FREY’S PROCEDURE - TO ANALYSE THE OUTCOME OF THIS PROCEDURE IN CHRONIC PANCREATITIS
Shilpa Mariappa Casaba^1, Venugopal HG^2, Nagesh N. S^3, Savitha Karlwad^4, Sathish O^5, Vinay B. N^6, Prasanna B^7

1Assistant Professor, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.
2Associate Professor, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.
3Professor and HOD, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.
4Senior Resident, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.
5Senior Resident, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.
6Professor, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.
7Senior Resident, Department of Surgical Gastroenterology and Liver Transplant, Bangalore Medical College and Research Institute, Bangalore.

ABSTRACT
BACKGROUND
Chronic Pancreatitis (CP) is a progressive inflammatory disease characterised by debilitating pain and pancreatic insufficiency. There is enormous personal and socio-economic impact on quality of life, inability to work and even shortening of life expectancy. Although, pancreaticoduodenectomy had been considered the standard surgical procedure for patients with CP because of its high post-op complications with exocrine and endocrine insufficiency, it is not preferred. This has led to a hybrid procedure described by Frey’s, which is used in our study for CP. We aim to analyse the short-term and long-term outcomes of Frey’s procedure at a tertiary care center in patients with chronic pancreatitis.

MATERIALS AND METHODS
A retrospective review of all CP patients who underwent Frey procedure were reviewed from January 2007-January 2016. Perioperative variables, short-term (30 days) and long-term (3 years) outcomes were reviewed. Data are frequency (%) or mean.

RESULTS
A total of 97 patients underwent Frey’s procedure. A total of 72 (70.7%) were men and 25 (29.3%) were women. Mean age was 38 years (range 14-66 years). Indications for surgery included intractable pain (n=97, 100%) and obstructive jaundice (n=4, 4.3%). 9 patients (32.6%) were diabetic preoperatively. Concomitant procedures include biliary drainage procedure was done for 4 patients (4.3%), i.e. choledochojunostomy and splenectomy for 2 patients (2.1%), cholecystectomy (n=6, 6%). Short-term outcomes include surgical site infection (n=10, 10%), pancreatic leak (n=6, 5.82%) and 2 patients required reoperation for bleeding and no mortality (30 days), diabetic ketoacidosis (n=2, 2%). Pancreatic carcinoma was detected in 3 (2.1%) patients. Long-term outcomes include pain free status (n=80, 86.9%), median follow-up of 3 years. Redo pancreatic procedure was performed in 1 (4.3%) for anastomotic leak.

CONCLUSION
Frey’s procedure is a safe and effective pain palliative option for CP patients with intractable pain. Because of its relatively low complication rate, it should be considered first choice of procedure for chronic pancreatitis patients.

KEYWORDS
Pain Abdomen, Chronic Pancreatitis, Frey’s Procedure, Endocrine Insufficiency, Diabetes.

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earlier days, because of its high postop complications, exocrine and endocrine insufficiency and difficulty managing post op pain has been major limitations. This has led to a growing enthusiasm for duodenum preserving pancreatic surgery. Frey described a hybrid procedure, which included head coring of pancreas and longitudinal pancreaticojejunostomy. Surgeons accepted this procedure very well because of its technical feasibility and low surgical risk. Surgical management is usually offered to most patients after medical treatment and endoscopic intervention have failed and is considered the last option of this step-up approach. Medical treatment for pain related to chronic pancreatitis usually fails as drug dependency occurs in most patients. Studies have shown that 40-70% of all patients with chronic pancreatitis require surgery. Indications for surgery are pain with non-resolving common bile duct stricture or duodenal stenosis and suspicion of malignancy.

In 85% of patients, pain is the most common symptom in chronic pancreatitis, its mechanism is still unclear. Several concepts have been hypothesised and pain probably results from a combination of them. The intraductal and interstitial hypertension theory is similar to a compartment syndrome, increased ductal pressure related to duct stricture or calculi and intraparenchymal hypertension as a result of fibrosis and oedema can activate intrapancreatic nociceptors, traditionally the head of pancreas.

**AIM**

Aim is to analyse the outcome of Frey’s procedure as the main indication is pain, head mass and obstructive jaundice. Main objective is to assess the pain in the follow-up after Frey’s surgery as the Frey’s procedure is mainly done to treat the pain.

**MATERIALS AND METHODS**

From January 2007-January 2016, patients who underwent Frey’s procedure for treatment of CP at our Department of Surgical Gastroenterology, Victoria Hospital, and BMC and RI were studied. The diagnosis of CP was based on the findings of clinical history, physical examination and radiological investigation. Radiological investigation consisted of a combination of USG, CECT and MRCP. Exocrine pancreatic insufficiency was defined as the presence of fat in faeces collected for 3 days after ingestion of fat in this same period, endocrine pancreatic insufficiency was determined for glucose levels >126 mg/dL and HbA1c. Bilirubin more than 3 was considered as biliary obstruction.

**Inclusion Criteria**

Patients meeting the following criteria considered eligible for surgery; presumed diagnosis of CP, clinical intractability of abdominal pain and enlarged pancreatic head using radiological criteria, Wirsung’s duct >5 mm and
recommendation of alcohol abstinence for at least 3 months.

Exclusion Criteria
Patients who were excluded were with a trophic pancreatic head and with a high suspicion of malignancy.

Preoperatively, patients with poor nutritional status were identified and assessed by patients’ nutritional status with a preoperative serum albumin <3.5 g/dl were defined as hypoalbuminemic and <3 gm received nutrition for 0-5-7 days before surgery. Pain control was achieved with staggered administrations of analgesics, sparing opioids and its derivations for patients with more severe pain.

Thromboprophylaxis with low molecular weight heparin was given postoperatively and antibiotic prophylaxis with 2gm ofceftriaxone was given at induction of anaesthesia.

All procedures were elective and performed by a skilled surgical team during the study period. Surgical technique followed recommendation described by Frey and smith (Figure 1) through a reverse hockey stick incision after extensive mobilisation of the pancreatic head with Kocher’s maneuver and exposure of the pancreas body and tail. Wirsung’s duct was identified using a syringe aiming toward the tail of pancreas. Then, the pancreatic duct was opened throughout its length longitudinally(Figure 2). At the tail of pancreas, the incision is extended 1-2 cm of the distal portion of the gland and the incision in the head to within 1 cm of the inner aspect of duodenum. At the head of gland, the pancreatic tissue was cored primarily leaving a rim of tissue along the inner aspect of duodenum and excavated down to the length of the pancreatic duct in depth; Santorini duct and uncinate process tissue were excised. Roux-en-Y loop was performed and passed through transverse mesocolon and the cored out head of the pancreas and main pancreatic duct are drained into Roux-en-Y limb of jejunum with a single layer of non-absorbable duct to mucosa anastomosis was done (Figure 3). A drain was placed adjacent to the pancreatic anastomosis. For patients with raised bilirubin, additional choledochojejunostomy was performed along with Frey’s for biliary drainage. In about 70% of the cases, resection of the fibrotic parenchyma is sufficient to relieve a common bile duct stricture. But, if the patients had raised bilirubin, a choledochojejunostomy was performed to relieve the obstruction. Splenectomy was done in 2 patients as the patients had hypersplenism due to left-sided portal hypertension.

All excised tissue was sent for histopathology for examination to confirm that there is no malignancy as pancreatic cancer is high in chronic pancreatitis. No postoperative mortality was noted in patients operated for Frey’s. Minor and major complications were recorded. A pancreatic fistula was defined according to the permanent of International Study Group on Pancreatic Fistula (ISGPF).

Only patients with at least 12 months of postoperative follow up were included.

### RESULTS
A total of 97 patients underwent Frey’s procedure in that 25 were females and 72 were males. Age group was from 14-66 years with a median age of 38 years excluding female patients. The male patients developed CP due to alcohol consumption. Out of 72 male patients, 5 of them had CP due to topical pancreatitis and 67 of them were due to alcohol consumption. Around 60 patients were smokers. All patients presented with abdominal pain, analgesics were used continuously in 72 patients, 60 of them had been hospitalised because of pain crisis. The median operative time was 320 minutes and blood loss was 250 mL, the median size of head of the pancreas was 6.0 cm and a pancreatic duct diameter of 8 (5-15) mm, pseudocysts were found in 12 patients.

<table>
<thead>
<tr>
<th>Major Complications</th>
<th>Number of Patients</th>
</tr>
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<tbody>
<tr>
<td>Pancreatic leak</td>
<td>6</td>
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<tr>
<td>Wound infection</td>
<td>10</td>
</tr>
<tr>
<td>Bleeding</td>
<td>02</td>
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<tr>
<td>Diabetic ketoacidosis</td>
<td>2</td>
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**Table 1**

<table>
<thead>
<tr>
<th>Minor Complication</th>
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<tbody>
<tr>
<td>Ileus</td>
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</tr>
<tr>
<td>Delayed gastric emptying</td>
<td>01</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>01</td>
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</table>

**Table 2**

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<th>Status</th>
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<tbody>
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<td>Normal</td>
<td>84</td>
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<tr>
<td>Diabetics</td>
<td>9</td>
</tr>
<tr>
<td>Obstructive jaundice</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table 3**

Main complications were pancreatic leak, around 6 of them developed in the immediate postoperative period, i.e. less than a week, which resolved on conservative management, 1 required re-surgery due to pancreatic leak, later patients were discharged in stable condition. The patients were followed for a minimum of 3 years. The patients were pain free for almost 2 years. Many patients developed wound infection may be due to prolonged surgery. Wound was cleaned thoroughly and daily dressings were done till the wound was clean. Two patients who developed haemorrhage on the first postoperative day were taken up for surgery to attain haemostasis. There was a small ooze from the surface at the head of the pancreas. One of these 2 patients who developed bleeding on the second postoperative day was taken up for re-laparotomy wherein bleeding was seen from the anastomatic site. There was a case of portal hypertension, which was found as a complication of chronic pancreatitis as he had portal cavernoma and plenty of collaterals. He developed delayed gastric emptying for which pyloromyotomy was done 2 years later. He has developed fundal varices and duodenal varices for which glue has been injected, which was suspected as he had melaena. Two patients developed diabetic ketoacidosis, which were managed conservatively.
One patient developed intestinal obstruction due to kinking of small bowel at distal aspect of the jejunojejunal anastomosis, which was relieved after reopening of the abdomen and release of the adhesive band. In 4 patients, choledochojejunoanastomostomy was done as they had raised bilirubin. It was a side-to-side anastomosis, postoperatively their jaundice was relieved. In 6 patients, they had choledolithiasis for which cholecystectomy was done.

Redopancreaticanastomosis was done in 1 patient. In 3 of the cases, histopathological examination came positive for malignancy.

DISCUSSION

Surgical intervention for CP is commonly accepted as the most effective therapeutic option for pain control and management of complications. Lateral pancreaticojejunostomy has been the choice of ductal decompression, since the second half of the last century. However, it is clear now that this is not a technique that solves all the problems for the patients with CP, especially, those when there is no pancreatic duct dilatation or the disease is predominantly in the head of the gland. This is because though remission of pain occurs in upto 80% of patients at 3 years approximately, 30% of patients subsequently develop recurrent pain after this period of time. This late pain recurrence was often attributed to persistence of pain or relapse of the disease in the pancreatic head. It was evident that Partington Rochelle's procedure failure was due to absence of adequate decompression of proximal main pancreatic duct, uncinate process and secondary head ducts within head of pancreas.

In this context, mixture of 2 techniques has been proposed by Beger and Frey combining this is a less aggressive form of decompression with ductal pancreatic resection with preservation of duodenum. Most CP patients for surgical treatment are in poor general condition with diabetes and are malnourished and therefore at higher risk of postoperative complaints. Thus, a less aggressive technique that leads to lower postoperative morbidity benefits this population.

The present series shows the experience of a single centre in the care of patients suffering from CP who underwent a specific surgical technique the Frey's procedure.

The overall morbidity and mortality in this study is on agreement with recent studies that show a range from 7.5%-39% of morbidity and 0-2.4% morbidity. Haemorrhagic, pancreatic fistula and abdominal collection were frequent complication. Pancreatic fistula rates ranged from 0-12%. The most common clinical complication is pulmonary as the patients were smokers often associated with alcoholism, which is the most frequent case of CP.

Malnutrition is often present in patient with CP, but there are many tools to assess patient nutrition status, such as serum albumin level and BMI. Serum albumin is a good and simple predictor of surgical risk and has a clear correlation. Hypoalbuminemia was associated with poor tissue healing, decreased collagen synthesis in the surgical wounds or the anastomosis and impairment of immune responses. Low albumin levels can be a good predictor of some types of independent predictor of poor surgical outcomes, especially sepsis and major infections. Gibbs et al. reported that a decrease in serum albumin from concentrations >4.6g/dL to <2 g/dL was associated with an exponential increase in mortality rates from <1% to 29% and morbidity rates from 10%-65%.

In the present study, serum hypoalbuminemia <3g was not operated upon, but he was improved nutritionally and was operated when the albumin level was 3 g/dL and above.

The long-term results related to pain control are in agreement with other studies with 91.4% of patient's pain free for a follow up of 36 months. Because, it is a subjective symptom, evolution of pain control as a criterion of surgical success in the postoperative follow up has to be looked up with caution as it may suffer interference from a number of psychological and social factors. The coexistence of mental disorders in patients with alcoholism and those dependent on narcotics can interfere with treatment outcome. Therefore, the service routine requires the cessation of alcohol, tobacco and narcotics abuse and offers psychosocial support for these patients to undergo the surgical procedure, so they can get better result not only consuming pain, but also for the overall recovery of the patient. Furthermore, some studies have shown that the return to alcoholism maybe a cause for pain recurrence in some patient with CP. The authors have observed that surgery is only part of a complex and multidisciplinary treatment that should start preparing the patient for surgery and continue during the whole postoperative period. Unfortunately, despite the monitoring of patients in the postoperative period, one-third of patients returned to drinking alcohol, most of them within first year.

In the current series, 9 patients were already diabetic, i.e. 9%, which is a frequency lesser to other published series ranging from 12%-26% except for Chaudhary et al.17 The development of diabetes de novo ranged from 10%-34% in published studies, wherein values lower than the one observed in this series of 36.7% what would have raised this rate is the extreme aggression to pancreatic parenchyma caused by the median alcohol intake of 278g per day per patient for a long period in this series, which is

<table>
<thead>
<tr>
<th>Re-Laparotomy</th>
<th>Number of Patients</th>
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<tbody>
<tr>
<td>Bleeding</td>
<td>2</td>
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<tr>
<td>Pancreatic leak</td>
<td>2</td>
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<table>
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<tr>
<th>Additional Procedures</th>
<th>Number of Patients</th>
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</thead>
<tbody>
<tr>
<td>Cholecystectomy</td>
<td>6</td>
</tr>
<tr>
<td>Choledochojejunostomy</td>
<td>4</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>2</td>
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</tbody>
</table>

significantly above the mean levels reported by Falconi et al. (100g/day). In one patient, there was significant pancreatic leak for which a redo surgery was done.

It is important to note that despite the complications and the inability to step the deterioration of glandular function. The main goal of surgery is to control pain, which was largely achieved. This can be noticed at follow up, which is an indirect sign of improved quality of life.

**CONCLUSION**
In conclusion, Frey’s procedure is a safe effective therapeutic option for surgical treatment of intractable pain because of its hybrid nature, combining both resection and drainage. The Frey’s procedure has been conceptualised based on the pathophysiology of chronic pancreatitis. The short and long-term outcome, especially pain relief and quality of life are better after the Frey’s procedure than after any other surgical procedure performed for chronic pancreatitis.

**REFERENCES**