo Clavien Grade I	3 (7 %)
Atelectasis	3 (7 %)
Dindo Clavien Grade II	9 (20.5 %)
Urinary tract infection	1 (2 %)
Pulmonary infection	1 (2 %)
Withdrawal syndrome	1 (2 %)
Delayed gastric emptying	1 (2 %)
Pancreatic fistula	4 (9 %)
Biliary fistula	1 (2 %)
Dindo Clavien Grade III	7 (16 %)
Intra-abdominal abscess	3 (7 %)
Parietal abscess	1 (2 %)
Parietal hematoma	1 (2 %)
Hemorrhage	2 (4.5 %)
Dindo Clavien Grade IV	2 (4.5 %)
Hemorrhagic shock	2 (4.5 %)

Table 2 Early postoperative complications requiring surgery

Delay	Diagnosis	Surgery required
Day 1	Hemorrhage	Stomach declotting + redo of the gastrojejunal anastomosis
Day 8	Hemorrhagic fistula	Ligature of the gastroduodenal artery
Day 24	Parietal hematoma	Hematoma evacuation
Day 35	Intra-abdominal hemorrhage	Redo of all anastomoses

and small bowel obstruction and peritonitis on the 12th month requiring adhesiolysis and lavage of the peritoneum.

The postoperative results are summarized in Table 3. Although 41 patients (93.2 %) presented with pain before surgery, 28 of these 41 cases (68.3 %) were judged to be pain free at the time of the last follow-up visit. During the follow-up, only one required regular analgesics (WHO class 3) because of chronic back pain despite successful surgery. The difference in the preoperative and postoperative parameters concerning the use of analgesics (preoperative analgesics: $n=41$, postoperative analgesics: $n=16$; $p<0.001$), especially class 3 analgesics (preoperative use of opiates: $n=27$, postoperative use of opiates: $n=1$; $p<0.001$), was statistically significant.

The development of diabetes did not significantly increase in the postoperative period ($p=0.08$). Eight patients (18.1 %) developed new diabetes mellitus postoperatively, while one case improved after surgery (patient on diet control only instead of oral drugs before surgery). Among our eight postoperative diabetic patients, two required diet control, seven required oral drugs only, four required insulin therapy only, and one required a combination of treatment. Exocrine insufficiency, increased from 28 patients (64 %) before surgery to 35 patients (79.5 %) postoperatively ($p=0.1$). The mean BMI significantly improved during the postoperative period (21.6 vs. 20.1 kg/m^2, $p<0.01$). Weight increased in 31 patients (70.5 %) with a mean of 4.3 kg (range: 1–24 kg).

Ten patients (26.3 %) were considered alcoholic during follow-up: four patients continued alcohol abuse pre and postoperatively and six patients relapsed after an initial withdrawal (mean withdrawal duration: 5.8 months, range: 1–15 months). Notwithstanding the small number of patients, postoperative alcohol abuse did not seem to significantly impact long-term results concerning the use of painkillers (10/28 in abstinent patients vs. 4/10, $p=0.81$), the development of diabetes (8/28 vs. 3/10, $p=0.93$) or exocrine insufficiency (24/28 vs. 7/10, $p=0.53$).

Table 3 General and functional results of the overall population ($n=44$)

Functional results	Preoperative	Postoperative	p
BMI (kg/m^2)	20.1±3	21.6±3.2	<0.01
Diabetes	7 (16 %)	14 (32 %)	0.08
Exocrine insufficiency	28 (64 %)	35 (79.5 %)	0.1
Analgesics	41 (93.2 %)	16 (31.7 %)	<0.001
WHO class 1 analgesics	38 (86.4 %)	15 (34.1 %)	<0.001
WHO class 2 analgesics	37 (84.1 %)	1 (2 %)	<0.001
WHO class 3 analgesics	27 (61 %)	1 (2 %)	<0.001

BMI body mass index, *WHO* World Health Organization

Results of Patients with Follow-up Longer than 5 Years

Twenty-one patients (47.7 %) were followed for more than 5 years (mean follow-up time: 71.2±14.7 months, range: 60–97.2 months) (Table 4). The general and functional results are summarized in Table 4. The results have remained stable and are still significantly different concerning weight and pain relief after 5 years.

Impact of a Preoperative Endoscopic Procedure

Thirty-two patients (72.7 %) underwent a previous endoscopic therapy with a mean of 1.8 procedures (range: 1–9). In 26 cases (81.3 %), prosthesis was inserted. Among the patients who had a successful stenting procedure ($n=26$), 22 (84.6 %) benefited from a pancreatic prosthesis only, one (3.8 %) benefited from a biliary prosthesis only and three patients (11.5 %) benefited from both pancreatic and biliary prostheses. Six patients (23.1 %) had various or not well-defined procedures including one alcohol celiac nerve plexus block, one cystogastrostomy, one endoscopic sphincterotomy, two extracorporeal shock wave lithotripsy and one nerve plexus neurolysis. The 26 stented patients underwent an average of 2.4 stenting procedures (range: 1–9), and the latest endoscopy was performed at a mean of 7.3 months (range: 1–36 months) before surgery. Eleven patients (34.4 %) showed progression or recurrence of pain after endoscopic treatment. Despite the small number of patients,

Table 4 Patients with follow-up longer than 5 years ($n=21$, 47.7 %)

Results	Preoperative	Postoperative	p
General results			
BMI (kg/m^2)	19.8±3.3	21.5±3.7	<0.01
Analgesics	20 (95.2 %)	9 (42.9 %)	0.0002
WHO class 1 analgesics	20 (95.2 %)	9 (42.9 %)	<0.001
WHO class 2 analgesics	19 (90.5 %)	0	<0.001
WHO class 3 analgesics	13 (90.5 %)	0	<0.001
Functional results			
Diabetes	2 (9.5 %)	6 (28.6 %)	0.12
Exocrine insufficiency	13 (61.9 %)	18 (85.7 %)	0.08
Enzyme supplementation	13 (61.9 %)	18 (85.7 %)	0.08

BMI body mass index, *WHO* World Health Organization

previous endoscopic stenting did not seem to be a predisposing factor for PF, biliary fistula or hemorrhage. However, it appeared to significantly increase the rate of global complications (8.3 % vs. 43.7 %; $p=0.035$), in particular those of a septic nature. A previous endoscopic procedure did not improve the results concerning postoperative pain (use of analgesics in 34.4 % vs. 41.7 %; $p=0.55$) because patients requiring preoperative stenting were likely to have a progressed disease (longer, more severe and frequent episodes). Among patients with preoperative Wirsung stenting (25 patients), 16 were considered pain-free at last follow-up visit and nine were still using painkillers regularly ($p=0.48$). Preoperative main pancreatic duct stenting did not seem to impact on long-term results concerning the management of pain.

Discussion

The present study supports the assumption that the Frey procedure can be performed without mortality and with low severe morbidity and that the general and functional results are persistent even after 5 years

The introduction of the Frey technique has led to controversial discussions concerning optimal surgical management, particularly in regard to the possible improvements in functional outcome, peri-operative morbidity and quality of life. The operative mortality for the Frey procedure is typically thought to be less than 1 %, and the morbidity rates range from 9 %[25] to 39 %.[26,27] In our study, perioperative mortality was nil, and complications occurred in 34.5 % with a surgical complication rate of 25 % (comparable to the results in Keck and Wellner's study).[13] Late morbidity is still high because of the comorbidity (alcohol, smoking) in many of those patients.[28] The 9 % rate of PF that we observed is close to the highest reported rates in the literature (between 0 % and 5 %) [27] but could be explained by the non-restrictive definition, which was not limited to severe grade C fistulas requiring reoperations. In patients with large main pancreatic duct (over 8 mm in diameter), the pancreaticojejunostomy was performed by sewing directly the duct to the jejunum and not to the pancreatic parenchyma. In these cases, the hard texture of pancreatic parenchyma did not prevent PF and the higher risk of fistula could be explained by the length of the anastomosis. The main medical complications were of a pulmonary nature. This may have been because of bias, since patients with chronic pancreatitis are often alcoholics and smokers and thus respiratory deficient. All cases of respiratory complications occurred in the patients operated on before 2006. Indeed Pessaux et al. advised in 2005 that these patients should be prepared preoperatively by respiratory physiotherapy,[9] which our study has proved to be efficient. Exocrine insufficiency was present postoperatively in 79.5 % of the whole cohort and in 86 % of patients followed over 5 years, but it was most of the time assessed by postoperative treatment with oral enzymes supplementation, which is systematically given in many centers after major pancreatic surgery. The various series of previously reported cases have documented percentages of de novo diabetes during the follow-up period that varied from 13 % to 25 %. In our series, 18 % of the patients developed new diabetes mellitus, which is less significant than the rate reported by Keck and Wellner[13] (34 % diabetes de novo) and by Strate et al.[12] (60 % diabetes mellitus). We also reported one case of diabetes improvement (but not complete recovery) after surgery probably related to improved dietary habits and abstinence from alcohol.

The long-term results for the use of analgesics were less optimistic than in a previously published report by Falconi et al.[11] Only 68 % of the patients were judged pain free after surgery versus 90 % in Falconi et al.'s study,[11] but no objective criteria to assess pain was defined in Falconi et al.'s paper. Our rate of 57 % patients still pain free after 5 years is similar to the 62 % rate for completely pain-free patients reported by Keck and Wellner.[13]

All patients with septic complications underwent previous endoscopic therapy. Endoscopic stenting seems to be a predisposing factor for this kind of complication, probably related to stent-associated pancreatic duct injuries, stent occlusion and bacterial colonization of the stent (relative risk = 3).[29] Unfortunately, we did not systematically obtain a bile sample for bacteriological study. Even if the small number of patient in each arm may impact the relevance of our results, in the whole population, preoperative Wirsung stenting did not seem to significantly impact long-term results concerning the use of painkillers (34.4 % vs. 41.7 %, $p=0.55$). However, the individual improvement of pain after Wirsung stenting could be a therapeutical test to predict good postoperative results after drainage or hybrid procedures and thus may help to select good responders to this surgery.

Among conservative procedures, lateral pancreaticojejunostomy using the Partington-Rochelle modification[30] has been most widely used due to its low morbidity and mortality. In long-term follow-up, the failure rate with the Partington-Rochelle procedure has been reported up to 30 % (reappearance of pain and use of opiates) versus 2 % prior to the 5-year follow-up and 0 % afterwards in our study with the Frey procedure. The most common reason of failure is a non-complete decompression of the ducts of Wirsung and Santorini as well as the collateral ducts located on the pancreatic head. The local resection of the pancreatic head, performed in the Frey procedure, improves the drainage of the different ducts and their tributaries in the pancreatic head compared with the Partington-Rochelle procedure.[7,10,31] Professor Frey himself has even advocated his procedure for small duct up to 3.5 mm.[32] In their review, Shrikhande et al.[33] concluded that the management of small

duct chronic pancreatitis should be tailored to the symptoms of the patient and that small duct chronic pancreatitis with head dominant disease should be treated with duodenum preserving pancreatic head resection or its modifications, i.e., the Frey procedure.

Compared with duodenum-preserving pancreatic head resection as described by Beger et al.,[27,34,35] the Frey procedure has lower surgical (20 % vs. 9 %, respectively; $p<0.05$)[27] and long-term morbidity rates.

The comparison of the Frey procedure versus pancreaticoduodenectomy (considered the standard surgical procedure for many years)[4,6] showed no significant differences in postoperative pain relief, mortality, and long-term morbidity;[36,37] however, the short-term results favored the organ-sparing procedure.[38] Pancreatic functional impairment with the Frey procedure was significantly reduced compared with that of pancreaticoduodenectomy.[36] This can be explained by the extensive resection including the removal of the duodenum and a large portion of the pancreas during pancreaticoduodenectomy. The Frey procedure was correlated to a higher quality of life, partly influenced by less nutritional, metabolic and gastrointestinal side effects (diarrhea, dumping syndrome, and reflux).

In patients with portal or mesenteric vein thrombosis and peripancreatic varices,[39] the Frey procedure was safer than the Beger procedure or pancreaticoduodenectomy because it did not require dissection of the pancreatic neck, which can be extremely difficult and dangerous with venous structures located posterior to the gland. A comprehensive review of the management of chronic pancreatitis was recently published.[40] In patients with chronic pancreatitis (instead of a primary malignancy), the decision to perform a total pancreatectomy is not an easy one because of the extensive nature of the surgery and the resulting endocrine deficiency, which almost always results in brittle insulin-dependent diabetes mellitus. But the development of autologous islet (auto islet) transplants has provided an opportunity to prevent development of insulin-dependent diabetes mellitus in such patients.[41]

We did not focus our study on quality of life outcome and did not insert subjective items into our standardized questionnaire. Thus, in our series we could not assess the postoperative and long-term quality of life. However, it appears to have been significantly increased in other studies.[9,11] Strate et al.[12] reported that 44 % of patients were successfully rehabilitated, i.e., they were able to return to professional work after this surgery.

In conclusion, the Frey procedure appears to be an effective and safe technique for pain relief in patients with chronic pancreatitis in the absence of neoplasia, with low mortality and morbidity rates. The benefits remain stable even after 5 years. However, new randomized controlled trials are needed to determine the most effective procedure for the management of patients with chronic pancreatitis.[42]

References

1. Andren-Sandberg A, Hoem D, Gislason H. Pain management in chronic pancreatitis. Eur J Gastroenterol Hepatol 2002; 14:957–70.
2. Tsiotou AG, Sakorafas GH. Pathophysiology of pain in chronic pancreatitis. Clinical implications from a surgical perspective. Int Surg 2000; 85:291–6.
3. Coffey R. Pancreaticoenterostomy and pancreatectomy. Ann Surg 1909; 50:1238–64
4. Andersen DK, Frey CF. The evolution of the surgical treatment of chronic pancreatitis. Ann Surg 2010; 251(1): 18–32.
5. Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. AMA Arch Surg 1958; 76:898–907.
6. Gourgiotis S, Germanos S, Ridolfini MP. Surgical management of chronic pancreatitis. Hepatobiliary Pancreat Dis Int 2007; 6:121–33.
7. Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. Pancreas 1987; 2:701–7.
8. Ho HS, Frey CF. The Frey procedure. Local resection of pancreatic head combined with lateral pancreaticojejunostomy. Arch Surg 2001; 136:1333–8.
9. Pessaux P, Kianmanesh R, Regimbeau JM et al. Frey procedure in the treatment of chronic pancreatitis short-term results. Pancreas 2006; 33:354–8.
10. Frey CF, Amikura K. Local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy in the management of patients with chronic pancreatitis. Ann Surg 1994; 220:492–507.
11. Falconi M, Bassi C, Casetti L et al. Long-term results of Frey's procedure for chronic pancreatitis: a longitudinal prospective study on 40 patients. J Gastrointest Surg 2006; 10:504–10.
12. Strate T, Taherpour Z, Bloechle C, et al. Long-term follow-up of a randomized trial comparing the Beger and Frey procedures for patients suffering from chronic pancreatitis. Ann Surg 2005; 241:591–8.
13. Keck T, Wellner UF. Long-term outcome after 92 duodenum-preserving pancreatic head resections for chronic pancreatitis: comparison of Beger and Frey procedures. J Gastrointest Surg 2010; 14:549–56.
14. Strate T, Bachmann K, Busch P, Mann O, Schneider C, Bruhn JP, Yekebas E, Kuechler T, Bloechle C, Izbicki JR. Resection vs drainage in treatment of chronic pancreatitis: long-term results of a randomized trial. Gastroenterology 2008; 134(5): 1406–11.
15. Lankisch PG, Andren-Sandberg A. Standards for the diagnosis of chronic pancreatitis and for the evaluation of treatment. Int J Pancreatol 1993; 14:205–12.
16. Schnelldorfer T., Adams D.B. Surgical treatment of alcohol-associated chronic pancreatitis: the challenges and pitfalls. Am Surg 2008;74(6):503–7.
17. Frey C, 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.
18. Frey CF, Reber HA. How I do it? J Gastrointest Surg 2005; 9:863–8.
19. WHO/ADA. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 1997; 20:1183–97.
20. Cancer pain relief guidelines. 1st edition. World Health Organization, Geneva, Switzerland 1986. The WHO analgesic ladder.
21. Dindo D., Demartine N., Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240:205–13.
22. Bassi C, Dervenis C, Butturini G et al. International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005; 138(1): 8–13.
23. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ,

Büchler MW. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007; 142(5): 761–8.
24. Epi Info Software Version 3.5.1 (January 2009). Community Health Assessment Tutorial Document version 2.0. Department of Health and Human Services, Centers for Disease Control and Prevention.
25. Frey CF, Mayer KL. Comparison of local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy (Frey procedure) and duodenum-preserving resection of the pancreatic head (Beger procedure). World J Surg 2003; 27:1217–30.
26. Izbicki JR, Bloechle C, Knoefel WT, et al. Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis: a prospective, randomized trial. Ann Surg 1995; 221:350–8.
27. Chaudhary A, Negi SS, Massod S, et al. Complications after Frey's procedure for chronic pancreatitis. IS J Surg. 2004; 188:277–81.
28. Izbicki JR, Bloechle C, Knoefel WT, et al. Surgical treatment of chronic pancreatitis and quality of life after operation. Surg Clin North Am 1999; 79:913–44.
29. Schnelldorfer T, Lewin DN, Adams DB. Do preoperative pancreatic stents increase operative morbidity for chronic pancreatitis? Hepatogastroenterology 2005; 52:1878–82.
30. Partington PF, Rochelle RE. Modified Puestow procedure for retrograde drainage of the pancreatic duct. Ann Surg 1960; 152:1037–43.
31. Paye F, Nicoluzzi E, Calicis B, Balladur P, Tiret E, Parc R. Influence de l'obstruction canalaire céphalique résiduelle sur les résultats de la dérivation pancréatico-jéjunale dans la pancréatite chronique. Gastroenterol Clin Biol 2001; 25: 755–60.
32. Frey CF. The surgical management of chronic pancreatitis: The Frey procedure. Adv Surg 1999; 32: 41–85.
33. Shrikhande SV, Kleeff J, Friess H, Büchler MW. Management of pain in small duct chronic pancreatitis. J Gastrointest Surg 2006; 10(2): 227–33.
34. Beger HG, Buechler M. Duodenum preserving resection of the head of the pancreas in chronic pancreatitis with inflammatory mass in the head. World J Surg 1990; 14:83–7.
35. Izbicki JR, Bloechle C, Broering DC, et al. 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 pancreatico-duodenectomy. Ann Surg 1998; 228:771–9.
36. Diener MK, Rahbari NN, Fischer L, et al. Duodenum-preserving pancreatic head resection versus pancreaticoduodenectomy for surgical treatment of chronic pancreatitis: a systematic review and meta-analysis. Ann Surg 2008; 247:950–61.
37. Huang JJ, Yeo CJ, Sohn TA, Lillemoe KD, Sauter PK, Coleman J, et al. Quality of life and outcomes after pancreaticoduodenectomy. Ann Surg 2000; 231:890–8.
38. Strate T, Bachmann K, Busch P, et al. Resection vs. drainage in treatment of chronic pancreatitis: long-term results of a randomized trial. Gastroenterology 2008; 134:1406–11.
39. Adam U, Makowiec F, Riediger H, et al. Pancreatic head resection for chronic pancreatitis in patients with extrahepatic generalized portal hypertension. Surgery 2004; 135:411–8.
40. Braganza JM, Lee SH, McCloy RF, McMahon MJ. Chronic pancreatitis. Lancet 2011; 377:1184–97.
41. Desai CS, Stephenson DA, Khan KM, Jie T, Gruessner AC, Rilo HL, Gruessner RW. Novel technique of total pancreatectomy before autologous islet transplants in chronic pancreatitis patients. J Am Coll Surg 2011; 213(6): 29–34.
42. Hartel M, Tempia-Caliera AA, Wente MN, et al. Evidence-based surgery in chronic pancreatitis. Langenbecks Arch Surg. 2003; 388:132–9.