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Review

Frey procedure for chronic pancreatitis: A narrative review

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ABSTRACT

Chronic pancreatitis is (CP) is a progressive inflammatory disease of the pancreas associated with disabling abdominal pain and gradual deterioration of exocrine and endocrine function. Up to 50% of patients with CP may require surgery during the course of the disease. The main indication for surgery is intractable abdominal pain not amenable to medical and endoscopic therapy. The type of surgery depends on pancreatic ductal diameter and associated parenchymal pathology like inflammatory head mass. Frey procedure (FP) is an effective method for control of pain in patients with enlarged pancreatic head. FP can be performed with a very low mortality and an acceptable morbidity. Compared with pancreaticoduodenectomy (PD), FP has favourable outcomes in terms of operation time, blood loss, morbidity, post-operative hospital stay, intensive care unit stay, and quality of life. FP has shorter operation time and lower morbidity in comparison to Beger procedure. But, long-term pain control and exocrine and endocrine dysfunctions are comparable between PD, Beger and FP. FP is technically easier than PD and Beger procedure. FP is thus a widely acceptable procedure for CP with enlarged pancreatic head in absence of a neoplasia.

1. Introduction

Chronic pancreatitis (CP) is a chronic inflammatory disorder of the pancreas characterized by disabling abdominal pain, relentless progression and gradual deterioration of exocrine and endocrine functions. There is no cure for this disease. So, all forms of treatment for CP are directed for palliation of symptoms. Intractable pain is the most distressing symptom of the disease. It may result in addiction to pain medication, dietary restriction, lifestyle modification, repeated hospitalization, absence from work and unemployment [1]. This leads to the consumption of a disproportionately high volume of resources. Hall et al. estimated that in the United Kingdom, CP costs £285.3 million per year (£79,000 per person per year) [2]. So, the primary goal of management of CP is control of pain. Other management issues are correction of pancreatic insufficiency and treatment of peripancreatic local complications. Current management is step-up approach; when all medical and endoscopic therapies fail to alleviate the pain and burden of CP, surgical interventions are considered. But for patients with advanced disease, medical and endoscopic treatments are frequently associated with inadequate symptom relief. Up to 50% of all patients may undergo surgical intervention at some time during their disease [3]. Current evidence suggests that surgery is more effective than endoscopic therapy in terms of more rapid, effective and sustained pain relief [4]. Moreover, few recent studies have shown better long-term pain control and preservation of exocrine and endocrine functions with early surgical interventions [5–7].

The goals of surgery for CP include: 1) pain relief, 2) control of pancreatitis associated complications of adjacent organs, 3) preservation of as much exocrine and endocrine functions as possible, 4) social and occupational rehabilitation, 5) improvement of quality of life. An ideal operation should address all these goals. More than 10 operations have been described for CP. This long list is unfortunately a testimony to the fact that there is no ideal surgical solution for this problem. Beginning in the early 1950s, decompression procedure was the most commonly performed operation for CP over more than 40 years. Although short-term pain relief was observed in 80% of patients, recurrent pain developed in up to 30% of patients over 3–5 years of follow-up [8–10]. From a technical point of view, the principal cause of failure of the Puestow operation is that the procedure does not address the inflammatory mass in the head of pancreas, so called the “pace

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maker" of pain in CP [11,12]. To address this issue, a variety of pancreatic head resection procedures have been advocated including pancreaticoduodenectomy (PD), Frey, and Beger. Both PD and Frey procedure (FP) have similar long-term outcomes. However, short-term results favor the organ-sparing procedure [13,14]. Of these three procedures, FP is technically easier. Although the long-term results of Frey and Beger procedures are equivalent, FP has shorter operation time and lower morbidity as compared with Beger procedure [15].

Over the past 14 years, we are performing Frey procedure regularly at our institution and we have found that Frey procedure is an effective procedure for chronic pancreatitis with enlarged pancreatic head. In contrast to Beger procedure, it does not require division of the neck of the pancreas in front of the portal vein and superior mesenteric vein confluence which is a tedious procedure in presence of portal hypertension with increased chances of venous injury and bleeding. Moreover, single pancreaticojejunal anastomosis is performed in Frey procedure which reduces the leak rate than Beger procedure where two anastomoses are required. For this reason, FP is now our preferred method of surgical management for CP with enlarged pancreatic head, especially if there is no suspicion of malignancy. PD is done only if there is a preoperative suspicion of malignancy.

2. Rationale for the Frey procedure

Frey procedure was first described by Frey and Smith in 1987 [16]. The operation was originally described for patients with chronic pancreatitis who have bulky head of the pancreas. The idea was that the enlarged complex head, full of fibrosis and obstructed ducts, cannot be adequately addressed by simply decompressing the main pancreatic duct according to the method of modified Puestow. Though the operative steps remained same, the conception was changed with the emergence of 'Pacemaker' theory of pain in chronic pancreatitis. According to this theory, the crucial triangle in chronic pancreatitis lies between the distal common bile duct, the duct of Wirsung, and the superior mesenteric portal vein. This triangle should be the target for local resection of pancreatic head in Frey's procedure. It has been hypothesized that lateral drainage by longitudinal pancreaticojejunostomy is unnecessary, at least in patients who do not have a 'chain of lakes' provided that the pacemaker, the pancreatic head is adequately cored out.

3. Evaluation before the Frey procedure

Chronic pancreatitis is diagnosed on the basis of clinical features and the identification of pancreatic ductal and/or parenchymal changes (calcification, atrophy, ductal dilatation) on imaging. Triphasic computed tomography (CT) scan of the abdomen with pancreas protocol is our preferred imaging for evaluation of the disease severity. Magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangio-pancreatography (ERCP) should be performed for evaluation and management of associated biliary obstruction. Upper G I endoscopy should be performed when there is a suspicion of portal hypertension. Endoscopic ultrasound (EUS) with guided FNA and measurement of tumor markers (serum CA 19.9 and CEA) should be performed when there is a clinical or radiological suspicion of malignancy. The indication for FP should be decided by a multidisciplinary team including gastroenterologists, radiologists, and gastrointestinal surgeons. FP should be performed when the pancreatic head is enlarged (>3.5 cm) (Figure- 1) with pancreatic duct diameter of 5 mm or more and there is no suspicion of malignancy. The technical feasibility of managing small duct disease has evolved over the years. If the pancreatic duct diameter is less than 3 mm, V-shaped excision of the anterior aspect of the pancreas is recommended [17]. Frey et al. [18] have found that sewing to the capsule of the pancreas rather than to the duct mucosa allowed them to decompress ducts as small as 3 mm in diameter. Baseline studies include assessment of exocrine, endocrine, and nutritional function, work status, analgesic intake, pain severity, and quality of life (if feasible). These data are compared with postoperative results to assess the expected success or failure of the operation. We routinely use Izbicki pain score (Table 1) for the assessment of pain severity [19] (see Fig. 1).

4. Surgical Technique

We perform the Frey procedure by a bilateral subcostal incision. Self-retaining Thompson retractor is routinely used. After thorough exploration and exclusion of unsuspected pancreatic cancer, we start our dissection by gently sweeping the hepatic flexure inferiorly. The base of the right portion of the transverse mesocolon is often densely adhered to the head of the pancreas. It is crucial to dissect the mesocolon and its vessels form the head of the pancreas by gentle sharp dissection and sweep it inferiorly for adequate exposure of the anterior surface of the head of the pancreas. Failure to do this critical step will make head coring impossible. Once the head of the pancreas and the anterior surface of the duodenum are fully exposed, a Kocher maneuver is performed and the infrapancreatic portion of the superior mesenteric vein is identified. Lesser sac is then entered to expose the body and the tail of the pancreas. The posterior surface of the stomach is often densely adhered to the anterior surface of the pancreatic body and tail and makes the dissection tedious. It requires a combination of sharp and blunt dissection. The next step is to ligate and divide the right gastroepiploic vessels to complete the exposure of the pancreas. The pancreatic duct is then accessed by aspiration with a 22 G needle either by palpation or by using intraoperative ultrasound. As majority of the cases pancreatic duct is dilated, simple palpation or a blind vertical incision with electrocautery at the midpoint of superior and inferior border of the pancreas in the body region will allow entering into the pancreatic duct. We have performed more than 250 cases of Frey' procedure over 14 years and in no case we required the help of intraoperative ultrasound. The pancreatic duct is then opened using electrocautery. The duct is opened throughout its length. The duct is opened to within 1 cm of the tail and into the pancreatic head. Before coring of the pancreatic head, we place a row of 3-0-polypropelene hemostatic sutures into the pancreatic head approximately 0.5 cm from the duodenum along the entire length of the C loop. These sutures allow for traction and hemostasis during the resection of the pancreatic head. We use electrocautery

Table 1
Izbicki Pain Score [19].

	Points
Frequency of pain attacks	
Daily	100
Several times a week	75
Several times a month	50
Several times a year	25
None	0
VAS	
No pain	0
Imaginative maximum of pain	100
Analgesic medication (Morphine-related analgesic potency)	
Morphine	100
Buprenorphine	80
Pethidine	20
Tramadol	15
Metamizole	3
Acetylsalicylic acid, etc.	1
Time of disease-related inability to work	
Permanent	100
Up to 1 year	75
Up to 1 month	50
Up to 1 week	25
No inability to work during the last year	0

Total Score = Sum of Single Median Values; Pain Score = Total Score Divided by 4.

for coring of the pancreatic head and uncinate process. Bleeding during coring can be controlled with cautery or with 4-0-polypropelene sutures. During head coring, it is crucial to place the left hand of the operating surgeon behind the head of the pancreas to palpate the thickness of the pancreatic head and to assess the depth of dissection. We prefer to remove slices of pancreatic tissue in coring out the head and uncinate process rather than removing the tissue as single specimen. By removing slices of tissue, we can periodically assess the thickness of the remaining parenchyma and palpate impacted calculi in the tributary ducts. To reduce the risk of penetrating the posterior capsule of the head, Frey and Amikura have recommended that the posterior limit of resection be the back wall of the opened duct of wirsung and duct to the uncinate [12]. All the intervening and overlying tissue in the pancreatic head including the duct of Santorini is excised keeping a 5 mm rim of pancreatic tissue in the duodenal sweep and on the right border of the superior mesenteric and portal vein (Fig. 2). The common bile duct will be visible or palpable to varying degrees after the head of the pancreas has been adequately cored out, crossing the posterior aspect of the cavity. If the operation is being done for biliary obstruction, all the fibrous tissue restricting the bile duct should be cautiously excised. We use fine scissors rather than cautery for this part of dissection so that the plane along the bile duct is not obscured by charred tissue. If there is difficulty in identifying the bile duct, one can remove the gallbladder and pass a dilator into the bile duct to guide the plane of dissection. If bile duct is opened inadvertently during this dissection, the duct should be opened widely and the edges to be tacked back to the surrounding fibrous tissue. It allows both bile and pancreatic secretion to drain in the Roux-en-Y jejunal limb used to cover the defect in the pancreas. Once the dissection is completed and hemostasis is secured, a Roux limb is prepared. Pancreaticojejunostomy is performed with a single layer of continuous sutures of 4-0-polypropelene. The operation is completed by performing a jejunojejunostomy approximately 60 cm distal to the pancreatic anastomosis. The Roux limb is kept slightly longer than the standard length used in post cholecystectomy biliary stricture (60 cm vs 40 cm) so that the same loop can be utilized for future biliary bypass without much trouble. All mesenteric and mesocolic gaps are closed. A closed system drain (Jackson Pratt) is placed superiorly along the pancreaticojejunostomy to the splenic hilum.

5. Perioperative management and follow-up

All patients should receive prophylactic antibiotic. We commonly use a combination of cefoperazone and sulbactum (based on antibiogram of our Institution). Antibiotic should be continued for 3 or more days if the patient had previously undergone biliary or pancreatic duct stenting. Thromboprophylaxis should be used routinely. In our institution, intermittent pneumatic compression device is used routinely for the prevention of deep venous thrombosis. Chemical thromboprophylaxis is used selectively. Peri-operative octreotide prophylaxis is not a routine. Postoperative pain control must be adequate for patients comfort as well as for the reduction of chest complications. Epidural analgesia or patient control analgesia can be used. We routinely use epidural analgesia for perioperative pain management. The epidural catheter is removed on postoperative day 4 and the patient is started on oral analgesic in a stepladder approach, non-narcotic analgesics being preferred. Drain fluid amylase should be estimated routinely on postoperative day 3 and 5. The drain should be removed when the output is less than 20 ml/day with a low amylase content and non-bilious in nature. All patients should be seen every 3 months for the first 2 years of surgery and every 6 months between 2 years and 5 years of surgery, and once in a year after 5 years. In the follow-up visit, following parameters should be recorded: body weight, pain control, analgesic requirement, need for enzyme supplementation, need for hospitalization, blood sugar level (both fasting and postprandial) and any complication related to chronic pancreatitis. If feasible, assessment of quality of life after the surgery can be performed. Patients should be encouraged to quit alcohol and smoking for better long-term results.

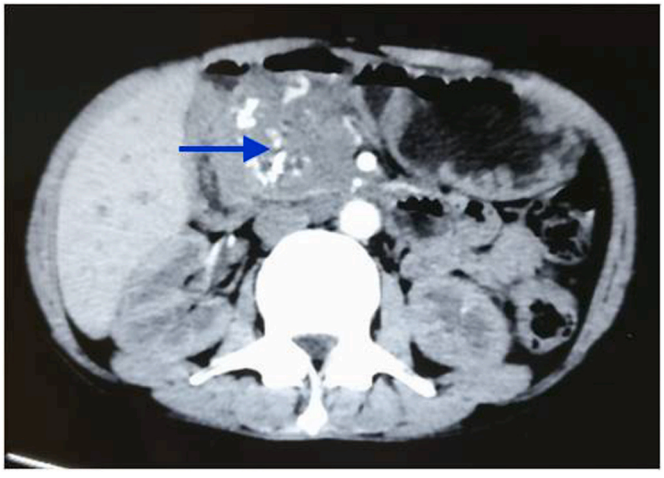

Fig. 1. Computed tomography scan of the abdomen showing an inflammatory pancreatic head mass (blue arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

6. Results of the Frey procedure

The results of the Frey procedure are quite favourable for a properly-selected patient. Short- and long-term results of the Frey procedure is presented in Table 2.

7. Short-term results

FP can be performed with a low mortality and acceptable perioperative morbidity. The mean or median postoperative hospital stay varies from 9 to 20 days [12,15,20–25,27]. Operative mortality varies from 0% to 3% [1,12,15,20–25,27]. Common causes of mortality are postpancreatectomy hemorrhage, chest infection and intraabdominal sepsis. Perioperative complications develop in 7%–42% of patients [1,12,15,20–25,27]. Common postoperative complications are wound infection, chest infection, intraabdominal abscess, pancreatic fistula, and intraabdominal hemorrhage. Chest infection is the most common medical problem in the early postoperative period. Ideally, all patients should stop smoking and continue chest physiotherapy for at least 6 weeks before operation to reduce the incidence of pulmonary complications [21]. The incidence of pancreatic fistula is low after surgery for CP. The incidence varies from 2% to 15% after the FP [1,12,15,20–25,27]. Most fistulas are grade A or B. The low incidence of pancreatic fistula could be explained by the hard texture of pancreatic parenchyma (which holds the suture better) and decreased secretary capacity of the pancreas in CP. The reported incidence of postoperative hemorrhage range from 0% to 9% [1,20–25,27] and it is one of the most common causes of re-exploration in the early postoperative period. In most cases, the source of bleeding is the cored out cavity of the pancreas. Delayed hemorrhage occurs due to erosion or pseudoaneurysm formation of the peripancreatic arteries.

The average weight of pancreatic tissue removed in FP varies in different studies. Frey and Amikura [12] described excision of 5.7 g per patient (range 2–11 g). In a Brazilian study, Gestic et al. [22] reported the average amount of pancreatic tissue removed after the FP was 17.4 g (range 5 g–78 g). Negi et al. [1] reported an average 9.5 g of tissue removed with an average head size of 6 cm. Ray et al. [27], in a recently published series showed that the median weight of pancreatic tissue removed was 8 g (range 5.5 g–35 g). More aggressive removal of pancreatic tissue during head coring may lead to intraoperative injury of bile duct or portal vein and the emergence of new-onset diabetes

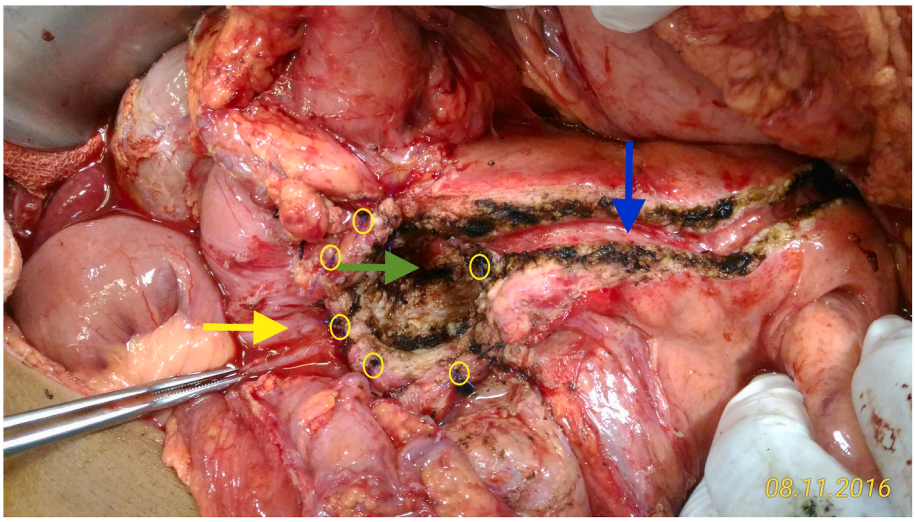

Fig. 2. Operative photograph showing cored out pancreatic head (green arrow) with longitudinally opened main pancreatic duct (blue arrow), duodenum (yellow arrow), and hemostatic sutures (yellow circles). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Short-and long-term outcomes after the Frey procedure.

Author (reference no)	N	Morbidity	PPH	POPF	Mortality	Post-OP Stay	Pain control	New-onset DM	New-onset EPI	Weight gain	Follow-up
		n (%)	n (%)	n (%)	n (%)	(days)	n (%)	n (%)	n (%)	n (%)	(months)
Frey and Amikura (12)	50	11 (22)	NS	1/50 (2)	0 (0)	13.5 (mean)	41/47 (87)	3/31 (12.9)	5/19 (26.3)	25/39 (64)	37 (mean)
Falconi et al. (20)	40	3 (7.5)	0 (0)	2/40 (5)	0 (0)	9 (median)	34/38 (88.8)	3/30 (10)	NS	26/40 (65)	60 (median)
Pessaux et al. (21)	34	7 (20.5)	3/34 (8.8)	4/34 (11.8)	0 (0)	16 (mean)	30/34 (88.2)	7/30 (23.3)	4/12 (33.3)	7/34 (79.4)	15 (mean)
Negi et al. (1)	60	25 (41.6)	2/60 (3.3)	4/60 (6.6)	2 (3.3)	NS	45/60 (75)	4/29 (13.7)	NS	NS	77 (median)
Gestic et al. (22)	73	21 (28.7)	2/73 (2.7)	5/73 (6.8)	0 (0)	10.6 (median)	64/70 (91.4)	22/60 (36.7)	25/51 (49)	NS	77 (median)
Roch et al. (23)	44	15 (34.5)	4/44 (9)	4/44 (9)	0 (0)	14 (median)	21/41 (68.3)	8 (18.1)	7 (16)	31 (70.5)	51.5 (mean)
Cauchy et al. (24)	33	17 (52)	0 (0)	5/33 (15)	0 (0)	19 vs 12	25/33 (76)	4/17 (23.5)	4/24 (16.6)	NS	51 (median)
Ueda et al. (25)	41	7 (17)	3/41 (7.3)	4/41 (10)	0 (0)	20 (mean)	26/29 (90)	2/29 (7)	NS	NS	47 (mean)
Li et al. (26)	75	NS	NS	NS	NS	NS	36/75 (48)	11/51 (21.57)	9/69 (13.04)	NS	50.4 (median)
Ray et al. (27)	138	43 (31)	6/138 (4)	11/138 (8)	0 (0)	9 (median)	103/122 (84)	28/89 (31.46)	31/113 (27.43)	89/122 (73)	65 (median)

N: number of patients; NS: not specified; PPH: post-pancreatectomy hemorrhage; POPF: postoperative pancreatic fistula; Post-OP: postoperative; DM: diabetes mellitus; EPI: exocrine pancreatic insufficiency.

mellitus (DM) and exocrine pancreatic insufficiency (EPI) in the short-term follow up. However, Gestic et al. [22] found no association between the amount of tissue removed and the incidence of new-onset DM or EPI. Moreover, inadequate head coring may lead to inadequate pain control and delayed development of biliary obstruction due to ongoing inflammation in the left over tissue in the pancreatic head.

An important intraoperative complication of FP is inadvertent injury of the intrapancreatic bile duct during head coring. If the bile duct is dilated (≥12 mm), biliary-enteric by-pass is the preferred treatment. If an undilated bile duct is opened inadvertently during head coring, the opening is increased to about 1.5 cm and the edges should be tacked back to the surrounding fibrous tissue within the cored out pancreatic head with 5-0- polydioxanone suture. It allowed both bile and pancreatic secretion to drain in the Roux-en-Y jejunal limb used for pancreaticojejunostomy. This group of patients may develop biliary stricture later on and needs long-term follow-up [28].

8. Long-term results

Most important aspect of any surgery for CP is adequate control of pain because pain is the most common and debilitating symptom for which the patient seeks medical advice. Long-term pain control after the FP varies from 48% to 91% [1,12,15,20–27]. Ten to 20% of patients experience persistent pain after the FP [1,12,15,20–27]. Several factors have been described as predictors of failure to achieve sustained complete pain relief following surgery. These include chronic pain more than 3 years, continuous pattern of pain, narcotic dependency before surgery, more than five endoscopic interventions prior to surgery, postoperative complications, and continued alcohol consumption [1,5,26,29]. Based on the observations that prolonged preoperative pain, multiple endoscopic interventions and narcotic abuse may adversely affects the outcomes of surgery, there is a tendency towards early surgery in CP patients. Few studies have already shown a better pain relief after early surgical intervention [5–7].

Nutrition and endocrine and exocrine functions are important elements in judging the success of an operation to relieve the pain or treat the complications of chronic pancreatitis. Weight gain has been reported in 64–79% of patients after FP [12,15,20,21,23,27]. Pancreatic endocrine and exocrine dysfunctions are common in long-term follow-up of patients with CP. It depends upon the types of intervention and the progression of the underlying disease process. The incidence of new-onset DM and new-onset EPI varies from 10 to 36% and 7–83% respectively depending upon the duration of follow-up and the methods of identification [1,12,13,20–24,27]. EPI does not play a major prognostic role. Occasionally, significant steatorrhoea leading to weight loss and increased susceptibility to infection have some prognostic significance. In majority of cases, EPI can easily be controlled by adequate pancreatic enzyme supplementation therapy. On the other hand, endocrine dysfunction has major prognostic role, particularly after surgical treatment of CP, because of possible hypoglycemia and DM-related organ dysfunctions. In a large prospective cohort study, Malka et al. [30] compared patients who underwent elective pancreatic surgery and with those who never underwent surgical intervention. The cumulative risk of DM was 83% ± 4% 25 years after the clinical onset of pancreatitis. The prevalence of DM did not increase in surgical group overall, but was higher 5 years after distal pancreatectomy than PPPD or drainage procedure. The author concluded that the risk of DM seems to be largely caused by progression of the disease. Pan et al. [31] showed that the incidence of DM was 28% over a median follow-up of 22 years. Risk factors for DM identified were: male sex, biliary stricture, steatorrhoea, alcohol abuse, and distal pancreatectomy. A recent systematic review [32] also reported a high incidence (39%) of new-onset DM after distal pancreatectomy. Relatively enriched distribution of islets cell in distal pancreas and additional tissue loss from surgical resection of already damaged pancreas may be the possible explanations. Recently, in a retrospective observational study, Ray et al. [27] had shown that the longer duration of disease and the longer follow-up period were associated with the development of new-onset DM. This can be explained by the fact that CP is a progressive disease and deterioration of exocrine and endocrine functions are the natural consequences of the disease rather than the result of intervention.

Re-operation after FP is well documented in the literature [1,7,15,22,25,27,33]. The incidence varies from 5% to 30%. The reported indications for re-operations were recurrence of pancreatitis in tail, recurrence of abdominal pain, biliary stricture, choledocholithiasis, malignancy can not be ruled out, duodenal obstruction, and incisional hernia.

9. Comparison with other procedures

Important studies comparing Frey procedure with Pancreaticoduodenectomy and Beger procedure have been presented in Table 3.

10. Frey procedure vs Whipple's or PPPD

One randomized controlled trial (RCT) [34] and four non-RCTs [35–38] compared FP with PD. In a RCT of 61 patients (Frey vs PPPD), Izbicki et al. [34] found a lower postoperative complication rate associated with the Frey procedure (19% vs 53.3%) and better quality of life (QOL) scores (71% vs 43%; p= <0.01). There was no significant difference in mortality, with one death in Frey group (3.2%), and no death in the PPPD group. Both operations were equally effective in controlling pain over 2-year follow-up (pain score decreased by 94% in FP and by 95% after PPPD). The FP thus appears to be as effective as a traditional PD in terms of pain relief, but is associated with less peri-operative morbidity and provides a better QOL. Outcomes of 15-year follow-up of the same study were reported by Bachmann et al. [14]. The author had shown that pain control was good and comparable between both groups, but the QOL was better after FP in regard of the physical status (p = 0.011). Though, there was no significant differences in terms of pain score, long-term mortality was significantly higher in PD group than the patients undergoing FP (53% vs 30%) resulting in a longer mean survival in FP (14.5 ± 0.8 vs 11.3 ± 0.8 years; p = 0.037). No correlation between exocrine and endocrine pancreatic function and pain was found, where as continuous alcohol consumption was associated with poorer outcome regarding quality of life and pain score (p < 0.001). The author concluded that Frey procedure provides better quality of life and long-term survival than PD and thus organ sparing procedure seems to be favourable in treatment of CP. Short-term outcomes are favourable in Frey group with a shorter operation time, less blood transfusion, lower morbidity, shorter length of hospital and

Table 3
Comparison of Frey procedure with Beger procedure and Pancreaticoduodenectomy.

Author	Number	Number	Operative morbidity Mortality		Pain control	DM	EPI	QOL	Duration of follow-up (months)
(reference)		n (%)	n (%)	n (%)	n (%)	n (%)			
Izbicki et al.	Frey	31	19.4%	1/31 (3.2)	28/31 (90)	32%	58%	71%	24 (median)
[34]	PPPD	30	53.3%	0 (0)	26/30 (87)	40%	83%	43%	
Hilderbrand et al.	Frey	39	20.5%	0 (0)	36/39 (92.3)	8/30 (26.7)	20/30 (66.7)	equal	50 (median)
[35]	PD	12	41.7%	0 (0)	8/12 (66.7)	4/6 (66.7)	5/6 (83.3)		
Aimoto et al.	Frey	6	1/6 (16.7)	0 (0)	6/6 (100)	1/6 (16.7)	0 (0)	better	70.8 (mean)
[36]	PPPD	10	2/10 (20)	0 (0)	9/10 (90)	4/10 (40)	1/10 (10)	119.8 (mean)	
Chiang et al.	Frey	25	20%	0 (0)	NS	NS	NS	NS	6 (mean)
[37]	PD	17	11.8%	0 (0)	NS	NS	NS		
Strate et al.	Frey	31	19.4	1/31 (3.2)	NS	13/23 (56.5%)	18/21 (86%)	equal	84 (median)
[13]	PPPD	30	53.3	0 (0)	NS	15/23 (65%)	22/23 (96%)		
Bachmann et al.	Frey	31	19.4%	1/31 (3.2)	7/21 (33.3)	81%	86%	better	180 (median)
[14]	PPPD	30	53.3%	0 (0)	6/14 (43)	86%	93%		
Kelemen et al.	Frey	13	0 (0)	0 (0)	7/12 (57.1)	*3/12 (25)*	10/12 (83.3)	equal	20.6 (mean)
Beger	32	8 (25)	0 (0)	17/27 (63.2)	*1/27 (3.7)*	23/27 (85.1)	41.5 (mean)		
[38]	PPPD	21	13 (61.9)	2 (9.5)	11/14 (78.5)	*6/14 (42.9)*	11/14 (78.5)	31.1 (mean)	
Izbicki et al.	Frey	22	9%	0 (0)	89	59	50	equal	18 (mean)
[39]	Beger	20	20%	0 (0)	95	65	50		
Keck et al.	Frey	50	30%	0 (0)	94	30/50 (60)	38/50 (76)	NS	43 (median)
[40]	Beger	42	40%	0 (0)	81	24/42 (57)	31/42 (74)	62 (median)	
Strate et al.	Frey	36	22%	0 (0)	NS	15/25 (60)	18/23 (78)	equal	104 (median)
[41]	Beger	38	32%	0 (0)	NS	14/25 (56)	22/25 (88)		
Bachmann et al.	Frey	36	22%	0 (0)	NS	83%	86%	equal	192 (median)
[42]	Beger	38	32%	0 (0)		77%	87%		

NS: not specified; Italics: new-onset DM; DM: diabetes mellitus; EPI: exocrine pancreatic insufficiency; QOL: quality of life.

intensive care unit stay as compared to PD [15,34–38]. Long-term pain control was similar between the two groups. QOL was better in Frey group. Although the RCT [42] showed similar exocrine and endocrine dysfunctions in long-term follow, non-RCTs [35,36] showed better preservation of pancreatic functions in the Frey group.

11. Frey procedure vs Beger procedure

One RCT [39] and two non-RCTs [38,40] compared Frey procedure with Beger procedure. Izbicki and Bloechle [39] had randomly assigned 42 patients of CP with inflammatory head mass to either a Beger (n = 20) or a Frey procedure (n = 22). There was no operative mortality in either group. Morbidity was 9% in Frey procedure and 20% after the Beger procedure. Pain was decreased by 95% and 94% after the Beger and the FP respectively. The QOL index was increased by 67% in both the groups. There was no difference in exocrine and endocrine insufficiency. The same study was continued and updated in 1997 to include 74 patients. In 2005, the long term results of these 74 patients with a median follow–up of 104 months were reported by Strate et al. [41]. Seven patients were not available for follow-up (Beger = 4; Frey = 3). There was no significant difference in late mortality (31% [8/26] versus 32% [8/25]). No significant differences were found regarding quality of life (global QL 66.7 [0–100] versus 58.35 [0–100]), pain score (11.25 [0–75] versus 11.25 [0–99.75]), exocrine (88% versus 78%) or endocrine insufficiency (56% versus 60%). After almost 9 years' long-term follow-up, the authors did not find any significant difference regarding mortality, quality of life, pain, or exocrine or endocrine insufficiency within the two groups and they have concluded that "The decision which procedure to choose should be based on the surgeon's experience". Outcomes at 16-year follow-up of the same study were published by Bachmann et al. [42] in 2014. No significant differences between the two groups regarding quality of life, pain control, or other somatic parameters were detected after a median of 16 years postoperatively. Mortality was comparable after Beger and FP at 39% vs. 34%, respectively, with postoperative survivals of 13.0 ± 1.1 years and 13.3 ± 0.9 years, respectively (p = 0.660). No statistically significant differences were found in rates of exocrine insufficiency (Beger 87% vs. Frey 86%; p = 0.953) or endocrine insufficiency (Beger 77% vs. Frey 83%; p = 0.655). When the impact of continuing consumption of alcohol on long-term outcome was analyzed, a strong decrease in quality of life was detected. Scores for cognitive functioning, emotional functioning, and global quality of life were significantly lower in patients with continuing consumption of alcohol. The pain score was also significantly lower in non-drinkers (3 [0–66] vs. 50 [24–96]; p < 0.001). Similarly in a non-randomized study, Keck et al. [40] had shown a shorter operation time in Frey group (360 vs 415 min, p= <0.01) with identical functional outcome in both Frey and Beger procedures but a tendency for better pain control with the Frey operation (62% vs 50%). Development of DM (60% vs 57%) (de novo 34% vs 17%) and EPI (76% vs. 74%) (de novo 34% vs. 33%) were identical in the follow-up period.

12. Conclusion

Based on the available literature, this review showed that Frey procedure a safe and effective procedure for chronic pancreatitis with enlarged pancreatic head provided cancer is not an issue. FP is relatively straightforward, although experience is required to optimize the extent of head resection and to identify and decompress the bile duct if required. It provides excellent pain control with good long-term quality of life which is comparable with Beger procedure and better than PD. Long-term exocrine and endocrine dysfunctions are comparable between the three procedures.

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Consent

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Declaration of competing interest

Nil.

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