






ORIGINAL ARTICLE

Quality of life after endoscopic procedures for chronic pancreatitis: A multicentre study

Mikael Parhiala^{1,2}  | Camilla Nøjgaard³ | Andreas Bartholdy³ | Anne Waage⁴ | Povilas Ignatavičius⁵ | Trond Engjom⁶ | Georg Dimcevski⁶  | Ingrid Kvåle Nordaas⁶ | Evangelos Kalaitzakis⁷ | Asbjørn M. Drewes⁸ | Amer Hadi⁷  | Søren S. Olesen⁸  | Jakob L. Poulsen⁸  | Johanna Laukkarinen^{1,2} | on behalf of the Scandinavian Baltic Pancreatic Club

¹Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

²Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland

³Pancreatitis Centre East (PACE), Copenhagen University Hospital Hvidovre, Copenhagen, Denmark

⁴Department of Surgery, Oslo University Hospital, Oslo, Norway

⁵Department of Surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania

⁶Department of Gastroenterology, Haukeland University Hospital, Bergen, Norway

⁷Division of Gastroenterology, Digestive Disease Center K, Bispebjerg University Hospital, Copenhagen, Denmark

⁸Department of Gastroenterology and Hepatology, Centre for Pancreatic Diseases, Aalborg University Hospital, Aalborg, Denmark

Correspondence

Mikael Parhiala, Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Elämäntieteiden tutkimuskeskus 2, PL 2000, Tampere 33521, Finland.

Email: mikael.parhiala@fmnet.fi

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Abstract

Background: Chronic Pancreatitis (CP) causes morphological changes in the pancreatic tissue, leading to complications and pain, which may require endoscopic interventions.

Objective: Our aim was to determine the frequency of endoscopic procedures (EP) in CP patients and to analyse pain and quality of life (QoL) in these patients after their EP.

Methods: This study included 1327 CP patients from the Scandinavian Baltic Pancreatic Club (SBPC) database including four countries and eight centres. We analysed patients undergoing EPs and gathered information on the EP, pancreatic function, pain, disease and duration. The EORTC C-30 QoL questionnaire was gathered prospectively and multivariable analysis was conducted on independent parameters between the groups. The reference population had no interventions ($n = 870$).

Results: 260 CP patients (22%) underwent EPs, median one year (range 0–39 years) after CP diagnosis. 68% were males. The median age was 59 (20–90) years. Most common aetiological factors were alcohol in 65% and smoking in 71%. Extracorporeal shock wave lithotripsy (ESWL) was used in 6% of the CP population and in 21% of the EP group. Biliary duct stenting was performed on 37% and pancreatic

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stenting was performed on 56% of the patients. There was no difference in pain patterns between patients who had pancreatic stenting and the reference population. The EP group had slightly better QoL ($p = 0.047$), functioning and fewer symptoms than the reference population, in the multivariable analysis there was no interaction effect analysis between the groups. The pancreatic stent group had better QoL and the same amount of pain than the reference group. The patients who needed later surgery (23%) had more pain ($p = 0.043$) and fatigue ($p = 0.021$).

Conclusions: One in five of the CP patients underwent EP. These patients scored higher on QoL responses and had better symptom scores. CP patients who had pancreatic stenting performed had the same pain patterns as the reference population. Randomised prospective trials are needed to determine the effect of endoscopy procedures on CP patients.

KEYWORDS

biliary stent, chronic pancreatitis, endoscopic retrograde cholangiopancreatography, extracorporeal shock wave lithotripsy, pancreatic stent, quality of life

INTRODUCTION

Persistent inflammation in chronic pancreatitis (CP) may lead to morphological changes in the pancreatic tissue causing ductal abnormalities, pancreatic fibrosis, pseudocysts and biliary obstruction. These changes may contribute to the development of chronic pain. Conservative management of CP includes patient education to avoid risk factors such as alcohol and smoking, pain management and treatment of pancreatic endocrine and exocrine insufficiency.¹⁻³

Invasive interventions are often needed to treat pain and complications such as biliary or pancreatic duct obstruction or pseudocysts and involve both endoscopic and surgical procedures. Endoscopic procedures (EP) may include pancreatic or bile duct dilation and stenting via ERCP (endoscopic retrograde cholangiopancreatography). Currently a stepwise approach is preferred, with endoscopy being a first- in-line treatment because of the vast range of possible treatment options and being less invasive and permanent than surgery.⁴⁻⁶ Estimates of frequency vary widely but studies show that 27%–76% of CP patients undergo EP,⁷⁻⁹ with a decline in procedures in the last 20 years due a rise in sensitive imaging modalities replacing ERCP.^{10,11}

EPs have been shown to provide pain relief with varying effect (36%–80%).¹²⁻¹⁵ Furthermore, CP and its complications impair quality of life (QoL), causing a chronic burden on the patient and the healthcare system.^{8,16,17} It is important from the patient's perspective to ascertain QoL status in CP patients needing endoscopic procedures for CP related complications and pain compared to CP patients in whom conservative treatment suffices. There are no studies as far we know where QoL is evaluated in CP patients needing endoscopy compared to patients not needing invasive treatments.

Our aim was to study the QoL and pain of CP patients after EP in a large population of CP patients reflecting real-world clinical practice. QoL in the CP cohort was measured once.

Key summary

Summarise the established knowledge on this subject

- Invasive interventions are often needed to treat chronic pancreatitis (CP) related complications and pain.
- Quality of life (QoL) and pain in CP patients after endoscopic procedures (EP) are not well described.

What are the significant and/or new findings of this study?

- Endoscopic procedures are extremely common (over 20%) in CP patients.
- QoL was better in CP patients with EPs, compared to the reference CP population.
- CP patients with EPs did not experience more pain compared to the reference CP population.
- More prospective studies are needed to determine the effect of EP on pain and QoL.

METHODS

This was cross-sectional multicentre study including data from the Scandinavian Baltic Pancreas Club (SBPC) database.¹⁸ The data were collected from 11th of January 2011 and extracted in 26th of November 2019. The study included eight centres in Europe (Finland, Norway, Denmark and Lithuania). We included patients meeting the M-ANNHEIM probable or definitive diagnostic criteria for CP.¹⁹ The baseline cohort comprised of 1327 patients; patients undergoing EP were identified from the baseline cohort ($n = 260$) and compared to patients who did not undergo and EP ($n = 870$) after exclusion of patients with missing procedural data and patients undergoing direct surgery without prior EP ($n = 197$) (Figure 1).

The data were collected by the respective centres and we also separately acquired data on the type and year of EP and the number of procedures performed. We also gathered data on pancreatic function, EPs, QoL, pain and CP aetiology. Exocrine pancreatic insufficiency (EPI) was screened for either by faecal fat collection, faecal elastase-1, or a C13 mixed triglyceride breath test. EPI was determined by reference to the United European Gastroenterology guidelines.²⁰ Endocrine insufficiency was defined using the American Diabetes Association classification for diabetes.²¹

QoL and symptoms were measured prospectively using the EORTC (European Organisation for Research and Treatment of Cancer) QLQ-C30 questionnaire. The QLQ-C30 is a 30-item questionnaire originally designed for cancer patients but also validated for CP patients.²² The EORTC QLQ-C30 is composed of the following 15 scales: Global health status/QoL and five functional scales: physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning and nine symptom scales: fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties.

We used the EORTC scoring manual for the QLQ-C30 questionnaires and responses were scored from 0 to 100. In the QoL and functioning scores, a higher score was taken to represent better QoL while for the symptoms score a lower score reflected fewer symptoms.

Ethical aspects

The study follows the ethical principles of the Declaration of Helsinki.²³ The study was approved by the Ethics Committee of Tampere University Hospital, Finland (Ethical committee code R15187). Each participating centre obtained approval from their local institutional

review boards. All the patients participating in this study had an informed written consent signed.

Statistical analyses

Unless otherwise specified, data are presented as medians (range) and the EORTC QLQ-C30 response scores are presented as means (SD). We used Pearson's exact test for categorical variables. The analysis of the normally distributed continuous variables was done using linear regression (EORTC QLQ-C30 Global health status/QoL) and Mann Whitney *U* test was used for non-normally distributed variables (The remaining EORTC QLQ-C30 parameters).

A multivariable analysis was conducted using a hierarchical regression analysis model. The Multivariable analysis was conducted separately for all quality of life variables, with the following independent variables: aetiology (alcohol, smoking, efferent duct and hereditary pancreatitis), age, disease duration, gender and pain. We measured the interaction effect of the variables using the R^2 -changes value. An R^2 -value of 0.01 was considered to affect the outcome by 1%. IBM SPSS® (Armonk, NY, USA) version 28 was used for the statistical analyses. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

The final study cohort comprised of 1130 patients of whom 260 patients (23%) had undergone EP(s) and 870 (77%) were conservatively managed (Figure 1). The data were registered a median one (0–39) year after the first EP. The EP group had a median age of 59 years (20–90) and 68% were male. The median BMI was 22.9 (15–48), similar to that

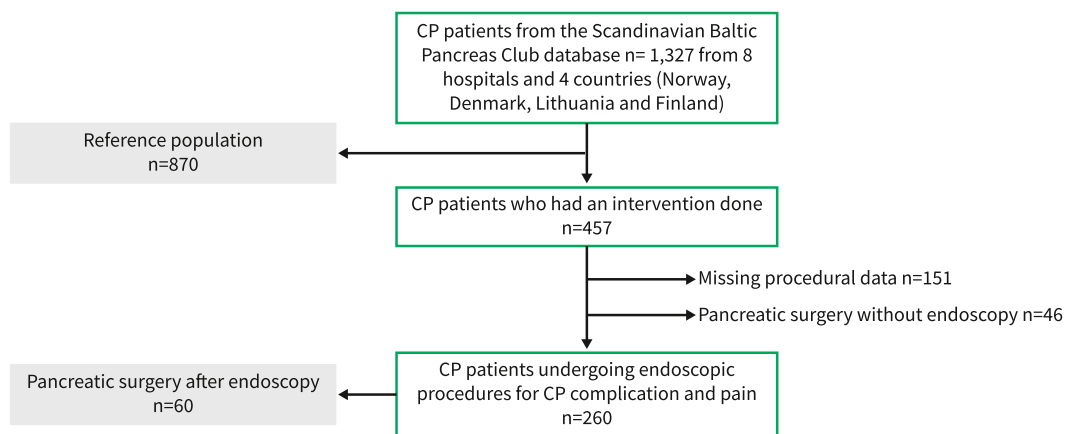


FIGURE 1 Flowchart of chronic pancreatitis (CP) endoscopy patients. The data were gathered from the Scandinavian Baltic Pancreas Club database and details concerning endoscopic procedures were collected separately. The final study group was formed of CP patients undergoing endoscopy for pancreatic complications or pain $n = 260$.

of the reference CP population. The median disease duration was 4 years (0–41) years. Patient characteristics are presented in Table 1.

Aetiology

In the EP group the most common aetiological risk factors were excessive alcohol consumption (65%) and smoking (71%), which were equally distributed among patients with and without EP. Efferent duct obstruction was more common in the EP patients (14% vs. 10%, $p < 0.001$) while hereditary pancreatitis was more common in the reference population (3.8% vs. 9.7%, $p = 0.003$) (Table 1).

Endoscopic procedures

Multiple EPs were performed in 44% ($n = 115$). Pancreatic stenting was performed in 56% ($n = 146$) and 72% of the patients had multiple pancreatic stenting procedures (median 2) (Table 2). We do not have data on the type of pancreatic stents used.

Biliary stenting was done in 37% ($n = 97$) of the EP patients. Pancreatic and biliary stenting were both performed in 13% ($n = 34$). Plastic biliary stents were used on 57%, metals stents 14% and both stents in 29%. Of the patients undergoing biliary stenting, 55% needed multiple biliary stents (median 2).

Endoscopic pseudocyst drainage was performed in 32% and percutaneous drainage in 8% of patients. Extracorporeal shock wave lithotripsy (ESWL) was used in 6% of the CP population and in 21% of the EP group.

Twenty-three per cent ($n = 60$) of the EP patients underwent pancreatic surgery later, median one (0–11) year after their first EP. These included 49% duodenum preserving pancreatic head resections (e.g. Frey procedure), 34% pancreatic resections (e.g. pancreaticoduodenectomy) and 17% drainage procedures (e.g. Puestow). Patients who did not have EP prior to surgery were omitted from the analysis. Of these 13% had duodenum preserving pancreatic head resections, 43% pancreatic resections and 13% drainage procedures.

The indication for surgery was pain in 57%, suspicion of malignancy in 13%, complication in 18% and 12% was unknown. The indications for patients with no EP before surgery were pain in 33%, suspicion of malignancy 26%, complications in 39% and finally 2% had an unknown indication.

Demographic details of patients needing EP and later pancreatic surgery are presented in Table 3.

Pain

After the EP, 42% of the patients were pain-free, 42% had intermittent pain and 17% constant pain. In the reference population

TABLE 1 Demographic of chronic pancreatitis patients who underwent endoscopic procedures.

Demographic	CP endoscopic group $n = 260$	CP reference population $n = 870$	p -value
Females/Males	32%/68%	33%/67%	0.729
Age (range)	59 (20–90) years	60 (18–89) years	0.221
BMI (range)	22.9 (15–48)	22.8 (13–46)	0.585
Time after diagnosis (range)	4 (0–41) years	2 (0–39) years	<0.001
Aetiology			
Alcohol	65.3%	60.3%	0.145
Nicotine	71.0%	68.0%	0.369
Nutritional	2.4%	3.9%	0.272
Hereditary	3.8%	9.7%	0.004
Efferent duct	14.0%	7.3%	<0.001
Immunological	2.4%	2.8%	0.734
Unknown	6.3%	6.5%	0.882
Pancreatic calcification	77.2%	67.3%	0.003
Pancreatic duct stones	48.7%	33.7%	0.003
Main duct dilation	73.2%	48.1%	<0.001
Pseudocysts	53.7%	35.1%	<0.001
Exocrine pancreatic insufficiency	61.5%	53.2%	0.020
Endocrine insufficiency	45.4%	40.1%	0.152

Note: The reference population consisted of chronic pancreatitis patients without interventions from the baseline population. Bold values are statistically significant ($p > 0.05$).

TABLE 2 Procedural demographic of endoscopic procedures done on chronic pancreatitis patients from the Scandinavian Baltic Pancreatic Club database.

	CP interventions <i>n</i> = 260	%	How many times median (range)
Biliary duct stenting	97	37%	2 (1–33)
Only plastic stents	51	57%	
Only metal stents	13	14%	
Both stents	26	29%	
Pancreatic duct stenting	146	56%	2 (1–24)
Both stenting	34	13%	
Spyglass EHL	1	0.4%	
ESWL	54	21%	
Endoscopic pseudocyst drainage	84	32%	1 (1–4)
Percutaneous pseudocyst drainage	20	7.7%	1 (1–7)
Had multiple endoscopic procedures	115	44%	2 (1–42)
Had later pancreatic surgery	60	23%	

TABLE 3 Clinical characteristics of chronic pancreatitis patients who had endoscopic procedures done and later pancreatic surgery.

	Surgery <i>n</i> = 60	No surgery <i>n</i> = 200	<i>p</i> -value
Pancreatic duct stenting	59%	57%	0.752
Multiple pancreatic stenting	48%	38%	0.330
Bile duct stenting	23 (44%)	67 (37%)	0.339
Both metal and plastic stent	4 (17%)	22 (33%)	0.159
Plastic stent	23 (100%)	54 (81%)	0.022
Metallic stent	4 (17%)	35 (52%)	0.004
ESWL	4 (7%)	50 (25%)	0.002
Calcification	82%	76%	0.397
Main duct dilation	64%	76%	0.094
Pseudocysts	40%	61%	0.012
Alcohol	65%	66%	0.927
Nicotine	58%	75%	0.018
Idiopathic pancreatitis	26%	2%	<0.001

Note: Bold values are statistically significant ($p < 0.05$).

there were more pain-free patients ($p = 0.008$) and less intermittent pain patients ($p = 0.035$).

Data on pain medication was available in 39% of the EP group and 44% of the reference population. Among EP patients, 31% used opioids which was more than in the reference population 13% ($p < 0.001$) while the proportions of patients without any pain medication were similar (60% vs. 63%, $p = 0.354$).

Out of the EP group, the patients who had pancreatic duct stenting performed had more opioid usage (26% vs. 13%, $p = 0.004$) than the reference population but there was no difference in pain patterns. Both groups had the same number of patients without pain medication (Table 4).

Quality of life

The EORTC QLQ-C30 QoL questionnaire results were available from 128 (49% of EP group) EP patients. The questionnaires were completed a median 4 years after their first intervention. We excluded patients who also had pancreatic surgery ($n = 32$), resulting in 96 (37% of the EP group) patients who were analysed in the final group.

The reference population here consisted of 382 (44%) patients who completed the EORTC QLQ-C30 questionnaire a median of two^{1–39} years after their diagnosis. The two groups did not differ in age, sex, alcohol or by aetiology but the reference population had a shorter disease duration ($p < 0.001$) and more smoking ($p = 0.029$).

TABLE 4 Outcomes of pancreatic duct stenting for chronic pancreatitis patients.

	Patients who had pancreatic stenting	CP reference population	p-value
	n = 128	n = 714	
Constant pain	13%	14%	0.852
Intermittent pain	40%	34%	0.172
Painless	47%	52%	0.251
	n = 73	n = 385	
Opioids	26%	13%	0.004
No pain medication	65%	63%	0.668

Note: Bold values are statistically significant ($p < 0.05$).

The EP group had a slightly better QoL (57 vs. 51, $p = 0.047$) and also better role, emotional and cognitive functioning responses (average 70 vs. 62 $p = 0.035$, 74 vs. 68 $p = 0.043$ and 77 vs. 71 $p = 0.046$ respectively) compared to the reference population. The CP reference population suffered more fatigue and appetite loss than the EP group (48 vs. 40, $p = 0.036$; and 36 vs. 27 $p = 0.045$ respectively) (Figure 2a).

In a separate analysis smoking affected QoL results but it did not have a statistically significant interaction effect between the two groups ($p = 0.905$). Disease duration did not affect QoL nor did it have a statistically significant effect between the groups ($p = 0.680$), the same was found for alcohol ($p = 0.334$), hereditary ($p = 0.898$), efferent duct aetiology ($p = 0.120$). When a multivariate analysis of the following variables was conducted, alcohol, smoking, hereditary, efferent duct pancreatitis, gender, age, disease duration or constant pain, all interaction effects ranged from 0% to 2%. Patients with painless pancreatitis had a 4.5% ($p = 0.001$) percent positive interaction with QoL towards the reference population (Supplementary material S1).

Among CP patients who had subsequently undergone pancreatic surgery after their EP, and thus were excluded from the original analysis, QoL was also analysed as a subgroup ($n = 32$). The questionnaires were completed a median three¹⁻¹⁶ years after surgery. They had worse QoL, functioning responses and more symptoms than the EP patients who did not have surgery ($n = 96$), but only pain ($p = 0.043$), financial difficulties ($p = 0.041$) and fatigue ($p = 0.021$) responses reached statistical significance (Figure 2b).

EP patients who had multiple endoscopic procedures ($n = 45$) compared to one procedure ($n = 51$) had the same QoL, functioning score and symptom scores. The patients who had pancreatic duct stenting performed had slightly better QoL ($p = 0.032$) but functioning and symptoms scores were the same as the reference population (Figure S1).

DISCUSSION

The present study including a large number of patients with CP gives input regarding QoL and pain scores. In our study population, one in five of the CP patients underwent EP and these patients scored higher on QoL responses and had better symptom scores.

We also found that CP patients on whom pancreatic stenting had been performed had the same pain patterns as the reference CP population.

Quality of life

Patients with CP undergo a variety of procedures for pain and management of complications. In our study, the EP patients' group had more morphological changes in the pancreatic tissue, which was as expected as these can contribute to abdominal complications and pain and also prolong the inflammation, thus increasing likelihood of need for EP.²⁴ Even though pancreatic complications impaired the patients' QoL, we found that patients who underwent EP for pancreatic complications had better global QoL, functioning and fewer symptoms than the reference population.^{16,17,25}

CP patients needing EP had better global QoL and better functioning and fewer symptoms than the reference population even though pancreatic complications impaired QoL. In 2021 Han et al. published a systematic review of QoL after EPs showing that EPs improve QoL.²⁶ Thirteen studies were analysed, most of them focussing on pancreatic duct stenting combined with ESWL. In our study we included biliary stenting (37%) and pseudocyst drainage (32%). We found that CP patients who underwent EP had slightly better function and fewer symptoms.

Patients with EP and later pancreatic surgery (23%) had worse outcomes on all EORTC C-30 parameters, but only pain, fatigue and financial difficulties were statistically significant. In our earlier study CP patients who underwent surgery for CP related pain had better outcomes if they did not have prior EP.²⁷ This could be due to delayed surgery because of prior endoscopic procedures. Hence, it is important to identify those patients likely to benefit from endoscopy or need early surgery for CP as earlier studies have shown that early surgery yields good results in relieving pain.^{13,28}

We cannot truly know why the EP group had better QoL than the patients needing no interventions. This could be because of patients being content that their pain and symptoms subsided due to the endoscopic procedures. Generally, only symptomatic patients should be treated and it may be that there are symptomatic CP patients

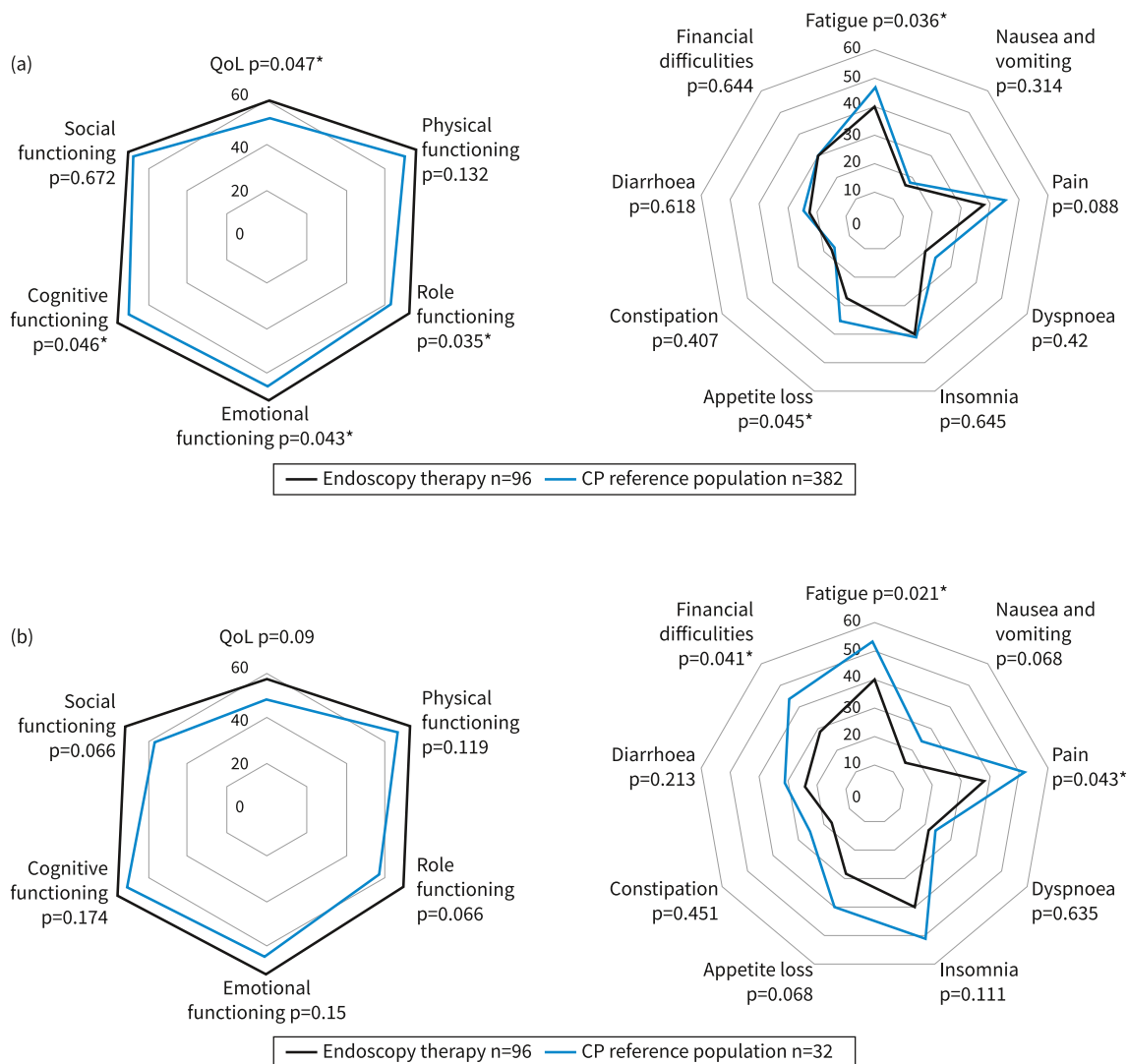


FIGURE 2 (a) EORTC QLQ-C30 quality of life of chronic pancreatitis (CP) patients who underwent endoscopic procedures had slightly better cognitive, emotional and role functioning and less appetite loss and fatigue the CP reference population. (b) When comparing CP patients who had later pancreatic surgery after endoscopic procedures, the surgical group had more fatigue, pain and financial difficulties. A higher score in QoL/functioning represents a better score. A lower score in symptoms represents a better score.

lacking adequate treatment. Another possible reason for EP patients having better QoL, is that patients who undergo endoscopic procedures may have a better relationship with pancreatologists, possibly leading to better treatment and improved abstinence from alcohol and smoking.²⁹

Pancreatic stenting and pain

The most prominent symptom of CP is chronic abdominal pain.¹⁷ CP-related pain is one of the main challenges in the treatment of CP. Conventionally it has been assumed that ductal pressure was higher in patients with pain, but it is now known that the mechanisms behind pain are more complex, involving factors such as inflammation, ischaemia, opioid hyperalgesia as well as peripheral and central sensitization of the nervous system.³⁰

In our study population most (60%) of the endoscopic procedures were pancreatic duct stenting. Symptomatic pancreatic strictures, duct stones and pancreatic leaks can be treated with endoscopic pancreatic duct stenting.³¹ Pancreatic duct stenting can offer pain relief in duct strictures in up to 90% in the short term, but in the long-term surgery may yield a better result.^{28,32,33}

Even though the EP patients used more opioids than the reference population, the number of patients with constant pain was the same as that in the reference population. In a recent study it was found that pain was independent on disease duration but did seem to decrease over time, probably due to medical treatment and interventions.³⁴ Endoscopic treatment alone does not seem to suffice for pain management but should be combined with appropriate pain medication.

Approximately 90% of CP patients have abdominal pain at some point during the course of the disease. We found that approximately

half of the patients undergoing pancreatic duct stenting were pain-free, which was approximately the same as reported in earlier studies and in our reference group (Table 4).^{35,36} However, in the EP group (31%) and the pancreatic stenting subgroup (26%), there was more opioid usage than in the reference group (13%).

There was no difference in pain response among patients needing multiple pancreatic stents compared to patients who had one pancreatic stent, which is reassuring as most patients needed multiple procedures. It should be noted, however, that any intervention will have a major effect on pain, and this is being explored in an ongoing study comparing EP + ESWL with sham interventions.^{37,38}

Plastic stents are habitually used for pancreatic duct strictures, which are either straight or more anatomically shaped S-model.⁵ In some cases, a self-expanding covered metal stent can be used in the pancreatic duct but seems to have a higher stent migration rate.³⁹

Other endoscopic procedures

Larger (over 5 mm) pancreatic obstructive stones can be treated with ESWL which can be combined with ERCP. In our study one in five CP patients undergoing ERCP had ESWL performed and approximately 30% of those undergoing ESWL had no ERCP. Patients with EWSL underwent less pancreatic surgery, which could be due to clinical differences and availability of ESWL in the treatment of calcific pancreatic masses. ESWL and ERCP in combination should be taken into account as an alternative to surgery in suitable patients with a calcific pancreatic mass if malignancy can be reliably ruled out.⁴⁰ An emerging alternative to ESWL is pancreatoscopy guided intraductal lithotripsy which has shown promising results.⁴¹

Nearly 40% of patients in the EP group and 7% of the whole CP population needed biliary stenting. CP-related benign biliary strictures can be treated with multiple plastic stents or self-expanding metal stents. Generally multiple procedures are needed for an optimal result.⁴² In our study half of the patients needed more than one stenting procedure; 57% had plastic stents and 14% metal stents and in 29% both stents were used (Table 2). Patients with metal biliary stents were less likely to undergo pancreatic surgery (Table 3).

Pseudocyst drainage is common in CP patients; one third of the EP patients in our group had endoscopic transmural drainage and 8% had percutaneous drainage. Pseudocysts were more common in the EP population than in the reference CP population. Also the EP group undergoing pancreatic surgery (Table 3) had fewer pseudocysts this could be due to recently developed techniques for endoscopic treatment of pseudocysts leading to a decrease in the need of surgical interventions in the treatment of pseudocysts. Only symptomatic pseudocysts should be treated. Symptoms may include pain, infection, obstruction, fistulas or bleeding.⁴³

This study is a multicentre cohort study from Northern Europe and provides an important overview of CP patients' long-term QoL and opioid use after endoscopic procedures. The SBPC is the largest registry on CP. A weakness of this study is that we did not have

enough data on QoL, pain and opioid use before EPs. Also, a majority of patients in the reference (68%) and EP (61%) were missing data on pain medication. Consequently, this only provides information on EP patients compared to CP patients with no EPs. The reference population is problematic as conservatively managed patients most likely differ from patients needing endoscopy, yet in our multivariable analysis we still found no significant differences affecting the EORTC QLQ-C30 analysis. Even though CP patients have a low QoL associated with complications and lifestyle, pancreatic morphology does not correlate with QoL, which should be taken into account when choosing invasive endoscopic procedures.⁴⁴

CONCLUSION

At least one in five CP patients needed EP for CP-related complications. Despite this, they did not seem to have lower QoL, but may even have better functioning QoL and fewer symptoms than reference CP population. There was no difference in pain patterns in patients who underwent pancreatic duct stenting compared to the reference population. It seems that CP patients who undergo EP have improved QoL, still a substantial number of the patients need later surgery. Prospective randomised clinical trials are needed on the effect of EPs on QoL in CP patients and to determine which patients need early surgical intervention and for which patients EP procedures suffice.

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CONFLICT OF INTEREST STATEMENT

Drs. Mikael Parhiala, Camilla Nøjgaard, Andreas Bartholdy, Anne Waage, Povilas Ignatavičius, Engjom Trond, Georg Dimcevski, Ingrid Kvåle Nordaas, Evangelos Kalaitzakis, Asbjørn M Drewes, Amer Hadi, Søren S Olesen, Jakob L Poulsen and Johanna Laukkarinen have no conflicts of interest or financial ties to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author (Mikael Parhiala) upon reasonable request.

ORCID

Mikael Parhiala  <https://orcid.org/0000-0002-5189-2251>

Georg Dimcevski  <https://orcid.org/0000-0003-2864-5129>

Amer Hadi  <https://orcid.org/0000-0002-9481-6021>

Søren S. Olesen  <https://orcid.org/0000-0003-3916-3168>

Jakob L. Poulsen  <https://orcid.org/0000-0002-0251-6049>

REFERENCES

- Singh VK, Yadav D, Garg PK. Diagnosis and management of chronic pancreatitis: a review. *JAMA*. 2019;322(24):2422–34. <https://doi.org/10.1001/jama.2019.19411>
- Löhr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al. HaPanEU/UEG Working Group. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United Eur Gastroenterol J*. 2017;5(2):153–99. Epub 2017 Jan 16. PMID: 28344786; PMCID: PMC5349368. <https://doi.org/10.1177/2050640616684695>
- Ashraf H, Colombo JP, Marcucci V, Rhoton J, Olowoyo O. A clinical overview of acute and chronic pancreatitis: the medical and surgical management. *Cureus*. 2021;13(11):e19764. PMID: 34938639; PMCID: PMC8684888. <https://doi.org/10.7759/cureus.19764>
- Dumonceau JM, Delhaye M, Tringali A, Arvanitakis M, Sanchez-Yague A, Vaysse T, et al. Endoscopic treatment of chronic pancreatitis: European society of gastrointestinal endoscopy (ESGE) guideline - updated August 2018. *Endoscopy*. 2019;51(2):179–93. Epub 2019 Jan 17. PMID: 30654394. <https://doi.org/10.1055/a-0822-0832>
- Udd M, Kylänpää L, Kokkola A. The role of endoscopic and surgical treatment in chronic pancreatitis. *Scand J Surg*. 2020;109(1):69–78. PMID: 32192421. <https://doi.org/10.1177/1457496920910009>
- Drewes AM, Bouwense SAW, Campbell CM, Ceyhan GO, Delhaye M, Demir IE, et al. Working group for the International (IAP – APA – JPS – EPC) Consensus Guidelines for Chronic Pancreatitis. Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatol*. 2017;17(5):720–31. Epub 2017 Jul 13. PMID: 28734722. <https://doi.org/10.1016/j.pan.2017.07.006>
- Rutter K, Ferlitsch A, Sautner T, Püspök A, Götzinger P, Gangl A, et al. Hospitalization, frequency of interventions, and quality of life after endoscopic, surgical, or conservative treatment in patients with chronic pancreatitis. *World J Surg*. 2010;34(11):2642–7. PMID: 20645098. <https://doi.org/10.1007/s00268-010-0713-z>
- Parhiala M, Sand J, Laukkanen J. A population-based study of chronic pancreatitis in Finland: effects on quality of life. *Pancreatol*. 2020;20(3):338–46. Epub 2020 Feb 21. PMID: 32147309. <https://doi.org/10.1016/j.pan.2020.02.005>
- Clark CJ, Fino NF, Clark N, Rosales A, Mishra G, Pawa R. Trends in the use of endoscopic retrograde cholangiopancreatography for the management of chronic pancreatitis in the United States. *J Clin Gastroenterol*. 2016;50(5):417–22. <https://doi.org/10.1097/MCG.0000000000000493>
- Parakh A, Tirkes T. Advanced imaging techniques for chronic pancreatitis. *Abdom Radiol (NY)*. 2020;45(5):1420–38. PMID: 31428813; PMCID: PMC7028513. <https://doi.org/10.1007/s00261-019-02191-0>
- Swensson J, Akisik F, Collins D, Olesen SS, Drewes AM, Frøkjær JB. Is Cambridge scoring in chronic pancreatitis the same using ERCP and MRCP? A need for revision of standards. *Abdom Radiol (NY)*. 2021;46(2):647–54. Epub 2020 Aug 1. PMID: 32740862. <https://doi.org/10.1007/s00261-020-02685-2>
- Mendieta PJO, Sagae VMT, Ribeiro IB, de Moura DTH, Scatimburgo MVCV, Hirsch BS, et al. Pain relief in chronic pancreatitis: endoscopic or surgical treatment? a systematic review with meta-analysis. *Surg Endosc*. 2021;35(8):4085–94. Epub 2021 May 4. PMID: 33948714. <https://doi.org/10.1007/s00464-021-08515-w>
- Issa Y, Kempeneers MA, Bruno MJ, Fockens P, Poley JW, Ahmed Ali U, et al. Dutch pancreatitis study group. Effect of early surgery vs endoscopy-first approach on pain in patients with chronic pancreatitis: the ESCAPE randomized clinical trial. *JAMA*. 2020;323(3):237–47. PMID: 31961419; PMCID: PMC6990680. <https://doi.org/10.1001/jama.2019.20967>
- Lee SH, Kim YS, Kim EJ, Lee HS, Park JY, Park SW, et al. Long-term outcomes of fully covered self-expandable metal stents versus plastic stents in chronic pancreatitis. *Sci Rep*. 2021;11(1):15637. Published 2021. <https://doi.org/10.1038/s41598-021-94726-z>
- Sofi AA, Khan MA, Ahmad S, Khan Z, Peerzada MM, Sunguk J, et al. Comparison of clinical outcomes of multiple plastic stents and covered metal stent in refractory pancreatic ductal strictures in chronic pancreatitis- a systematic review and meta-analysis. *Pancreatol*. 2021;21(5):854–61. <https://doi.org/10.1016/j.pan.2021.03.017>
- Machicado JD, Amann ST, Anderson MA, Abberbock J, Sherman S, Conwell DL, et al. Quality of life in chronic pancreatitis is determined by constant pain, disability/unemployment, current smoking, and associated Co-morbidities. *Am J Gastroenterol*. 2017;112(4):633–42. Epub 2017 Feb 28. PMID: 28244497; PMCID: PMC5828017. <https://doi.org/10.1038/ajg.2017.42>
- Olesen SS, Juel J, Nielsen AK, Frøkjær JB, Wilder-Smith OH, Drewes AM. Pain severity reduces life quality in chronic pancreatitis: implications for design of future outcome trials. *Pancreatol*. 2014;14(6):497–502. Epub 2014 Oct 7. PMID: 25455540. <https://doi.org/10.1016/j.pan.2014.09.009>
- Olesen SS, Poulsen JL, Drewes AM, Frøkjær JB, Laukkanen J, Parhiala M, et al. The Scandinavian Baltic Pancreatic Club (SBPC) database: design, rationale and characterisation of the study cohort. *Scand J Gastroenterol*. 2017;52(8):909–15. Epub 2017 May 4. <https://doi.org/10.1080/00365521.2017.1322138>
- 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;42(2):101–19. Epub 2007 Mar 12. PMID: 17351799. <https://doi.org/10.1007/s00535-006-1945-4>
- Löhr JM, Dominguez-Munoz E, Rosendahl J, Besselink M, Mayerle J, Lerch MM, et al. HaPanEU/UEG Working Group. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United Eur Gastroenterol J*. 2017;5(2):153–99. Epub 2017 Jan 16. PMID: 28344786; PMCID: PMC5349368. <https://doi.org/10.1177/2050640616684695>
- American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2019. *Diabetes Care*. 2019;42(Suppl1):S13–28. <https://doi.org/10.2337/dc19-S002>
- Fitzsimmons D, Kahl S, Butturini G, van Wyk M, Bornman P, Bassi C, et al. Symptoms and quality of life in chronic pancreatitis assessed by structured interview and the EORTC QLQ-C30 and QLQ-PAN26. *Am J Gastroenterol*. 2005;100(4):918–26. <https://doi.org/10.1111/j.1572-0241.2005.40859.x>
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–4. <https://doi.org/10.1001/jama.2013.281053>
- Drewes AM, Bouwense SAW, Campbell CM, Ceyhan GO, Delhaye M, Demir IE, et al. Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatol*. 2017;17(5):720–31. Epub 2017 Jul 13. <https://doi.org/10.1016/j.pan.2017.07.006>
- Olesen SS, Nøjgaard C, Novovic S, Jensen NM, Nørregaard P, Dahl EE, et al. Pain and aetiological risk factors determine quality of life in patients with chronic pancreatitis, but a brick in the puzzle is missing. *Pancreatol*. 2020;20(7):1347–53. Epub 2020 Sep 10. PMID: 32948. <https://doi.org/10.1016/j.pan.2020.09.004>
- Han SY, Papachristou GI, Shah RJ, Conwell DL. Effect of pancreatic endotherapy on quality of life in chronic pancreatitis patients: a systematic review. *World J Gastrointest Endosc*. 2021;13(8):336–55. <https://doi.org/10.4253/wjge.v13.i8.336>
- Parhiala M, Waaga A, Ignatavičius P, Olesen SS, Poulsen JL, Trond E, et al. Surgical strategies for chronic pancreatitis in a 1,327- patient

- Scandinavian Baltic pancreatic Club (SBPC) register. *Pancreatology*. 2023;23(1):28–34. <https://doi.org/10.1016/j.pan.2022.12.004>
28. Boregowda U, Echavarría J, Umopathy C, Rosenkranz L, Sayana H, Patel S, et al. Endoscopy versus early surgery for the management of chronic pancreatitis: a systematic review and meta-analysis. *Surg Endosc*. 2022;36(12):8753–63. Epub ahead of print. PMID: 35922602. <https://doi.org/10.1007/s00464-022-09425-1>
29. Srivoleti P, Yang AL, Jin DX, Banks PA, McNabb-Baltar J. Provider type influences adherence to lifestyle changes in chronic pancreatitis. *Pancreatology*. 2021;21(1):42–5. <https://doi.org/10.1016/j.pan.2020.11.021>
30. Talukdar R, Reddy DN. Pain in chronic pancreatitis: managing beyond the pancreatic duct. *World J Gastroenterol*. 2013;19(38):6319–28. <https://doi.org/10.3748/wjg.v19.i38.6319>
31. Han S, Attwell AR, Tatman P, Edmundowicz SA, Hammad HT, Wagh MS, et al. Adverse events associated with therapeutic endoscopic retrograde pancreatography. *Pancreas*. 2021;50(3):378–85. PMID: 33835969; PMCID: PMC8041157. <https://doi.org/10.1097/MPA.0000000000001769>
32. Shah BB, Rodge GA, Goenka U, Afzalpurkar S, Goenka MK. A prospective study of fully covered self-expandable metal stents for refractory benign pancreatic duct strictures. *Clin Endosc*. 2022;55(6):793–800. Epub ahead of print. PMID: 35368176.1157. <https://doi.org/10.5946/ce.2021.211>
33. Tringali A, Bove V, Vadalà di Prampero SF, Boškoski I, Familiari P, Perri V, et al. Long-term follow-up after multiple plastic stenting for refractory pancreatic duct strictures in chronic pancreatitis. *Endoscopy*. 2019;51(10):930–5. Epub 2019 Aug 2. PMID: 31378858. <https://doi.org/10.1055/a-0959-6163>
34. Vipperla K, Kanakis A, Slivka A, Althouse AD, Brand RE, Phillips AE, et al. Natural course of pain in chronic pancreatitis is independent of disease duration. *Pancreatology*. 2021;21(3):649–57. Epub 2021 Feb 2. PMID: 33674197. <https://doi.org/10.1016/j.pan.2021.01.020>
35. Bhullar FA, Faghieh M, Akshintala VS, Ahmed AI, Lobner K, Afghani E, et al. Prevalence of primary painless chronic pancreatitis: a systematic review and meta-analysis [published correction appears in *Pancreatology*]. *Pancreatology*. 2022;22(1):20–9. <https://doi.org/10.1016/j.pan.2021.11.006>
36. Shalimar, Midha S, Hasan A, Dhingra R, Garg PK. Long-term pain relief with optimized medical treatment including antioxidants and step-up interventional therapy in patients with chronic pancreatitis. *J Gastroenterol Hepatol*. 2017;32(1):270–7. <https://doi.org/10.1111/jgh.13410>
37. Drewes AM, Kempeneers MA, Andersen DK, Arendt-Nielsen L, Besselink MG, Boermeester MA, et al. Controversies on the endoscopic and surgical management of pain in patients with chronic pancreatitis: pros and cons!. *Gut*. 2019;68(8):1343–51. <https://doi.org/10.1136/gutjnl-2019-318742>
38. Olesen SS, Drewes AM, Gaud R, Tandan M, Lakhtakia S, Ramchandani M, et al. Combined extracorporeal shock wave lithotripsy and endoscopic treatment for pain in chronic pancreatitis (SCHOKE trial): study protocol for a randomized, sham-controlled trial. *Trials*. 2020;21(1):338. Published 2020 Apr 16. <https://doi.org/10.1186/s13063-020-04296-0>
39. Sherman S, Kozarek RA, Costamagna G, Reddy DN, Tarnasky P, Shah RJ, et al. Soft self-expandable metal stent to treat painful pancreatic duct strictures secondary to chronic pancreatitis: a prospective multicenter trial. *Gastrointest Endosc*. 2023;97(3):472–81. e3. <https://doi.org/10.1016/j.gie.2022.09.021>
40. Geusens D, van Malenstein H. The role of extracorporeal shock wave lithotripsy in the treatment of chronic pancreatitis. *Acta Gastroenterol Belg*. 2021;84(4):620–6. <https://doi.org/10.51821/84.4.027>
41. de Rijk FEM, Stassen PMC, van der Wiel SE, Boermeester MA, Issa Y, Kempeneers MA, et al. Long-term outcomes of pancreatoscopy-guided electrohydraulic lithotripsy for the treatment of obstructive pancreatic duct stones. *Endosc Int Open*. 2023;11(3):E296–304. Published 2023 Mar 24. <https://doi.org/10.1055/a-2035-8969>
42. Hu B, Sun B, Cai Q, Wong Lau JY, Ma S, Itoi T, et al. Asia-Pacific consensus guidelines for endoscopic management of benign biliary strictures. *Gastrointest Endosc*. 2017;86(1):44–58. <https://doi.org/10.1016/j.gie.2017.02.031>
43. Kitano M, Gress TM, Garg PK, Itoi T, Irisawa A, Isayama H, et al. International consensus guidelines on interventional endoscopy in chronic pancreatitis. Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with the International Association of Pancreatology, the American Pancreatic Association, the Japan Pancreas Society, and European Pancreatic Club. *Pancreatology*. 2020;20(6):1045–55. Epub 2020 Jul 10. PMID: 32792253. <https://doi.org/10.1016/j.pan.2020.05.022>
44. Steinkohl E, Olesen SS, Drewes AM, Frøkjær JB. Progression of pancreatic morphology in chronic pancreatitis is not associated with changes in quality of life and pain. *Scand J Gastroenterol*. 2020;55(9):1099–107. <https://doi.org/10.1080/00365521.2020.1794022>

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