

Results of Frey's Procedure for Chronic Pancreatitis: A Retrospective Single-Center Study in Vietnam

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1. Abstract

1.1. Introduction: Surgical treatment of chronic pancreatitis is indicated for intractable pain. Frey's method is an accepted treatment for this disease. The present study aimed to describe a single-center experience in the treatment of Frey's procedure for chronic pancreatitis.

1.2. Methods: This was a retrospective review of cases of chronic pancreatitis who underwent Frey's procedure from 2010 January to 2018 December in 108 Military Hospital. The results of Frey's method, including demographics, indication for surgery, mortality, morbidity, pain relief, weight gain, and pancreatic endocrine function, were evaluated.

1.3. Results: The median age was 50.5 ± 10.0 years; 84.7 % of patients were male. The median pre-operative body mass index (BMI) was 19.3 ± 2.8 kg/m². Almost all patients had abdominal pain, 57/59 (96.6%) of them daily. The etiology of pancreatitis was chronic alcohol abuse in 51 patients (86.4%). The significant indication for surgery was intractable pain (74.6%). There was no postoperative mortality. Postoperative morbidity occurred in 9 patients (15.3%), including pancreatic fistula in two (3.4%), and gastrointestinal bleeding in four (6.8%). Long-term relief of abdominal pain was achieved in 84.9% of cases. Only seven patients (13.2%) developed new-onset diabetes mellitus after Frey's procedure during the follow-up period.

1.4. Conclusions: Frey's procedure was a safe and effective therapeutic option for the surgical treatment of patients with intractable pain caused by chronic pancreatitis with dense calcification or stones

in the head of that pancreas and dilation of the main pancreatic duct.

2. Introduction

Chronic pancreatitis is characterized by fibrosis and inflammation of the pancreas in individuals with genetic, environmental, and other risk factors such as hypertriglyceridemia. Chronic pancreatitis is characterized by pancreatic atrophy, fibrosis, ductal strictures and distortion, calcifications, dysplasia, exocrine insufficiency and diabetes, and chronic pain [1].

Forty to 75 percent of patients with CP fail medical and endoscopic therapies and are considered for surgery, most commonly for debilitating abdominal pain. The goals of surgery are to effectively and durably relieve pain, minimize short- and long-term morbidity, and preserve pancreatic parenchyma and, therefore, long-term pancreatic function [2-4]. Several specific procedures have been described, including the Whipple, pylorus-preserving pancreaticoduodenectomy, distal pancreatectomy, total pancreatectomy, and a duodenal-preserving resection of the pancreatic head. The choice of surgical procedure should be determined by the degree and extent of main pancreatic duct dilation and gland morphology. Resection is considered in patients who have failed other forms of therapy and in those who are not candidates for a drainage procedure (usual patients with predominantly small duct disease [5]. In 1987, Frey and Smith described anterior resection of the head of the pancreas combined with drainage of the main pancreatic duct using longitudinal pancreaticojejunostomy [6]. Frey's procedure can prevent decompression failure of the Wirsung duct, Santorini duct, and small ducts in the head of the

pancreas.

In Vietnam, Trinh Hong Son introduced Frey's procedure in 2002, and this procedure has been indicated for most patients with CP. However, there are few reports in the literature on the long-term results of Frey's procedure. In particular, Vietnamese studies on the short- and long-term outcomes of Frey's procedure are limited. This retrospective study aimed to evaluate the results of Frey's procedure for patients with CP at a single Vietnamese institution.

3. Methods

3.1. Patient Selection

This was a retrospective study of 59 patients who underwent Frey's procedure for CP from January 2010 and December 2018 in 108 Military Central Hospital in Vietnam. All patients were diagnosed with CP by clinical history, physical examination, ultrasonography, computed tomography, endoscopic ultrasonography, Endoscopic Retrograde cholangiopancreatography (ERCP), and histological findings.

Frey's procedure was indicated in patients who failed medical and endoscopic therapy, developed complications, and recommendation of alcohol abstinence for at least three months [7]. Exclusion criteria were an atrophic pancreatic head and a high suspicion of malignancy. Clinical characteristics and short – and long – term results were evaluated. Preoperative variables include demographics, etiology, duration of symptoms, the intensity of pain, analgesic requirements, presence of diabetes mellitus or steatorrhea, presence of pseudocyst, biliary obstruction (jaundice), duodenal obstruction, pseudoaneurysm, prior treatment. Similarly, intraoperative findings like the presence of a large head, ductal stones, calcifications, and any complications were confirmed as of previous imaging. Also, effective results like intraoperative blood loss and operative time noted. Exocrine pancreatic dysfunction was based on the presence of steatorrhea. The fecal elastase level was evaluated as well. Endocrine pancreatic dysfunction was based on diabetes militus diagnosis, which was defined as blood glucose level >200 mg/ dL 2 hours after a 75g oral glucose load or glycated hemoglobin (HbA1c) >6.5. Surgical complications had been defined as per the Clavien Dindo classification system. The significant difficulty was defined as Clavien-Dindo classification grade III and IV of surgical complications [8]. Postoperative pancreatic fistulas were scored using the International Study Group on Pancreatic Fistula Definition (ISGPS) [9]. Also, the number of postoperative hospital stay was noted. In the analysis of long-term results, data of patients with a follow-up of more than 12 months were analyzed. Pain intensity was estimated with a pain analog scale. A scale of 0 to 10 was used, where 0 indicated no pain and 10 indicated severe, unbearable, continuous pain. A score of 0 to 1 was taken as no pain.

3.2. Surgical Technique

The surgical procedure was performed, as described by Frey and Smith [6]. After extensive mobilization of the pancreatic head with Kocher's maneuver and the anterior surface of the pancreas from

pancreatic head to tail is exposed. The confirmation of the dilated MPD by puncture with fine needle or ultrasonography, the MPD is incised from the anterior surface. The MPD is fully opened from pancreatic head to tail (Figure. 1). After ligation of the anterior loop of the gastroduodenal artery by suturing and placing hemostatic sutures, maximum excision of pancreatic parenchyma of the pancreatic head, including uncinated process is performed (Figure 1). Pancreatic stones and calcifications in the pancreatic head should be removed as much as possible. The complete decompression of the pancreatic ducts in the head of the pancreas and full-length drainage of the MPD from the head to the tail is the most important part of the surgery to prevent the recurrence of pancreatitis. Excised tissue should be sent for histopathological examination to rule out malignancy. The jejunum was dissected 40 cm distal to the Treitz ligament and opened the antecolic side. Longitudinal side-to-side pancreatico-jejunojejunostomy was performed using a 4-0 absorbable multifilament continuous suture, and 3-0 non absorbable monofilament interrupted suture and finished with side-to-side jejunojejunal anastomosis (Figure 1). A drain was placed adjacent to the pancreatic anastomosis.

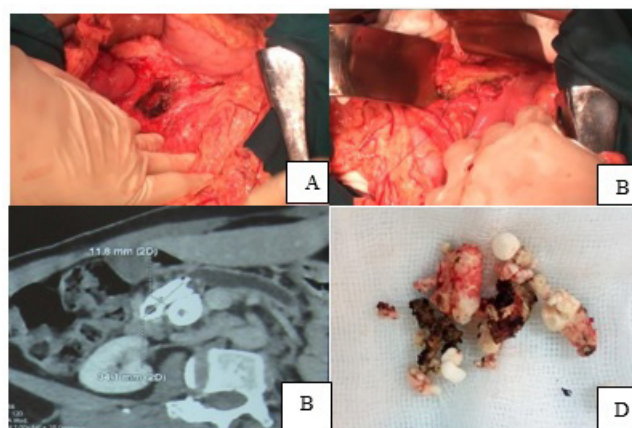


Figure 1: Several large stones in pancreatic head in abdomen pelvic CT scan. (A) Frey's procedure. (B) Longitudinal side-to-side pancreaticojejunojejunostomy. (C) Preoperative CT scan. (D) Pancreas Stone.

3.3. Statistical Analysis

Categorical variables were compared by the chi-square test, Fisher exact tests, and Wilcoxon signed-rank test. Continuous variables are presented as mean (\pm standard deviation) and were compared using an independent 2-sample t-test or the Mann-Whitney U-test. A P-value <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA).

4. Results

Between January 2010 and December 2018, 59 patients who underwent a Frey's procedure for the treatment of chronic pancreatitis in 108 Military Central Hospital were studied.

4.1. Patients

(Table 1) shows the clinical characteristics of patients who under-

went Frey's procedure. Of the series of 59 patients, 50 were males (84.7%), and 9 were females (15.3%), with a mean age of 50.5 ± 10 (SD) years (range: 33–77 years). The body mass index (BMI) of these patients was 19.3 ± 2.8 kg/m² and preoperative weight loss (49.2%). The etiology of chronic pancreatitis was related to constant alcohol use in 51 patients (86.4%). A stone in the pancreatic duct or a parenchyma calcification was identified in 57 patients (96.6%). They presented symptoms of abdominal pain 57 patients (96.6%), and requiring analgesic medication, jaundice (13.6%), diarrhea (13.6%). Three patients had choledocholithiasis, and three patients had gallbladder stones. Preoperative complications due to pancreatitis choledocholithiasis were observed in 37 patients (59.3%), including pancreatic pseudocyst in 12 (20.3%), and bile duct stenosis or occlusion in 23 (39%). Diabetes mellitus was evident in 13 patients (22%) before Frey's procedure.

Table 1: Clinical characteristics of patients

Male/female	50/9
Age (years)	50.5 ± 10.0 (33 – 77)
Body mass index (kg/m ²)	19.3 ± 2.8 (14.1 – 26.4)
Alcohol	51 (86.4%)
Pancreatic stone or calcification	57(96.6)
Abdominal pain	57 (96.6%)
Severe	23 (39%)
Moderate	21(35.6%)
Little	13 (22%)
Weight loss	29 (49.2%)
Diarrhea	8 (13.6%)
Jaundice	8 (13.6%)
Bilirubin total(μ l)	20.2 ± 29.1 (11.2-181)
Amylase (U/l)	214.2 ± 271.6 (24-1293)
Glucose(mmol/l)	7.7 ± 5.4 (4.6-41.2)
Preoperative complication due to pancreatitis	
Pancreatic pseudocyst	12 (20.3%)
Bile duct stenosis or occlusion	23 (39%)
Bile duct stone	3 (5.1%)
Gallbladder stone	3 (5.1%)
Preoperative Diabetes mellitus	13 (22%)
CP, chronic pancreatitis	

(Table 2) describes the treatment of chronic pancreatitis before Frey's procedure. A pancreatic stent was successfully inserted in 2 patients (3.4%). Endoscopic biliary drainage was performed in 3 patients (5.1%). Also, pseudocyst drainage was conducted in two cases (3.4%) before surgery by ultrasound-guided percutaneous drainage. The patients with CP requiring surgical treatment by Frey's procedure often had more than one indication (Table 2), which included intractable pain in 44 patients (74.6%), recurrent episodes of acute pancreatitis in 29 patients (49.1%), bile duct stenosis or obstruction in 23 patients (39%).

4.2. Short-Term Results of Frey's Procedure

The early postoperative outcomes are shown in (Table 3). The main intraoperative complications including: transection of intrapancreatic bile duct (8.5%), splenic injury (1.7%), portal vein injury (5.1%). The median operative time was 137.4 ± 29 (range: 90 - 250) minutes. The median intraoperative blood loss was 482.5 ± 301.2 ml (range:

50 - 1250) ml. There was no mortality. Surgically related complications occurred in 9 patients (15.3%). Postoperative pancreatic fistulae (ISGPF grade B) were observed in 2 patients (3.4%); all were treated with surgically placed drains, and none required further surgical intervention. Gastrointestinal hemorrhage occurred in 4 patients (%) and was associated with a pancreatic fistula in one patient. The median postoperative hospital stay was 14.6 ± 7.6 (range: 6-41) days. Histological examinations of all resected specimens confirmed the diagnosis of CP, and no carcinoma was seen.

Table 2: Preoperative therapy and Indications of surgery

Treatment before Frey's procedure	
Pancreatic stenting (ERCP)	2(3.4%)
Biliary stenting (ERCP)	3(5.1%)
Pseudocyst drainage	2 (3.4%)
Indications for surgery	
Intractable pain	44 (74.6%)
Bile duct stenosis or obstruction	23 (39%)
Recurrent episodes	29 (49.1%)

Table 3: Short-term results of the Frey's procedure

Intraoperative complications (n, %)	
Splenic injury	1 (1.7%)
Portal vein injury	3 (5.1%)
Intrapaneatic bile duct injury	5 (8.5%)
Operation time (minutes)	137.4 ± 29 (90 - 250)
Operative blood loss (ml)	482.5 ± 301.2 (50 - 1250)
Intraoperative blood transfusion	5 (8.5%)
Morbidity	9 (15.3%)
Pancreatic fistula	2 (3.4%)
Gastrointestinal hemorrhage	4 (6.8%)
Pneumonia	1(1.7%)
Wound infection	2 (3.4%)
Coil embolization of the gastroduodenal artery	1 (1.7%)
Postoperative hospital stay (days)	14.6 ± 7.6 (6-41)

4.3. Long-Term Results of Frey's Procedure

All patients were completed 12 months or more of follow-up. Six patients were lost to follow-up, and 53 patients who attended more than 12 months of follow-up were analyzed. The follow-up rate was 85% (53/59). The follow-up period was 49.1 ± 26.4 (range: 12 -116) months, and their long-term results are listed in (Table 4).

Table 4: Long-term results 53 patients after Frey's procedure

Persistent abdominal pain	8 (15.1%)
Use of analgesia	3 (5.7%)
Hospital readmission	
Acute Pancreatitis	6 (11.3%)
Obstructive jaundice	2 (3.8%)
Choledocholithiasis	7 (13.2%)
Reoperation	9 (17%)
Gastrointestinal bypass and biliary bypass	2 (3.8%)
Choledocholithotomy and choledochojejunostomy	7 (13.2%)
New onset of diabetes after surgery	7 (13.2%)
Weight gain	30 (56.6%)

Persistent abdominal pain was present in eight patients (15.1%), but only three patients (5.7%) required the regular use of analgesic medication. Long-term pain relief was achieved in 84.9% (45/53) of cases. In 51 patients with alcoholic pancreatitis, 27 patients (52.9%) stopped drinking, and 18 patients (35.3%) reduced the amount of drinking, but still drank every day. Six patients (11.8%) continued to drink in the same way as before Frey's procedure. Hospital readmission was required in 15 patients (28.3%). Six patients who required readmission had continued alcohol consumption after Frey's procedure. Six patients had acute pancreatitis and were treated conservatively. Obstructive jaundice occurred in 2 patients and required gastrointestinal and biliary bypass procedures. Seven patients had choledocholithiasis and required surgically (choledocholithotomy and choledochojunostomy). Overall, by the end of the study, 13.2% (7/53) of the patients had developed new-onset diabetes mellitus during the follow-up period. Most patients were medicated with pancrelipase supplementation, and only 4 (7.5%) patients developed steatorrhea after Frey's procedure. Our results showed that 56.5% of patients gained weight gain after Frey's procedure.

5. Discussion

There are regional differences in the prevalence of chronic pancreatitis by etiology. Alcohol-related pancreatitis is more common in Vietnam.

Surgical treatment for CP is often required when conservative therapy cannot control the intractable pain due to excessive pancreatic inflammation. When choosing among surgical options, one must consider the areas of the pancreas that are involved in chronic pancreatitis and whether the pancreatic duct is dilated [5].

Two primary forms of surgical interventions are presently performed for CP patients with the aim of improved drainage of the pancreatic duct: drainage and resection procedures. Any of these surgical interventions should be aiming to relieve pain while at the same time, preserving as much of the pancreatic parenchyma and being as safe as possible [5, 10].

Of the surgical drainage procedures, lateral pancreaticojejunostomy using the Partington–Rochelle modification is well recognized and widely used because of its safety and efficacy.¹¹ These draining procedures preserve a maximum of pancreatic tissue; however, the major disadvantage of these procedures is that the frequently associated inflammatory mass in the pancreatic head, and therefore the underlying cause of the disease is not addressed. Nowadays, the only suitable indication for a simple drainage procedure and for longitudinal pancreaticojejunostomy is in patients with isolated pancreatic duct pathology (dilated duct of > 7mm) without an inflammatory mass in the pancreatic head. For the select group of patients, long term pain relief of this drainage operation has been shown to be around 60-70%. It has been reported that about 30% of patients do not benefit from lateral pancreaticojejunostomy at long-term as recurrent pancreatitis may occur in the pancreas head due to undrained Wirsung and/or Santorini ducts and their branches [12, 13].

Frey's performed by coring out the head of the pancreas and leaving a small remnant along the duodenal wall and combined this procedure with a longitudinal incision of the left-sided central pancreatic duct for optimal drainage. For reconstruction, a longitudinal pancreaticojejunostomy using a Roux-en-Y loop used for drainage of the pancreatic head cavity and the left-sided main duct [6].

Frey's procedure could be the standard operation for CP patients with dense calcification or stones in the head of the pancreas and dilation of the main pancreatic duct and can be performed for almost all patients with CP and dilation of the MPD. In this study, 57/59 (96.6%) patients had stones in the pancreatic duct or a parenchyma calcification.

In one trial, 72 patients with painful obstructive CP were randomly assigned to endoscopic or surgical intervention. Endoscopic therapy consisted of endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and stenting (52 percent of patients) and/or stone removal (23 percent), while surgery consisted of a resection (80 percent) or drainage (20 percent) procedure. At five years, more patients who underwent surgery were pain-free than those who underwent endoscopy (34 versus 15 percent); the rates of partial pain relief were similar (52 percent after surgery versus 46 percent after endoscopy) [14, 15].

The initial report by Frey included 50 patients; 89 percent of patients had pain relief, 64 percent experienced significant weight gain, and only 11 percent had progression of diabetes.¹⁶ Frey's results have been validated by other series both at his institution and others, with reported pain relief rates of 62 to 91 percent and morbidity rates of 8 to 39 percent [17-21]. In our study, relief of abdominal pain was achieved in 45/53 patients (84.9%) in the long term, while only three patients (5.7%) required the regular use of analgesic medication after Frey's procedure. These results were similar to those of previous reports [22-24].

The rate of intraoperative complications in this study is higher than in other studies, especially complications: transection of the intrapancreatic bile duct (8.5%), portal vein injury (5.1%). The additional procedures performed included one distal pancreatectomy, one splenectomy, eight cholecystectomies, and nine choledochojunostomy and related to these complications.

Our study also revealed similar results with no mortality and 15.3% morbidity. Two patients developed postoperative pancreatic fistula, but all of these patients could be treated conservatively in our study. However, four patients developed postoperative gastrointestinal hemorrhage. Three of these four patients were treated by conservative management. The patient was found to have bleeding from the gastroduodenal artery into the Roux-en-Y limb through the pancreaticojejunostomy and was treated with endovascular coil embolization of the gastroduodenal artery. No patients required relaparotomy to resolve postoperative complications.

Gestic et al. reported two reoperations as a result of bleeding were

performed, the first one was in postoperative day two because of bleeding in the spleen and retroperitoneum, and the other one was in postoperative day 12 because of bleeding from the pancreatic excised face. In these two patients, the pancreatojejunostomy was taken down, the hemorrhage controlled, and anastomosis was redone. Careful hemostasis is very important in Frey's procedure, and we should pay careful attention to the possibility of postoperative hemorrhage, including gastrointestinal bleeding, and sustained hypotension with tachycardia after Frey's procedure [20].

Six patients required hospital readmission after the Frey's procedure because of the recurrence of acute pancreatitis. The cause of the exacerbation, in that case, was recurrent pancreatitis in the head of the pancreas after Frey's procedure to prevent the recurrence of pancreatitis, extensive resection of the parenchyma in the pancreatic head is essential to decompress the whole pancreatic head completely. Ueda et al. reported hospital readmission in four patients (13%). All four patients who required readmission had continued alcohol consumption after Frey's procedure [25].

Pancreatic exocrine and endocrine functions after Frey's procedure were well preserved in our study. Most of the patients who underwent Frey's procedure received pancrelipase supplementation, and 7.5% developed steatorrhea. Pancrelipase replacement therapy likely prevents symptomatic pancreatic exocrine insufficiency. About pancreatic endocrine function, previous reports showed that 10–20% of patients had new-onset diabetes mellitus [16, 23, 26]. In this study, seven patients (13.2%) had new-onset diabetes mellitus. Ueda et al. reported only two patients (7%) had new-onset diabetes mellitus [25].

Our results and other reports showed that Frey's procedure revealed less morbidity, good long-term pain relief, and preservation of pancreatic endocrine function [16, 22, 23, 25, 27]. Frey's procedure can be a standard surgical procedure for CP with severe pancreatic head inflammation. However, Frey's procedure cannot be applied to patients with CP without diffuse dilation of the main pancreatic duct and a possibility of malignancy.

6. Conclusion

In conclusion, based on short- and long-term results, this study demonstrates that Frey's procedure was a safe and effective therapeutic option for the surgical treatment of patients with intractable pain caused by chronic pancreatitis with dense calcification or stones in the head of that pancreas and dilation of the main pancreatic duct.

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