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Original Article

Short- and long-term outcomes of selective use of Frey or extended lateral pancreaticojejunostomy in chronic pancreatitis

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Abstract

Background: Surgery is the most effective treatment in patients with painful chronic pancreatitis and a dilated pancreatic duct. Studies reporting the outcomes of selected surgical approach according to the pancreatic head size in these patients are lacking.

Method: This was a retrospective, observational single-centre study of consecutive patients who underwent either a Frey procedure or extended lateral pancreaticojejunostomy (eLPJ) for pain due to chronic pancreatitis with a dilated main pancreatic duct (5 mm or more) between 2006 and 2017. A Frey procedure was used in patients with pancreatic head enlargement (40 mm or more) and eLPJ (full-length pancreaticojejunostomy, including transection of the gastroduodenal artery) in others. A biliodigestive bypass was added in the case of biliary obstruction.

Results: Overall, 140 of 220 patients met the eligibility criteria: 70 underwent a Frey procedure and 70 an eLPJ. Hepaticojejunostomy was added in 17.1 per cent of patients (Frey: 24.3 per cent; eLPJ: 10.0 per cent ($P = 0.025$)). Major morbidity occurred in 15.0 per cent of patients (Frey: 21.4 per cent; eLPJ: 8.6 per cent ($P = 0.033$)). After a median 7.8 years of follow-up, the mean (s.d.) decrease in Izbicki pain score was 33 (27) points (34 (28) points after a Frey procedure; 32 (26) points after an eLPJ). Pain relief was reported as 'very much' by 87.5 per cent of patients (Frey: 86.1 per cent; eLPJ: 88.9 per cent) and as 'partial' by 11.1 per cent (Frey: 13.8 per cent; eLPJ: 8.3 per cent).

Conclusion: Selective-use of either a Frey procedure or eLPJ in patients with symptomatic chronic pancreatitis was-associated with low morbidity and long-term pain relief. Adding a-biliodigestive bypass did not increase morbidity.

Introduction

Chronic pancreatitis is a progressive inflammatory disease of the pancreas, with abdominal pain the predominant symptom[1,2]. The majority of patients have calcifying chronic pancreatitis with the development of parenchymal and intraductal stones[3,4]. A subset of these patients has inflammatory enlargement of the pancreatic head leading to local complications such as stenosis of the pancreatic or biliary duct or the duodenum. The pathophysiology of pain in chronic pancreatitis is multifactorial, and several explanatory mechanisms have been suggested, but, so far, none of the results is conclusive[5,6]. One hypothesis is that ductal obstruction leads to a dilated duct (more than 5 mm), with hypertension in the pancreatic tissue, which induces pain[7,8]. This is supported by the fact that drainage and decompression of a dilated pancreatic duct in this situation provides excellent pain reduction in the majority of patients[9–11]. Another hypothesis is that the head of the pancreas functions as a pacemaker of pain and that by removing the inflammatory mass in the head, the greatest reduction in pain can be achieved[1].

Based on the outcome of three randomized trials[9,12,13], current guidelines state that surgery is the most effective treatment in patients with painful chronic pancreatitis and a dilated pancreatic duct[2,14]. The different surgical options can be divided into drainage procedures, resection procedures, and combined procedures[2]. There is longstanding controversy over whether to perform partial resection of the pancreatic head in patients with chronic pancreatitis. Some have argued that this approach should be routinely performed to prevent ongoing inflammatory processes, while others believe that only surgical drainage is sufficient[1,11,15,16]. Consequently, the choice of surgical technique varies widely between countries, centres, and surgeons. Recent guidelines advise the Frey procedure in the case of an enlarged pancreatic head (40 mm or more) and a dilated pancreatic duct (5 mm or more), whereas lateral pancreaticojejunostomy is indicated in patients with a normal-sized pancreatic head (less than 40 mm) and a dilated pancreatic duct (5 mm or more)[1,2,14].

Such a selective surgical approach of either a Frey procedure or a full-length pancreaticojejunostomy, including transection of the gastroduodenal artery (extended lateral pancreaticojejunostomy

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(eLPJ)), has been the standard at our centre for more than two decades. However, large series with long-term follow-up of this approach, focusing on Frey and eLPJ, including the concomitant addition of hepaticojejunostomy in the case of biliary obstruction, are lacking. Therefore, we report herein the long-term outcomes of a surgical strategy comprising selective use of the Frey procedure and eLPJ in symptomatic, dilated duct chronic pancreatitis.

Methods

This retrospective single-centre cohort study was performed according the STROBE guidelines[17]. Reporting of data adhered as much as possible to the new International Study Group for Pancreatic Surgery (ISGPS) standards[18].

Patients and eligibility

All adult patients who underwent surgical treatment for chronic pancreatitis between 2006 and 2017 in the Amsterdam UMC, location Academic Medical Centre, were identified. The time period of 2006 to 2017 was chosen in order to exclude overlap with the previous series from our group[11], and to guarantee a minimum follow-up of 2 years. Only patients with an established diagnosis of chronic pancreatitis according the M-ANNHEIM diagnostic criteria were selected[19]. Patients were included if they had undergone a Frey procedure or eLPJ for chronic pancreatitis. Patients were excluded if they underwent another type of surgery than Frey or eLPJ; if they did not provide informed consent for participation in this study; and if they had undergone prior pancreatic surgery.

Patients are referred nationwide to the Amsterdam UMC for surgical treatment of chronic pancreatitis. There are six other centres in the Netherlands that perform surgery for chronic pancreatitis, but the majority of patients are referred to the Amsterdam UMC. All patients had been discussed in a multidisciplinary team meeting with gastroenterologists, pancreatic surgeons, and abdominal radiologists according to a treatment algorithm that essentially remained similar during the entire study period. Patients with a dilated (more than 5 mm) main pancreatic duct due to symptomatic chronic pancreatitis with the use of opioids and without the possibility of duct clearance using endoscopy or extracorporeal shockwave lithotripsy underwent surgery. During this time period a group of five surgeons performed the operations, all of whom worked in close collaboration and followed the same treatment algorithm and surgical technique. Several patients in this cohort were also included in the multicentre ESCAPE randomized trial, in which early surgery was compared to the endoscopy-first approach[13].

Ethics

This study was reviewed and approved by the medical ethical committee of the Amsterdam UMC, location Academic Medical Centre, with reference number E2-172, and received an exemption status, owing to its descriptive nature. All patients provided written informed consent.

Surgical technique

Frey procedure

Patients with a dilated pancreatic duct, including an enlarged pancreatic head (40 mm or more) or large parenchymal or intraductal stones located in the pancreatic head, had a duodenum-preserving pancreatic head resection according to the Frey procedure (*Fig. 1a*)[20]. The Frey procedure is performed by coring out the pancreatic head, leaving a semi-circular cuff

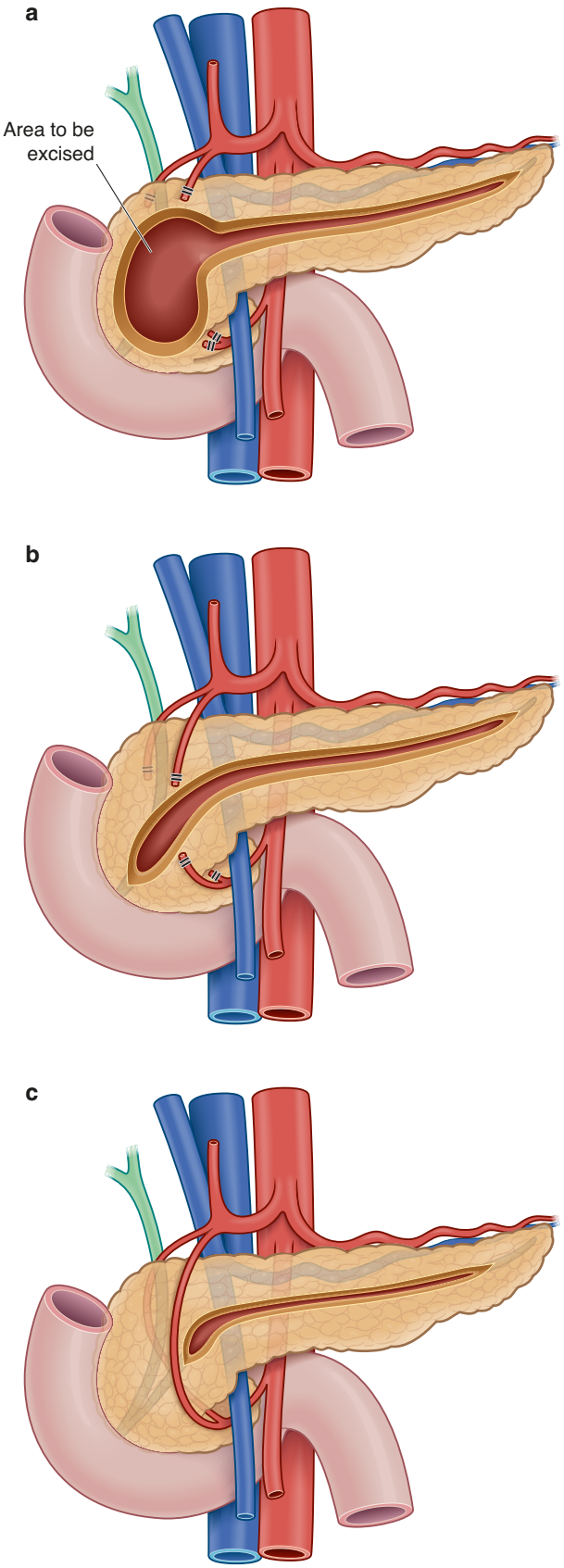

Fig. 1 Surgical procedures for chronic pancreatitis

a Frey procedure as used in the present study. **b** Extended lateral pancreaticojejunostomy (eLPJ) as used in the present study. **c** Lateral pancreaticojejunostomy according Partington-Rochelle (not used in present study).

of 1 cm of pancreas along the duodenum. This includes exposing and ligating the gastroduodenal artery on both sides of the pancreatic duct (below and above). For the pancreaticojejunostomy, the pancreatic duct is incised over the full length until 1 cm from the tip of the pancreatic tail to the head. The reconstruction is done as described for the eLPJ. Additionally, a biliodigestive anastomosis is performed in the case of clinical signs of stenosis of the intrapancreatic common bile duct, either by a separate choledochoduodenostomy or by a hepaticojejunostomy on the same bowel loop as the pancreaticojejunostomy; both include a cholecystectomy.

Extended lateral pancreaticojejunostomy

Patients with a dilated pancreatic duct due to stones or strictures but without an enlarged inflammatory pancreatic head (less than 40 mm) underwent an eLPJ. In contrast to the lateral pancreaticojejunostomy (LPJ), according Partington-Rochelle (*Fig. 1c*), in the eLPJ (*Fig. 1b*) the trajectory of the pancreatic duct is opened over the full length, from 1–2 cm from the tip of the pancreatic tail up to 1 cm from the ampulla. Before opening the duct from the pancreatic body towards the head and the tail, the gastroduodenal artery is exposed and ligated on both sides (below and above) of the pancreatic duct. For reconstruction, a blind ending proximal jejunal loop is anastomosed side to side to the full length pancreatic duct, in a Roux-Y construction. Additionally, a biliodigestive anastomosis is performed in the case of stenosis of the intrapancreatic segment of the common bile duct, by either a separate choledochoduodenostomy or a by hepaticojejunostomy on the same bowel loop as the pancreaticojejunostomy; both include a cholecystectomy.

Clinicopathological data and questionnaires

Clinicopathological data were extracted from medical records for all included patients. Around June 2019, surviving patients were asked to self-complete a one-off questionnaire regarding long-term outcomes. Morphological characteristics on preoperative computed tomography or magnetic resonance imaging were re-evaluated by a pancreatic radiologist (C.Y.N.).

Outcomes

The primary outcome was pain relief at long-term follow-up described as a decrease in Izbicki pain score. Secondary outcomes were decrease in visual analogue scale points (VAS; range 0–100), rates of partial and complete pain relief, pain relief on a 3-point semi-quantitative scale, opioid use, postoperative complications, short- and long-term reoperation rates, quality of life, pancreatic function, and mortality. The Izbicki pain score is a validated, chronic pancreatitis-specific pain score with a scale ranging from 0 to 100, with 100 as the worst pain score. It consists of four items regarding frequency of pain, intensity of pain, use of pain medication, and disease-related inability to work.[9,21] A decrease in the VAS and Izbicki pain score was calculated per patient by the long-term VAS/Izbicki score minus the preoperative VAS/Izbicki pain score. A VAS below 10 was considered as complete pain relief and a VAS between 10 and 40 as partial pain relief. Semi-quantitative pain relief was measured on a 3-point self-rated scale: 'very much', 'partial', or 'no' pain relief. Postoperative complications were registered according to the Clavien-Dindo classification, where complications are subdivided into five categories, increasing in severity (*Table S1*)[22]. Quality of life was assessed using the Short Form 36 (SF-36) quality-of-life questionnaire, which is a commonly used and validated questionnaire[23]. Pancreatic exocrine insufficiency was confirmed when a patient was using pancreatic enzyme-replacement therapy and/or had a faecal elastase-1 test of less than 200 μg/g. Diabetes mellitus was confirmed when a patient was using diabetes medication. Mortality among the included patients was recorded in three categories: in hospital, within 30 days, and within 90 days.

Statistical methods

Depending on a normal or non-normal distribution, mean(s.d.) or median with i.q.r. was used to present summary statistics. Categorical data were statistically compared using the χ^2 test or Fisher exact test. Continuous data were compared using the Student's *t* test or Mann–Whitney U test. *P*-values were two-tailed and $P < 0.05$ was considered to represent a statistically significant difference. Analyses were performed using SPSS Statistics version 25 (IBM, Armonk, New York, USA).

Results

Patients

Between 2006 and 2017, a total of 185 patients underwent surgical treatment of chronic pancreatitis. In total, 49 patients were excluded. Of these, 21 were excluded because they underwent another type of surgery for chronic pancreatitis (11 distal pancreatectomy, eight pancreatoduodenectomy, two only hepaticojejunostomy); 17 were excluded because they did not provide informed consent; and seven were excluded because of previous pancreatic surgery. Eventually, 140 consecutive patients were included with confirmed chronic pancreatitis and informed consent; 70 underwent a Frey procedure and 70 eLPJ (*Fig. 2*). The mean age of the included patients was 51 (10) years and 65.7 per cent were male. The aetiology of chronic pancreatitis was similar in both groups with alcohol (58.3 per cent) being the most common. In total, 75 of the 140 patients (53.6 per cent (Frey: 38; eLPJ: 37)) completed the long-term follow-up questionnaire at a median follow-up of 94 months (i.q.r. 56–123) months (7.8 years).

Preoperative and morphology characteristics

At the time of surgery, patients had a chronic pancreatitis diagnosis for a median of 19 (i.q.r. 6–48) months. Preoperatively, the degree of pain, assessed by the Izbicki pain score, was significantly higher in patients who underwent a Frey procedure compared with patients who underwent eLPJ (69 (18) *versus* 60 (21); $P = 0.044$). Some 68.9 per cent of patients used opioids, as patients with recurrent pain episodes who did not have a pain attack at the time of surgery were also included. The majority (57.8 per cent) of patients had undergone endoscopic treatment before surgery, with a median of 2 (i.q.r. 1–4) procedures. Preoperatively, 62.6 per cent of patients had exocrine insufficiency and 33.8 per cent had diabetes mellitus.

The mean diameter of the pancreatic head was 39 (8) mm (Frey: 41 (8); eLPJ: 37 (7) mm ($P = 0.001$)). The mean size of the pancreatic duct was 8 (3) mm and in 90.7 per cent of the patients the main obstruction was located in the head of the pancreas. In the Frey group, calcifications were present more often than in the eLPJ group (92.2 *versus* 79.0 per cent; $P = 0.035$). Therefore, both intraductal pancreatic head stones (78.1 *versus* 56.5 per cent, $P = 0.012$) and parenchymal pancreatic head stones (82.8 *versus* 59.7 per cent, $P = 0.004$) were present more often in patients undergoing a Frey procedure. See *Table 1* for all preoperative and morphological characteristics.

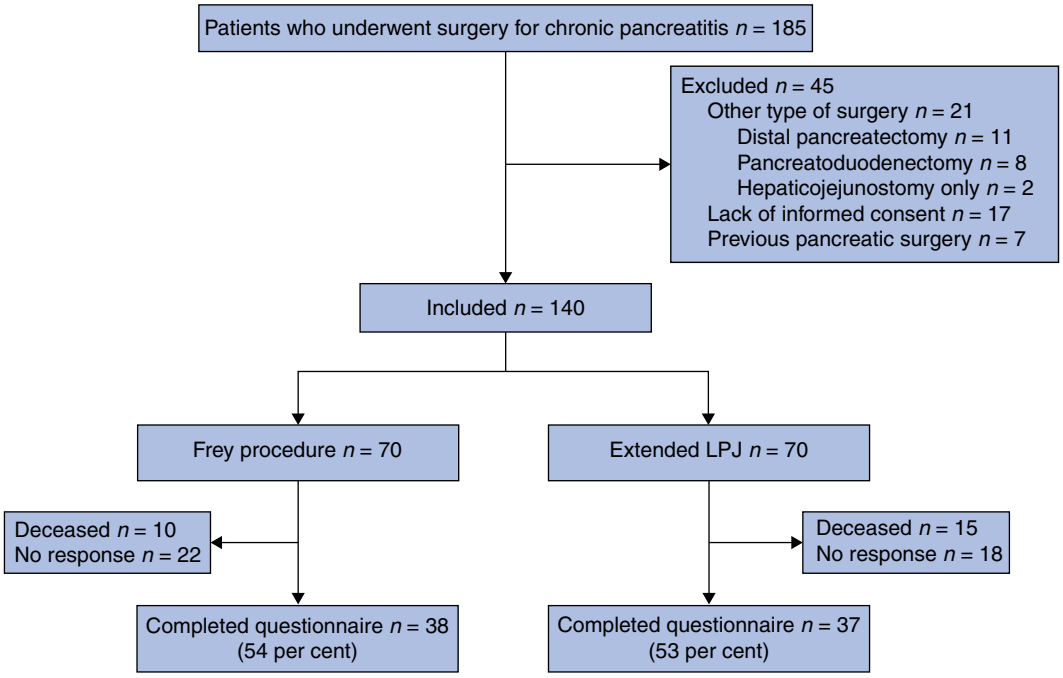

Fig. 2 Flowchart of patient selection

LPJ, lateral pancreaticojejunostomy.

Indication and surgical characteristics

The indication for surgery was recurrent or continuous pain in 96.4 per cent of patients. The indication for a Frey procedure was pancreatic head enlargement in 40 of 70 patients (57.1 per cent) and large parenchymal or intraductal stones in the head in 28 of 70 patients (40.0 per cent). In two other patients, cysts in the head were present for which a Frey procedure was performed. Perioperative characteristics were not statistically different between the two groups. Severe postoperative complications according to the Clavien-Dindo classification (Grade III or more) occurred in 15.0 per cent of patients (Frey: 21.4 per cent; eLPJ: 8.6 per cent ($P = 0.033$)). Detailed complications per patient are listed in *Table S2*; there was more leakage of the pancreaticojejunostomy (PJ) anastomosis with the Frey procedure ($n = 8$) than with the eLPJ ($n = 2$). The short-term reoperation rate (less than 30 days) was 7.9 per cent (Frey: 10.0 per cent; eLPJ: 5.7 per cent ($P = 0.346$)). The in-hospital and 30-day mortality rate was 1.4 per cent; one patient died after a myocardial infarction during surgery and one had a distributive shock following diffuse intestinal ischaemia without a clear cause. The 90-day mortality rate was 2.1 per cent. All surgical characteristics are presented in *Table 2*.

Biliodigestive bypass

A biliodigestive anastomosis was performed in 17.1 per cent of procedures and more often performed during the Frey procedure than during eLPJ (24.3 per cent *versus* 10.0 per cent; $P = 0.025$). Of the 24 patients with a biliodigestive anastomosis, 12 had a hepaticojejunostomy (Frey: nine patients; eLPJ: three patients) and 12 a choledochoduodenostomy (Frey: eight patients; eLPJ: four patients); all included a cholecystectomy.

Long-term outcomes

Long-term follow-up was 94 months (7.8 years) in 75 of 140 patients who completed the questionnaires. At the long-term follow-up, the mean decrease in Izbicki pain score was 33 (27) points (34 (28) points after a Frey procedure and 32 (26) points after eLPJ). The mean decrease in VAS (0–100) was 58 (30) points (61 (28) points after a Frey procedure and 55 (31) points after eLPJ).

There were no significant differences between the two groups regarding both pain scores. The proportion of patients with complete or partial pain relief, defined as a VAS score of less than 40, was 64.4 per cent (66.7 per cent with a Frey procedure and 62.2 per cent with eLPJ; $P = 0.914$). Pain relief on a 3-point semi-quantitative scale was scored as 'very much' by 87.5 per cent of patients (Frey: 86.1 per cent; eLPJ: 88.9 per cent) and as 'partial' in 11.1 per cent (Frey: 13.8 per cent; eLPJ: 8.3 per cent). Thirty-eight per cent of the patients in both groups were still using opioids at the long-term follow-up. Exocrine insufficiency and diabetes mellitus were comparable among the groups. Quality of life, measured by the SF-36, was comparable in all domains for the two treatment groups, but more than half of all patients scored lower than the Dutch average score of 50 on both the physical and mental component scales. Long-term outcomes are presented in *Table 3*.

Discussion

In this single-centre cohort study, the surgical strategy of selective use of either a Frey procedure or eLPJ in patients with pain due to chronic pancreatitis and a dilated pancreatic duct had low morbidity, and resulted in long-term pain relief and a low rate of new-onset diabetes. Although one-third of patients reported pain during follow-up, 100 per cent of patients after a Frey procedure and 97.2 per cent of patients after eLPJ reported 'very much' or 'partial' pain relief. Severe complications occurred more often after the Frey procedure than after an eLPJ (21.4 *versus* 8.6 per cent), but reoperation rates, length of stay, exocrine and endocrine insufficiency, and mortality were comparable for both procedures. Adding a biliodigestive anastomosis did not appear to increase the complication rate.

Table 1 Patients and preoperative characteristics

	Total $n = 140$	Frey procedure $n = 70$ (50.0%)	eLPJ $n = 70$ (50.0%)	*P*
Age (years), mean (s.d.)	51 (10)	50 (10)	51 (10)	0.762
Sex				0.154
Male	92 (65.7)	50 (71.4)	42 (60.0)	
Female	48 (34.3)	20 (28.6)	28 (40.0)	
Duration of pain (months), median (i.q.r.)*	35 (16–78)	39 (19–83)	32 (12–71)	0.451
Duration of chronic pancreatitis (months), median (i.q.r.)	19 (6–48)	19 (8–45)	19 (4–51)	0.770
Aetiology of chronic pancreatitis				0.131
Alcoholic	77 (58.3)†	43 (66.2)‡	34 (50.7)§	
Idiopathic	36 (27.3)	13 (20.0)	23 (34.3)	
Biliary	8 (6.1)	5 (7.7)	3 (4.5)	
Hereditary	5 (3.8)	3 (4.6)	2 (3.0)	
Pancreas divisum	4 (3.0)	0 (0.0)	4 (6.0)	
Other¶	2 (1.5)	1 (1.5)	1 (1.5)	
Previous endoscopic treatment	78 (57.8)‡	40 (59.7)§	38 (55.8)	0.653
Total no. of endoscopic procedures per patient, median (i.q.r.)	2 (1–4)	2 (1–3)	2 (1–5)	0.447
Izbicki pain score (0–100), mean (s.d.)*	64 (20)	69 (18)	60 (21)	**0.044**
VAS (0–100), mean (s.d.)	89 (13)	92 (9)	87 (16)	0.099
Pain pattern*				0.947
Continuous pain	55 (75.3)	27 (75.0)	28 (75.7)	
Recurrent pain	18 (24.7)	9 (25.0)	9 (24.3)	
Opioid use	91 (68.9)†	46 (70.8)‡	45 (67.2)§	0.655
Weak opioids	26 (19.7)	10 (15.4)	16 (23.9)	
Strong opioids	65 (49.2)	36 (55.4)	29 (43.3)	
Exocrine insufficiency	82 (62.6)#	38 (58.5)‡	44 (65.7)§	0.332
Diabetes mellitus	46 (33.8)**	27 (39.1)††	19 (28.4)§	0.184
Insulin dependent	13 (9.6)**	9 (13.0)††	4 (6.0)§	0.163
Morphological characteristics	137 (98)§	70 (100)	67 (96)§	
Enlarged pancreatic head (≥ 40 mm)	65 (47.4)§	40 (57.1)	25 (37.3)§	**0.020**
Max. diameter pancreatic head (mm), mean (s.d.)	39 (8)§	41 (8)	37 (7)§	**0.001**
Max. diameter pancreatic duct (mm), mean (s.d.)	8 (3)§	8 (3)	7 (3)§	**0.045**
Main obstruction cause				0.075
Stone	92 (77.3)‡‡	53 (84.1)†	40 (70.2)§§	
Stricture	27 (22.7)	10 (15.9)	17 (29.8)	
Main obstruction location				0.321
Head	117 (90.7)¶¶	63 (92.6)§	54 (88.5)#	
Corpus	10 (7.8)	5 (7.4)	5 (8.2)	
Tail	2 (1.6)	0 (0)	2 (3.3)	
Calcifications	108 (85.7)##	59 (92.2)***	49 (79.0)†	**0.035**
Intraductal	96 (76.2)##	53 (82.8)***	43 (69.4)†	0.159
Head	85 (67.5)	50 (78.1)	35 (56.5)	**0.012**
Body	29 (23.0)	13 (20.3)	16 (25.8)	0.463
Tail	36 (28.6)	16 (25.0)	20 (32.3)	0.369
Parenchymal	97 (77.0)##	56 (87.5)***	41 (66.1)†	**0.004**
Head	90 (71.4)	53 (82.8)	37 (59.7)	**0.004**
Body	61 (48.4)	40 (62.5)	21 (33.9)	**0.004**
Tail	62 (49.2)	33 (51.6)	29 (46.8)	0.588

Data are *n* (%) unless otherwise indicated. *Data only available for patients who completed the questionnaire (total 75 patients (Frey: 38; LPJ: 37). †Missing in eight patients. ‡Missing in five patients. §Missing in three patients. ¶One patient with familial adenomatous polyposis and one with a pancreaticobiliary maljunction. #Missing in nine patients. **Missing in four patients. ††Missing in one patient. ‡‡Missing in 21 patients. §§Missing in 13 patients. ¶¶Missing in 12 patients.##Missing in 14 patients. ***Missing in six patients. eLPJ, extended lateral pancreaticojejunostomy; VAS, visual analogue score.

According to recent guidelines, the Frey procedure is indicated in patients with a dilated pancreatic duct and enlarged pancreatic head, whereas a LPJ is indicated in case of a dilated pancreatic duct and a normal pancreatic head size[1,2,14]. This is the first large cohort with long-term follow-up to investigate and compare the results of these two surgical procedures in chronic pancreatitis for their respective indications. A previous, smaller study compared the short-term results of the Frey procedure in 22 patients with LPJ in 28 patients[24]. In that study, both procedures had an equivalent benefit in reducing the requirement for analgesia: 64 per cent after the Frey procedure *versus* 71 per cent after LPJ, with a median follow-up of 36 months ($P = 0.761$). In the present study, there were comparable results in both groups with regard to pain relief, measured by the Izbicki pain score and VAS score, after a median follow-up of 94 months. Several studies have investigated Frey and LPJ separately. LPJ procedures provide pain relief in 71–87 per cent of patients with chronic pancreatitis with a mean follow-up of 67 months[11,24–26]. Frey relieves pain in 68–90 per cent of patients with chronic pancreatitis within a mean follow-up of 57 months[27–30]. However, various methods are used for quantifying pain relief, which makes it difficult to generalize these results. In our study, pain relief based on the Izbicki pain score and VAS score was somewhat lower, but the pain relief results according the 3-point semi-quantitative scale were higher, compared to the above-described studies. When taking all pain scores in our study together, it can be concluded that both the Frey procedure and eLPJ provided good long-term pain relief.

In the present study, the rate of complications was significantly higher after the Frey procedure compared with after the eLPJ (21.4 per cent *versus* 8.6 per cent; $P = 0.033$), but reoperation rates, length of hospital stay, and ICU admissions did not differ. In a previous,

Table 2 Surgical characteristics

	Frey procedure n = 70 (50%)	eLPJ n = 70 (50%)	P
Indication for surgery			0.366
Pain	66 (94.3)	67 (98.5)†	
Other*	4 (5.7)	1 (1.5)	
Perioperative characteristics			
Duration of surgery (min), mean (s.d.)	334 (74)‡	327 (71)§	0.561
Blood loss (ml), median (i.q.r.)	400 (200–650)¶	300 (210–550)#	0.669
Biliodigestive bypass	17 (24.3)	7 (10.0)	**0.025**
Hepaticojejunostomy	9 (12.9)	3 (4.3)	
Choledochoduodenostomy	8 (11.4)	4 (5.7)	
Length of stay (days), median (i.q.r.)	9 (8–12)**	9 (8–11)	0.852
ICU	5 (7.1)	4 (5.7)	0.512
Postoperative complications ≥ Grade III (CD classification)††	15 (21.4)	6 (8.6)	**0.033**
Grade IIIA	5	1	
Grade IIIB	5	1	
Grade IV	4	3	
Grade V	1	1	
Short-term reoperation (< 30 days)‡‡	7 (10.0)	4 (5.7)	0.346
Time interval short-term reoperation (days), median (i.q.r.)	3 (0–9)	3 (0–12)	0.924
Long-term reoperation (≥ 30 days)‡‡	8 (11.4)	4 (5.7)	0.227
Time interval long-term reoperation (days), median (i.q.r.)	410 (318–751)	311 (131–1590)	0.497
Mortality			
In hospital	1	1	> 0.999
30-day	1	1	> 0.999
90-day	1	2	> 0.999

Data are *n* (%) unless otherwise indicated. *Other indications for a Frey procedure were biliary obstruction (three patients) and duodenal obstruction (one patient), and another indication for a lateral pancreaticojejunostomy was suspicion of pancreatic malignancy (one patient).†Missing in two patients. ‡Missing in eight patients. §Missing in five patients. ¶Missing in 49 patients. #Missing in 57 patients. **Missing in one patient. ††Definitions and details regarding complications are presented in *Tables S1 and S2*. ‡‡Reasons for reoperation within 30 days of the primary surgery were postoperative bleeding (three patients), fascial dehiscence (three patients), leakage of anastomosis (two patients), duodenal perforation (one patient), intestinal ischaemia in one patient and neurosurgery in another patient. Reoperation after 30 days after primary surgery was performed mainly due to incisional hernias (10 patients), in one patient a pylorus-preserving pancreaticoduodenectomy was performed owing to persisting pain, and one patient required a revision of the gastroenterostomy that was made at primary surgery. eLPJ, extended lateral pancreaticojejunostomy; CD, Clavien-Dindo.

large-cohort study of patients in our centre, the complication rate after head resection procedures (Frey, Beger, or pancreatoduodenectomy) was higher than after LPJ (30 *versus* 21 per cent)[11]. No other large-cohort study has compared complications from Frey and LPJ procedures, but in the study of Sakorafas *et al.*, a similar complication rate after LPJ was reported in 120 patients (8 per cent)[31]. In that study only eight patients underwent a Frey or Beger procedure, with a complication rate of 20 per cent. In a meta-analysis including a larger cohort undergoing Frey procedures, the postoperative complication rate was 21 per cent[32]. Reasons for the higher complication rates with a Frey procedure are unknown. It is plausible that the coring out of the pancreatic head of the pancreas could increase the complication rate, especially more leakage of the PJ anastomosis (eight *versus* two; *Table S2*). Given the overall outcomes, it seems fair to conclude that a Frey procedure is not required or advised in patients without an enlarged pancreatic head.

The discussion on the optimal type of surgical intervention for chronic pancreatitis is surprisingly persistent and has been ongoing for several decades. Some have argued that the debate may be related to unexplained differences in the phenotype of chronic pancreatitis between countries, including a higher rate of enlarged pancreatic heads in some countries than in others[33]. This would naturally lead to different use of drainage *versus* resection procedures. A study that compared patients with chronic pancreatitis from Boston, USA, and Freiburg, Germany, found a median pancreatic head size of 45 mm in Germany *versus* and 26 mm in the USA ($P < 0.001$)[33]. In our Dutch cohort, the mean pancreatic head diameter was 39 mm, and therefore the Frey procedure and eLPJ were evenly performed, with equivalent results for their selective indications.

Our technique for LPJ differs somewhat from other centres. Many authors describe using the technique of Partington-Rochelle[9,11,24,26,34]. According to this technique, the pancreas is opened from tail to just left of the mesenteric vessels, without transecting the gastroduodenal artery as it crosses the pancreas[34]. Therefore, a 'classic' Partington-Rochelle does not drain the ductal system in the pancreatic head, which could lead to persistent pain after surgery. In the present study, the 'extended LPJ' (eLPJ) was used, in which the complete pancreatic duct, including Wirsung and Santorini, is drained by opening the pancreatic duct from 1–2 cm of the tip of the pancreas tail to about 1 cm of the ampulla. This requires transection of the right gastroepiploic vein and artery, and ligation of the gastroduodenal artery cranial and caudal from the pancreatic duct[16]. It is possible that more studies actually use an eLPJ but describe it as a Partington-Rochelle procedure. The results of an eLPJ may differ from those of a Partington-Rochelle procedure. Future studies should report clearly on the exact type of LPJ used. Moreover, studies use various methods for quantification of pain relief and this also hampers comparison of outcomes.

The addition of a hepaticojejunostomy or choledochoduodenostomy to a duodenum-preserving pancreatic head resection has been described by several studies, all with low morbidity rates[35–37]. In our study, the morbidity rates were relatively low, including in patients with additional biliodigestive bypass. Some centres may perform pancreatoduodenectomy in patients with painful chronic pancreatitis and a biliary obstruction. However, a Frey procedure or eLPJ with a synchronous biliodigestive bypass in patients is potentially a better, more parenchyma-sparing option.

Worldwide, total pancreatectomy with islet auto-transplantation (TP-IAT) is increasingly being adopted in patients with small duct chronic pancreatitis or hereditary pancreatitis[2]. However, TP-IAT has also been advised as first-line surgical treatment, replacing LPJ or the Frey procedure[38,39]. It has been stated that the LPJ, Beger, and Frey procedures only lead to transient pain relief

Table 3 Long-term outcomes

	Total $n = 75$	Frey procedure $n = 38$ (50.7%)	eLPJ $n = 37$ (49.3%)	P
Long-term follow-up (months), median (i.q.r.)	94 (56–123)	92 (49–128)	95 (58–110)	0.937
Decrease in Izbicki pain score (0–100), mean (s.d.)*	−33 (27)†	−34 (28)‡	−32 (26)§	0.808
Decrease in VAS (0–100), mean (s.d.)*	−58 (30)‡	−61 (28)‡	−55 (31)§	0.402
Pain relief	47 (64.4)§	24 (66.7)§	23 (62.2)	0.914
Complete (VAS < 10)	25 (34.2)	13 (36.1)	12 (32.4)	
Partial (VAS < 40)	22 (30.1)	11 (30.6)	11 (29.7)	
No pain relief (VAS ≥ 40)	26 (35.6)	12 (33.3)	14 (37.8)	
Pain relief on a 3-point semi-quantitative scale	71 (98.6)‡	36 (100)§	35 (97.2)¶	0.469
Very much pain relief	63 (87.5)	31 (86.1)	32 (88.9)	
Partial pain relief	8 (11.1)	5 (13.8)	3 (8.3)	
No pain relief	1 (1.4)	0 (0.0)	1 (2.8)	
Opioid use	28 (38.4)§	14 (37.8)¶	14 (38.9)¶	0.926
Weak opioids	10 (13.7)	3 (8.1)	7 (19.4)	
Strong opioids	18 (24.7)	11 (29.7)	7 (19.4)	
BMI (kg/m2), mean (s.d.)	24 (4)¶	23 (4)¶	25 (5)	0.156
Exocrine insufficiency (enzyme use)	59 (78.7)	32 (84.2)	27 (73.0)	0.235
Pre-existent	41 (69.5)	21 (65.6)	20 (74.1)	
New onset	18 (30.5)	11 (34.4)	7 (25.9)	
Diabetes mellitus	43 (57.3)	24 (63.2)	19 (51.4)	
Pre-existent	26 (34.7)	16 (42.1)	10 (27.0)	
New onset	17 (22.7)	8 (21.1)	9 (24.3)	0.743
Insulin dependent	11 (14.7)	6 (15.8)	5 (13.5)	0.779
Current smoking	45 (60.0)	25 (65.8)	20 (54.1)	0.065
Current alcohol use	15 (20.3)¶	8 (21.6)¶	7 (18.9)	0.076
SF-36 domain scores, mean (s.d.)				
Physical functioning	75 (25)	79 (20)	71 (29)	0.214
Social functioning	70 (29)	69 (28)	71 (31)	0.821
Role limitations (physical problems)	53 (47)	50 (48)	56 (47)	0.579
Role limitations (emotional problems)	73 (41)	76 (38)	70 (44)	0.569
Bodily pain	76 (25)	73 (24)	79 (27)	0.309
Mental health	72 (21)	72 (21)	72 (21)	0.877
Vitality	55 (22)	56 (21)	55 (4)	0.864
General health perception	49 (26)	47 (24)	50 (27)	0.581
Physical component scale	44 (11)	44 (10)	45 (12)	0.942
Mental component scale	46 (12)	46 (12)	46 (12)	0.907

Data are *n* (%) unless otherwise indicated. *Delta of preoperative pain score minus postoperative pain score at long term. †Missing in five patients. ‡Missing in three patients.§Missing in two patients. ¶Missing in one patient.

and that, in the long term, pain recurs in up to 50 per cent of patients[38]. A recent meta-analysis on TP-IAT, which included 15 studies and 1255 patients, reported an opioid-free rate of 63 per cent at 1 year after TP-IAT[40]. The most recent and currently largest cohort of TP-IAT shows that 80 per cent of the patients have pain relief (3-point semi-quantitative pain relief: better, same, or worse, as compared with pre-TPIAT) 10 years after TP-IAT, with persistent opioid use in 38 per cent of patients. In our cohort, with nearly 8 years of follow-up, results after the Frey procedure and eLPJ were comparable; self-reported pain relief was 97.2–100 per cent and 38.4 per cent of patients are still using opioids. However, after TP-IAT, the risk of insulin-dependent diabetes is 70 per cent at 1 year after TP-IAT, increasing to 80 per cent at the 10-year follow-up[38,40]. In our study, only 14.7 per cent of the patients had new-onset diabetes at nearly 8 years after surgery. It therefore seems that, in the long-term, the Frey procedure and eLPJ still outperform TP-IAT as first-line surgical treatments in patients with symptomatic dilated duct chronic pancreatitis.

The majority (57.8 per cent) of patients had undergone endoscopic treatment before surgery. As our centre is a surgical expert centre for chronic pancreatitis, these numbers are potentially not an adequate representation of clinical practice in the Netherlands. For a better representation, we refer to one of our papers on the Dutch Chronic Pancreatitis Registry (CARE registry)[41].

The results of our study should be interpreted in light of several limitations. Firstly, the retrospective design in which patients were asked about their preoperative situation may have resulted in recall bias for some outcomes like the preoperative Izbicki pain score. However, for the main outcomes, only data on the current situation at the long-term follow-up were obtained from the questionnaire. Secondly, although the strategy in our centre has been the same for over two decades, the Frey procedure was also used in some patients with a smaller pancreatic head. Most likely, this was done in patients with larger stones in the pancreatic head duct or uncinate process. Thirdly, the questionnaire response rate was relatively low (53.6 per cent), which could be related to this specific disease but may have led to selection bias. Fourthly, pain relief as primary outcome is very subjective and difficult to generalize. Our study addressed this limitation by measuring the pain relief four ways (a decrease in VAS, a decrease in Izbicki score, pain relief using VAS, and pain relief using a 3-point semi-quantitative scale), leading to very different results. This is not only a limitation for the present study, but for the complete literature on surgery in chronic pancreatitis. Therefore, we should strive to use one standard tool for pain assessment in all studies on surgery in chronic pancreatitis, as advised by the recently published ISGPS standards for reporting on surgery for chronic pancreatitis[18,42]. We adhered as much as possible to these reporting standards; however, not all proposed outcomes could be reported as some data were not available. Replication studies from other countries and continents are needed, including on the impact of adding a biliodigestive anastomosis.

Disclosure. The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

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