

THE EFFECT OF PUESTOW PROCEDURE ON CHRONIC PANCREATITIS

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Abstract

A Puestow procedure is an option for patients suffering from chronic pancreatitis with ductal dilation and severe intractable pain. **Objectives:** To evaluate the effect of the procedure on pain, endocrine and exocrine function through a period of one year in a high volume tertiary center. **Methods:** The study included fourteen patients undergoing Puestow procedure who were followed up for the improvement of pain, blood glucose level and steatorrhea over a period of one year. **Results:** A dramatic response in pain (intensity/ frequency/consequences) and fasting blood glucose level occurred after one year. While for the postprandial blood glucose level, it showed an improvement that reflects a remarkable control of blood glucose level. Regarding the steatorrhea, the improvement was not statistically significant. There was a rise in percentage of patients with no fat detected in stool; however, some patients with 'few' fat in stool showed an increased fecal fat at the end of the year. **Conclusion:** The dramatic relief of pain after the Puestow procedure is a life-changing step for patients suffering from a painful experience. The disability that this disease causes could be reversed through a procedure that is less invasive than other pancreatic surgeries, carrying less morbidity and mortality.

Keywords: Chronic Pancreatitis- Puestow Procedure - Pancreatic Surgery - Pancreas – Steatorrhea.

INTRODUCTION

Chronic pancreatitis (CP) is a complex disorder that causes a significant and chronic incapacity in patients with a substantial burden on the society. It leads to a progressive and irreparable destruction of the pancreatic parenchyma, which results in fibrosis, and consequent loss of pancreatic function. This may cause steatorrhea, malabsorption, diabetes and unbearable pain. Pain, often in combination with obstruction (duodenum, bile duct, pancreatic duct, portal vein), remains the main indication for surgical intervention.^[1] Major advances have been made in the etiology and pathogenesis of this disease, and the role of genetic predisposition is increasingly coming to the fore. However, advances in noninvasive diagnostic modalities allow for better diagnosis of chronic pancreatitis at an early stage of the disease. The impact of these advances on surgical treatment is beginning to emerge; for example, patients with certain genetic predispositions may be better treated with total pancreatectomy versus less invasive procedures.^[2]

Patients typically present with deeply penetrating and dull epigastric pain, which classically radiates to the back. The pathophysiological mechanisms for pain in CP are incompletely understood. An increasingly discussed hypothesis is that neural inflammatory cell infiltration leads to pancreatic neuritis with enlarged nerves, changes in neural plasticity, and formation of a dense intra-pancreatic neural network. Since the underlying pain mechanisms are just beginning to be understood, treatment of chronic unbearable CP pain is often empirical and insufficient, with surgery being the treatment of choice.^[2]

Therefore, surgical treatment can improve the quality of life in patients not only by relieving pain and retaining the secretory function of the pancreas, but also by effectively removing the risk factors for cancer. Many factors such as disease location (head, body, tail of the pancreas, or diffuse disease) or the suspicion of cancer can often affect the surgical approach.^[3] Considerable controversy remains with respect to the surgical management of chronic pancreatitis. Modern understanding of the neurobiology of pain in chronic pancreatitis suggests that a window of opportunity exists for effective treatment of the intractable pain, after which central sensitization can lead to an irreversible pain syndrome. Effective surgical procedures exist for chronic pancreatitis; however, the timing of surgery is unclear.³ A Puestow procedure, or a longitudinal pancreaticojejunostomy, is an option for patients suffering from chronic pancreatitis with ductal dilation and severe intractable pain (who have failed non-operative therapy). For optimal treatment of patients with chronic pancreatitis, close collaboration between a multidisciplinary team including gastroenterologists, surgeons, and pain management physicians is needed. Due to the small number of Puestow procedures performed at individual centers, the current study examines the 1-year outcomes following this procedure in a high volume tertiary center.^[4]

PATIENTS AND METHODS

This case series study was conducted on 14 patients undergoing Puestow procedure in Cairo University Hospitals during the period from June 2020 until January 2021. The study evaluates the effect of the procedure on pain, endocrine and exocrine function. Pre-operative assessment of severity will be done using the Chronic Pancreatitis Obstructive Prognosis Score (COPPS)(Fig.1).^[7] All patients who were diagnosed with chronic pancreatitis through history and radiological findings, with dilated pancreatic duct (with or without stones) were included in the study. Magnetic resonance cholangiopancreatography (MRCP) provided a noninvasive evaluation of ductal changes with a high resolution and sensitivity. However, patients with non-dilated pancreatic duct or chronic abdominal pain due to other causes were excluded from the study. An informed written consent was obtained from each participating patient.

	1 point	2 points	3 points
NRS (1-10), most intense day within the past 7 d	0-2	3-6	7-10
HbA1c, %	>6.0	5.5-6.0	<5.5
CRP, mg/L	<3.1	3.1-20	>20
BMI, kg/m ²	>25	18-25	<18
Thrombocytes, Gpt/L	150-400	100-150	<100, >400

COPPS A = 5-6 points COPPS B = 7-9 points COPPS C = 10-15 points

CRP, C-reactive protein; NRS, numeric rating scale for pain: 0 = no pain, 10 = worst imaginable pain.

Figure 1: Chronic Obstructive Pancreatitis Prognosis Score (COPPS) ⁷

Regarding the postoperative follow-up, patients will be assessed at six months interval and at the end of the year. The assessment will be based on three factors: first, the intensity, frequency, and consequences (IFC) score of pain.^[8] Second, the fasting and 2 hours postprandial levels of blood glucose were measured (mg/dl) in all patients, and their insulin requirements for diabetic control was recorded. Finally, the exocrine function was assessed by the steatorrhea and the presence of fecal fat on stool analysis. They will be graded as nil, few, some or many. The primary outcome of this study was the pain score of patients pre-operatively, at six and twelve months post-operatively. The secondary outcome was the fasting, two hours postprandial glucose level and fecal fat of patients pre-operatively, at six and twelve months post-operatively. Complications in the form of leakage, pancreatic fistula, sepsis and recurrence of pain after post-operative resolution were additional outcomes. Data analysis packages will be SPSS version twenty one. Qualitative data were presented by number and percentage; quantitative data will be presented by mean, standard deviation, median and Interquartile range. ANOVA test was used to detect correlations between early surgical intervention and pain control. Level of significance was considered if p is equal to or below 0.05.^[9]

Intensity (I) was given a score of 0 to 8 on the following scale:

- No pain I₀
- Insignificant pain (only on direct questioning) I₂
- Mild pain I₄
- Moderate pain (analgesics regularly required but no drug dependency) I₆
- Severe pain (Drug dependency present and sleep disturbed regularly) I₈

Scores	0	1	2	3	4
(F) Frequency					
of pain episodes/year	3	4-6	7-9	10-12	12
duration in hrs/episode	<12	12-24	24-48	48-78	72
(C) Consequence					
Work loss in months/year	0	1	2-4	5-8	8
No. of hospitalizations/year	0	4	5-8	9-12	12

Figure 2: Intensity, Frequency and Consequences (IFC) Scoring System⁸

RESULTS

The study showed a male predominance of 57.10%, while females were 42.90%. Regarding the age of the patients, it ranged from fourteen to fifty five years old with a mean of 35.79. Preoperatively, 85.70% of patients had pancreatic duct stones, 85.70% had fecal fat on stool analysis and 78.60% were diagnosed with diabetes mellitus. According to the COPPS, the studied patients were classified in to the B (71.40%) and C (28.60%) groups with no patients meeting the criteria of the A group found in

this study. Chart 1 conveys a dramatic improvement in the mean IFC score (from a mean of 13.14 to 4.86) over the whole year. Although 78.6% of patients were diabetic on presentation, chart 2 shows a significant improvement of the fasting blood glucose from a mean of 153.21 mg/dl to 103 mg/dl at 6 months and 102.64 at 12 months (p value: 0.007 and 0.024 respectively). Furthermore, the two hours postprandial blood glucose level showed an improvement from a mean of 204.43 mg/dl to 149.29 mg/dl after one year (chart 3), reflecting a remarkable control of blood glucose level (p value: 0.001) with no development of new onset diabetes. While for the exocrine function that was reflected through the grade of steatorrhea, the improvement was not significant. Table 1 conveys the rise in percentage of patients with no fat detected in stool (from 14.3% to 50%), however, the percentage of patients with 'many' fat in stool rose from 21.4% to 35.7% (p value: 0.527). The presence of patients developing 'many' fat in stool, after having 'few' or 'some', abolishes any significance regarding the surgery related improvement of steatorrhea.

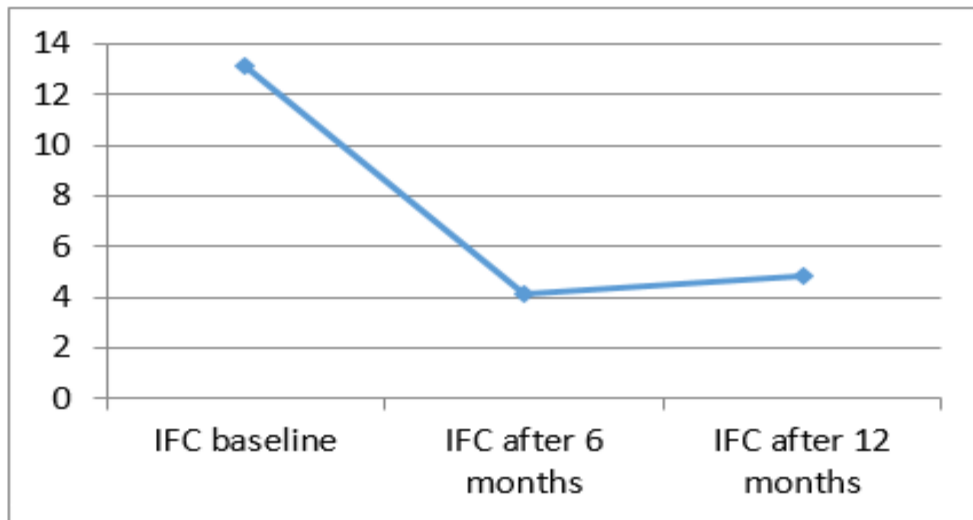


Chart 1: Post-operative Pain (IFC)

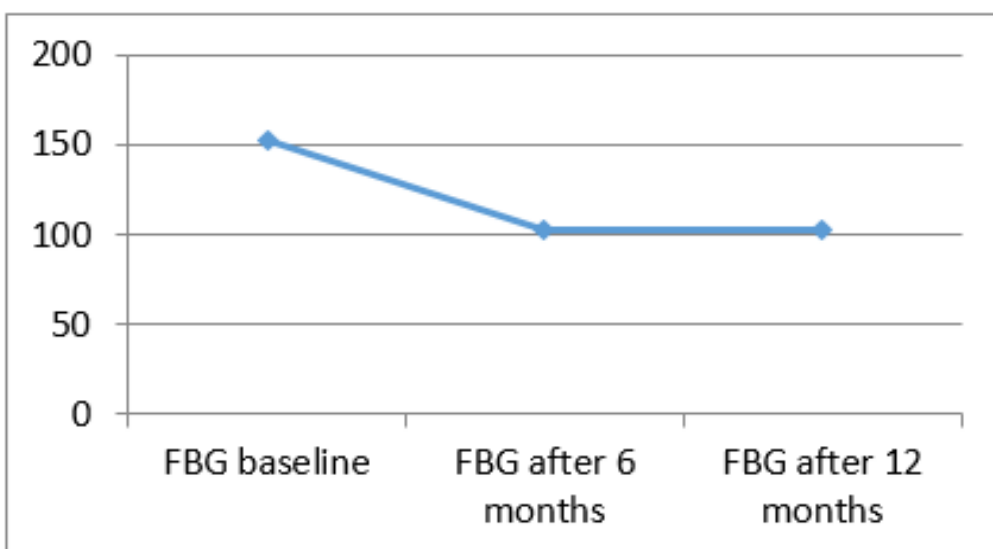


Chart 2: Post-Operative Fasting Blood Glucose Level

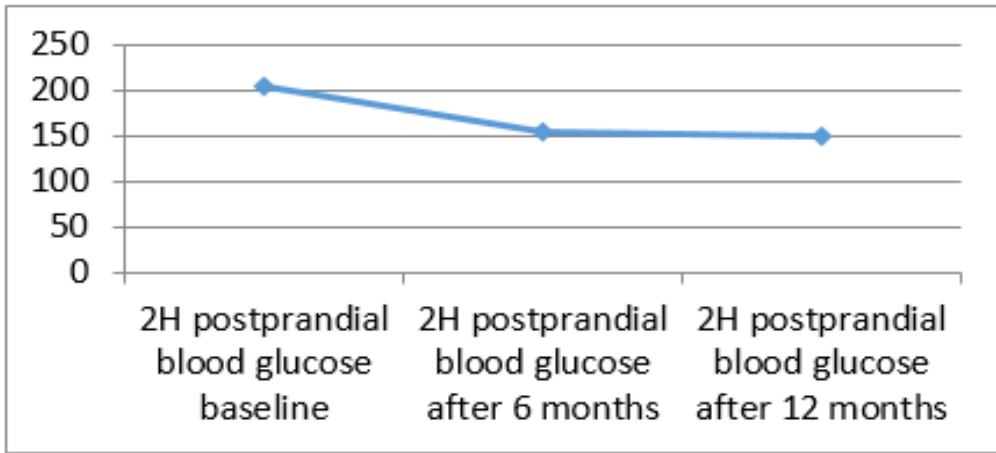


Chart 3: Post-operative Two Hours Postprandial Blood Glucose Level

Table 1: Post-operative fecal fat

		baseline		After 6 months		After 12 months	
		Count	%	Count	%	Count	%
Fecal fat	Nil	2	14.3%	5	35.7%	7	50.0%
	few	4	28.6%	2	14.3%	0	0.0%
	some	5	35.7%	5	35.7%	2	14.3%
	many	3	21.4%	2	14.3%	5	35.7%
P value		-----		0.398		0.527	

Regarding the postoperative morbidity, only one patient (7.10%) out of fourteen was re-explored for intestinal obstruction after three days and a revision of a stenosed jejunojunostomy was done. Since only two categories of patients are present in this study (COPPS B and C), a comparison was done regarding the degree of improvement. This comparison aims to detect a correlation between the degree of disease severity and the extent of response to surgery. Chart 4 shows the degree of postoperative pain improvement in both categories compared to each other. Tables 2 and 3 show the degree of improvement in postoperative fasting and postprandial glucose levels comparing both categories.

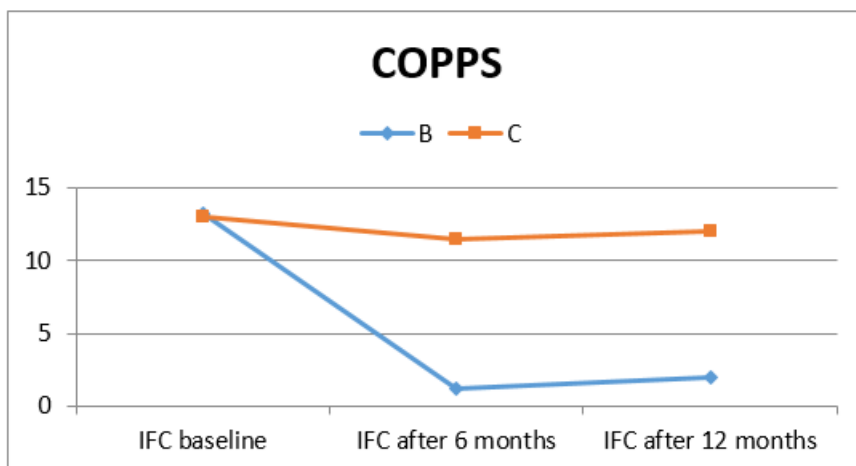


Chart 4: Post-operative Pain in COPPS B and C

Table 2: Post-operative fasting blood glucose level in COPPS B and C

	COPPS										P value
	B					C					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
FBG baseline	170.30	115.70	117.00	81.00	370.00	110.50	0.58	110.50	110.00	111.00	0.635
FBG after 6 months	108.20	18.41	110.00	81.00	130.00	90.00	0.00	90.00	90.00	90.00	0.106
FBG after 12 months	106.70	15.45	115.00	81.00	120.00	92.50	2.89	92.50	90.00	95.00	0.106

Table 3: Post-operative postprandial blood glucose level in COPPS B and C

	COPPS										P value
	B					C					
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
2H postprandial blood glucose baseline	220.20	115.22	160.00	141.00	420.00	165.00	5.77	165.00	160.00	170.00	0.539
2H postprandial blood glucose after 6 months	160.20	15.35	160.00	141.00	180.00	145.00	5.77	145.00	140.00	150.00	0.054
2H postprandial blood glucose after 12 months	155.00	13.33	155.00	135.00	170.00	135.00	5.77	135.00	130.00	140.00	0.024

DISCUSSION

Based on the severity of the disease, which patient will mostly benefit from the Puestow procedure was a question evaluated in this study. Chart 4 shows better pain control in the COPPS B group in comparison to the COPPS C group, while charts 5 and 6 show no statistical difference between COPPS B and C groups in postoperative fasting and postprandial blood glucose level. However, the results of this comparison proved to be statistically not significant with high p values (tables 2 and 3). Increasing the number of studied patients in each COPPS group and including patients from the COPPS A group may yield different results. Apart from the overall significant improvement of pain in the studied patients, only one patient (7.1%) did not show any improvement on the follow up criteria. Pre-operatively, the patient was classified as COPPS C. With negative genetic studies [pancreatitis panel] and follow up imaging showing drained non dilated pancreatic duct with no stones, the obstructive and the genetic components of pancreatitis were excluded from being causes of persistent unrelieved pain. The response that this case showed postoperatively, revealed the importance of understanding the actual underlying etiology and the severity of the disease in order to direct the patients to the best surgical procedure (resection vs. drainage).

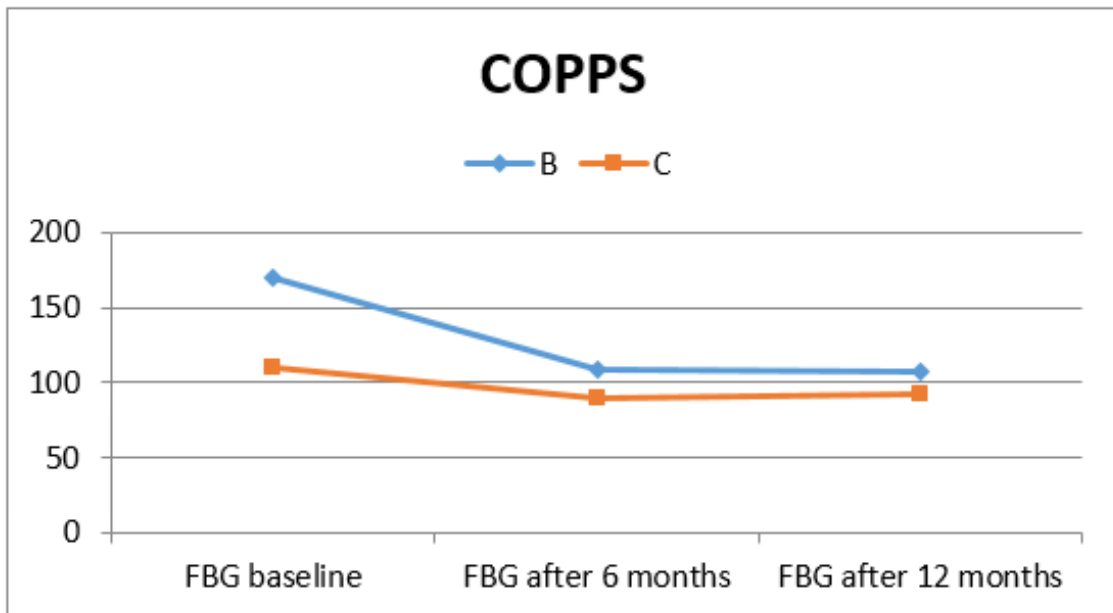


Chart 5: Post-operative fasting blood glucose level in COPPS B and C

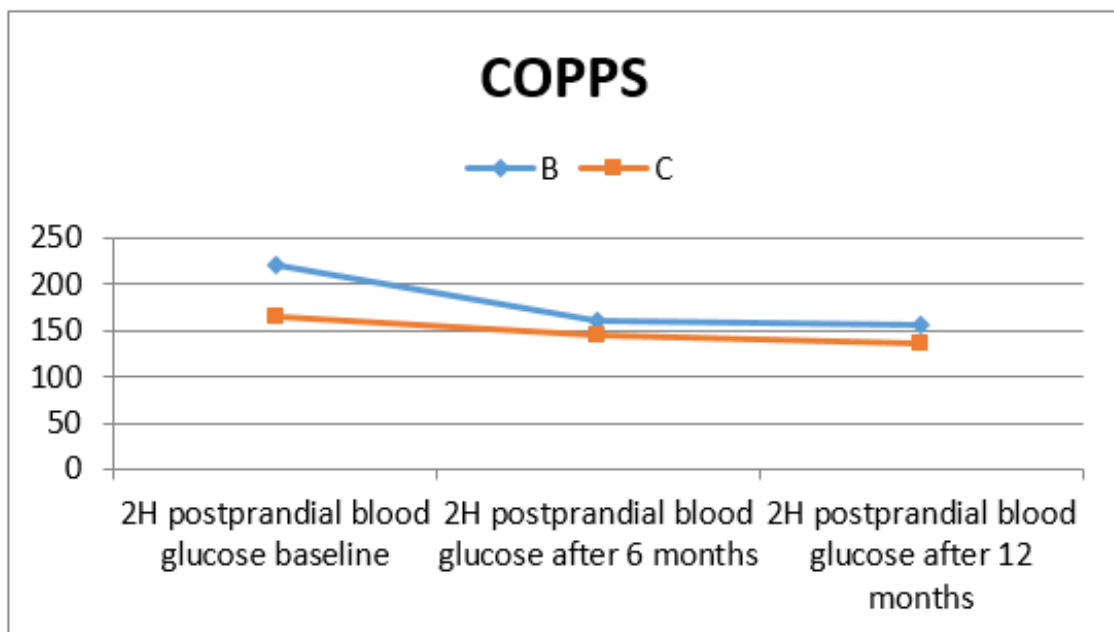


Chart 6: Post-operative postprandial blood glucose level in COPPS B and C

In consistency with our findings regarding pain resolution, Kim and Hong in 2016 followed up eleven patients after undergoing a laparoscopic Puestow procedure for more than two years. All patients showed pain resolution with no relapses recorded.^[10] While in 2019, Hodgman et al retrospectively studied thirteen patients over a period of fifteen years. Pain improved in only 60% while 30% faced post-operative morbidity between ileus and development of intra-abdominal abscess.^[11] Although having a similar number of patients with a longer period of follow-up, patients in our study showed a better resolution of pain with less postoperative morbidity. Back in 2013, Abhishek et al performed Puestow procedure for forty five patients and followed them for three years. Recurrent pain requiring

hospitalization occurred in 16.7%, 7% of patients required revision surgery, morbidity appeared in 13% and mortality occurred in 7%. However, recurrence of pain, the need for a revision surgery or mortality were not found in our study.^[12]

A systematic review in 2014 done by Yang et al focused on the impact of early surgery on intractable pain and quality of life. The review did not only explain the effect of surgery on pain relief but also revealed an important factor that alters the response to surgery. The timing of surgery is a critical issue that relates the degree of pain relief to the duration of the chronic pancreatitis (before drainage) period. Early surgery and a shorter period of CP were associated with an increased likelihood of partial or complete postoperative pain relief.^[13] Relying on the hypothesis of the clinical pain syndrome, continuous pancreatic nociceptive afferent injury can result in peripheral and central sensitization leading to neuronal hyperresponsiveness, which can result in a continual state of pain independent of peripheral nociceptive input. Central sensitization is associated with reduced efficacy of invasive endoscopic and surgical treatments directed at the pancreas. The poor correlation between structural changes in the pancreas and the severity of pain, and the persistence of pain in patients who have had a total pancreatectomy, lend credibility to this central sensitization hypothesis.^[14]

The Dutch pancreatitis study group in 2012 highlighted two independent risk factors, the repeated pre-operative endoscopic management and the use of pre-operative opioids as part of the medical management. They concluded their results with a clear explanation of why drainage of obstructed pancreatic ducts does not relieve pain. They stated that ‘allowing pancreatic pain to exist for a prolonged period of time is associated with peripheral and central nerve sensitization that leads to a self-perpetuating pain state.’^[15] The study by Usama et al (part of the Dutch pancreatitis group) showed that repetitive endoscopic interventions lacking a successful pain relief are associated with a less favorable outcome when surgery is eventually performed. Additionally, each endoscopic intervention is associated with a relatively small risk for morbidity but the cumulative risk may be substantial.^[16] This may explain why the aforementioned patient did not show any improvement in pain post-operatively. Pre-operatively she had underwent several trials of endoscopic stenting and drainage resulting in the prolongation of the chronic pancreatitis “pain stimulation” period. The rise of the ESCAPE trial in 2021 showed that early surgery outperforms conservative treatment and endoscopy, which may have significant implications for daily clinical practice. If the present step-up approach of conservative treatment and endoscopy is followed, one should bear in mind not to miss an early window of opportunity to operate on a surgically treatable chronic pancreatitis. Future research should focus on the many aspects of pain in chronic pancreatitis and the impact of our interventions to improve patient selection for invasive treatment.^[17]

Regarding the glycemic control, shortening of the period of continuous irritation to the pancreatic tissue and the ongoing fibrosis and atrophy lowered the odds of developing denovo diabetes mellitus after drainage.^[13] In our study, the 2 hours post-prandial glucose levels improved 26.9% (from 204.43 mg/dl to 149.29 mg/dl). This indicates the preservation of the residual pancreatic function instead of regaining the lost function.^[18] The possible explanation for the improvement in endocrine function after decompressive surgery may lie in the fact that the islet cells may be “normal”. It is postulated that the obstruction of the pancreatic duct (together with the dense intralobular and perilobular fibrosis) creates a compartment syndrome and supposedly, the insulin deficiency results from poor islet perfusion and poor insulin absorption due to raised interstitial pressures. The enhanced perfusion of the islets of Langerhans may increase insulin transfer and absorption, thereby resulting in an improvement of the glycemic control. It is unlikely that stenting of the pancreatic duct would have resulted in a similar improvement because pain reduction after stenting only occurred in 54% of patients and may only be transient.^[19]

Few limitations were encountered during this study and their effect might have altered the accuracy of the results. First, the variation of the disease severity among the studied patients. All patients were diagnosed with chronic pancreatitis but not all of them had the same pre-operative duration of the disease, or the same number of endoscopic attempts before seeking the surgical option. Although similar to several studies discussing the effect of the same procedure, the small number of patients should have been increased to improve the accuracy of the results. A one-year follow up was enough to reveal the post-operative effect but not sufficient to discover relapses or development of de novo pancreatic insufficiency. The choice of the follow up criteria depended mainly on the availability of laboratory resources. The fecal elastase, C peptide and pancreatic polypeptide levels might have given a clearer picture of the residual pancreatic function and might have discovered attempts of regaining pancreatic functions.^[13]

CONCLUSION

In the end, nearly all patients experienced resolution of pain with no relapses for one year except for the only patient that has been discussed previously. Regarding the diabetic patients, a better glycemic control was apparent during the follow up period. In addition, there was no development of new onset diabetes mellitus. Apart from the dramatic resolution of pain and the assumed preservation of the endocrine function, the maintenance of the exocrine function is still questionable. Therefore, the role of this procedure in limiting the progression of disease by relieving the obstruction is hardly presumed. The pain may not resolve with resolution of obstruction due to the persistence of a systemic trigger that is left untreated after the drainage procedure. Timing of surgery is another factor in chronic pancreatitis patients that needs to be discussed in multidisciplinary groups in expert centers. This offers an advantage of not missing an early window of opportunity to operate on a surgically treatable chronic pancreatitis.

Despite the ambiguity of preserving the residual pancreatic function, the dramatic relief of pain after the Puestow procedure is considered a life-changing step for patients suffering from a painful experience. The disability and the social burden that this disease causes, could be reversed through a procedure that is less invasive than other pancreatic surgeries, carrying less morbidity and mortality. Future research should focus on the many aspects of pain in chronic pancreatitis and the impact of our interventions to improve patient selection for invasive treatments.

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Statements and Declarations

On behalf of all Co-Authors, I shall bear full responsibility for the submission. I confirm that all authors listed on the title page have contributed significantly to the work, have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission.

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