

Surgical strategies for chronic pancreatitis in a 1,327- patient Scandinavian Baltic pancreatic Club (SBPC) register



Mikael Parhiala ^{a, b}, Anne Waage ^c, Povilas Ignatavičius ^d, Søren S. Olesen ^e, Jakob L. Poulsen ^e, Engjom Trond ^f, Georg Dimcevski ^f, Ingrid Nordaas ^{f, g}, Amer Hadi ^h, Evangelos Kalaitzakis ⁱ, Asbjørn M. Drewes ⁱ, Camilla Nøjgaard ^j, Johanna Laukkarinen ^{a, b, *}, on behalf of the Scandinavian Baltic Pancreatic Club

^a Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland

^b Faculty of Medicine and Health Technology, Tampere University, Finland

^c Department of Surgery, Oslo University Hospital, Oslo, Norway

^d Department of Surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania

^e Centre for Pancreatic Diseases, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Denmark

^f Department of Gastroenterology, Haukeland University Hospital, Norway

^g Department of Clinical Medicine, University of Bergen, Norway

^h Division of Gastroenterology, Digestive Disease Center K, Bispebjerg Hospital, Copenhagen, Denmark

ⁱ Herlev Copenhagen University Hospital/Herlev, University of Copenhagen, Copenhagen, Denmark

^j Pancreatitis Centre East (PACE), Copenhagen University Hospital Hvidovre, Copenhagen, Denmark

ARTICLE INFO

Article history:

Received 30 May 2022

Received in revised form

29 August 2022

Accepted 7 December 2022

Available online 11 December 2022

Keywords:

Chronic pancreatitis

Surgery

Pain

Quality of life

ABSTRACT

Background: Chronic pancreatitis (CP) may cause intermittent or continuous pain and complications requiring invasive interventions. No specific recommendations for surgical interventions have been presented. Our aim was to determine the surgical treatment strategies for the treatment of CP in the Scandinavian and Baltic countries.

Methods: This multi-centre cross sectional study included 1327 CP patients from eight centres. The data was gathered from the Scandinavian Baltic Pancreatic Club (SBPC) database. Patients who underwent pancreatic surgery were analysed. The baseline CP population from the eight centres was used as a reference. The information registered included comorbidities, pancreatic function, previous interventions, time and type of surgery and the EORTC-30 quality of life (QOL) questionnaire.

Results: Overall, 95/1327 (7%) patients underwent pancreatic surgery. Fifty-one (54%) of these underwent pancreatic surgery for chronic pain (PSCP) and formed the final study group. Median follow-up time was two (range 0–8) years after surgery and seven (1–46) years after diagnosis. The most common surgical procedures were pancreatic resection combined with drainage (54%) followed by pancreatic resections (32%) and drainage procedures (14%). Postoperatively, 47% of the patients were pain free with or without pain medication while 16% had chronic pain episodes, this did not differ from the base CP population. In QOL questionnaires, PSCP patients reported the same QOL but worse social functioning and more symptoms compared to the CP population.

Conclusions: Pancreatic surgery for CP is rare: surgical procedures were performed on only 7% of the CP patients in the SBPC database. In half of the patients the indication was pain. Most of these patients underwent endoscopic procedures before surgery. Half of the patients reported being pain-free after surgery.

© 2022 IAP and EPC. Published by Elsevier B.V. All rights reserved.

Abbreviations: CP, Chronic Pancreatitis; ERCP, Endoscopic retrograde cholangiopancreatography; PD, Pancreaticoduodenectomy; QoL, Quality of Life; EPI, Exocrine pancreatic insufficiency; PSCP, Pancreatic Surgery for Chronic Pain.

* Corresponding author. Dept. of Gastroenterology and alimentary tract surgery, Tampere University Hospital, Elämäntie 2, PL 2000, 33521, Tampere, Finland.

E-mail address: johanna.laukkarinen@pshp.fi (J. Laukkarinen).

1. Introduction

Chronic pancreatitis (CP) causes sustained inflammatory changes in the pancreatic tissue leading to fibrosis and calcifications, which in turn can lead to pancreatic ductal strictures and

dilation. Over time the pancreatic tissue loses function, leading to exocrine pancreatic insufficiency (EPI) and endocrine insufficiency. The main risk factors for CP are excessive alcohol consumption and smoking [1–4].

In CP patients, chronic pain is the leading symptom and cause of poor quality of life (QOL). Several theories have been proposed to explain the mechanism underlying pancreatic abdominal pain. High pancreatic ductal pressure may be related to pain although many other factors also come into play. Chronic inflammation can cause neuropathy and lead to irreversible sensitization of the central nervous system, causing patients to suffer continuous pain despite the disappearance of inflammation in the pancreatic tissue. Pancreatic ischaemia and oxidative stress have also been associated with pancreatic pain. Other causes of pain in CP patients can be attributed to complications such as pseudocysts and bile duct obstruction [5–12].

CP patients may need invasive endoscopic or surgical procedures, either for pain or to treat complications. Endoscopic procedures include pancreatic and bile duct stenting and pseudocyst drainage. Surgical interventions are intended to improve pancreatic drainage and to remove fibrotic and calcified tissue. The choice of surgery is based on the symptoms and imaging findings, involving resection, drainage, or a combination of these [13,14]. So far there are no specific recommendations for surgical interventions.

Our objective was to determine the surgical treatment strategies for the treatment of CP in the Scandinavian and Baltic countries.

2. Methods

This was a cross-sectional multicentre study including data from the Scandinavian Baltic Pancreatic Club (SBPC) database [15]. The data was collected from 2016 to the extraction date in 2019 and included data from eight centres across northern Europe. Among the patients included, 1327 met the M-ANNHEIM definitive diagnostic criteria, which include one or more of the following: pancreatic calcifications, moderate or marked ductal pancreatic ductal lesions according to the Cambridge classification, pancreatic exocrine insufficiency (pancreatic steatorrhea markedly reduced by pancreatic enzyme replacement therapy) or a typical histological specimen of the pancreas [16,17]. Patients who underwent

pancreatic surgery and the base CP group were analysed (Fig. 1). The surgery group consisted of CP patients who underwent pancreatic surgery for CP pain. CP patients from the same eight centres who did not have any surgery were used as a basegroup. Patients undergoing emergency pancreatic surgery (for example, necrosectomy) or who had a gastroenteroanastomosis or a hepaticojejunostomy without pancreatic intervention were excluded from the final analysis.

The base population (n = 1327) consisted of CP patients without any surgical intervention from the same eight centres included in the SBPC database.

The data were registered by the respective centres and included type and year of surgery, indications and complications. From the SBPC database we gathered data on pancreatic function, endoscopic therapies, QOL, pain and CP aetiology. Exocrine pancreatic insufficiency (EPI) was characterized by the use of faecal elastase-1, faecal fat collection or a C13 mixed triglyceride breath test. EPI was defined according to previously published guidelines [18].

QOL was measured using the QLQ-C30 questionnaire. The EORTC scoring manual was used for the QLQ-C30 questionnaires and responses were scored from 0 to 100. A higher score on QOL/functioning indicates better quality of life as also does lower score on symptoms (e.g., pain or insomnia).

2.1. Ethical aspects

The study was approved by the Ethics Committee of Tampere University Hospital, Finland (ETL code R15187). Also each participating centre obtained a separate approval from their local institutional review boards.

2.2. Statistical analyses

Data are presented as medians (range) or numbers (%) unless otherwise specified. The statistical analyses were performed using Pearson's Chi-Square or Fisher's exact test. The analysis of the continuous variables was done using Mann Whitney U test. The QLQ C30 responses were presented in a radar plot. A boxplot with whiskers was used to show the pain results and disease duration before surgery, the middle line indicating a median value, the box

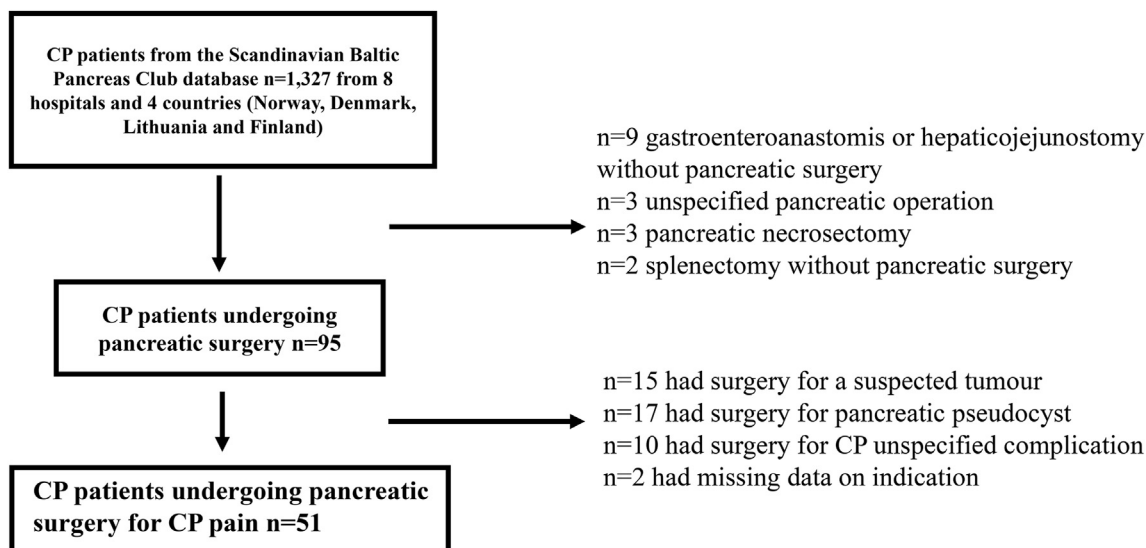


Fig. 1. Flowchart of CP surgery patients. The data were gathered from the Scandinavian Baltic Pancreas Club database and details concerning surgery were collected separately. The final study group was formed of CP patients undergoing surgery for pain n = 51.

indicating the interquartile range and whiskers the range. A p-value of under 0.05 was considered statistically significant. The IBM SPSS® (Armonk, NY) version 26 was used for all statistical analysis.

3. Results

Of the 1331 CP patients in the database, 95 (7%) patients underwent pancreatic surgery. Indication for surgery was pain in 51 (54%), complications to CP in 27 (28%) and suspected malignancy in 15 (16%) of the patients. In two (2%) patients' data on indication was lacking.

The 51 patients who underwent pancreatic surgery for chronic pain (PSCP group) formed the final study group and were analysed. The median follow-up time was two (range 0–8) years after surgery. The median age at the time of surgery was 48 (range 18–71) years and n = 17 (33%) of the patients were female. Surgery was performed a median of three years (0–28) after the diagnosis. Ductal lesions were present in 74% and pancreatic calcifications in 91% of the patients. Seventy-four-point five percent (74.5%) of the patients underwent endoscopic retrograde cholangiopancreatography (ERCP) prior to surgery. Pancreatic resection combined with drainage (n = 28 (54%), Frey, Berne and Beger procedures) was the most common procedure, followed by pancreatic resections alone (n = 17 (33%); pancreaticoduodenectomy, distal resections and total pancreatectomies) and drainage alone (n = 7 (13%); Puestow/Partington-Rochelle and pseudocyst drainage) (Table 1 and Fig. 2). Post-operative diabetes was diagnosed in 39% and 41% had EPI.

Patients in the base group were older with a median age of 59 (range 15–109) vs. 51 (range 19–73) years. Idiopathic pancreatitis, calcifications and ductal dilation were more often diagnosed in the PSCP group. Endoscopic procedures were more often also performed in the PSCP group, 75% vs. 26%, (p = 0.000). Diabetes occurred equally in both groups but EPI was less common in the surgery group post-operatively. There was no difference in the number of patients with high pain scores and pain medication after

surgery (Table 1).

Deaths were registered separately from all eight centres a median of 12 years after surgery (range 1–31) in 88% (45/51) of the patients. During this follow-up time, only one patient (2%) died of unknown causes one year after surgery.

3.1. Pain

After surgery, 16% of the patients suffered chronic pain episodes, 36% had recurring or intermittent pain episodes and 47% were pain free with or without medication. The patients with constant pain had longer disease duration before surgery than the CP patients without constant pain (11 (1–28) vs. 3 years, p = 0.034 (Fig. 3).

Of the 33 patients with data on pain medication two (range 1–7) years after surgery, 30% took strong pain medication (morphine, tramadol, buprenorphine), 6% had paracetamol or a nonsteroidal anti-inflammatory drug and 64% had no pain medication.

3.2. Quality of life (QLQ C30) responses

More than a half of patients (n = 31 (61%)) from the PSCP group completed the EORT QLQ C30 questionnaire. In the QLQ C30 responses, the PSCP group had worse social functioning (p = 0.028) but QOL and other functioning responses did not differ from those of the base CP population (n = 514). In symptom responses, the PSCP group reported more constipation, nausea and insomnia (p = 0.009, p = 0.002 and p = 0.001). (Fig. 4).

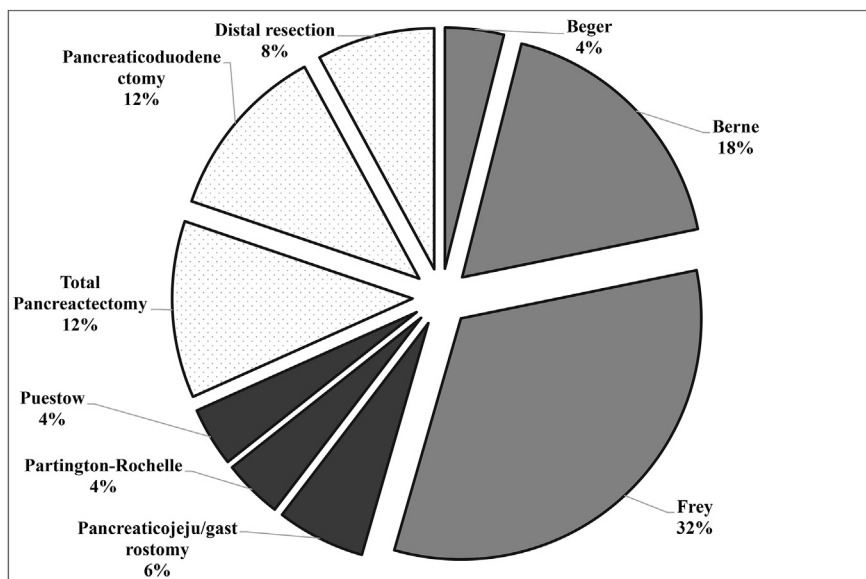
In the PSCP group, patients with prior ERCP (n = 25) had worse physical, role and social functioning (p = 0.017, p = 0.04 and p = 0.04) and more severe fatigue and pain symptom scores (p = 0.041 and p = 0.006) than patients without prior ERCP (n = 6).

When comparing surgical procedures in the PSCP group, pancreatic drainage resulted in most patients with constant pain (p = 0.015). Patients with combined pancreatic resection and drainage had the least amount of constant pain (drainage 50%, resection 23% and combined 4%) p = 0.013 (Fig. 4). Total

Table 1
Demographic table of CP patients who underwent pancreatic surgery for pain. Pain and pancreatic insufficiency were measured post-operatively in the surgical group.

	Surgery for CP pain n = 51	All CP n = 1327	Surgery vs control p-value
Male/Female	67%/33%	67%/33%	p = 0.976
Age when surgery	48 (18–71 years)	N/A	
Age when visit	51 (19–73 years)	59 (15–109) years	p = 0.000
Time after diagnosis	6 (0–39 years)	3 (0–61 years)	p = 0.001
Aetiology			
Alcohol	60%	61%	p = 0.936
Nicotine	60%	69%	p = 0.231
Immunological	0%	2.3%	p = 0.308
Hereditary	6.7%	9.7%	p = 0.578
Efferent duct	0%	10%	p = 0.030
Unknown	30%	7.0%	p = 0.000
Calcification	91%	69%	p = 0.003
Ductal dilation	74%	57%	p = 0.031
Pseudocysts	41%	43%	p = 0.850
ERCP	75%	26%	p = 0.000
Biliary stenting	19%	12%	p = 0.039
Pancreatic stenting	33%	17%	p = 0.002
Pancreatic function and pain after surgery			
	Surgery for CP pain n = 44	Control CP group n = 1107	Surgery vs control p-value
Diabetes	39%	44%	p = 0.491
PEI	41%	60%	p = 0.019
No (post-operative) pain *	47%	47%	p = 0.940
Continuous (post-operative) pain *	15.9%	16.4%	p = 0.926
Morphine*	21.2%	18.5%	p = 0.695
No pain medication*	64.0%	57.0%	p = 0.434

*Pain and pain medication was measured after surgery, except for the control group.



Drainage procedure	13%	n=7
Pancreatic resection	33%	n=17
Duodenum preserving pancreatic head resection	54%	n=28
Total	100%	n=52

Fig. 2. Type of pancreatic surgery performed with indication of chronic pancreatitis pain in the eight centres.

A.

	n	Female/ Male %	Surgery done time after diagnosis median (range)	Pancreatic main duct dilation	Pancreatic calcification	Alcohol	Smoking	Prior ERCP	Surgery type			
									Pancreatic drainage n=6	Pancreatic resection n=13	DPPHR n=25	
Painless without medication or intervention	16	36%	38%/62%	3 (1-23) years	77%	92%	38%	46%	69%	17%	38%	40%
Painless with medication or intervention	5	11%	40%/60%	1 (1-8) years	67%	100%	75%	50%	80%	0%	15%	12%
All Painless	21	48%	38%/62%	3 (1-23) years	75%	94%	47%	47%	71%	17%	54%	52%
Recurring pain	16	36%	31%/69%	3(1-8) years	73%	93%	63%	75%	81%	33%	23%	44%
Constant pain	7	16%	29%/71%	11 (1-28) years	100%	86%	71%	57%	76%	50%	23%	4%
Constant pain vs recurring and painless	p-value	0.737	0.802	0.034	0.13	0.488	0.412	0.865	0.812	0.0014	0.4	0.013

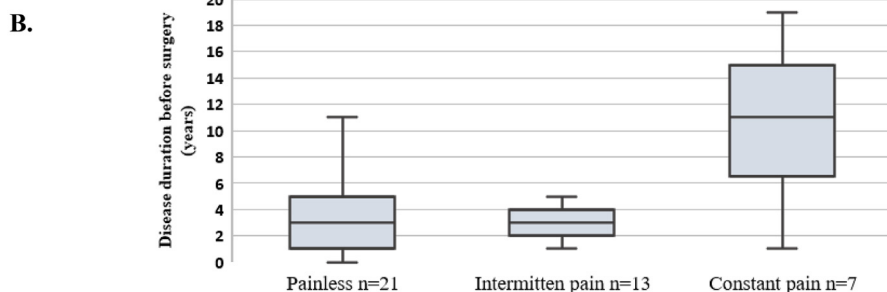


Fig. 3. **A.** Results of surgery in CP patients who underwent pancreatic surgery for pain. Duodenum preserving pancreatic head resections (DPPHR) seemed to have less pain. **B.** Patients with constant pain after surgery had a longer disease duration before surgery. Boxplot with whiskers with the middle line indicating a median value, the box indicating the interquartile range and whiskers the range.

pancreatotomy was performed on six patients, four with islet autotransplantation. One (17%) of these patients had opiate use and chronic pain.

Of the 15 patients undergoing surgery for a suspected tumour, 11 had completed the pain scores and EORTC QLQ-C30 responses. None of them had constant pain and 55% were pain free with or without medication. On EORTC QLQ-C30 responses they had a statistically better score in role functioning ($p = 0.029$), fatigue ($p = 0.049$) and pain ($p = 0.009$) than the base CP population.

4. Discussion

CP can lead to burdensome abdominal pain which may

necessitate endoscopic treatment or pancreatic surgery. The optimal treatment and timing for CP remains uncertain. We aimed to ascertain the surgical treatment strategies in CP and to study QOL in these patients.

We found that pancreatic surgery for CP is rare: surgical procedures were performed on only 7% of the CP patients in the SBPC database. In most of the patients the indication was pain, and half of them reported being pain free after surgery.

The first surgical procedure reported for CP was pancreaticoduodenectomy (PD) While PD involves resecting the duodenum together with the pancreas a CP-specific duodenum preserving surgical technique has been developed, for example the Frey, Puestow, Berger and Berne modifications [19–25]. The Beger

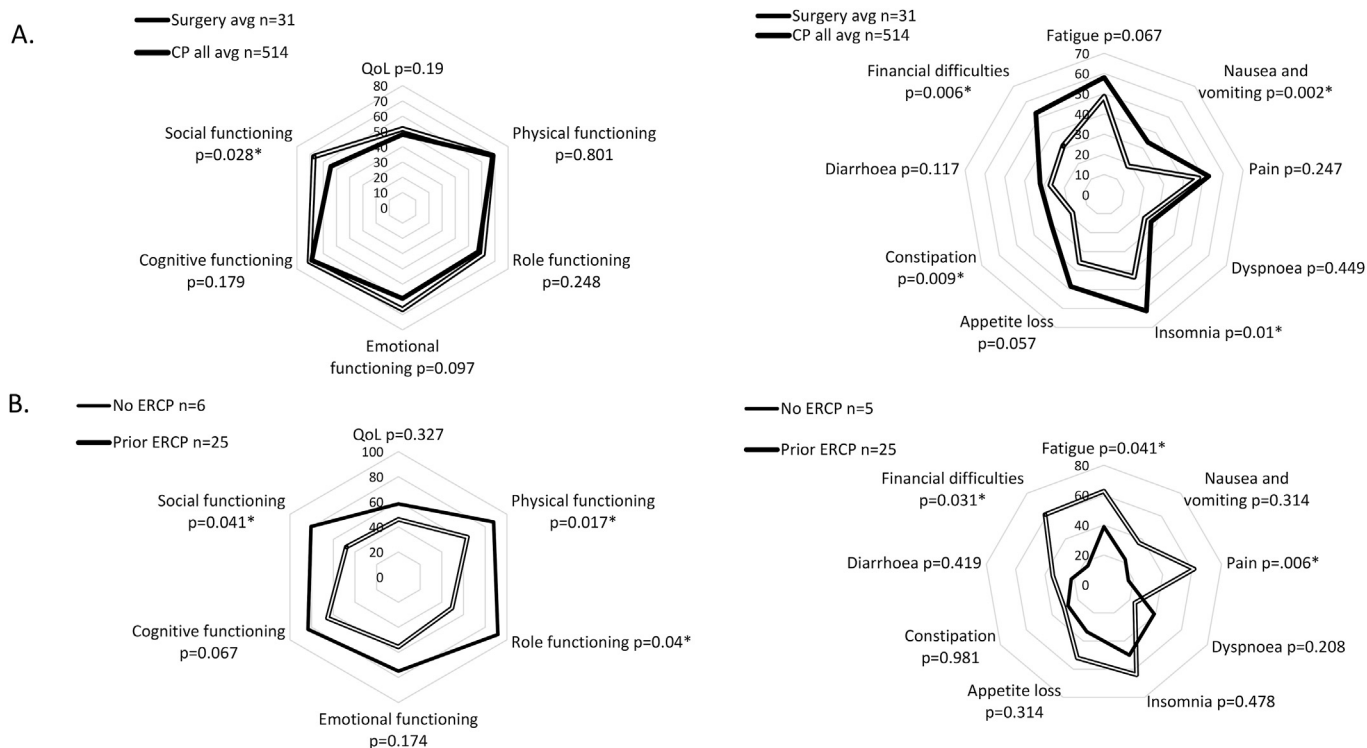


Fig. 4. EORTC C30-QOL and functioning in CP patients who had pancreatic surgery for pain. A higher score in QOL/functioning represents a better score. A lower score in symptoms represents a better score. **A.** The surgery group appeared to have a similar QOL to the control group. **B.** The CP patients who did have any prior endoscopic procedures done before surgery had a better quality of life and fewer symptoms, e.g., pain.

procedure involves the resection of the pancreatic head and the pancreas is divided above the portal vein. In the Frey procedure the pancreatic head is opened and resected following a lateral jejunostomy. A Berne modification has subsequently been developed which involves carving out the inflamed pancreas mass from the head of the pancreas and does not involve dividing the pancreatic tissue [26–30].

In our study, combined pancreatic drainage and resection was most common (55%), Frey’s procedure being the primary procedure of choice (33% of total). Pancreatic resection was done in 31% and drainage procedures in 14%. Numerous pancreatic surgery techniques are in use and there seems to be no predominant style. In the ESCAPE trial, 59% of the procedures were drainage and 37% were combined drainage and resection and in a Finnish cohort study pancreatic resection (70%) was the most common technique in CP with combined drainage and resection being (30%) while pure drainage procedures were very rare (1%). This differs from the meta-analysis by Ratnayake et al. where 67% of the procedures were combined pancreatic resections [31–33].

Presumably the difference in pancreatic surgery techniques is based on the surgeons’ and clinics’ own customs. The type of pancreatic surgery for CP should be determined by the anatomy of the afflicted pancreas. The international consensus guidelines recommend a Berne or Frey-type procedure over PD or Pylorus preserving-PD [34]. In patients with CP and a dilated main duct without an inflamed mass in the pancreatic head and no bile duct stenosis or portal vein stenosis, a lateral jejunostomy may suffice [35].

The selection of a surgical technique for patients with CP should be based on the anatomical characteristics of the pancreas to be operated on. In our study, CP patients with only pancreatic drainage for pain had more symptoms and post-operative pain than those patients who underwent resection or combined resection and

drainage procedures. Patients with combined pancreatic resection and drainage procedures had the least amount of constant pain. Further studies are needed to determine the optimal strategies for surgical interventions.

In our study there was no difference in pain and pain medication between the base CP group and the PSCP group. We did not have access to detailed preoperative data. The PSCP group had a lower incidence of pancreatic insufficiency, possibly due to the inflammation subsiding slowly after surgery. Similar findings have been reported in earlier studies [30,31,36].

CP patients undergoing pancreatic surgery for pain had more pain post-operatively if they had already undergone ERCP. In our study CP patients who had undergone ERCP before surgery received more pain medication than patients who had not undergone ERCP prior to surgery. Moreover, no post-operative morphine was needed in patients undergoing their first surgery without prior endoscopic treatment and early surgery also seems to achieve better pain relief.

Similar results have been reported in other studies such as the Dutch ESCAPE trial, where an endoscopy-first approach resulted in more pain at 18 months while quality of life remained the same. In our study CP patients with no prior surgery had higher QOL scores [31]. Another Dutch randomized trial compared endoscopy and pancreatic surgical drainage [37]. In the two-year follow-up the surgical group were more pain free than patients treated with the endoscopic approach (40% vs. 16% respectively $p = 0.007$). A Czech randomized trial compared endoscopy to surgery and the surgical group had more painless (with or without pain medication) patients than the endoscopy group at five-year follow-up (surgery 32% vs. endoscopy 15% $p = 0.002$) [38]. In our study, 12% of the patients underwent total pancreatectomy for CP. These patients had approximately the same amount of constant post-operative pain and opiate use than the rest of the surgery group.

Our study has some limitations. We were not able to collect complete preoperative data from all the patients on pain, medication and QOL before the surgical interventions. Even though the SBPC register is the largest CP register in existence, surgical operations are rare, and thus the overall number of patients meeting our inclusion criteria is still fairly small. Although this is a cross-sectional study the numbers are too small for multivariate analyses. It should be noted that the time factors after surgery differ, not being consecutive causes limitations in the causality between surgery and outcomes. We assume that the surgery group have an altogether more severe disease spectrum than the conservatively managed population. The International Study Group of Pancreatic Surgery in 2020 released a standard for reporting details prior to and after surgery, including the use of opiates, pancreatic insufficiency and quality of life. According to this, the morphology of the pancreas and the outcome of surgery should also be reported. In the future adhering to these standards will result in a more reliable comparison of surgical outcomes and better care for CP patients [39].

There is preliminary data to suggest that pancreatic surgery for CP may not only slow down the inflammation but also delay the development of pancreatic insufficiency. In our population CP patients treated surgically for pancreatic pain had less EPI and endocrine insufficiency than the base population. Similar results have been reported in earlier studies [40,41].

More studies are needed to determine which CP patients benefit from surgery and when an endoscopic approach may suffice for pain relief.

We conclude that surgery for CP is rare. Surgical procedures were performed in only 7% of the CP patients in the SBPC database. In half of the patients the indication was pain. Most of these patients underwent endoscopic procedures before surgery. Half of the patients reported being pain free after surgery, either with or without pain medication. Patients who underwent a resection or combined resection and drainage seemed to achieve better pain and symptom control than the patients who underwent surgical drainage only. Further studies are needed to determine the optimal strategies for surgical interventions.

Acknowledgements

This study was financially supported by the Medical Research Fund of Pirkanmaa Hospital District [grant numbers: V026, X024 and AA039] and the Sigrid Jusélius Foundation [grant number: MS424]. Mary & Georg C. Ehrnrooth Foundation [Grant number: 202110011]. The authors have no conflicts of interest to declare.

References

- [1] Agarwal S, Sharma S, Gunjan D, Singh N, Kaushal K, Poudel S, Anand A, Gopi S, Mohta S, Sonika U, Saraya A. Natural course of chronic pancreatitis and predictors of its progression. *Pancreatology* 2020 Apr;20(3):347–55. <https://doi.org/10.1016/j.pan.2020.02.004>. Epub 2020 Feb 14. PMID: 32107194.
- [2] Lévy P, Domínguez-Muñoz E, Imrie C, Löhr M, Maisonneuve P. Epidemiology of chronic pancreatitis: burden of the disease and consequences. *Unit Eur Gastroenterol J* 2014 Oct;2(5):345–54.
- [3] Etamad B, Whitcomb DC. Chronic pancreatitis: diagnosis, classification, and new genetic developments. *Gastroenterology* 2001;120(3):682–707.
- [4] Olesen SS, Nøjgaard C, Poulsen JL, et al. Chronic pancreatitis is characterized by distinct complication clusters that associate with etiological risk factors. *Am J Gastroenterol* 2019;114(4):656–64.
- [5] Olesen SS, et al. Pain severity reduces life quality in chronic pancreatitis: implications for design of future outcome trials. *Pancreatology* 2014 Nov-Dec;14(6):497–502.
- [6] Sureshkumar S, Omang A, Anandhi A, Rajesh BS, Abdulbasith KM, Vijayakumar C, et al. Efficacy of pregabalin and antioxidants combination in reducing pain in chronic pancreatitis: a double blind randomized trial. *Dig Dis Sci* 2021.
- [7] Olesen SS, Phillips AE, Faghih M, Kuhlmann L, Steinkohl E, Frøkjær JB, Bick BL, Ramsey ML, Hart PA, Garg PK, Singh VK, Yadav D, Drewes AM. Pancreatic

Quantitative Sensory Testing (P-QST) Consortium. Overlap and cumulative effects of pancreatic duct obstruction, abnormal pain processing and psychological distress on patient-reported outcomes in chronic pancreatitis. *Gut* 2021 Oct 21. <https://doi.org/10.1136/gutjnl-2021-325855>. *gutjnl-2021-325855*, Epub ahead of print. PMID: 34675068.

- [8] Sand J, Nordback I. Kroonisen haimatulehduksen aiheuttama kipu: a review. *Lääketieteellinen Aikakausk Duodecim* 2011;127(10):995–1001.
- [9] Tjora E, Dimcevski G, Haas SL, Erchinger F, Vujasinovic M, Löhr M, Nøjgaard C, Novovic S, Zalite IO, Pukitis A, Hauge T, Waage A, Roug S, Kalaitzakis E, Lindkvist B, Olesen SS, Engjom T. Scandinavian Baltic Pancreatic Club. Patient reported exposure to smoking and alcohol abuse are associated with pain and other complications in patients with chronic pancreatitis. *Pancreatology* 2020 Jul;20(5):844–51. <https://doi.org/10.1016/j.pan.2020.05.001>. Epub 2020 May 11. PMID: 32507681.
- [10] Drewes AM, Olesen AE, Farmer AD, Szigethy E, Rebours V, Olesen SS. Gastrointestinal pain. *Nat Rev Dis Prim* 2020 Jan 6;6(1):1. <https://doi.org/10.1038/s41572-019-0135-7>. PMID: 31907359.
- [11] Kleeff J, Whitcomb DC, Shimosegawa T, Esposito I, Lerch MM, Gress T, Mayerle J, Drewes AM, Rebours V, Akisik F, Muñoz JED, Neoptolemos JP. Chronic pancreatitis. *Nat Rev Dis Prim* 2017 Sep 7;3:17060. <https://doi.org/10.1038/nrdp.2017.60>. PMID: 28880010.
- [12] Poulsen JL, Olesen SS, Malver LP, Frøkjær JB, Drewes AM. Pain and chronic pancreatitis: a complex interplay of multiple mechanisms. *World J Gastroenterol* 2013 Nov 14;19(42):7282–91. <https://doi.org/10.3748/wjg.v19.i42.7282>. Published online 2013 Nov 14.
- [13] Drewes AM, Bouwense SAW, Campbell CM, Ceyhan GO, Delhaye M, Demir IE. Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatology* Sep-Oct 2017;17(5):720–31. <https://doi.org/10.1016/j.pan.2017.07.006>. Epub 2017 Jul 13.
- [14] Singh I, Vikesh K, Yadav D, Dhiraj, Garg Pramod K. Diagnosis and management of chronic pancreatitis: a review. *JAMA* 2019 Dec 24;322(24):2422–34. <https://doi.org/10.1001/jama.2019.19411>.
- [15] Olesen SS, Poulsen JL, Drewes AM, Frøkjær JB, Laukkarinen J, Parhiala M, et al. The Scandinavian Baltic Pancreatic Club (SBPC) database: design, rationale and characterisation of the study cohort. *Scand J Gastroenterol* 2017 Aug;52(8):909–15. <https://doi.org/10.1080/00365521.2017.1322138>. Epub 2017 May 4.
- [16] Schneider A, Löhr JM, Singer MV. The M-ANNHEIM classification of chronic pancreatitis: introduction of a unifying classification system based on a review of previous classifications of the disease. *J Gastroenterol* 2007 Feb;42(2):101–19. <https://doi.org/10.1007/s00535-006-1945-4>. Epub 2007 Mar 12. PMID: 17351799.
- [17] Sarner M, Cotton PB. Classification of pancreatitis. *Gut* 1984;25(7):756–9. <https://doi.org/10.1136/gut.25.7.756>.
- [18] Löhr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch, et al. HaPanEU/UEG Working Group. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *Unit Eur Gastroenterol J* 2017 Mar;5(2):153–99. <https://doi.org/10.1177/2050640616684695>. Epub 2017 Jan 16. PMID: 28344786; PMCID: PMC5349368.
- [19] Bachmann K, Tomkoetter L, Kutup A, Erbes J, Vashist Y, Mann O, Bockhorn M, Izbicki JR. Is the Whipple procedure harmful for long-term outcome in treatment of chronic pancreatitis? 15-year follow-up comparing the outcome after pylorus-preserving pancreatoduodenectomy and Frey procedure in chronic pancreatitis. *Ann Surg* 2013 Nov;258(5):815–20.
- [20] Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. *AMA Arch Surg* 1958 Jun;76(6):898–907.
- [21] Roch A, Teyssedou J, Mutter D, Marescaux J, Pessaux P. Chronic pancreatitis: a surgical disease? Role of the Frey procedure. *World J Gastrointest Surg* 2014 July 27;6(7):129–35.
- [22] Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. *Pancreas* 1987;2(6):701–7.
- [23] Ni Q, Yun L, Roy M, Shang D. Advances in surgical treatment of chronic pancreatitis. *World J Surg Oncol* 2015;13:34.
- [24] Mihaljevic AL1, Kleeff J, Friess H. Beger's operation and the Berne modification: origin and current results. *J Hepatobiliary Pancreat Sci* 2010 Nov;17(6):735–44. <https://doi.org/10.1007/s00534-009-0179-2>. Epub 2009 Oct 2.
- [25] Dutta AK, Chacko A. Head mass in chronic pancreatitis: inflammatory or malignant. *World J Gastrointest Endosc* 2015;7(3):258–64. <https://doi.org/10.4253/wjge.v7.i3.258>.
- [26] Bachmann K, Tomkoetter L, Kutup A, Erbes J, Vashist Y, Mann O, et al. Is the Whipple procedure harmful for long-term outcome in treatment of chronic pancreatitis? 15-year follow-up comparing the outcome after pylorus-preserving pancreatoduodenectomy and Frey procedure in chronic pancreatitis. *Ann Surg* 2013 Nov;258(5):815–20.
- [27] Puestow CB, Gillesby WJ. Retrograde surgical drainage of pancreas for chronic relapsing pancreatitis. *AMA Arch Surg* 1958 Jun;76(6):898–907.
- [28] Partington PF, Rochelle RL. Modified Puestow procedure for retrograde drainage of the pancreatic duct. *Ann Surg* 1960;152:1037–43.
- [29] Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. *Pancreas* 1987;2(6):701–7.
- [30] Mihaljevic AL, Kleeff J, Friess H. Beger's operation and the Berne modification: origin and current results. *J Hepatobiliary Pancreat Sci* 2010 Nov;17(6):735–44. <https://doi.org/10.1007/s00534-009-0179-2>. Epub 2009 Oct 2.
- [31] Issa Y, Kempeneers MA, Bruno MJ, Fockens P, Poley JW, Ahmed Ali U, et al.

- Effect of early surgery vs endoscopy-first approach on pain in patients with chronic pancreatitis: the ESCAPE randomized clinical trial. *JAMA* 2020 Jan 21;323(3):237–47. <https://doi.org/10.1001/jama.2019.20967>.
- [32] Parhiala M, Sand J, Laukkanen J. Surgery for chronic pancreatitis in Finland is rare but seems to produce good long-term results. *World J Clin Cases* 2021;9(35):10927–36. <https://doi.org/10.12998/wjcc.v9.i35.10927>.
- [33] Ratnayake CBB, Kamarajah SK, Bpt Loveday, Nayar M, Oppong K, White S, et al. A network meta-analysis of surgery for chronic pancreatitis: impact on pain and quality of life. *J Gastrointest Surg* 2020;24(12):2865–73. <https://doi.org/10.1007/s11605-020-04718-z>.
- [34] Kempeneers MA, Issa Y, Ali UA, Baron RD, Besselink MG, Büchleret, et al. International consensus guidelines for surgery and the timing of intervention in chronic pancreatitis. *Pancreatology* 2020;20(2):149–57. <https://doi.org/10.1016/j.pan.2019.12.005>.
- [35] Isaji S. Has the Partington procedure for chronic pancreatitis become a thing of the past? A review of the evidence. *J Hepatobiliary Pancreat Sci* 2010 Nov;17(6):763–9. <https://doi.org/10.1007/s00534-009-0181-8>. Epub 2009 Sep 25. PMID: 19779664.
- [36] Ma KW, So H, Shin E, Mok J, Yuen K, Cheung TT, Park DH. Endoscopic versus surgical intervention for painful obstructive chronic pancreatitis: a systematic review and meta-analysis. *J Clin Med* 2021;10(12):2636. <https://doi.org/10.3390/jcm10122636>.
- [37] Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med* 2007;356(7):676–84. <https://doi.org/10.1056/NEJMoa060610>.
- [38] Dite P, Ruzicka M, Zboril V, Novotný I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy* 2003;35(7):553–8. <https://doi.org/10.1002/jhbp.795>.
- [39] Siriwardena AK, Windsor J, Zyromski N, Marchegiani G, Radenkovic D, Morgan C, et al. Standards for reporting on surgery for chronic pancreatitis: a report from the international study group for pancreatic surgery (ISGPS). *Surgery* 2020;168(1):101–5. <https://doi.org/10.1016/j.surg.2020.02.007>.
- [40] Maartense S, Ledebøer M, Bemelman WA, Ringers J, Frølich M, Masclee AA. Effect of surgery for chronic pancreatitis on pancreatic function: pancreatico-jejunostomy and duodenum-preserving resection of the head of the pancreas. *Surgery* 2004 Feb;135(2):125–30. <https://doi.org/10.1016/j.surg.2003.09.004>. PMID: 14739846.
- [41] Yang CJ, Bliss LA, Schapira EF, Freedman SD, Ng SC, Windsor JA, Tseng JF. Systematic review of early surgery for chronic pancreatitis: impact on pain, pancreatic function, and re-intervention. *J Gastrointest Surg* 2014 Oct;18(10):1863–9. <https://doi.org/10.1007/s11605-014-2571-8>. Epub 2014 Jun 19. PMID: 24944153.