

Short- and Long-term Results of Modified Frey's Procedure in Patients with Chronic Pancreatitis: A Retrospective Japanese Single-Center Study

MASAKI TANAKA, IPPEI MATSUMOTO*, MAKOTO SHINZEKI,
SADAKI ASARI, TADAHIRO GOTO, HIRONORI YAMASHITA,
JUN ISHIDA, TETSUO AJIKI, TAKUMI FUKUMOTO,
and YONSON KU

Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe, 650-0017, Japan

Received 6 January 2014/ Accepted 16 January 2014

Key words: modified Frey's procedure, lateral pancreaticojejunostomy, chronic pancreatitis, short- and long-term results, drainage procedure

ABSTRACT

BACKGROUND: The study aim was to determine the short- and long-term results of surgical drainage procedure for chronic pancreatitis at a single center in Japan.

METHODS: The records of 28 consecutive patients were retrospectively reviewed. All patients underwent surgery at Kobe University Hospital between June 1999 and April 2013. Long-term follow-up was performed in all patients for a median period of 77 months.

RESULTS: The 26 men (93%) and 2 women (7%) had a mean age of 47 years. The etiology of pancreatitis was chronic alcohol abuse in 24 patients (86%). The major indication for surgery was persistent symptoms (97%). Modified Frey's procedure in 21 patients, lateral pancreaticojejunostomy (LPJ) in 6 patients, LPJ and distal pancreatectomy in one patient, were performed. There was no postoperative mortality. Postoperative morbidity occurred in 6 patients (21%). The percentage of pain-free patients after surgery was 97%, and further acute exacerbation was prevented in 97%. Two patients (6%) required subsequent surgery for infectious pancreatic cyst and intraabdominal abscess. Of the patients that completed follow-up, 13 (46%) had diabetes mellitus, including 5 patients (19%) with new-onset diabetes, and 6 patients (19%) developed pancreatic exocrine insufficiency.

CONCLUSIONS: Modified Frey's procedure is safe, feasible, and effective to manage chronic pancreatitis. The technique prevents further exacerbations and maintains appropriate pancreatic endocrine and exocrine function.

ABBREVIATION

CP, chronic pancreatitis; CT, computed tomography; mFrey, modified Frey's procedure; LPJ, lateral pancreaticojejunostomy; US, ultrasonography

INTRODUCTION

Patients with chronic pancreatitis (CP) suffering from severe and disabling pain present a therapeutically challenging problem [1]. Patients commonly present with pain and with exocrine or endocrine insufficiency. All therapeutic efforts in CP are directed towards the relief of pain as well as the management of the associated complications [2]. Recent prospective randomized controlled trials reveal that surgery is more effective than endoscopic treatment in terms of pain relief, preserving state of physical health, and requiring fewer procedures, over both the short and long term [3]. It is desirable for the patient with CP that the surgical treatment is a low-risk and easily-implemented procedure, which exerts the effective relief of symptoms, the rectification of the common bile duct obstruction and the augment exocrine or endocrine insufficiency [4]. Two main surgical approaches are used in the treatment of CP: One is involved in the decompression of diseased and obstructed pancreatic ducts, and the other is involved in the resection of the enlarged pancreatic head. In drainage procedures as described by Partington and Rochelle [5], the pancreatic duct is opened longitudinally and then a lateral pancreaticojejunostomy (LPJ) is performed. In a resectional procedure such as pylorus-preserving pancreaticoduodenectomy [6], it is mandatory to remove the pancreatic head with the

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affected neural tissue because the head of the pancreas functions as a “pacemaker” of CP. The hybrid procedures have been shown to be safe and effective such as duodenum-preserving pancreatic head resection and local resection of the head of the pancreas combined with LPJ (Frey procedure) for the past few decades [4, 7]. Modified Frey's procedure, a LPJ with limited anterior resection of the pancreas head, have been widely performed to achieve pain relief and preserve exocrine and endocrine function [8, 9]. We conducted modified Frey's procedure by limiting the coring out of the pancreatic head to include only the area anterior to the main pancreatic duct because most CP patients in countries like Japan where the inflammatory head mass is rarely encountered [9, 10]. However, there are few reports regarding the short- and long-term results in the large series of the surgical drainage procedures [11-13].

We herein evaluate the safety and efficacy of modified Frey's procedure or LPJ for CP at a single institution over both short- and long-term.

MATERIALS AND METHODS

Study design

Thirty-eight patients with CP were performed surgery at the Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Kobe University Hospital between June 1999 and April 2013. Five pancreaticoduodenectomies (PDs), 5 distal pancreatectomies (DPs), and 28 drainage procedures, were performed. Of these, patients who underwent drainage procedures, consisted of modified Frey's procedure and LPJ, were reviewed retrospectively. All patients were diagnosed with CP by clinical history, ultrasonography (US), computed tomography (CT), magnetic resonance imaging, magnetic resonance cholangiopancreatography, and endoscopic retrograde cholangiopancreatography. Clinical characteristics of patients and short- and long-term results after surgery were evaluated. Only the patients with a follow-up period of more than 6 months were included in the analysis for long-term results. All patients gave written informed consent for surgical treatment according to our institutional guidelines.

Surgical technique

An upper midline incision or transverse abdominal incision was used. After dividing the gastrocolic ligament to enter the lesser sac, the upper and lower edges of the pancreas were clearly delineated from the head of the pancreas to the tail. The main pancreatic duct was identified by intraoperative US. The main pancreatic duct was opened longitudinally, leftward toward the tail. A rightward ductotomy was then completed into the head of the pancreas. Opening of the main pancreatic duct should be extended to the head side and tail side as much as possible to gain the complete drainage of the duct system. Pancreatic stones in the main and branch duct were removed whenever possible. A limited wedge resection of the anterior parenchyma in front of the Wirsung duct was performed (modified Frey's procedure). The original Frey's procedure involved coring out the anterior and posterior parenchyma of the main pancreatic duct. This procedure emphasized resection of the parenchyma as much as possible: some surgeons even resected the parenchyma posterior to the main pancreatic duct.

However, we focused on the decompression effect achieved by opening the anterior surface of the main pancreatic duct with minimal parenchyma resection, to preserve the parenchyma as much as possible and avoid injury to the common bile duct or portal vein. When coring out of pancreatic head was difficult for technical reasons, LPJ was performed. The Roux-en-Y limb was then constructed. The Roux limb was opened longitudinally at the anti-mesenteric side, matching the length of the opened main pancreatic duct. Longitudinal side-to-side pancreaticojejunostomy was performed. The anastomosis was begun at the tail of the pancreas and consisted of two layers of suture, first applied to the inferior side from tail to head, then repeated on the superior side. A closed silicone drain was placed superiorly, along the pancreaticojejunostomy to the splenic hilum.

Definitions

Postoperative mortality included all deaths occurring during the current hospitalization or within 30 days of surgery. Major and minor postoperative complications were classified according to the Clavien-Dindo classification of surgical complications [14]. Pancreatic fistulae were defined and classified according to the criteria of the International Study Group on Pancreatic Fistula (ISGPF) [15]. All patients were seen every 3 to 6 months after surgery. Patients underwent clinical and laboratory evaluation at each visit, and the following characteristics were recorded: pain, analgesic treatment, pancreatic enzyme substitution, endocrine status, body weight, digestion status, episodes of acute pancreatitis, and hospital readmissions. Diabetes mellitus was defined as a fasting blood glucose > 126 mg/dL and serum glycosylated hemoglobin A1c (HbA1c) level > 6.5% [16]. Pancreatic exocrine insufficiency was defined as the presence of steatorrhea [17].

RESULTS

The clinical characteristics of patients undergoing LPJ are shown in Table I. A total of 26 men (93%) and 2 women (7%) were evaluated; their median age was 47 years (range, 16–73 years).

Table I. Characteristics of patients

Patients details	Number (%)
Male, female	26, 2
Age (years)	47 (16-73)
Etiology	
Alcoholic	24 (86%)
Idiopathic	3 (11%)
Pancreas divisum	1 (3%)
Pancreatic stone	26 (93%)
Diameter of main pancreatic duct, mm, mean, SD	9.3 ± 3.2
Diameter of pancreatic head, cm, median (range)	2.4 (1.8-3.5)
Chronic abdominal pain	15 (54%)
Acute exacerbation	18 (64%)
Preoperative complications	17 (61%)
Common bile duct stenosis	3 (11%)
Pancreatic pseudocyst	12 (43%)
Splenic vein thrombosis	2 (7%)
Diabetes mellitus	8 (28%)
Insulin-dependent	7 (25%)
Oral antidiabetics	1 (3%)

The etiology of chronic pancreatitis was related to chronic alcohol use in 24 patients (86%). A stone in the pancreatic duct or a parenchyma calcification was identified in 26 patients (93%). Median diameter of the pancreas head was 2.4 cm (1.8–3.5 cm). Mean diameter of the main pancreatic duct was 9.3 mm. Persistent daily abdominal pain was present in 15 patients (54%) requiring the regular use of analgesic medication. Severe abdominal pain due to recurrent exacerbation was present in 18 patients (64%). Preoperative complications were observed in 17 patients (61%): pancreatic pseudocyst in 12 (43%); common bile duct stenosis in 3 (11%); Splenic vein thrombosis 2 (7%). Diabetes mellitus was present in 8 patients (28%). A total of 28 surgeries were performed with modified Frey's procedure in 21 (75%) patients and LPJ in 6 (21%) patients. The additional procedures performed included one (4%) LPJ with distal pancreatectomy (Table II).

Table II. Surgical procedure

	Number (%)
Modified Frey's procedure	21 (75%)
LPJ	6 (21%)
LPJ + distal pancreatectomy	1 (3%)

The early postoperative outcomes are listed in Table III. The median operative time was 355 minutes. The median intraoperative blood loss was 662 ml. There was no mortality. Postoperative complications of Clavien-Dindo grade III or higher occurred in 6 patients (21%). ISGPF grade A or B postoperative pancreatic fistula was not found, but grade C postoperative pancreatic fistula was occurred in one patient who required surgical drainage. Gastrointestinal hemorrhage occurred in two patients (7%). Both patients required endovascular intervention. In one case, the patient had bleeding from drain and underwent emergent angiography on postoperative day 8. Angiography revealed bleeding from the posterior superior pancreaticoduodenal artery (PSPDA). This was successfully treated using transcatheter arterial embolization of the PSPDA. The other patient underwent angiography on postoperative day 9 due to melena. The patient was found to have bleeding from the gastroduodenal artery (GDA) and was treated with endovascular coil embolization of the GDA. One patients required relaparotomy to resolve postoperative bile leakage on postoperative day 1. The median postoperative hospital stay was 20 days. All patients were completed 6 months or more of follow-up. The median follow-up period in these 28 patients was 77 months (range, 6–182 months), and their long-term results are listed in Table IV. Only one patient (3%) required the regular use of analgesic medication because of sustained abdominal pain. Twenty-seven patients were judged to be pain-free at the time of their final follow-up

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Table III. Short-term results

Perioperative details	Number		
	All (n=28)	mFrey ^a (n=21)	LPJ ^b (n=7)
Operative time, min, median (range)	355 (240-611)	380 (240-611)	341 (284-543)
Intraoperative blood loss, mL, median (range)	662 (20-2823)	684 (20-2823)	544 (235-1350)
Intraoperative blood transfusion	4 (14%)	4 (19%)	0
Mortality	0	0	0
Morbidity			
Clavien-Dindo grade III and higher complication	6 (21%)	5 (23%)	1 (13%)
Pancreatic fistula	1 (3%)	1 (4%)	0
Delayed gastric empty	1 (3%)	0	1 (13%)
Gastrointestinal hemorrhage	2 (7%)	2 (9%)	0
Biliary leakage	2 (7%)	2 (9%)	0
Intra-abdominal abscess	2 (7%)	1 (4%)	1 (13%)
Relaparotomy	3 (11%)	2 (9%)	1 (13%)
Endovascular arterial embolization	2 (7%)	2 (9%)	0
Postoperative hospital stay, days, median (range)	20 (11-108)	22 (11-108)	19 (13-51)

^a mFrey, modified Frey's procedure; ^b LPJ, lateral pancreaticojejunostomy

Table IV. Long-term results

Late postoperative details	Number (%)		
	All (n=28)	mFrey ^a (n=21)	LPJ ^b (n=7)
Sustained abdominal pain	1 (3%)	1 (4%)	0
Hospital readmission	5 (19%)	3 (21%)	2 (28%)
Peripancreas abscess	1 (3%)	1 (4%)	0
Gastric ulcer	1 (3%)	0	1 (13%)
Cholangitis	1 (3%)	1 (4%)	0
Infectious pancreatic cyst	2 (6%)	1 (4%)	1 (13%)
Reoperation	2 (6%)		
Cystogastrostomy	1 (3%)	1 (4%)	0
Drainage	1 (3%)	1 (4%)	0
Diabetes mellitus	13 (46%)	10 (47%)	3 (42%)
Insulin-dependent	6 (21%)	4 (19%)	2 (28%)
Oral antidiabetic	7 (25%)	5 (23%)	2 (28%)
New onset of diabetes	5 (19%)	3 (21%)	2 (28%)
New onset of insulin-dependent diabetes	1 (3%)	1 (4%)	0
Pancreatic exocrine insufficiency	6 (19%)	4 (19%)	2 (28%)

visit, yielding a long-term pain relief rate of 97%. Five patients (19%) were readmitted to the hospital during the follow-up period. Two patients (6%) had infectious pancreatic cyst. Intra-abdominal abscess, cholangitis, and gastric ulcer were occurred in one patient each. Of these five patients, 2 patients required reoperation. One patient who had intra-abdominal abscess underwent surgical drainage 5 years after the primary surgery. One patient underwent gastrocystostomy for new-onset infectious pancreatic cyst 4 months after the primary surgery. Among the 24 patients with alcoholic CP, 9 patients (37%) could not stop drinking after the operation. Of the nine patients, 2 patients had diabetes mellitus, and another 2 patients had pancreatic exocrine insufficiency after

the surgery. In 9 patients who could not stop drinking, 3 patients died (complication of diabetes mellitus, liver failure, and lung cancer), 3 patients were alive at the investigation. Remaining 3 patients were lost to follow up at 4, 6, and 9 years after surgery. On the other hands, in 15 out of 24 patients with alcoholic chronic pancreatitis, who could stop drinking after surgery, one patient died at 3 years after surgery with unknown reason, 11 patients were alive at the investigation, and 3 patients were lost to follow up at 3, 3, and 4 years after surgery.

During the postsurgical follow-up period, 13 patients (46%) were diagnosed with diabetes mellitus. Six patients (21%) were treated with insulin, 7 (25%) with oral antidiabetic medication. New-onset diabetes developed in 5 patients (19%) during the follow-up period, but only one (3%) developed new-onset of insulin-dependent diabetes after surgery. All 8 patients who had diabetes mellitus preoperatively sustained diabetes mellitus after primary surgery (Fig. 1). Six patients (19%) were diagnosed with pancreatic exocrine insufficiency.

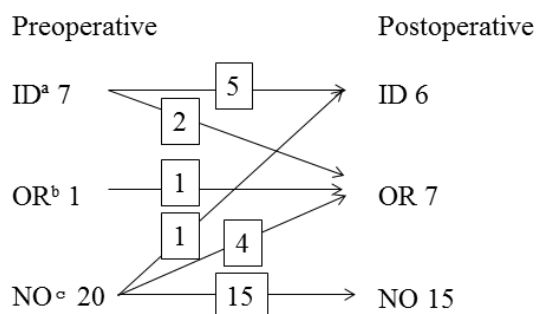


Figure. 1
Relation of pre and post operative diabetes mellitus in patients with chronic pancreatitis
^a ID, Insulin-dependent;
^b OR, Oral antidiabetics;
^c NO, Normal

DISCUSSION

In the various surgical drainage procedures available for patients with CP, LPJ using the Partington-Rochelle modification [5] and Frey's procedure [4] is widely used due to its safety and feasibility [1, 10]. Although the primary indication for surgery in patients with CP is daily unrelenting abdominal pain associated with chronic narcotic dependence, the majority of patients underwent surgery for acute pancreatitis exacerbation and chronic unrelenting abdominal pain in our study. It is important to evaluate the success rates of various surgical procedures for achieving pain relief, as well as for ameliorating or abolishing recurrent exacerbations of CP. Extended drainage operations, a combination of limited pancreatic head resection and drainage, were established to treat patients with pancreatic head masses. Recently, a modified Frey's procedure was developed to minimize the extent of pancreatic head resection [9]. This modified Frey's procedure focuses on the decompression effect achieved by opening the anterior surface of the main pancreatic duct with a small spindle-shaped resection. This procedure provides minimal parenchyma resection to preserve the parenchyma as much as possible and avoids injury to the common bile duct or portal vein. Since CP patients in Japan rarely present enlarged pancreatic head mass [10], modified Frey's procedure has been performed as a standard procedure in our institution. Recently, it has been reported that the median diameter of the pancreatic head in patients with CP is 2.6 cm in Americans and 4.5 cm in Germans ($P < 0.001$) [18]. In our subjects, the mean diameter of the pancreatic head in patients with CP is 2.4 cm (range 1.8-3.5 cm). In Japanese patients with CP, the inflammatory pancreatic head masses are smaller than those of Americans and Germans. Therefore, modified Frey's procedure or LPJ might be justified [10, 19].

For the short-term results, operative morbidity (Clavien-Dindo grade III or more) was 21 % without mortality in our study. Our results are in accordance with recent reports with operative mortality of less than 1% and morbidity ranging from 4% to 40% (averaging 20%) after surgical drainage [1, 8, 11-13, 17, 20-24]. The late arterial hemorrhage after several surgical drainage procedures for CP has been reported to range 1.0% to 4.5%. In previous reports, patients with the late arterial hemorrhage required emergent reoperation to obtain permanent hemostasis [8, 13]. In our study, the late arterial hemorrhage occurred in two patients, they were successfully treated by emergent endovascular intervention. When multidetector-row CT with contrast is able to identify suspected arterial bleeding, endovascular intervention and transcatheter arterial embolization should be the first treatment of choice [25].

In our study, the abdominal pain relief was achieved in 97% of the patients during long-term follow-up period. In a recent review by Nealon et al, surgical drainage procedures relieved abdominal pain relief in 86% of patients and prevented recurrent acute exacerbations in 91% [20]. Our results were comparable to other large series with 48 to 91% of pain relief [1, 9, 11-13, 17, 20, 21, 23]. We found that the long-term pancreatic

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endocrine and exocrine function after surgery were well maintained. The previous reports of surgical drainage procedures showed that the percentages of new-onset diabetes developed in 17 % to 34% during the follow-up period [1, 9, 11-13, 17]. In our study, 19% of the patients developed new-onset diabetes, which is comparable to the rate of the previous reports, but only one patient (3%) developed new-onset insulin-dependent diabetes during the follow-up period. It is noted that no patients with diabetes mellitus preoperatively were improved diabetes mellitus postoperatively. Early surgical intervention might prevent the progression of endocrine insufficiency. In our study, 19% of the patients developed pancreatic exocrine insufficiency, which is less than the rate of previously reported several extended drainage procedures that varied from 60% to 80% [1, 11-13, 17]. It is thought that more pancreatic parenchyma could be preserved by modified Frey's procedure or LPJ comparing to other extended drainage procedures. Other reason of this discrepancy may be due to the differences of pancreatic exocrine insufficiently definition.

The short- and long-term results of modified Frey's procedure and LPJ procedure were shown in Table III and IV. It is likely that there were no differences between the two procedures in short- and long-term results. In our study, LPJ procedure was performed only when pancreatic head could not underwent coring out by technical reasons intraoperatively. In other words, in receiving LPJ patients, the diameter of the pancreas head was small.

The limitation of our study was its retrospective nature with a moderate number of patients. However, to the best of our knowledge, this is the second report of short- and long- term results of surgical drainage including modified Frey's procedure in Japan. Because the morphology of CP in Japan is different from other countries, based on our results, a prospective multicenter randomized trial will be needed in Japan to evaluate the efficacy of this procedure.

In conclusion, modified Frey's procedure is safe, feasible, and effective to manage CP. The technique prevents further exacerbations and maintains appropriate pancreatic endocrine and exocrine function.

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