

Comprehensive Outcomes of the Frey Procedure: A Single-center Perspective

Vimalakar R Eppa¹, Raju Musham², Gayatri Senapathy³

Received on: 30 June 2024; Accepted on: 16 August 2024; Published on: 27 December 2024

ABSTRACT

Introduction: Chronic pancreatitis is a severe, ongoing inflammation of the pancreas, characterized by significant abdominal pain and deficiencies in both exocrine and endocrine functions. This condition greatly reduces overall well-being, induces psychological distress, and results in a considerable economic burden. The primary indication for surgical intervention is uncontrollable pain. Frey's procedure is the preferred surgical option.

Objectives: This research aims to assess the effectiveness of long-term pain management in individuals with chronic pancreatitis who have undergone the Frey procedure, using a validated pain assessment tool. Additionally, it evaluates exocrine and endocrine insufficiencies along with overall quality of life.

Materials and methods: This is a retrospectively analyzed prospective study conducted at KIMS-Sunshine Hospital, Secunderabad. We evaluated 48 patients who underwent the Frey procedure from 2016 to 2021, each with a follow-up period of at least 1 year. The assessment comprised the validated Izbicki pain score along with evaluations of exocrine and endocrine functions, quality of life using the SF-6 questionnaire, and nutritional status, considering factors such as steatorrhea, glycemic control, and weight gain.

Results: The total number of patients enrolled was 52. Four patients were identified intraoperatively as having malignancy by frozen section and were therefore converted to the Whipple procedure. Therefore, 48 patients (30 = male, 18 = female, mean age 35.2 years) were analyzed in this study. About 6 patients underwent hepaticojejunostomy along with Frey's procedure in view of benign biliary stricture.

In this study of 48 patients, the preoperative mean overall pain score was 66.67. Postoperative mean overall pain scores were recorded at 3, 12, 36, and 60 months, showing values of 6.27, 6.37, 8.26, and 8.42, respectively. These results indicate a clear and statistically significant ($p < 0.05$) reduction in pain both in the immediate and extended follow-up periods.

In the first 3 months following surgery, there was weight gain in most of the patients (65%). Though some patients showed mild weight loss subsequently on long-term follow-up, it was not statistically significant (p -value = 0.041).

The SF-36 quality of life questionnaire indicated a general improvement in quality of life for the entire group, largely attributable to a reduction in pain. Preoperatively, the mean physical component score (PCS) and mental component score (MCS) were 25.37 ± 6.67 and 26.28 ± 9.94 , respectively. These scores increased to 57.78 ± 15.56 and 48.30 ± 26.82 at 3 years, with a p -value of < 0.05 .

Conclusion: Frey's procedure is safe and effective in relieving pain in chronic calcific pancreatitis (CCP) with improved quality of life and seems to be better than PD stenting. However, it has no role in the control of exocrine and endocrine pancreatic insufficiency.

Keywords: Abdominal pain, Chronic calcific pancreatitis, Frey's procedure.

Euroasian Journal of Hepato-Gastroenterology (2024): 10.5005/jp-journals-10018-1445

INTRODUCTION

Chronic pancreatitis is a severe, ongoing inflammation of the pancreas, characterized by significant abdominal pain and deficiencies in both exocrine and endocrine functions.¹ The primary and most debilitating symptom of chronic pancreatitis is persistent pancreatic pain, which can lead to narcotic dependency, dietary restrictions, lifestyle modifications, and frequent hospitalizations. This pain often has a greater impact on quality of life than the resulting exocrine and endocrine deficiencies.¹ With no specific treatment targeting the underlying disease process, management focuses primarily on alleviating symptoms and complications. Therefore, effective pain management is a key therapeutic goal, necessitating ongoing evaluation of new treatment methods.² While medical and endoscopic treatments are commonly used, surgery is required for approximately 40–75% of patients and generally provides faster, more effective, and lasting pain relief compared to endoscopic methods.³

^{1,2}Department of Surgical Gastroenterology, KIMS-Sunshine Hospitals, Hyderabad, Telangana, India

³Department of Radiology, KIMS-Sunshine Hospitals, Hyderabad, Telangana, India

Corresponding Author: Vimalakar R Eppa, Department of Surgical Gastroenterology, KIMS-Sunshine Hospitals, Hyderabad, Telangana, India, Phone: +91 9573201103, e-mail: vimalakarreddy@gmail.com

How to cite this article: Eppa VR, Musham R, Senapathy G. Comprehensive Outcomes of the Frey Procedure: A Single-center Perspective. *Euroasian J Hepato-Gastroenterol* 2024;14(2):182–186.

Source of support: Nil

Conflict of interest: None

Surgical intervention is primarily indicated for persistent abdominal pain that does not respond to medication, jaundice caused by peri-choledochal inflammation, and suspected

malignancy. The choice of surgical intervention is influenced by factors such as the extent of ductal enlargement, pancreatic structure, and the presence of inflammation in the pancreatic head. The swollen pancreatic head is frequently regarded as the main source of pain, and its removal is considered essential for relieving symptoms.⁴ While pancreaticoduodenectomy can provide effective pain relief, there is an increasing preference for procedures that preserve the duodenum and involve drainage of the pancreatic duct.⁵ Two procedures that have gained prominence are Beger's procedure and Frey's procedure. Although the long-term outcomes of the Frey and Beger procedures are similar, the Frey procedure generally offers a shorter operation time and reduced morbidity compared to the Beger procedure.⁶ Frey's procedure is preferred by many pancreatic surgeons because it avoids resection of the pancreatic neck and involves only a single anastomosis.⁶ This innovative technique, first described by Frey and Smith in 1987, involves a local resection of the pancreatic head along with longitudinal pancreaticojejunostomy. The primary source of pain in chronic pancreatitis is the area located between the distal common bile duct, the duct of Wirsung, and the junction of the superior mesenteric and portal veins. In Frey's procedure, this specific area is targeted for local resection of the pancreatic region to relieve pain.⁴

The objective of this study is to evaluate pain management before and after Frey's procedure in patients with chronic pancreatitis. This assessment includes the use of a validated pain score and an analysis of nutritional status, exocrine and endocrine function, and overall quality of life.

MATERIALS AND METHODS

This study is retrospective, with data analyzed prospectively, conducted at KIMS-Sunshine Hospitals. It includes 48 patients who underwent the study between 2016 and 2021, each with a follow-up period of at least 1 year.

Ethical approval was granted by the Institutional Review Board, and written informed consent was obtained from all patients involved in the study.

Chronic pancreatitis was diagnosed based on the criteria set by the Marseilles criteria, based on clinical symptoms and morphological changes in the pancreas identified through imaging studies.⁷

All patients underwent a CT pancreatic protocol, which included a precontrast scan followed by a biphasic postcontrast study: One phase at 30–45 seconds for the pancreatic parenchymal phase and another at 65 seconds for the portal phase.

The pancreatic parenchyma was examined for any mass lesions. The width of the pancreatic duct was measured, and the presence and extent of intraductal calculi were recorded. Ductal dilation was defined as a maximum diameter of 6 mm or greater (Fig. 1).

Magnetic resonance cholangiopancreatography (MRCP) was additionally performed in patients who were found to have dilated CBD with dilated IHBR. Magnetic resonance cholangiopancreatography images in these patients were additionally assessed for the presence of CBD Stricture and to rule out other causes of biliary obstruction such as choledocholithiasis and neoplasm. Upper GI endoscopy and serum CA 19.9 are performed in every case. Exocrine and endocrine functions, nutritional status, work status, analgesic use, and pain severity were all assessed. The Izbicki pain score was utilized to assess pain

severity (Table 1).⁸ Exocrine (Table 2), endocrine, quality of life, and nutritional status were analyzed in terms of steatorrhea, glycemic control, weight gain, and the SF-36 questionnaire.⁹

Inclusion Criteria

All age-groups of patients with diagnosed CCP have the following:

- Persistent pain.
- Main duct disease with intraductal calculi.
- Ductal dilation of 6 mm or greater.

Of the 48 patients who fit the above criteria, 18 patients also had CCP with biliary stricture; they underwent Frey's with Hepaticojejunostomy.

Exclusion Criteria

- Suspected malignancy.
- Severe portal hypertension.

Operative Technique

In our unit, Frey's procedure is performed through a bilateral subcostal incision. After a thorough exploration to rule out unsuspected pancreatic cancer, we begin dissection with extensive Kocherization. Skipping this crucial step can make head-coring difficult. We then enter the lesser sac to expose the body and tail of the pancreas. The right gastroepiploic vessels are ligated and divided to fully expose the pancreas.

Next, we access the pancreatic duct, either by using a 23-G needle for aspiration or through palpation. The duct is then exposed and opened along its entire length, extending up to 2 cm from the tail distally and into the pancreatic head. Extensive coring of the head is done with a thin rim of pancreatic tissue over the portal vein (Fig. 2). Roux en-Y pancreatojejunostomy was performed.

Postoperatively, the patients are followed up every 3, 12, 36, and 60 months after surgery. In our study population, all the patients had a minimum follow-up up to 1 year.

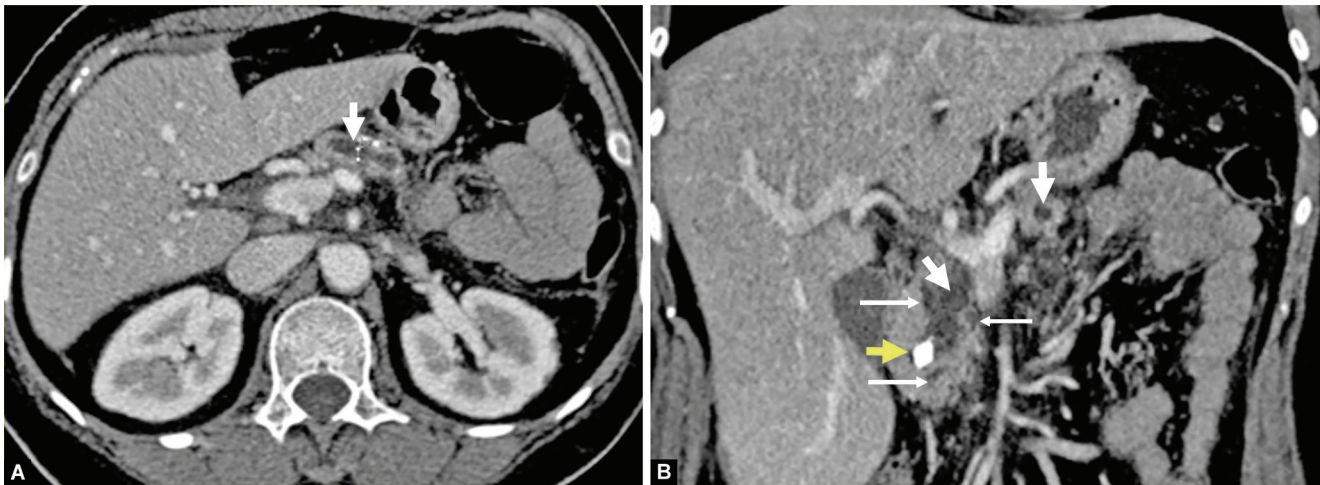
Statistical Analysis

Continuous data are presented as medians (interquartile range, IQR). Student's *t*-test was applied to normally distributed continuous data, while the Wilcoxon test was used for non-normally distributed continuous data. The χ^2 test or Fisher's exact test was employed for categorical data, as appropriate. An odds ratio (OR) with a 95% confidence interval was estimated using the final regression model. A *p*-value of ≤ 0.05 was considered statistically significant. All *p*-values reported are two-tailed and were not adjusted for multiple comparisons. Statistical analysis was conducted using SPSS® version 15.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

The total number of patients enrolled was 52. Total of 4 patients were identified intraoperatively as having malignancy by frozen section and were therefore converted to the Whipple procedure. Therefore, 48 patients (30 = male, 18 = female, mean age 35.2 years) were analyzed in this study. Our cohort stretched from the youngest patient, a tender 6-year-old, to the most seasoned among us, a venerable soul at 75 years of age. About 6 patients underwent hepaticojejunostomy along with Frey's procedure in view of benign biliary strictures.

Around 18 (37.5%) of 48 patients had previously undergone Pancreatic Duct Stenting multiple times elsewhere.



Figs 1A and B: Contrast-enhanced computed tomography abdomen in pancreatic protocol in a patient with chronic pancreatitis. (A) Axial image at the level of body of pancreas; (B) coronal reformatted image at the level of uncinate process, reveal diffuse volume loss in the pancreas with dilatation of the pancreatic duct (white arrows in A and B) which measured 7 mm in diameter. Obstructing intraductal calculus (yellow arrow) was seen in the distal ventral duct. Also seen are dilated side duct branches in the uncinate process (long white arrows in B)

Table 1: Pain score model

Frequency of pain	Points
Daily	100
Several times a week	75
Several times a month	50
Several times a year	25
None	0
Analgesics medication	
Morphine	100
Buprenorphine	80
Pethidine	20
Tramadol	15
Paracetamol	5
Disease related inability to work	
Permanent	100
<1 year	75
<1 months	50
<1 week	25
No inability in last year	0

Table 2: Scoring system for diarrhea and bloating sensation

Frequency	Frequency points
Daily	100
Several times a week	75
Several times a month	50
Several times a year	25
None	0

Pain

In this study, there was a notable improvement in the overall pain score (Table 3 and Fig. 3, Pain scores at preoperative and postoperative).

Stent vs Surgery

After propensity score matching, in the 18 patients who had pancreatic duct stenting, the mean overall pain scoring prior to

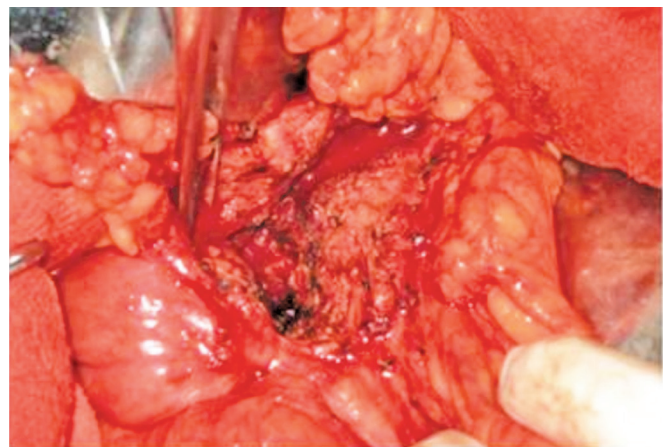


Fig. 2: Head coring with lay opened duct

surgery was 54.24 and the overall pain score was 6.27 postsurgery. We can hence infer that pain relief from stenting is much less when compared to that achieved by Frey’s procedure. However, in view of the small sample size of our study population, more studies with greater numbers are recommended to establish this observation (Table 4).

Weight

Most patients (n = 31, 65%) showed weight gain post-surgery (mean = 48.6, Standard deviation = 7.02) on short-term follow-up. However, some (n = 17, 35%) showed mild weight loss on follow-up, though this number was not statistically significant (p-value 0.041). The short-term weight gain was considered to be due to the release of ductal obstruction, but the long-term assessment of weight analysis post-procedure requires further studies.

Steatorrhea

Steatorrhea (passing bulky, oily, foul-smelling stools floating on the pan) was seen in 25 patients preoperatively and persisted following surgery, 5 new patients developed post-surgery. It shows that there was ongoing fibrosis.

Table 3: Comparison of preoperative and postoperative VAS pain score, frequency of pain, analgesia required, and inability to work

	Preoperative (mean)	Postoperative (mean) immediate 3 months	Postoperative (mean) immediate 1 year	Postoperative (mean) 36 months	Postoperative (mean) 60 months	p-value
VAS	85.14	5.45	5.30	5.45	5.54	<0.05
Frequency of pain	90.57	6.29	6.20	6.32	6.32	<0.05
Analgesia requirement	20	8.10	8.00	8.5	8.5	<0.05
Inability to work	90.95	10.90	10.95	12.1	13.2	<0.05
Mean overall pain score	66.67	6.27	6.37	8.26		<0.05

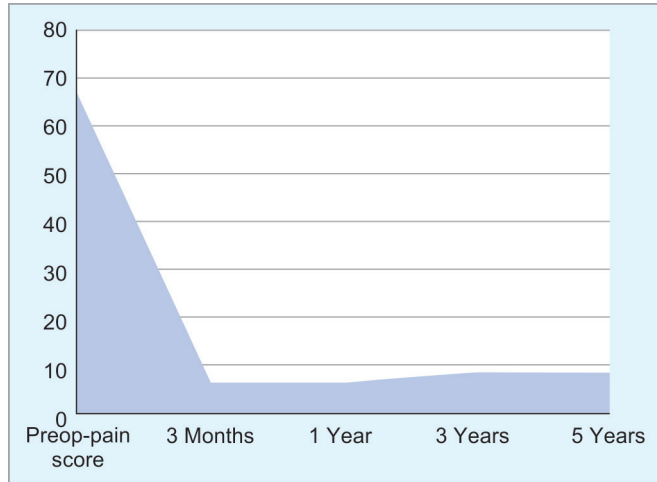


Fig. 3: Pain scores at preoperative and postoperative

Table 4: Scores in the stent group and surgery group

	Pain score in stent group (6 months)	Pain score in surgery group (6 months)	p < 0.05
Mean overall pain score	54.24	6.27	

Glycemic Status

During the course of the disease there was worsening of DM (preoperatively 16 (32%) patients had DM, of them 6 were on insulin and remaining on OHD). New onset DM was seen in 12 (24%) patients within the span of 1-year post-surgery. The need for insulin was increased in the preoperative group. We can, thus infer surgery has no role in glycemic control, however, studies with larger samples are required to establish this (Tables 5 to 7).

Quality of Life

The SF-36 quality of life questionnaire indicated an overall improvement in quality of life for the entire study group, primarily due to pain reduction. Prior to surgery, the mean physical component score (PCS) and mental component score (MCS) were 18.3 ± 7.26 and 22.28 ± 9.4 , respectively. These scores improved to 56.7 ± 8.56 and 42.3 ± 16.82 postoperatively, with a p-value of <0.05. (Fig. 4, SF-36 Analysis)

Post OP Complications

Grade A Pancreatic leak was seen in 4 patients; 2 patients underwent re-explanation for bleeding with 0 mortality. Our data infers that safe procedure to undergo surgery.

Table 5: Preoperative vs postoperative weight analysis

Weight	Mean	Std. deviation	p-value
Preoperative	46.7	7.02	0.041
Immediate postoperative	48.6	7.56	
Postoperative 3 years	42.3	6.220	

Table 6: Steatorrhea in preop vs postoperative

Steatorrhea	
Preoperative	25
Postoperative after 3 months	30 (including the 25 preop-onset)
Postoperative after 1 year	36
Postoperative after 3 years	39

Table 7: Glycemic control in preop vs postoperative group

Preoperative	Postoperative	Total	p-value < 0.05 (pre-SX vs postinsulin requirement)
16	12 (New onset)	28 (24 months follow-up)	
OHA	Insulin	OHA	Insulin
10	6	11	1
		16	12

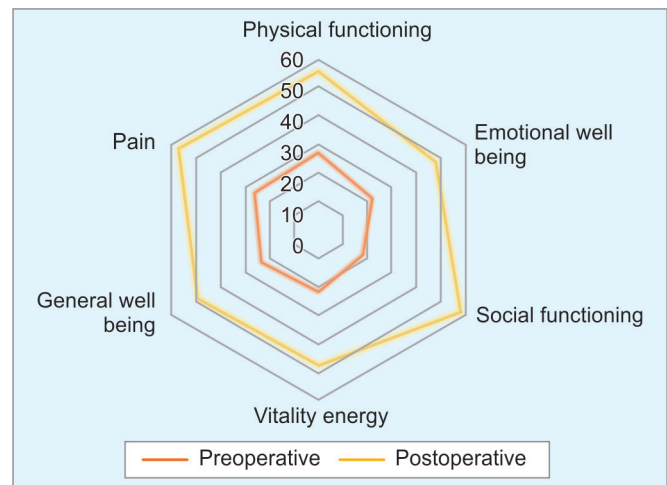


Fig. 4: SF-36 analysis

DISCUSSION

Although multiple theories have been suggested to explain the onset of pain in chronic pancreatitis, the two most widely accepted hypotheses are ductal hypertension and neuropathic changes.^{8,10} Building on these theories, ductal drainage and pancreatic

head resection have become the main surgical approaches for managing chronic pancreatitis. Recent reports suggest that these procedures are effective in alleviating pain for patients with this condition.^{11,12} This study has shown that Frey's procedure led to significant and sustained pain relief over a median follow-up of 3 years.

As concluded in similar previous studies conducted by Gestic et al., Fanconi et al., and Masaki Tanaka et al. Our study also concluded that the immediate and extended outcomes of overall pain score following Frey's procedure were better.^{13,14}

Dhruba Narayan Sah et al. concluded that Frey's procedure is a safe option for patients with chronic pancreatitis, based on a sample of 26 patients. Our study, which included a larger cohort of 48 patients, supports the same conclusion.¹⁵

A multicenter randomized trial from Holland compared 19 cases of endotherapy with 20 cases of surgical drainage. In this study, four patients who initially underwent endotherapy eventually required surgical intervention. Pain relief was achieved in 32% of patients after endotherapy, whereas 75% experienced relief following surgery. Furthermore, Izbicki pain scores and SF-36 quality of life scores were significantly higher in the surgery group.¹⁶ Our findings reached a similar conclusion.

In a study conducted by Yanming Zhou et al., which included 23 studies, Frey's procedure led to weight gain in 60.5% of patients. The study also observed a reduction in insulin requirements, with some patients no longer needing insulin after surgery. Additionally, there was a slight improvement in exocrine function one-year postprocedure, but in the overall study, there was no improvement in exocrine/endocrine function.¹⁷

Frey, Falconi, Roch, Rajendra, and their colleagues found that in some patients with pre-existing insulin-dependent diabetes mellitus, insulin requirements decreased or were eliminated after surgery, likely due to better dietary habits and quitting alcohol.¹⁷ However, our study showed a deterioration in endocrine function.

Studies conducted by L Soundarya Rajan et al.¹⁸ and Satyajith Rath et al.¹⁹ concluded that Quality of life increased in every domain following Frey's procedure, this was proven with statistical significance in our study as well.

A Brazilian review article by Gestic et al.¹⁴ concluded that the morbidity rate associated with Frey's procedure was 28.7% (most common being infections: Pneumonia, SSI, and UTI) with no mortality. In our study, the rate is 12.5%, with no mortality.

CONCLUSION

Frey's procedure is safe and effective in relieving pain in CCP with improved quality of life and seems to be better than PD stenting. However, it has no role in the control of exocrine and endocrine pancreatic insufficiency.

REFERENCES

1. Jarnagin. Management of chronic pancreatitis: Conservative, endoscopic, and surgical, 6th edition. William R Jarnagin (Ed). Netherlands: Elsevier Health Sciences; 2017. pp. 90–98.

2. Zhao X, Cui N, Wang X, et al. Surgical strategies in the treatment of chronic pancreatitis: An updated systematic review and meta-analysis of randomized controlled trials. United States: Lippincott Williams and Wilkins; 2017; pp. 9–10.
3. Evans JD, Wilson PG, Carver C, et al. Outcome of surgery for chronic pancreatitis. *Br J Surg* 1997;84(5):624–629. PMID: 9171747.
4. Rajendran R, Amudhan A, Prabhakaran R, et al. Head coring for chronic calcific pancreatitis without pancreatic head mass: Short-term outcome analysis. *Int J Hepatobiliary Pancreat Dis* 2014;4:62–69. DOI: 10.5348/ijhpd-2014-24-OA-12.
5. Ho HS, Frey CF. The Frey procedure. *Archives of surgery*. 2001; 136(12):1353–1358. DOI: 10.1001/archsurg.136.12.1353.
6. Frey CF, Amikura K. Local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy. *J Hepatobiliary Pancreat Surg* 1995;2(1):25–31. DOI: 10.1007/BF02348284.
7. Sarner M, Cotton PB. Classification of pancreatitis. *Gut* 1984;25(7): 756–759. DOI: 10.1136/gut.25.7.756.
8. Izbicki JR, Bloechle C, Knoefel WT, et al. Duodenum-preserving resection of the head of the pancreas in chronic pancreatitis. A Prospective, Randomized Trial. *Ann Surg* 1995;221(4):350–358. DOI: 10.1097/0000658-199504000-00004.
9. Cech DJ, Martin S Tink. Evaluation of Function, Activity, and Participation. In: *Functional Movement Development Across the Life Span*. Elsevier; 2012. pp. 88–104.
10. Bockman DE, Buchler M, Malfertheiner P, et al. Analysis of nerves in chronic pancreatitis. *Gastroenterology* 1988;94(6):1459–1469. DOI: 10.1016/0016-5085(88)90687-7.
11. Ebbelhøj N, Svendsen LB, Madsen P. Pancreatic tissue pressure: Techniques and pathophysiological aspects. *Scand J Gastroenterol* 1984;19(8):1066–1068. PMID: 6533777.
12. Keus E, van Laarhoven CJHM, Eddes EH, et al. Size of the pancreatic head as a prognostic factor for the outcome of Beger's procedure for painful chronic pancreatitis. *Br J Surg* 2003;90(3):320–324. DOI: 10.1002/bjs.4043.
13. Tanaka M, Matsumoto I, Shinzaki M, et al. Short- and long-term results of modified Frey's procedure in patients with chronic pancreatitis: A retrospective Japanese single-center study. *Kobe J Med Sci* 2014;60(2):E30–E36. PMID: 25339257.
14. Gestic MA, Callejas-Neto F, Chaim EA, et al. Surgical treatment of chronic pancreatitis using Frey's procedure: A Brazilian 16-year single-center experience. *HPB* 2011;13(4):263–271. DOI: 10.1111/j.1477-2574.2010.00281.x.
15. Sah DN, Bhandari RS, Singh YP, et al. Early outcome of Frey's procedure for chronic pancreatitis: Nepalese tertiary center experience. *BMC Surg* 2019;19(1):139. DOI: 10.1186/s12893-019-0592-7.
16. Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med* 2007;356(7):676–684. DOI: 10.1056/NEJMoa060610.
17. Zhou Y, Shi B, Wu L, et al. Frey procedure for chronic pancreatitis: Evidence-based assessment of short- and long-term results in comparison to pancreatoduodenectomy and Beger procedure: A meta-analysis. *Pancreatol* 2015;15(4):372–379. DOI: 10.1016/j.pan.2015.05.466.
18. Soundararajan L, Ulagendrapuram S, Prabhakaran R, et al. Frey's procedure - does it improve quality of life? A single center experience of long-term outcome following Frey's procedure. *International Surgery Journal* 2020;7(3):733. DOI: 10.18203/2349-2902.isj20200814.
19. Rath S, Meher S, Basu A, et al. Quality of Life after Frey's procedure in patients with chronic pancreatitis. *J Clin Diagn Res* 2016;10(3):PC10-5. DOI: 10.7860/JCDR/2016/16736.7417.