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# Long-term outcomes of surgery for chronic pancreatitis: A single-center experience

Abdullah Altaf[1], Syed Tatheer Abbas[1], Nusrat Yar Khan[1], Abu Bakar Hafeez Bhatti[2]

[1]Department of Hpb Surgery and Liver Transplantation, Shifa International Hospital Islamabad Pakistan, Islamabad, Pakistan
[2]Department of Surgery, Shifa Tameer-e-Millat University Faculty of Medicine, Islamabad, Pakistan

## ABSTRACT

**Objective:** There are limited data on the long-term outcomes after surgery for chronic pancreatitis. The aim of the current study was to assess the long-term pain relief and survival outcomes following surgical intervention for chronic pancreatitis.

**Material and Methods:** This was a single-center retrospective cohort study that included 36 patients who underwent surgery for chronic pancreatitis. The study analyzed 30-day morbidity and mortality rates, long-term pain relief, and endocrine and exocrine insufficiency. Additionally, 10-year overall survival rates were assessed.

**Results:** The 30-day morbidity rate was 12/36 (33.4%), with no reported mortality. The median preoperative and postoperative visual analog scale scores were 9 (8-9) and 1 (1-2), respectively (p<0.001). Among 34 patients with severe pain, 33 (97%) reported substantial improvement. Long-term mortality was 6/36 (16.7%), and the 1-year, 5-year, and 10-year overall survival rates were 97%, 90%, and 85%, respectively. Factors associated with inferior survival included preoperative diabetes mellitus (p<0.001), hospital admissions after surgery (p=0.002), failure to gain weight after surgery (p=0.001), post-operative body mass index <18.5 kg/m$^2$ (p=0.029), and poor pain control after surgery (p=0.004). Conversely, preoperative endoscopic stent placement (p=0.031) was linked to improved 10-year overall survival.

**Conclusion:** Surgery offers long-term pain relief for chronic pancreatitis, and outcomes can be optimized through early identification and management of high-risk factors.

**Keywords:** Chronic pancreatitis, endoscopic retrograde cholangiopancreatography, Frey's procedure, long-term survival

## INTRODUCTION

Chronic pancreatitis (CP) is a progressive inflammatory disorder that leads to irreversible destruction of the pancreatic parenchyma. This condition significantly impacts a patient's quality of life due to persistent pain, pain-related disability, and concurrent co-morbidities that often result in hospital admissions and the use of opioids (1-3). Diagnostic delays are common due to the non-specific symptoms and limited value of radiological investigations in the early stages of CP (4).

The more advanced stages of CP are characterized by uncontrolled pain, exocrine and endocrine insufficiency, and in rare cases, pancreatic cancer (5,6). Treatment typically follows a step-up approach, beginning with conservative measures, then proceeding to endoscopic interventions, with surgery considered as a last resort (7).

Approximately 40-75% of CP patients eventually require surgery, which aims to provide pain relief, manage complications, and improve quality of life (8). Despite the positive outcomes of surgery for CP, the optimal timing for intervention is still debated (9-11). Various surgical procedures can be performed, including drainage, resectional, and combined resection and drainage procedures, depending on the anatomical features of the pancreas and surrounding structures (8,12-15).

Although there has been progress in understanding the pathophysiology of CP, there are still gaps in its management. Many CP patients experience delays in receiving medical care, and not all are suitable candidates for surgery. Long-term data on these patients are limited, but it is known that infections, cardiovascular issues, and diabetes-related complications are major factors contributing to long-term mortality (6).

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**Corresponding Author**
**Abu Bakar Hafeez Bhatti**

**E-mail:** abubakar.hafeez@yahoo.com
**ORCID ID:** orcid.org/0000-0002-4875-603X

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As a specialized unit for hepato-pancreatico-biliary conditions, our team treats both adult and pediatric patients with advanced CP requiring surgery. The purpose of this study is to present the short-term and long-term outcomes of surgery for CP from a single center.

## MATERIAL and METHODS

This single-center retrospective cohort study examined patients who underwent surgery for CP between March 2012 and October 2022, with a minimum follow-up of six months (n=36). The study was approved by the Shifa International Hospital Ethics Review Committee (date: 06.09.2023) and Institutional Review Board (IRB #0313-23) and was conducted in accordance with the Declaration of Helsinki and STROBE guidelines.

### Patient Details

The diagnosis of CP was based on a typical history of recurrent episodes of abdominal pain, nausea or vomiting, and any concurrent symptoms of exocrine or endocrine insufficiency (steatorrhea, or diabetes mellitus), combined with radiological evidence of CP such as pancreatic atrophy, pancreatic duct dilation or disruption, pancreaticolithiasis, and parenchymal calcifications on abdominal ultrasound and computed tomography (CT). In patients with atypical features, magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography (ERCP) were performed to establish the diagnosis (4). Idiopathic CP was a diagnosis of exclusion, while other etiologies were confirmed on radiological investigations, such as the presence of gallstones on ultrasound pancreatic divisum on CT.

Pain was assessed using the visual analogue scale [(VAS), range: 0-10], frequency and duration of pain attacks, and the need for painkillers. Good pain control was defined as a post-operative VAS score ≤3. We assessed long-term pain relief and patients were contacted in 2023 to extract information regarding pain control. Post-operative complications were categorized according to the Clavien-Dindo classification (16). Patients were considered to have endocrine insufficiency if there was a known history of diabetes mellitus, confirmed by fasting blood glucose levels >125 mg/dL, or when patients were on diabetic medications. Exocrine insufficiency was considered if there was steatorrhea or if patients required enzyme replacement therapy for better control of bowel movements. Body mass index (BMI) was categorized as underweight (<18.5 kg/m$^2$), normal (18.5 kg/m$^2$-25 kg/m$^2$), overweight (25 kg/m$^2$-30 kg/m$^2$), and obese (>30 kg/m$^2$). All patients were discussed in a multidisciplinary team meeting, and Frey's procedure was performed for patients with diffuse and multifocal involvement of the pancreas (12).

### Statistical Analysis

Clinicopathological data were extracted from electronic medical records and patient files, and all patients were followed until June 2023. Patient demographics, clinical presentation, details of diagnostic workup and endoscopic intervention, operative details, and post-operative outcomes were analyzed. The primary objective of the study was to determine long-term overall survival (OS) and pain relief after surgery. Additionally, endocrine and exocrine insufficiency, postoperative hospitalizations, change in weight, and BMI after surgery were examined. Continuous data were presented as median with interquartile range and were compared using the Mann-Whitney U test. Kaplan-Meier survival analysis was used to determine OS, and the log-rank test was used to determine significance. Survival was calculated by subtracting the date of death from the date of surgery. All statistical tests were two-tailed, and a p-value of less than 0.05 was considered statistically significant. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, v26).

## RESULTS

### Patient Details

The median age was 24.5 years (range 12.2-45.0), with 12 (33.3%) patients under 16 years old. The median preoperative BMI was 20.8 (range 16.7-23.9) kg/m$^2$, and the median time from symptoms to diagnosis was 30 (range 19.5-55) months (Table 1). All patients required painkillers, and 13 (36.1%) had 10 or more hospitalizations before surgery. The median pancreatic duct diameter on imaging was 5.7, (range 4-8.4) mm, with 20 (55.6%) patients having a duct diameter >5 mm. Out of 36 patients, 33 (91.7%) underwent ERCP before surgery, and 14 (38.9%) had ERCP with pancreatic duct stenting. Preoperative biopsy was performed on 4 (11.1%) patients due to suspicion of malignancy, but all cases were negative.

### 30-day Outcomes

Out of 36 patients, 31 (86.1%) underwent Frey's procedure, and five (13.9%) had Whipple's procedure (Table 2). The 30-day morbidity rate was 12/36 (33.4%), with no mortality. Two patients had grade 4 complications, including pneumonia (n=1) and sepsis (n=1).

### Long-term Outcomes

The median follow-up was 71.1 months (range 16.1-90.3). The 1,5, and 10-year OS rates were 97%, 90%, and 85% (Figure 1). During follow-up, there were 6 (16.7%) mortalities, attributed to exocrine insufficiency (n=3), diabetes and its complications (n=2), and pneumonia (n=1). Preoperative diabetes mellitus (p<0.001), multiple hospital admissions after surgery (p=0.002), failure to gain weight after surgery (p=0.001), post-operative BMI <18.5 kg/m$^2$ (p=0.029), and poor pain control after surgery (p=0.004) were associated with inferior long-term survival (Table 3). Preoperative endoscopic stent placement (p=0.031) was associated with improved 10-year OS.

| **Table 1.** Patient characteristics, radiological and endoscopic details | |
|---|---|
| **Variables** | **Number (n=36)** |
| Age in years, median (IQR) | 24.5 (12.25-45) |
| **Sex, n (%)** | |
| Male | 19 (52.8) |
| Female | 17 (47.2) |
| **Etiology, n (%)** | |
| Idiopathic | 21 (58.3) |
| Gallstones | 11 (30.6) |
| Pancreatic divisum | 2 (5.6) |
| Autoimmune | 2 (5.6) |
| Duration of symptoms, median (IQR), months | 30 (19.5-55) |
| Number of preoperative hospitalizations, n (%) | 6.5 (2.3-14.8) |
| Patients with ≥10 hospitalizations, n (%) | 13 (36.1) |
| Visual analog scale score, median (IQR) | 9 (8-9) |
| **Severity of abdominal pain, n (%)** | |
| Severe | 34 (94.4) |
| Moderate | 2 (5.6) |
| Patients on analgesics, n (%) | 36 (100) |
| Patients with comorbidities, n (%) | 6 (16.7) |
| Preoperative BMI, median (IQR), kg/m$^2$ | 20.8 (16.7-23.9) |
| **BMI categories, n (%)** | |
| <18.5 kg/m$^2$ | 12 (33.3) |
| 18.5-24.9 kg/m$^2$ | 19 (52.8) |
| 25-29.9 kg/m$^2$ | 4 (11.1) |
| >30 kg/m$^2$ | 1 (2.8) |
| Preoperative exocrine insufficiency, n (%) | 9 (25) |
| Preoperative endocrine insufficiency, n (%) | 5 (13.9) |
| Preoperative insulin dependence, n (%) | 3 (8.3) |
| Preoperative jaundice, n (%) | 5 (13.9) |
| Pancreatic duct diameter, median (IQR), mm | 5.7 (4-8.4) |
| **Pancreatic duct diameter, n (%)** | |
| <3 mm | 4 (11.1) |
| 3-5 mm | 12 (33.3) |
| >5 mm | 20 (55.6) |
| Parenchymal calcifications, n (%) | 26 (72.2) |
| **Pancreatic strictures, n (%)** | |
| Diffuse/generalized | 3 (8.3) |
| Head | 9 (25) |
| Neck | 2 (5.6) |
| Body | 2 (5.6) |
| Distal bile duct and pancreatic duct | 9 (25) |
| Pancreatolithiasis, n (%) | 14 (38.9) |
| Preoperative ERCP, n (%) | 33 (91.7) |
| Preoperative ERCP stenting, n (%) | 14 (38.9) |
| **Number of ERCPs, n (%)** | |
| One | 23 (63.9) |
| Two | 6 (16.7) |
| Three or more | 4 (11.1) |
| Preoperative biopsy, n (%) | 4 (11.1) |

IQR: Interquartile range, ERCP: Endoscopic retrograde cholangiopancreatography, BMI: Body mass index.

| **Table 2.** Operative details and short-term outcomes | |
|---|---|
| **Variables** | **Number (n=36)** |
| **Surgical procedure, n (%)** | |
| Frey's procedure | 31 (86.1) |
| Whipple's procedure | 5 (13.9) |
| Cholecystectomy | 36 (100) |
| Hepaticojejunostomy | 7 (19.4) |
| Operative time, median (IQR), minutes | 300 (240-420) |
| Intraoperative blood loss, median (IQR), mL | 400 (200-600) |
| 30-day post-operative morbidity, n (%) | 12 (33.4) |
| Grade 1 | 2 (5.6) |
| Wound infection | 2 (5.6) |
| Grade 2 | 8 (22.3) |
| Chyle leak | 2 (5.6) |
| Wound infection | 6 (16.7) |
| Grade 3 | **0 (0)** |
| Grade 4 | 2 (5.6) |
| Pneumonia | 1 (2.8) |
| Sepsis | 1 (2.8) |
| Grade 5 | 0 (0) |
| Intensive care unit stay, median (IQR), days | 1 (1-2) |
| Hospital stay, median (IQR), days | 5 (5-6) |

IQR: Interquartile range.

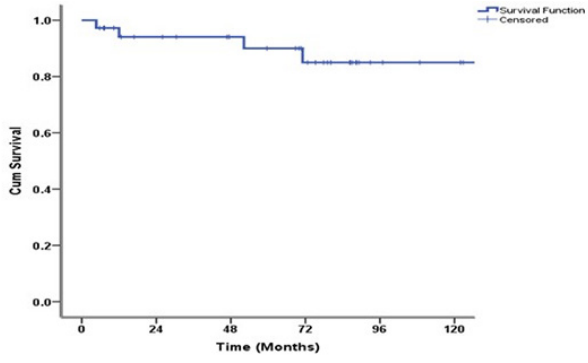


**Figure 1.** Estimated 1, 5 and 10-year overall survival in patients who underwent surgery for chronic pancreatitis.

### Pain Control, Pancreatic Function, BMI

The VAS score improved for all patients after surgery, with a median preoperative and postoperative VAS score of 9 (8-9) and 1 (1-2) ($p<0.001$). Complete pain control was achieved in 19 (52.8%) patients, and 14 (38.9%) reported substantial improvement with occasional episodes of mild pain. Notably, out of 34 patients with severe pain before surgery, 33 (97%) experienced substantial improvement. Overall, good pain control was achieved in 28/36 (77.8%) patients (VAS ≤3).

**Table 3.** Factors associated with 10-year overall survival after surgery for chronic pancreatitis

| Variables | 10-year OS (%) | p-value |
|---|---|---|
| Sex | | 0.229 |
| Male | 90 | |
| Female | 79 | |
| Etiology | | 0.584 |
| Idiopathic | 71 | |
| Gallstones | 91 | |
| Preoperative exocrine dysfunction | | 0.688 |
| Present | 74 | |
| Absent | 83 | |
| Preoperative diabetes mellitus | | <0.001 |
| Present | 40 | |
| Absent | 86.5 | |
| Preoperative BMI | | 0.230 |
| <18.5 kg/m$^2$ | 64.2 | |
| ≥18.5 kg/m$^2$ | 91.7 | |
| Preoperative hospitalizations | | 0.054 |
| ≤2 | 66.7 | |
| >2 | 90.7 | |
| Preoperative ERCP and stenting | | 0.031 |
| Yes | 100 | |
| No | 72 | |
| Pancreatic duct diameter | | 0.590 |
| <3 mm | 100 | |
| 3-5 mm | 83.3 | |
| >5 mm | 81.6 | |
| Pancreatic stricture | | 0.330 |
| Yes | 92 | |
| No | 69.3 | |
| Pancreatolithiasis | | 0.867 |
| Yes | 79.6 | |
| No | 85.9 | |
| Pancreatic calcifications | | 0.737 |
| Yes | 86.2 | |
| No | 77.1 | |
| Preoperative jaundice | | 0.118 |
| Yes | 60 | |
| No | 88 | |
| Post-operative pain relief | | 0.004 |
| Yes | 92.6 | |
| No | 60 | |
| Post-operative weight gain | | 0.001 |
| Yes | 94.4 | |
| No | 60 | |
| Post-operative BMI | | 0.029 |
| <18.5 kg/m$^2$ | 65.6 | |
| ≥18.5 kg/m$^2$ | 88 | |
| New onset exocrine insufficiency | | 0.073 |
| Yes | 75 | |
| No | 85.5 | |
| Post-operative hospitalizations | | 0.002 |
| ≤2 | 93.1 | |
| >2 | 52.5 | |

BMI: Body mass index, ERCP: Endoscopic retrograde cholangiopancreatography, OS: Overall survival.

## DISCUSSION

In this study, we report long-term outcomes with surgical management of CP. Due to no cases of alcohol-related CP, a relatively young age at the time of surgery, and zero short-term mortality, a 10-year OS rate of 85% was achieved. To the best of our knowledge, this is the first study from Pakistan examining long-term outcomes after surgery for CP. A number of preoperative and postoperative factors were associated with long-term survival and can serve as useful markers to establish nutritional goals, devise follow-up plans, and evaluate pancreatic endocrine and exocrine function.

Overall, we found surgical intervention to be safe and effective, with excellent long-term survival after surgery, comparable to contemporary reports on surgical outcomes in CP (6,17). Factors such as smoking, alcohol and opioid use, concomitant diabetes mellitus, poor pain control despite surgery, and low BMI have been associated with mortality in CP (18-20). Inferior long-term survival was also significantly associated with preoperative diabetes mellitus and more than two hospital admissions after surgery. More importantly, preoperative endoscopic stent placement, weight gain, and pain relief with surgery were associated with improved survival. These factors can be used to devise follow-up plans in patients with CP. More intensive post-operative surveillance strategies and clearly defined nutritional goals are needed when these factors are present.

Surgery is performed in CP for unrelenting and troublesome pain (21). Complete pain control is achieved in 37% compared to 17% (p=0.008), of patients undergoing surgical versus endoscopic therapy (22). The role of surgery versus endoscopy in patients with early CP remains debatable. In the ESCAPE trial, early surgery was associated with lower pain scores compared with endoscopic management (11). In a recent systematic review and meta-analysis, surgery was associated with better overall pain control [odds ratio (OR) 0.33, 95% confidence interval (CI) 0.23-0.47, p<0.001, $I^2$=4%]. However, considering that surgical intervention is a significant undertaking, the authors concluded that surgery should be considered when endoscopy fails (23). Out of 36 patients in the current study, 33 (91.7%) underwent ERCP and 14 (38.9%) had pancreatic stent placement. Due to ineffective pain control by endoscopy, surgical intervention was performed. On the last follow-up, 19 out of 36 (52.8%) patients were completely pain-free, and 33 out of 36 (91.7%) patients with severe pain reported substantial pain relief after surgery. Therefore, the step-up approach starting with medical management, endoscopy, and finally surgery appears to be a reasonable option in CP.

The impact of surgery on long-term endocrine and exocrine function in CP remains less clearly understood. Two recently concluded systematic reviews reported conflicting results. Hughes and colleagues have shown that there is no difference in endocrine failures following surgical therapy [48 out of 135 (36%)], or endoscopic therapy [49 out of 124 (40%)], [OR (95% CI) 0.71 (0.30-1.69), p=0.44]. Similarly, no significant difference in exocrine failure rate following surgery [39 out of 55 (71%)] and endoscopy [43 out of 57 (75%)] [OR (95% CI) 0.62 (0.12-3.12), p=0.56] was reported (22). On the other hand, Ma et al. (23) reported less endocrine insufficiency after surgery compared to endoscopy [OR 2.10, 95% CI 1.20-3.67, p=0.01, $I^2$=0%]. Steatorrhea and diabetes mellitus are reported in 13-19% and 14.7-43.8% of patients, respectively (24). Hence, the progressive deterioration of pancreatic function after surgery might represent one of the biggest challenges in managing these patients in the long term and is a major cause of morbidity, and incurred treatment costs. With regard to the choice of surgical procedure, Frey's procedure is commonly used in CP (25,26). Whipple's procedure is reserved for patients with a suspicious mass in the head of the pancreas and head-dominant pathology. We also preferred Frey's procedure as it was indicated in the majority of our patients with CP, was relatively easy to perform, and was associated with low morbidity.

### Study Limitations

Our study had the limitations typical of a retrospective, non-randomized study. As a referral center and quaternary care hospital, we see very few patients with early CP. Nevertheless, we report the impact of surgery on long-term pain relief, pancreatic function, and OS in patients with advanced CP. We have reported 10-year OS based on Kaplan-Meier curves, and five patients had an actual follow-up longer than ten years. We did not compare outcomes of surgery with endoscopy because, in a non-randomized setting and with a unique referral pattern, we couldn't carry out such a study. In 21 (58.3%) patients, the etiology of CP could not be determined. This is much higher than reports from the West, but similar results have been reported from India (27).

## CONCLUSION

The current study shows that the majority of patients with CP achieve pain relief through surgery. More importantly, Frey's procedure in these patients is associated with excellent short-term and long-term outcomes. Not all patients benefit from surgery, and we need to refine patient selection in CP. Moreover, risk factors for inferior long-term survival should be identified, permitting tailored follow-up protocols.

### Ethics

**Ethics Committee Approval:** The study was approved by the Shifa International Hospital Ethics Review Committee (date: 06.09.2023) and Institutional Review Board (IRB #0313-23) and was conducted in accordance with the Declaration of Helsinki and STROBE guidelines.

**Informed Consent:** A verbal informed consent was provided by the participants of the study.

### Footnotes

#### Author Contributions

Concept - A.A., A.B.H.B.; Design - A.A., A.B.H.B.; Supervision - N.Y.K., A.B.H.B.; Data Collection or Processing - S.T.A., A.A.; Analysis or Interpretation - S.T.A., A.A., A.B.H.B.; Literature Search - S.T.A., A.A., A.B.H.B.; Critical Review - N.Y.K., A.B.H.B.; Writing - A.A., A.B.H.B.

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