

**Short-term clinical outcomes of Frey’s procedure for chronic pancreatitis - our experience.**

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**Conflicts of Interest:** Nil

**Abstract**

**Importance:** Even though recent evidence suggests that early surgical intervention in patients with chronic pancreatitis is superior to the traditional step-up approach, many centers in India prefer to reserve surgery for patients not responding to conservative and endoscopic management mainly due to apprehensions about the morbidity and mortality associated with pancreatic surgeries. In this study, we present our experience in managing cases of chronic pancreatitis with Frey’s procedure and the short-term outcomes associated with Frey’s procedure including surgical safety, peri operative complications, and most importantly pain relief.

**Objective:** To analyze the surgical safety and short-term clinical outcomes of Frey’s procedure in patients with chronic pancreatitis.

**Design, setting, and participants:** It was a retrospective analysis of a prospectively data conducted at ESIC MC and PGIMSR, Rajajinagar, Bangalore. A total of 16 patients with chronic pancreatitis with dilated main pancreatic duct and severe chronic abdominal pain who had undergone Frey’s procedure between January 2018 and 2 December 2018 were included in this study. Patients were followed up for a minimum of 3 years till August 2022.

**Intervention:** There were 16 patients with chronic pancreatitis who had undergone Frey’s procedure during the study period. In Frey’s procedure, the anterior surface of the pancreatic duct is unroofed completely and ductal stones are extracted following which head coring is performed, and a standard Roux-en-Y is used to perform longitudinal Pancreatico jejunostomy. This procedure effectively decompresses the dilated

pancreatic duct and removes pancreatic head tissue which is believed to be the pacemaker of pain in chronic pancreatitis.

**Main outcome measures:** The primary outcome of this study was to assess pain relief following Frey's procedure at the end of the follow-up period using the Izbicki score. The secondary outcomes included complications (intraoperative and postoperative), exocrine insufficiency, endocrine insufficiency, and quality of life.

**Results:** A total of 17 patients (ages ranged 22–54, male – 10, female-6) underwent Frey's procedure during the study period. Alcohol was etiology in seven patients while the majority (56.3%) were nonalcoholic. Half of the patients had tropical pancreatitis. Intractable pain was present in all cases along with pseudocyst in three cases. The mean preoperative Izbicki scores were  $61.09 \pm 9.86$ . Five patients had diabetes and four patients had steatorrhea. The postoperative period was uneventful and no major complications or mortality were reported. The mean duration of hospitalization was about eleven days. At the end of three years follow-up period, 13 patients (81.3%) had complete pain relief and 3 patients (18.7%) had partial pain relief. Steatorrhea resolved in two of the patients with exocrine insufficiency post-operatively. None of the patients newly developed exocrine or endocrine insufficiency.

**Conclusions:** Our preliminary findings indicate that Frey's treatment may be a safe choice for patients with chronic pancreatitis, offering sufficient pain relief without affecting pancreatic endocrine and exocrine function, with tolerable perioperative morbidity. endocrine and exocrine function.

**Keyword:** pancreatic, preliminary, endocrine

## **Introduction**

Chronic pancreatitis is a multi-factorial fibro inflammatory syndrome in which repetitive episodes of pancreatic inflammation lead to irreversible destruction of the pancreatic parenchyma as evidenced by fibrosis on histology [1]. The most characteristic clinical feature of chronic pancreatitis is chronic upper abdominal pain, which significantly lowers the quality of life. In most patients, unrelenting severe chronic upper abdominal pain is the only symptom that brings them to the hospital [2]. As the disease progresses there is significant destruction of acinar cells and islet of Langerhans cells leading to exocrine and endocrine insufficiency. Exocrine insufficiency presents with steatorrhea, malnutrition, and symptoms of deficiency of fat-soluble vitamins (A, D, E, and K). Endocrine insufficiency leads to a difficult to manage form of diabetes i. e. Type III diabetes wherein patients are at a high risk of developing hypoglycemia due to concomitant destruction of alpha cells of islet of Langerhans which produce glucagon [2,3]. Traditionally the management of chronic pancreatitis was done with a step-up approach, Initially, lifestyle modifications and then medical therapy (pancreatic enzyme replacements, analgesics, etc.), and endoscopic procedures used to be tried, and then patients not responding to these interventions used to be referred for surgical management [3,4,5]. Recent studies such as the ESCAPE trial which was a multicentric randomized control trial conducted across 30 Dutch hospitals suggest that early surgical intervention is better than a step-up approach [6,7,8].

## **Methods**

### **Study design, Inclusion, and Exclusion Criteria**

This was a retrospective review of prospectively collected data of surgically treated cases of chronic

pancreatitis who underwent Frey's procedure from January 2018 to December 2018 at the department of general surgery at ESIC MC & PGIMSR. Follow-up was performed three years for all patients who underwent Frey's treatment. The exclusion criteria, aside from patients undergoing procedures other than Frey's procedure, were lost to follow up and inadequate data. Pancreaticoduodenectomy was performed in one of the patients which chronic pancreatitis with head mass as there was a high suspicion of malignancy, he was excluded from this study. A total of 16 cases of chronic pancreatitis had undergone Frey's procedure during the study period. Based on the ductal architecture, pancreatic head enlargement, suspected malignancy, and related locoregional complications, our center will determine what surgical procedure to perform. Frey's technique was all cases of chronic pancreatitis with intractable pain and low risk of malignancy [9]. Regarding the timing of surgery, we offer surgical treatment to all patients with radiological evidence of calcific pancreatitis with ductal dilatation with unremitting upper abdominal pain. All patient's underwent open Frey's procedure as per our unit policy.

#### **Frey's Procedure [10]**

A bilateral subcostal incision (Rooftop) is made to access the peritoneal cavity. The abdomen is then thoroughly examined and an extended Kocher maneuver is performed. The gastrocolic ligament is then divided. After entering the lesser sac, the anterior surface of the pancreas is visualized. The main pancreatic duct is opened longitudinally, proximally, and distally as in the Partington-Rochelle modification of the longitudinal pancreatic jejunostomy. The superior mesenteric vein below the pancreas and the portal vein above it are identified and preserved in plain sight. Absorbable

sutures are placed parallel to, and not less than 3-4 mm from, the duodenum along the inner aspect of the duodenum for hemostatic purposes. The head of the pancreas is cored out using cautery and sharp dissection, leaving a cuff of the pancreas along the inner aspect of the duodenum. Every attempt is made to preserve the anterior pancreaticoduodenal arcade. The excised pancreatic tissue is always sent to pathology to avoid overlooking a pancreatic carcinoma simulating chronic pancreatitis. Care is taken not to injure the common bile duct, which is intubated with a Bakes dilator to assess its course. A rim of pancreatic tissue is preserved along the inner aspect of the duodenum to encompass the blood supply to the duodenum from the superior and inferior pancreaticoduodenal arteries. Medially, a margin of at least 4-5 mm of the pancreatic head should be left between the portal superior mesenteric vein to avoid dividing the pancreas or injuring these venous structures. When the coring-out of the head and the uncinate process is completed, there should be only a short segment of the pancreatic duct (1- 1.5 cm in length) remaining, and this segment of the duct should be probed to remove all calculi from it. The probe should pass freely into the duodenum. The anterior surface of the intrapancreatic common duct is exposed relieving it from constriction by fibrosis or pseudocysts. Posteriorly, a shell or rim of the pancreas should remain between the cored-out head and uncinate process and the inferior vena cava. With the hand behind the head of the pancreas, it is not difficult to judge the depth of the incision. That this shell of tissue remains is essential to prevent the egress of intestinal contents into the retroperitoneum after the cored-out head of the pancreas is drained in continuity with the filleted open main pancreatic duct in the body and tail of the pancreas using

a Roux-en-Y limb of jejunum. The end of the Roux-en-Y jejunal limb is closed with a stapler reinforced by inverting Lembert sutures. For the pancreatic jejunostomy anastomosis, we perform a single layer anastomosis with Prolene 3-0 in a continuous fashion.

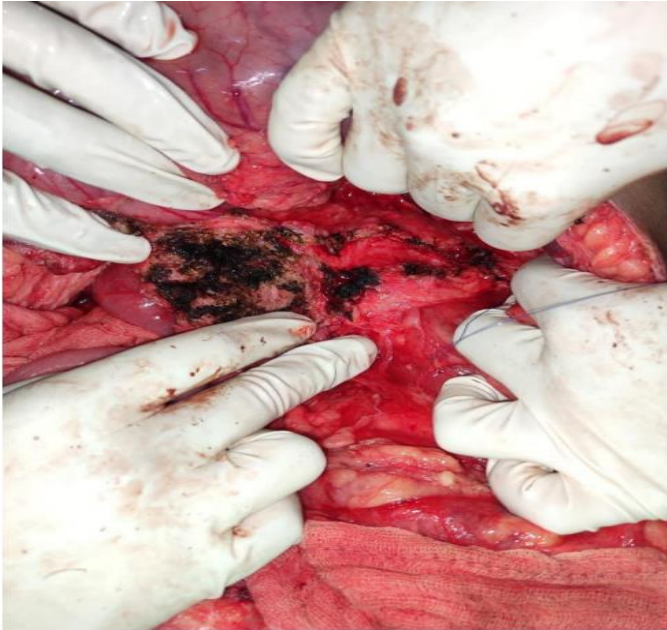


Figure 1: Unroofed Pancreatic duct with coring of the pancreatic head.



Figure 2: Completed long itudinal Pancreatico jejunostomy.

#### **Antibiotics were started**

depending on the patient's clinical condition, sepsis symptoms, or previous cholangitis. In high-risk patients,

deep vein thrombosis prophylaxis was administered with low molecular weight heparins.

The drain was usually removed on day three, after the assessment of the clinical amylase value and the drain volume in the drain fluid. Patients were discharged after they had started ambulating and tolerating oral feeds.

At admission and during hospitalization the baseline characteristics of the patients; demographics, symptoms, cause of pancreatitis, history of alcohol consumption and smoking, the pattern of pain, the severity of pain, radiological findings, perioperative complications, exocrine insufficiency, and endocrine insufficiency were recorded. Postoperatively the patients were followed up on an outpatient basis for at least six months.

Perioperative events had been defined as per the Clavien Dindo classification system of surgical complications. Major complications were defined as events occurring within 30 days requiring intervention (IIIa – under local anesthesia, IIIb – under general anesthesia), intensive care organ support (IVa – single organ, IVb – multiorgan), and death (V) [11].

Primary outcome I e. Pain relief was assessed using a validated pain score specifically designed for chronic pancreatitis I e. Izbicki score. It consists of four questions regarding frequency of pain, the intensity of the pain (VAS score), use of analgesics, and disease-related inability to work.

Based on these questions a pain score can be calculated ranging from 0 (no pain) to 100 (severe, debilitating pain). Pain relief was defined as complete pain relief (Izbicki pain score 10 and pain level decrease >50%), or no relief (Izbicki pain score > 10 and pain level decrease of <50%) [12]. All 16 patients were followed up for a minimum of six months.

There was no loss of follow-up.

Secondary outcomes were perioperative complications. Exocrine insufficiency was defined as the presence of steatorrhoea, or the need for pancreatic enzyme replacement therapy (> 1-year history; overt steatorrhoea without treatment).

Endocrine insufficiency was defined by the presence of prediabetes (HbA1c 5.7-6.4%) or overt diabetes mellitus (HbA1c >6.4%).

Both exocrine insufficiency and endocrine insufficiency were defined as described by Cahen et al; those who had pancreatic insufficiency at both baseline and follow-up (insufficiency persisted); those

who did not have insufficiency at baseline but in whom insufficiency developed during follow-up (insufficiency developed); those who had insufficiency at baseline but not at follow-up (insufficiency resolved), and those who did not have insufficiency at baseline or follow-up (sufficiency persisted) [7].

### Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 25.0 software (SPSS Company, Chicago, IL, USA). Quantitative data were expressed as mean  $\pm$  standard deviation or median (whenever applicable) and range. Statistical difference between preoperative and post operative pain scores was examined using the paired t-test.

The Chi-square test or Fisher's exact test was used to compare categorical variables, as appropriate. P values of < 0.05 were considered statistically significant.

### Results

A total of 16 patients with chronic calcific pancreatitis underwent Frey's procedure during the study period. They were followed up for 3 years.

### Characteristics of the patients included in the study

The baseline characteristics of the patients before surgery are outlined in Table 1.

Mean age of the patients was 39 years, 62% (n=10) were men and 6% (n=6) were women. 7 (43.8%) patients had alcoholic chronic pancreatitis and 9 patients had tropical calcific pancreatitis (56.3%). Imaging showed ductal dilatation in all of the patients. The mean ductal diameter was 8.44 mm (SD  $\pm$  1.094).

7 (56.3%) patients had ductal dilatation alone. 9 (43.8%) patients had a pancreatic head mass with ductal dilatation. Pancreatic parenchymal calcifications were found in all of the patients. 3 (18.8%) patients had pseudocysts.

The mean Izbicki pain score before the intervention was 61.09 (SD-9.861). 7 (43.8%) of the patients denied smoking, 5 (31.3%) were past smokers and 4 (25%) were current smokers. 6 (37.5%) patients denied alcohol consumption, 2 (12.5%) patients used to consume alcohol in the past and 8 (50%) gave history of current alcohol consumption.

4(25%) patients had steatorrhea; rest of the people did not give history suggestive of exocrine insufficiency. 5 (31.3%) were diabetic (HbA1c>6.4%), 3 patients were in a pre-diabetic state (HbA1c>6.4%) and 8 patients were non-diabetic (HbA1c<5.7%) The mean duration of symptoms was 1 year and 5 months.



Table 1: Baseline characteristics of the patients included in this study.

Age, mean ± SD, years	39.38 ± 10.38
Men, No. (%)	10 (62.5%)
Women, No. (%)	6 (37.5%)
Cause of Pancreatitis	
Alcoholic	7 (43.8%)
Tropical Calcific Pancreatitis	9 (56.3%)
Body Mass Index	21.16 ± 1.486
Pattern of Pain	
• Continuous	8 (50%)
• Intermittent	8 (50%)
Radiological Features	
• Duct dilatation alone	7 (56.3%)
• Mass+duct dilatation	9 (43.8%)
• Parenchymal calcifications	16 (100%)
• Pseudocyst	3 (18.8%)
• Pseudoaneurysm	0 (0%)
MPD Diameter mm ± SD	8.44 ± 1.094
Izbicki Pain Score	61.09 ± 9.861
Duration of symptoms (years)	1.44 ± 0.403
Smoker	
• Current	4(25%)
• Past	5(31.3%)
• Never	7 (43.8%)
Alcohol consumption	
• Current	8 (50%)
• Past	2 (12.5%)
• Never	6 (37.5%)
Exocrine Function	
• Steatorrhea	4 (25%)
• No Steatorrhea	12 (75%)
Endocrine Function	
• Normal (HbA1c- <5.7%)	8 (50%)
• Pre diabetes (HbA1c- <5.7%)	3 (18.8)
• Diabetes (HbA1c- >6.4%)	5 (31.3%)

### Perioperative Outcomes

Table 2 outlines the perioperative events. The mean duration of the procedure was 236 minutes (SD-42.57). 4 (25%) patients required intra-operative or immediate post operative blood transfusion.

None of the patients developed major complications as per Clavien Dindo classification.

Mean duration of ICU stay was 3.93 days (SD1.12) and the mean duration of hospital stay was 10.9 days (SD-4.9). Post operative period of all of the patients was uneventful and all the patients included in this study survived.

Table 2: Perioperative Outcomes.

Duration of procedure (minutes)	236 ± 42.57
Number of patients requiring Intraoperative or Immediate postoperative blood transfusion	4 (25%)
Major complications (Clavien Dindo Grade III) and above	0
Duration of ICU stay, days ± SD	3.93 ± 1.12
Duration of hospitalization, days ± SD	10.9 ± 4.9
Mortality	0

Primary outcome Primary outcome has been outlined in Table-3. As described above the primary outcome was recorded as complete pain relief (Izbicki pain score 10 and pain level decrease >50%), or no relief (Izbicki pain score > 10 and pain level decrease of<50%) A clear statistical difference was noted in the intensity of pain before the procedure and at the end of the follow up period (p<0.01). 13 patients (81.3%) had complete pain relief and 3 (18.7%) patients had partial pain relief which was managed on outpatient basis with analgesics.

### Secondary Outcomes

Secondary outcome of this study was to assess exocrine and endocrine functions post operatively at the end of the study period. Findings have been outlined in Table-3. None of the patients developed endocrine and exocrine insufficiency following the procedure. Those who had endocrine insufficiency 8(50%) continued to have it and those who had endocrine sufficiency 8 (50%) continued to have it in the post operative period. Endocrine insufficiency did not resolve following the procedure.

Table 3: Comparison of Pain and Pancreatic endocrine and exocrine insufficiency before and after Frey’s procedure.

Izbicki Score	9.15 ± 2.16
Pain relief	
• No relief	0
• Partial relief	3 (18.7%)
• Complete relief	13 (81.3%)
Exocrine Insufficiency	
• Sufficiency persisted	13 (81.3%)
• Insufficiency persisted	1 (6.3%)
• Insufficiency resolved	2 (12.5%)
• Insufficiency developed	0

Exocrine Insufficiency	
• Sufficiency persisted	8 (50%)
• Insufficiency persisted	8 (50%)
• Insufficiency resolved	0
• Sufficiency resolved	0

## Discussion

Considering the high prevalence of calcific pancreatitis in southern India and its impact on the quality of life of the patient and the economic burden associated with repeated hospitalizations, surgery seems like a promising option and a one-stop solution for the patients. The true prevalence of chronic pancreatitis cannot be determined as patients with unexplained abdominal pain may have chronic pancreatitis which eludes the diagnosis. A survey on chronic pancreatitis in the Asia Pacific conducted by Garg and Tandon suggested a prevalence of 114-200 cases per 100,000 which is way more than the global average of 8-10 per 100,000 cases [13]. This high prevalence of calcific pancreatitis in southern India is due to a distinctive form of chronic pancreatitis called Tropical chronic pancreatitis (TCP). Tropical chronic pancreatitis is a juvenile chronic calcific nonalcoholic pancreatitis of unknown etiology seen only in tropical countries of the developing world. It constitutes about 70% of all cases in India [13]. Most patients with TCP develop the illness before the age of 40 years with a mean age of onset being 24 years. TCP typically presents with severe abdominal pain, severe malnutrition, and endocrine and exocrine insufficiency. Almost all patients with TCP develop multiple large intraductal and parenchymal calcifications. The exact pathophysiology of this disease process is not known, however, several etiological factors have been implicated including protein-energy malnutrition, casava consumption, and deficiency of micronutrients and microminerals [14]. Another very dreadful consequence of TCP is the development of malignancy, especially in

untreated cases. Other causes of chronic pancreatitis include alcohol consumption, genetic factors like hereditary pancreatitis, cystic fibrosis, idiopathic and Benign pancreatic duct obstruction (due to trauma, sphincter of Oddi dysfunction, Pancreas divisum, etc.) [15,16]. Prevalence of tropical calcific pancreatitis in the south Indian population favors surgical drainage over the traditional step-up approach or endoscopic drainage.

Although the step-up (endoscopy first) looks like a good approach in the Western population where alcoholic chronic pancreatitis remains the leading cause, the situation in India is a little different. Due to the high prevalence of tropical chronic pancreatitis which accounts for about two third of the cases of chronic pancreatitis in India and its propensity to cause extensive pancreatic parenchymal calcifications and multiple large intraductal calculi, endoscopic treatment is seldom effective in the long term. Repeated hospital admissions and endoscopic procedures with working days lost due to illness and poor quality of life make the step-up approach expensive [6,7,8]. Also, by the time a patient is referred to a surgeon after repeated failed conservative and endoscopic interventions it would be too late; In such patients even with surgery achieving pain relief would be difficult (due to neuropathic pain) and postoperative recovery would also be troublesome owing to malnutrition [4]. Recently there has been mounting evidence that early surgical intervention is associated with better short-term and long-term outcomes [6,7,8]. Our study further validates the efficacy and safety of early surgery in patients with Chronic Pancreatitis.

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