

Frey's procedure for chronic pancreatitis: a 10-year single-center experience in Korea

Hyung Sun Kim, Joo Hyung Lee, Joon Seong Park, Dong Sup Yoon

Pancreatobiliary Cancer Clinic, Department of Surgery, Gangnam Severance Hospital, Yonsei University, Seoul, Korea

Purpose: Chronic pancreatitis (CP) is progressive inflammatory disease that leads to irreversible destruction of the pancreatic parenchyma. The main indications for surgical intervention in cases involving CP are intractable pain, suspicion of malignancy, and failure of other methods. However, there is no report related to Frey's procedure in Korea; hence, we aimed to investigate and analyze our institution's experience and determine the benefits of surgical treatment for CP.

Methods: This was a retrospective study of 24 patients with CP who underwent Frey's procedure at Gangnam Severance Yonsei University between January 2007 and December 2017. Preoperative exocrine and endocrine pancreatic function, perioperative finding (blood loss, operation time), postoperative complications were evaluated. Statistical analytics were chi-square test, Fisher exact tests, and Wilcoxon signed-rank test and Mann-Whitney U-test.

Results: Surgery was performed due to alcohol-derived CP in 12 of 24 patients (50%) and due to pancreatic stones in 15 of 24 patients (62.5%). Two patients had postoperative complications which were managed conservatively. After surgery, 7 of 24 patients were prescribed with exocrine medication. Comparison of the preoperative and postoperative conditions showed that glycated hemoglobin had no significant differences. After surgery, only 5 patients (21%) complained of intermittent abdominal pain.

Conclusion: In conclusion, Frey's procedure appears to be a less burdensome surgical procedure. Thus, it could be the first option for management of patients with large pancreatic stone.

[Ann Surg Treat Res 2019;97(6):296-301]

Key Words: Chronic pancreatitis, Pancreaticojejunostomy, Patient outcome

INTRODUCTION

Chronic pancreatitis (CP) is progressive inflammatory disease that leads to irreversible destruction of the pancreatic parenchyma. Patients experience chronic pain and dyspepsia or diabetes mellitus (DM) owing to the permanent loss of exocrine and endocrine pancreatic functions [1-3]. They also experience acute pain, which necessitates the use of medications, such as opioid painkillers, and hospitalization for intravenous injection. The abdominal pain is caused by increased pressure in the main pancreatic duct (MPD) owing to pancreatic inflammation,

which is similar to what is observed in compartment syndrome, and direct contact with the sensory nerve [4-6].

The main indications for surgical intervention in cases involving CP are intractable pain, suspicion of malignancy, and failure of other methods, such as medical and endoscopic management [7,8]. The basic goals of surgical procedures include ductal decompression and drainage. Among the surgical methods, Frey's procedure, which is known for its short operation time and fewer complications, is the preferred surgical treatment modality for CP in many areas around the world. However, there are still very few reports related to Frey's

Received May 27, 2019, Revised October 14, 2019,
Accepted October 24, 2019

Corresponding Author: Joon Seong Park

Department of Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, 20 Eonju-ro 63-gil, Gangnam-gu, Seoul 06229, Korea
Tel: +82-2-2019-2444, Fax: +82-2-3462-5994

E-mail: JSPARK330@yuhs.ac

ORCID: <https://orcid.org/0000-0001-8048-9990>

Copyright © 2019, the Korean Surgical Society

© Annals of Surgical Treatment and Research is an Open Access Journal. All articles are distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

procedure in Korea; hence, we aimed to investigate and analyze our institution's experience and determine the benefits of surgical treatment for CP.

METHODS

This was a retrospective study of 24 patients with CP who underwent Frey's procedure at Gangnam Severance Yonsei University between January 2007 and December 2017. The diagnosis of CP was based on clinical history, physical examination, and endoscopic ultrasound, CT, and endoscopic retrograde cholangiopancreatography (ERCP) findings (Fig. 1A, B). Exocrine pancreatic dysfunction was based on the presence of steatorrhea. The fecal elastase level was evaluated as well. Endocrine pancreatic dysfunction was based on DM diagnosis, which was defined as blood glucose level >200 mg/dL 2 hours after a 75-g oral glucose load or glycated hemoglobin (HbA1c) >6.5. Major complication was defined as Clavien-Dindo classification grade III and IV of surgical complications [9]. Postoperative pancreatic fistulas were scored using the International Study Group on Pancreatic Fistula definition [10]. The study protocol was approved by the institutional review board at Gangnam Severance Hospital, Yonsei University of Korea (3-2019-0011). Informed consent was obtained from all participants.

Surgical procedure

The surgical procedure was performed as described by Frey

and Smith [11]. The dilated MPD was incised from the anterior surface of the pancreas. The opening of the MPD was extended as much as possible to the pancreatic tail and then to the head, which was cored out. The jejunum was dissected 40 cm distal to the Treitz ligament and opened antecolic side. Longitudinal side-to-side pancreaticojejunostomy was performed using a 4-0 absorbable multifilament continuous suture and 3-0 nonabsorbable monofilament interrupted suture and finished with side-to-side jejunojejunal anastomosis (Fig. 1C, D). A closed suction drain was inserted into the anterior and posterior space of the pancreaticojejunostomy site.

Statistical analysis

Categorical variables were compared by 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).

RESULTS

Baseline characteristics

Twenty-four patients (men, 19; women, 5) with mean age of 50.33 ± 11.33 years were included. Of 24 patients, 16 and 14 had alcohol experience and smoking history, respectively. They presented symptoms of abdominal pain (18 of 24, 75%), weight

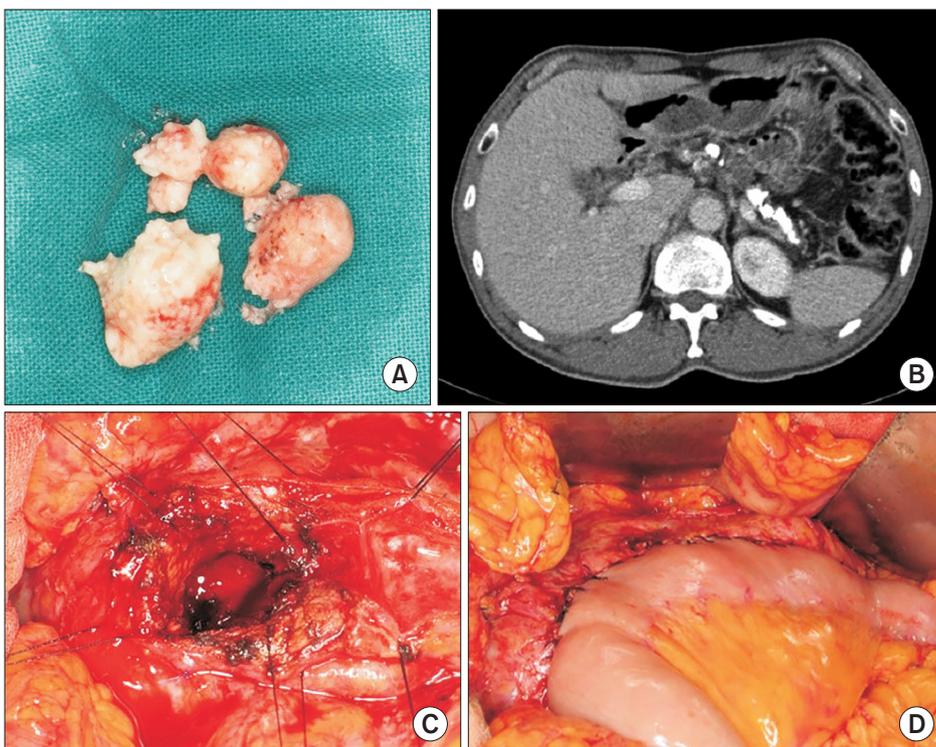


Fig. 1. Several large stones within main pancreatic duct in abdomen pelvic CT scan. (A) Pancreas Stone. (B) Preoperative CT scan. (C) Frey's procedure. The main pancreatic duct was opened. (D) Longitudinal side-to-side pancreaticojejunostomy.

Table 1. Baseline characteristics of chronic pancreatitis patients

Patient No.	Sex	Age (yr)	Height (cm)	Alcohol	Smoking	Clinical symptom
1	M	58	170.0	Yes	Yes	Abdominal pain
2	F	49	152.0	No	No	Abdominal pain
3	F	47	153.8	Yes	No	Abdominal pain
4	M	38	176.0	Yes	No	Abdominal pain
5	M	63	172.0	No	No	Weight loss
6	M	43	168.0	Yes	Yes	None
7	M	61	171.9	Yes	Yes	Abdominal pain
8	M	67	169.0	Yes	Yes	Abdominal pain
9	M	54	161.9	Yes	Yes	Diarrhea, weight loss
10	M	67	170.0	Yes	Yes	Intermittent abdominal pain
11	M	51	165.0	Yes	Yes	Diarrhea
12	M	61	165.1	Yes	No	Abdominal pain
13	F	24	156.1	Yes	No	Abdominal pain
14	M	43	166.9	No	No	Abdominal pain
15	F	62	152.0	No	No	Intermittent abdominal pain
16	F	32	159.4	No	No	None
17	M	58	172.0	Yes	Yes	None
18	M	36	166.7	Yes	Yes	Abdominal pain
19	M	50	172.8	No	Yes	Intermittent abdominal pain
20	M	46	171.6	Yes	Yes	Abdominal pain
21	M	41	177.0	Yes	Yes	Abdominal pain
22	M	59	166.7	No	Yes	Abdominal pain, weight loss, diarrhea
23	M	44	161.9	Yes	No	Abdominal pain
24	M	54	171.0	No	Yes	Abdominal pain

Table 2. Preoperative characteristics of chronic pancreatitis patients

Patient No.	BMI (kg/m ²)	Preoperative ESWL	Diabetes medication	HbA1c (%)	CT: pancreatic duct Diameter (cm)
1	21.97	No	Medication	8.1	1.30
2	21.25	No	Insulin injection	7.9	1.30
3	23.79	No	Medication	6.5	0.95
4	23.36	No	None	6.0	1.10
5	20.16	No	Insulin injection	7.7	0.90
6	21.74	No	Insulin injection	6.5	0.90
7	19.73	No	Medication	8.3	1.10
8	22.49	No	Insulin injection	7.6	0.80
9	23.65	No	Medication	6.1	1.30
10	17.47	No	Insulin injection	7.3	1.00
11	16.90	No	Medication	Not identified	0.90
12	25.71	No	None	Not identified	1.10
13	21.96	No	None	Not identified	1.00
14	18.78	No	None	Not identified	1.20
15	22.78	No	None	5.7	0.90
16	17.44	No	Medication	8.0	1.30
17	24.68	No	Medication	8.7	0.70
18	21.37	No	Insulin injection	14.7	0.80
19	25.12	No	None	Not identified	0.60
20	21.20	No	Insulin injection	9.5	0.50
21	27.45	No	None	5.2	2.00
22	24.40	No	Medication	8.3	1.30
23	16.44	Yes	None	6.0	0.70
24	20.35	No	Insulin injection	8.0	0.90

BMI, body mass index; ESWL, extracorporeal shock wave lithotripsy; HbA1c, glycated hemoglobin.

loss (3 of 24, 12.5%), and diarrhea (3 of 24, 12.5%), but 3 patients (3 of 24, 12.5%) had no typical CP symptoms; One patient had progressive CP with atrophic change, and 1 patient had newly developed diabetes. The other patient had no symptoms but underwent operation to slow the progression of pain and CP (Table 1).

Surgery was performed due to alcohol-derived CP in 12 of 24 patients (50%) and due to pancreatic stones in 15 of 24 patients (62.5%). Only 1 patient had extracorporeal shock wave lithotripsy (ESWL) before surgery.

Preoperative endocrine and exocrine dysfunction

Sixteen patients (16 of 24, 66.6%) were diagnosed with and treated for DM before surgery (8 patients: oral medication, 8 patients: insulin injection). Exocrine deficiency was defined as

fecal elastase level <200. Thirteen patients (13 of 24, 54.2%) had exocrine deficiency before surgery (Table 2).

Perioperative finding and postoperative complications

Operative factors such as operation time and blood loss were similar among patients, with mean operation time of 286.67 ± 97.9 minutes and mean estimated blood loss of 432.91 ± 329.22 mL. Two patients had postoperative complications (postoperative chyle leakage and postoperative pancreatic fistula grade A), which were managed conservatively (Table 3).

Postoperative endocrine and exocrine dysfunction

After surgery, 7 of 24 patients were prescribed with exocrine medication (pancreas enzyme supplement), which they are

Table 3. Perioperative and postoperative characteristics of chronic pancreatitis patients

Patient No.	Hospital days	Time (min)	Blood loss (mL)	Surgical complication	Postoperative pain killer medication
1	13	590	690	None	No
2	12	330	500	None	No
3	12	240	250	None	No
4	9	360	900	None	Intermittent medication
5	7	240	50	None	No
6	10	250	200	None	No
7	9	260	530	None	No
8	19	300	850	Postop chyle	Intermittent medication
9	9	240	250	None	No
10	11	320	700	None	No
11	10	210	700	None	No
12	13	340	1,200	None	Intermittent medication
13	9	280	250	None	No
14	6	210	250	None	No
15	312	240	50	None	No
16	11	360	200	None	No
17	9	450	1,000	None	No
18	13	390	500	None	Long standing opioid medication
19	7	150	500	None	No
20	16	310	230	None	Intermittent medication
21	9	210	350	None	No
22	8	240	80	POPF grade A	No
23	28	150	50	None	No
24	8	210	110	None	No

Postop, postoperative; POPF, postoperative pancreatic fistula.

Table 4. Comparison between preoperative and postoperative patient results with Wilcoxon signed-rank test

	BMI (kg/m ²)		Body weight (kg)		HbA1c (%)	
	Pre	Post	Pre	Post	Pre	Post
Mean ± SD	21.71 ± 3.16	20.99 ± 3.11	59.75 ± 11.18	57.94 ± 11.33	7.74 ± 2.19	7.48 ± 1.40
P-value	0.003		0.001		0.629	
Z	-3.249		-2.968		-0.484	

BMI, body mass index; HbA1c, glycated hemoglobin; SD, standard deviation.

taking until now. Comparison of the preoperative and postoperative conditions showed that HbA1c had no significant differences ($Z = -0.484$; $P = 0.629$). Body weight and body mass index (BMI) statistically decreased after surgery ($Z = -2.968/-3.249$, $P = 0.001/0.003$) (Table 4).

DISCUSSION

The most common etiology of CP is alcohol consumption. The incidence of CP due to alcohol consumption has been increasing in Korea [12,13].

There are many reasons for surgery, and pain is one of the most important symptoms for choosing the procedure. In this study, 15 patients (62.5%) complained of abdominal pain before surgery, but only 5 patients (21%) complained of intermittent abdominal pain after surgery. In these 5 patients, abdominal pain recurred when they consumed alcohol or overate. Two patients had a pain attack within 2 years. Therefore, abdominal pain was major surgical indications in Frey procedure for CP patients.

There are many surgical procedures for CP such as pancreatic resection, Whipple's procedure, pylorus-preserving pancreatoduodenectomy, distal pancreatectomy, total pancreatectomy, duodenum-preserving pancreatic head resection (Beger's procedure), and local pancreatic head resection with longitudinal pancreatojejunostomy (Frey's procedure) [14]. We have summarized Beger's and Frey's procedures, which are widely used as surgical treatment of CP [11,15-18]. Beger's procedure is organ sparing procedure, however, this procedure is technically more demanding, because of 2 anastomoses. This procedure is used for patients with a combination of CP and inflammatory mass in the head of pancreas. Frey's procedure has the advantage of a short operation time and single anastomosis, but has the disadvantage of removing the pancreatic parenchyma. The patients with obstruction in the left-sided pancreatic duct and with less severe inflammation in head of pancreas are indications for Frey's procedure.

Operation time was also shorter than other major surgeries (pancreaticoduodenectomy, distal pancreatectomy, Beger's procedure) and the estimated blood loss was less than other major surgery in our study. Frey's procedure had shorter operation time and lower complication rate than these procedures [14].

Many studies comparing Frey's and Beger's procedures have reported lower morbidity (9% vs. 20%), increased quality of life, and better pancreatic function in patients who underwent Frey's procedure. Furthermore, the average operation time in our institution was shorter than that of another study [19]. Four patients were readmitted due to recurrent abdominal pain.

Development of interventions such as ERCP, ESWL, and other techniques for pancreatic duct stone is improving [20,21].

In Korea, many cases of ESWL case have been reported [22]. However, some of them have been reported to have undergone surgery due to large pancreatic stone.

Several studies have compared endoscopic and surgical approaches for CP. The results of these studies indicate that the surgical approach is associated with higher pain relief (86% vs. 61%) and more increase in weight (47% vs. 29%) [23]. In another study, a comparison of endoscopic with ESWL and surgical approach showed better physical quality of life after surgery [24].

Despite the difficulty of endoscopic intervention in large pancreatic stones, surgical intervention for pancreatic duct stone in CP patients were not considered as first-line treatment in many institutions. The reasons for this are postoperative complications and postoperative endocrine and exocrine dysfunctions. Comparison of preoperative and postoperative status has not shown poor results in CP patients. Furthermore, results showed that active surgical treatment had a good effect of pain management on patients with CP.

Other studies reported several complications such as pancreatic fistula and postoperative bleeding with abdominal abscess after Frey's procedure [25,26]. However, there were no major complications in our institution. Another study concluded that patients with pancreatic stenting before operation had higher rates of postoperative pancreatic fistula than patients with nonpancreatic stenting [27]. In our case, previous pancreatic stenting did not increase the risk of pancreatic fistula.

The BMI and body weight of the patients decreased in comparison with those before the operation. The BMI and body weight were measured at the first outpatient checkup only 7 to 10 days after discharge, which could be the reason why no nutritional improvement was noted after surgery. Other studies have shown an increase in postoperative nutritional index after Frey's procedure [1].

In conclusion, Frey's procedure appears to be a less burdensome surgical procedure. Thus, it could be the optimal option for management of patients with CP with pancreatic stone.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Gestic MA, Callejas-Neto F, Chaim EA, Utrini MP, Cazzo E, Pareja JC. Surgical treatment of chronic pancreatitis using Frey's procedure: a Brazilian 16-year single-centre experience. *HPB (Oxford)* 2011;13:263-71.
2. Kilburn DJ, Chiow AKH, Leung U, Siriwardhane M, Cavallucci DJ, Bryant R, et al. Early experience with laparoscopic frey procedure for chronic pancreatitis: a case series and review of literature. *J Gastrointest Surg* 2017;21:904-9.
3. Spanier BW, Dijkgraaf MG, Bruno MJ. Epidemiology, aetiology and outcome of acute and chronic pancreatitis: an update. *Best Pract Res Clin Gastroenterol* 2008;22:45-63.
4. Demir IE, Tieftrunk E, Maak M, Friess H, Ceyhan GO. Pain mechanisms in chronic pancreatitis: of a master and his fire. *Langenbecks Arch Surg* 2011;396:151-60.
5. Sakorafas GH, Tsiotou AG, Peros G. Mechanisms and natural history of pain in chronic pancreatitis: a surgical perspective. *J Clin Gastroenterol* 2007;41:689-99.
6. Poulsen JL, Olesen SS, Malver LP, Frokjaer JB, Drewes AM. Pain and chronic pancreatitis: a complex interplay of multiple mechanisms. *World J Gastroenterol* 2013;19:7282-91.
7. Gourgiotis S, Germanos S, Ridolfini MP. Surgical management of chronic pancreatitis. *Hepatobiliary Pancreat Dis Int* 2007;6:121-33.
8. van der Gaag NA, Gouma DJ, van Gulik TM, Busch OR, Boermeester MA. Review article: surgical management of chronic pancreatitis. *Aliment Pharmacol Ther* 2007;26 Suppl 2:221-32.
9. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205-13.
10. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005;138:8-13.
11. Frey CF, Smith GJ. Description and rationale of a new operation for chronic pancreatitis. *Pancreas* 1987;2:701-7.
12. Ryu JK, Lee JK, Kim YT, Lee DK, Seo DW, Lee KT, et al. Clinical features of chronic pancreatitis in Korea: a multicenter nationwide study. *Digestion* 2005;72:207-11.
13. Kim O, Baik S. Alcohol consumption, cigarette smoking, and subjective health in Korean elderly men. *Addict Behav* 2004;29:1595-603.
14. Roch A, Teyssedou J, Mutter D, Marescaux J, Pessaux P. Chronic pancreatitis: a surgical disease? Role of the Frey procedure. *World J Gastrointest Surg* 2014;6:129-35.
15. Frey CF, Mayer KL. Comparison of local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy (frey procedure) and duodenum-preserving resection of the pancreatic head (beger procedure). *World J Surg* 2003;27:1217-30.
16. Buchler MW, Friess H, Bittner R, Roscher R, Krautzberger W, Muller MW, et al. Duodenum-preserving pancreatic head resection: long-term results. *J Gastrointest Surg* 1997;1:13-9.
17. Frey CF. The surgical management of chronic pancreatitis: the Frey procedure. *Adv Surg* 1999;32:41-85.
18. Beger HG, Krautzberger W, Bittner R, Buchler M, Limmer J. Duodenum-preserving resection of the head of the pancreas in patients with severe chronic pancreatitis. *Surgery* 1985;97:467-73.
19. Tan CL, Zhang H, Li KZ. Single center experience in selecting the laparoscopic Frey procedure for chronic pancreatitis. *World J Gastroenterol* 2015;21:12644-52.
20. Korpela T, Udd M, Tenca A, Lindström O, Halttunen J, Myrskylalo S, et al. Long-term results of combined ESWL and ERCP treatment of chronic calcific pancreatitis. *Scand J Gastroenterol* 2016;51:866-71.
21. Tandan M, Talukdar R, Reddy DN. Management of pancreatic calculi: an update. *Gut Liver* 2016;10:873-80.
22. Lee BU, Kim MH, Choi JH, Choi JH, Kim HJ, Park DH, et al. Safety and effectiveness of successive extracorporeal shock wave lithotripsy for pancreatolithiasis under intravenous bolus pethidine administration alone. *Korean J Gastroenterol* 2014;63:231-8.
23. Dite P, Ruzicka M, Zboril V, Novotny I. A prospective, randomized trial comparing endoscopic and surgical therapy for chronic pancreatitis. *Endoscopy* 2003;35:553-8.
24. Cahen DL, Gouma DJ, Nio Y, Rauws EA, Boermeester MA, Busch OR, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med* 2007;356:676-84.
25. Chaudhary A, Negi SS, Masood S, Thombare M. Complications after Frey's procedure for chronic pancreatitis. *Am J Surg* 2004;188:277-81.
26. Egawa S, Motoi F, Sakata N, Kitamura Y, Nakagawa K, Ohtsuka H, et al. Assessment of Frey procedures: Japanese experience. *J Hepatobiliary Pancreat Sci* 2010;17:745-51.
27. Amudhan A, Balachandar TG, Kannan DG, Rajarathinam G, Vimalraj V, Rajendran S, et al. Factors affecting outcome after Frey procedure for chronic pancreatitis. *HPB (Oxford)* 2008;10:477-82.