Endoscopic Ultrasound-Guided Celiac Plexus Block Can Be a Useful Procedure for Pain Relief in Chronic Pancreatitis When Used Selectively

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Background and Objectives: Endoscopic ultrasound (EUS)-guided celiac plexus block (CPB) for pain relief in chronic pancreatitis (CP) has wide variation in results as reported in the literature. The objective was to find out the efficacy of EUS-CPB in painful CP from our region where phenotype of CP is different from West and to find out factors favoring response to EUS-CPB.

Methods and Results: Patients with known CP who underwent EUS-CPB were assessed for response to CPB. Response to EUS-CPB was recorded as more than 50% reduction in visual analogue scale (VAS) score for pain severity at 1 week, 4 weeks, 12 weeks and 24 weeks after procedure. Factors between responders and nonresponders were analyzed. Among 29 patients who underwent EUS-CPB during the study period, response was seen in 72.4% patients after the procedure. The mean time to response to EUS-CPB was 1.22 (± 0.43) days. Mean duration of response was 8 months (± 4.73). Short duration of painful CP (≤ 2 years) was seen in 15 patients (51.72%) and long duration (> 2 years) was seen in 14 (48.27%). Among responders (21/29), those patients who had short duration of disease had significantly lower median VAS score at 12 weeks, (1 versus 3, p-value = 0.026) and at 24 weeks, (1.5 versus 2.5, p-value = 0.049), as compared to those with longer duration of disease. Overall, 83.3% males responded as compared to 54.54% females (p = 0.04). Significant proportion of subjects who responded either stopped or used analgesics occasionally (p = 0.0001). There was no statistically significant difference in response to EUS-CPB with respect to age, prior history of endoscopic retrograde cholangiopancreatography (ERCP), etiology of CP, prior history of surgery, or whether only EUS-CPB was done (p > 0.05 for all).

Conclusion: EUS-CPB can be effective when used in select group of painful CP patient who are not immediate candidates for surgery especially in early course of disease. It can be offered to patients with persistent pain despite optimum medical therapy. When effective, it can reduce need for analgesic medication at least in short to medium term.

Keywords
► endoscopic ultrasound-guided celiac plexus block/neurolysis
► management of pain in chronic pancreatitis
► celiac ganglion
► celiac plexus neurolysis
► endotherapy in chronic pancreatitis
Introduction

Pain is the most distressing symptom of chronic pancreatitis. Variable results to different modalities used for pain management are due to complexity of various neurogenic pathways and multiple factors resulting in pain in chronic pancreatitis. Step-up approach has been well accepted in the management of pain in chronic pancreatitis. Endoscopic treatment is considered first-line modality for pancreatic duct (PD) strictures and stones. However, there is discordance among technical success that can be around 85 to 86% and clinical success that ranges from 51 to 60% only. Celiac plexus interventions in form of endoscopic ultrasound-guided celiac plexus block (EUS-CPB) and endoscopic ultrasound-guided celiac plexus neurolysis (EUS-CPN) have been well-established endoscopic modality for relieving pain when medical management fails in patients with chronic pancreatitis and pancreatic cancer who are not immediate surgical candidates for any reason. Injection of ethanol (neurolysis) and bupivacaine (block) disrupts the pain signal transmission to spinal cord and central nervous system, thereby interfering with pain perception in chronic pancreatitis. In clinical practice EUS-CPB is preferred over EUS-CPN for chronic pancreatitis as neurolysis can result in retroperitoneal fibrosis and carries the risk of adverse events more than EUS-CPB. EUS-CPN has an inferior result in chronic pancreatitis as compared to pancreatic cancer. Therefore, offering EUS-CPN to patients of chronic pancreatitis may not be appropriate outside of research setting.

Previous studies have shown variable result for success with EUS-CPB for duration and degree of pain relief in chronic pancreatitis. This has been mainly due to difference in techniques, approach, and selection of patients. One of the systematic reviews showed overall clinical success rate of 51% for EUS-CPB. Because the effect of CPB is temporary, serial procedures are often advocated in those having response to index procedure. There is not enough data for efficacy of EUS-CPB in Indian population. There is also a debate among experts regarding when and in which group of patients this procedure should be offered in chronic pancreatitis.

In this background, we aimed to assess the efficacy of EUS-CPB in patients with CP, ascertain potential predictors of response, and explored whether adding EUS-CPB early as opposed to late during course of CP provided more benefits.

Materials and Methods

We retrospectively analyzed data from prospectively maintained records of patients with CP who underwent EUS-CPB between January 2019 and May 2023 in a tertiary care hospital.

All the patients included were proven cases of painful chronic pancreatitis based on their previous history, clinical examination, and at least one cross-sectional imaging. All the patients were on optimum pharmacological treatment and pain persisted needing use of frequent analgesics. These patients were given oral and/or intravenous tramadol as and when required for pain relief. Together with this they were given pancreatic enzyme replacement therapy using uncovered preparations, selenium containing antioxidants, proton-pump inhibitors, and appropriate dietary management. Alcohol abstinence was re-enforced and diabetic management was done wherever indicated. In certain patients in addition to above tricyclic antidepressants (nortriptyline 10–25 mg and pregabalin 75 mg) were also tried.

EUS-CPB was done in following patients: (a) those CP patients with persistent pain despite optimum medical management requiring frequent analgesics where endoscopic retrograde cholangiopancreatography (ERCP) was not indicated due to small duct disease (absence of PD stone and/or stricture) in 15 patients; (b) those patients where pain persisted despite optimum medical management and ERCP (which was done based on ductal anatomy as per the institutional protocol) in 14 patients. In cases where there were multiple large calculi, extracorporeal shock wave lithotripsy followed by ductal clearance was done. In cases of PD strictures, stricture dilatation followed stenting was done. Repeated sessions of ERCP were done in patients with strictures with gradual upgradation of stent size. In these cases, EUS-CPB was used as an additional therapy for pain relief if pain persisted after ERCP, while the patients were still under repeated ERCP protocol. Also, any additional cause of pain like peptic ulcer disease, pancreatic mass, and common bile duct stricture was ruled out by appropriate imaging before EUS-CPB.

Option of surgery in patients with refractory pain was discussed and EUS-CPB was offered only to those who were either not an immediate surgical candidate or who declined surgical interventions at that moment. EUS-CPB was also offered in cases of refractory pain post-surgery.

The primary objective of the study was to know efficacy of EUS-CPB in reducing pain in patients of chronic pancreatitis not responding to routine pharmacological management. The secondary objective was to compare various factors among responders of EUS-CPB versus nonresponders of EUS-CPB. In addition, we tried to analyze whether doing EUS-CPB early during painful chronic pancreatitis is more useful than adding it late.

Duration of chronic pancreatitis was classified as those with less than or equal to 2 years as short duration of painful chronic pancreatitis and those with more than 2 years as long duration of painful chronic pancreatitis. Baseline demographic details, duration of chronic pancreatitis (short vs long), type of disease (only parenchymal or parenchymal with ductal stones/strictures), use of pain killers after procedure, and pain score (visual analog scale [VAS]) before and 1 week, 4 weeks, 12 weeks, 24 weeks after the procedure were recorded and analyzed. Patients were offered ERCP based on their ductal disease as per standard protocol. Patients less than 12 years of age, coagulation abnormality, ongoing infections, distorted anatomy, and follow-up less than 6 months were excluded. A response to EUS-CPB was defined as more than 50% reduction in pain as per VAS pain score and reduction or absence of use of pain killers.
Procedure
Baseline coagulation profile was done for all the patients before procedure. Preprocedure 500 mL of bolus intravenous normal saline over 1 hour was given and it was continued at 100 mL/h during and for 6 hours postprocedure. In addition, 1 gm of intravenous ceftriaxone was given to all patients before the procedure. All cases were done under propofol sedation with continuous vitals monitoring. Linear echoendoscope from Olympus (GF-UCT180) with ultrasound processor (EU-ME2 system) was used in all cases. At first, a detailed evaluation of pancreatic anatomy and PD status was done. Then the origin of celiac trunk from aorta was identified from gastroesophageal junction/proximal gastric body. Left adrenal was then identified by torquing clockwise from celiac trunk. Celiac plexus was identified in the space between celiac trunk and left adrenal. Distance between the probe and 2 mm above celiac take-off was measured and an avascular path was identified. Needle used were either 20G EUS-CPN needle from ((ECHO-20-CPN; Cook Medical) or 22G fine-needle aspiration needle (Expect; Boston Scientific, Natick, Massachusetts, United States). Stylet was removed and needle was primed with normal saline before puncture. Needle was punctured and advanced till just 2 mm anterior to celiac trunk. After needle puncture, 2 mL sterile saline was injected to confirm position. Then suction was applied for 10 seconds to the syringe to look for any blood return. Then few milliliters of saline flush were used to clear needle of any gastric wall contaminant. Once the needle was in position, 20 mL of 0.25% bupivacaine was injected followed by injection of 40 mg of triamcinolone acetate in aliquots of 5 mL in all cases. Additional 40 mg of triamcinolone acetate was injected in some cases where it was feasible as per sonographers preference. Central injection technique was used in all cases where injection was done either just anterior or slight left lateral to celiac trunk (Fig. A-D). Wherever identified, intraganglion injection was also done in addition to central injection where additional 20 mg (2.5 mL) of triamcinolone acetate was injected in the ganglions (only 5 cases). Two milliliter of saline flush through the needle was given before withdrawal to clear needle and avoid spillage. Postprocedure intravenous hydration and continuous vital monitoring to look for any hypotension was done. Patients were discharged either on same day or next day with a course of oral antibiotics for 5 days. Other medical treatment for chronic pancreatitis was continued as before. Patients were advised to use analgesics only if pain was severe on emergency basis on follow-up. Follow-up was done during follow-up clinic visits or over telephonic interview in some cases.

Institutional ethics committee approval was taken.

Statistical Analysis
SPSS software was used for statistical analysis. Descriptive statistics were depicted by mean and standard deviation. Nonparametric variables were depicted by median and range. Mann–Whitney U test was used for categorical variable. p-Value less than 0.05 was considered significant.

Results
Study Population
A total of 29 patients underwent EUS-CPB for refractory pain due to chronic pancreatitis during the study period. The mean age of patients was 42.24 years (± 15.61) where majority were males (62.1%). All patients were documented to have chronic pancreatitis by magnetic resonance cholangiopancreatography, ERCP, or EUS criteria. Ethanol was the commonest etiology for chronic pancreatitis that was followed by biliary and idiopathic. Mean duration of painful chronic pancreatitis was 3.32 years, where short duration disease (≤2 years) was seen in 15 patients (51.72%) and long duration disease (>2 years) was seen in 14 (48.27%) patients. Only parenchymal disease/small duct disease was seen in 15 patients (51.27%). PD stricture was seen in seven (24.13%) patients and PD calculi seen in three (10.34%) patients, while both PD stricture and calculi were seen in four (13.7%) patients.

Fourteen of 29 patients had a history of undergoing ERCP prior to EUS-CPB because of ductal disease. Nine of them underwent once, 1 underwent twice, 3 underwent thrice, and 1 underwent 4 times ERCP prior to EUS-CPB. Mean time for EUS-CPB procedure after ERCP was 37.12 weeks. Two patients had prior history of surgery for CP before EUS-CPB was done. Only EUS-CPB without ERCP was done in 15 of 29 patients (51.72%) as they were not the candidates for ERCP (Table 1).

Effectiveness of EUS-CPB
Twenty-one of 29 (72.4%) subjects had response to EUS-CPB. Sixteen of them developed response within 1 day and 5 of
them in 2 days. The mean time to response to EUS-CPB was 1.22 (± 0.43) days. Mean duration of response was 8 months (± 4.73). Five patients experienced adverse events possibly attributed to EUS-CPB. Hypotension occurred in 3 patients who were treated with intravenous fluids and none of them required any vasopressors. Transient bradycardia occurred in one subject and mild bleeding occurred in one of the subjects. None of these complications were life threatening and all were managed conservatively.

**EUS-CPB Responders versus Nonresponders—Comparative Analysis**

Comparative analysis was made in those who responded to EUS-CPB and those who did not. As per gender, 83.3% males responded as compared to 54.54% females (p = 0.04). Significant proportion of subjects who responded either stopped or used analgesics occasionally (p < 0.0001); however, those who did not responded required frequent analgesics. Median VAS score at 12 (2 vs. 6, p = 0.00) and 24 weeks (2 vs. 7, p = 0.001) remained significantly lower in responders as compared to nonresponders. One of the patients with prior history of Frey’s procedure responded, whereas the other patient with prior surgery did not respond. There was no statistically significant difference in response to EUS-CPB with respect to age, duration of disease, etiology of disease, prior history of ERCP, or whether only EUS-CBP was done (Table 2).

**Comparison between Those with Short Duration (n = 15) versus Long Duration of Painful CP (n = 14)**

Among short duration group, only parenchymal disease was present in nine (60%) and ductal disease in six (40%) patients. Whereas among long duration group, only parenchymal disease was present in six (43%) patients and ductal disease in eight (57%) patients. Overall response to EUS-CPB was seen in 12 (80%) patients in short duration group and in 9 (64.3%) patients in long duration group that was statistically not significant (p = 0.345). Duration of response was 7.18 ± 2.44 months in short duration versus 8.31 ± 5.33 months in long duration (p = 0.857). When analysis was made only in responders (n = 21), those patients who had short duration of pain (n = 12) as compared to those with longer duration of pain (n = 9) had lower median VAS score at 12 weeks, 1 versus 3, p-value = 0.026 and at 24 weeks, 1.5 versus 2.5, p-value = 0.049 (Fig. 2).

<table>
<thead>
<tr>
<th>Characteristics (total 29 patients of chronic pancreatitis)</th>
<th>Mean ± SD / n (%)</th>
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<tr>
<td>Age (y)</td>
<td>42.24 (15.61)</td>
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<tr>
<td>Males Females</td>
<td>18 (62.07) / 11 (37.93)</td>
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<tr>
<td>Duration of CP, no. of participants (%)</td>
<td>15 (51.73) / 14 (48.27)</td>
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<tr>
<td>Short (&lt; 2 y) Long (≥ 2 y)</td>
<td></td>
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<tr>
<td>Nature of CP, no. of participants (%)</td>
<td>7 (24.13) / 3 (10.34) / 4 (13.7) / 15 (51.73)</td>
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<tr>
<td>PD stricture PD calculi Both stricture and calculi Only parenchymal disease</td>
<td></td>
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<tr>
<td>ERCP done before CPB (%)</td>
<td>14 (48.27)</td>
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<tr>
<td>No. of ERCP session before CPB (1/2/3/4)</td>
<td>9/1/3/1</td>
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<tr>
<td>Time for CPB after ERCP (weeks)</td>
<td>37.12 ± 14.75</td>
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<tr>
<td>Only CPB without ERCP, no. of participants (%)</td>
<td>15 (51.73)</td>
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<tr>
<td>Complications after CPB (%)</td>
<td>5/29 (17.25) / 1 (10.3) / 3 (17.2) / 1 (3.4)</td>
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<tr>
<td>Bradycardia Hypotension Bleeding</td>
<td></td>
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<tr>
<td>Response to CPB (%)</td>
<td>21 (72.42)</td>
</tr>
<tr>
<td>Time to response to CPB in days</td>
<td>1.22 ± 0.43</td>
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<tr>
<td>Duration of response to CPB in months</td>
<td>8 ± 4.73</td>
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<tr>
<td>Use of pain killers after EUS-CPB</td>
<td>14 (48.3) / 11 (37.9) / 4 (13.8)</td>
</tr>
<tr>
<td>No Occasional Frequent</td>
<td></td>
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Abbreviations: CP, chronic pancreatitis; ERCP, endoscopic retrograde cholangiopancreatography; EUS-CPB, endoscopic ultrasound-guided celiac plexus block; PD, pancreatic duct; SD, standard deviation.
Pain management in chronic pancreatitis can be extremely challenging. Though role of CPB has been controversial for pain management in chronic pancreatitis, it has been clearly advocated in a randomized controlled trial by Santosh et al, that if used, EUS-guided approach is better than fluoroscopy-guided approach.\(^3\) Response rate in their study was 70% after EUS-CPB as compared to 30% in percutaneous fluoroscopic-guided approach (\(p < 0.044\)).\(^3\) A systematic review involving two randomized controlled trial comparing percutaneous approach (computed tomography-guided and fluoroscopy-guided) versus EUS approach showed that EUS-CPB group was more effective to reduce pain at 4 weeks after procedure; however, there was no difference in complication rates between the two approaches.\(^11\) Correct patient selection
and correct techniques are key to its success. Though long-term pain relief may not be achieved, it is an important procedure for those patients who are not responding to medical management and/or endotherapy, requiring frequent analgesics or hospitalization for pain relief and are not an immediate surgical candidate. In chronic pancreatitis patients who are having small duct disease or predominantly parenchymal disease, pain management options apart from chronic opioid use are very limited. Radical pancreatic surgeries, including total pancreatectomy, pancreaticoduodenectomy, duodenum-preserving pancreatic head resections and its modifications, are some of the options that have shown to provide good pain relief in small duct CP. But not all patients are candidates or are willing for these major surgeries and accessibility to experienced centers in performing these complex surgeries is also limited in India. There has been a previous randomized controlled trial showing surgery being superior to endoscopic therapy for long-term pain relief in obstructive pancreatitis. However, recent recommendations suggest using surgical option only if first-line endoscopic interventions have been exhausted or unsuccessful in cases of obstructive chronic pancreatitis. But therapeutic decision making in small duct CP disease is more complex and should involve consideration of multiple factors including patients’ preference, patients’ expectations, cost, and availability of expertise. EUS-CPB can be an extremely useful adjunct in these situations specially serving as a bridge to a definitive surgery.

A previous systemic review analyzing both percutaneous and EUS-guided approach has shown a wide range of pain relief after CPB in CP (25%–96%), with median response after EUS-guided CPB being 68%. Contrary to previous reports, initial success rates for pain relief after EUS-CPB were found to be higher in our study. This may be due to a different phenotype of chronic pancreatitis in our population. We often encounter idiopathic painful CP patients who are not a good candidate for endotherapy because of ducal anatomy and are not responding to medical management. Neural remodeling with perineural inflammation plays an important role in these patients. Also, there is evidence that as the duration of disease progresses, neuronal plasticity, peri-neural inflammation, neuronal damage increases, and eventually both peripheral (intra pancreatic) and central nervous system get involved thereby making patients less responsive to standard pain-relieving medications and procedures. As reflected in our study also that median VAS score among responders was significantly less in those patients with shorter duration of painful CP as compared to longer duration; we should consider offering this procedure at a relatively early stage of disease. This may be due to irreversible neural modulation and remodeling both at peripheral level and central level that occurs at a later stage of CP making the CPB less effective. Similar results have been reported when EUS-CPN has been used for pain relief in pancreatic cancer, where an early intervention is a positive predictor of response.

Pain is a predominant symptom in chronic pancreatitis in India as demonstrated in a prospective study of 1086 patients where pain was present in 971 patients (94%). Among them 85 subjects underwent surgery; however, pain relief was seen in only 31 patients (36.5%). So, there is an unmet need for procedures providing pain relief in chronic pancreatitis in Indian scenario. In some of our patients, EUS-CPB was also offered in the setting of obstructive pancreatitis where pain persisted after drainage procedure like ERCP. The ERCP status of the patient did not affect their response to EUS-CPB thereby suggesting that ductal hypertension is not the only factor responsible for pain in these patients and decision of offering EUS-CPB should not be affected by their ERCP status provided adequate ERCP is being performed.

Males had a better response then females in our study. Exact reason for this is not apparent and this finding may just be a chance because of small number of patients in the current study and needs further evaluation.

Sey et al reported that for every 10 years increase in patients age, they were 1.6 times more likely to have response to EUS-CPB. However, response to EUS-CPB did not differ according to age in our study. They also reported that those who had positive response to EUS-CPB at first attempt had better response if this procedure was repeated later when the pain-relieving effects had weaned off as compared to initial nonresponders. In our study, in only small number of patients who had initial response serial blocks were offered and we also found similar trend. Thus, only who are initial responders should be offered this procedure again. In their review article, Maydeo et al elegantly describes approach for pain management in chronic pancreatitis where they suggest optimizing pharmacology therapy first, and ruling out extrapancreatic causes of pain, doing ERCP where indicated followed by evaluating for surgery if pain is persistent. In addition, they suggest modest response to EUS-CPB of around 59% with short-term pain relief of 3 months.

Literature suggests that EUS-CPB is a relatively safe procedure with majority having minor adverse events like transient hypotension and diarrhea like what was seen in our study. Proper fluid loading of patients in peri-procedural period is key to prevent significant hypotension. Prophylactic antibiotics were given to all our patients as though uncommon; infections can occur after steroid injection in EUS-CPB procedure. EUS-CPB can be safely performed as a day care procedure after a careful 3 to 4 hours of postprocedure observation. Very rarely serious adverse events after EUS-CPN (0.2%) and EUS-CPB (0.6%) like retroperitoneal abscess, bleeding, paralysis, abdominal ischemia, pneumothorax, peritonitis, and death have been reported in the literature; however, we did not encounter any major adverse events. Limitations of our study is that it had a small sample size, was retrospective in nature and wide variety of patients of chronic pancreatitis were included.

To conclude, EUS-CPB is a useful adjunct in the armamentarium of endoscopists dealing with a small but important subset of challenging patients of CP who are not having pain relief despite optimum medical and endotherapy and who are not an appropriate candidate for surgery. At least, it provides an immediate relief in 60 to 80% of patients if done correctly. Careful patient selection by including patients with shorter duration of disease course, older patients, and initial responders will maximize the chances of success of EUS-CPB.
However, this procedure should be only performed by an experienced endosonologist after thorough discussion with the patient and relatives about the temporary nature of pain relief and variable degree of success after EUS-CPB.

Further large randomized studies in select group of patients are needed to establish the role of EUS-CPB in patients of painful chronic pancreatitis. Since the phenotype of chronic pancreatitis in India is different from the West, we need guidelines from India specific for EUS-guided celiac plexus intervention like we have for EUS-guided biliary drainage.24,25

**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>EUS</td>
<td>Endoscopic ultrasound</td>
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<tr>
<td>EUS-CPB</td>
<td>Endoscopic ultrasound-guided celiac plexus block</td>
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<tr>
<td>EUS-CPN</td>
<td>Endoscopic ultrasound guided celiac plexus neurolysis</td>
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<tr>
<td>CP</td>
<td>Chronic pancreatitis</td>
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<tr>
<td>VAS</td>
<td>visual analogue scale</td>
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<tr>
<td>ERCP</td>
<td>Endoscopic retrograde cholangiopancreatography</td>
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<tr>
<td>PD</td>
<td>Pancreatic Duct</td>
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<tr>
<td>MRCP</td>
<td>Magnetic Resonance Cholangiopancreatography</td>
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**Ethical Approval**

Institutional review board approval was taken for this study.

**Authors' Contributions**

Nikhil Sonthalia did the procedures, designed research, and statistical analysis and wrote the manuscript; Vikram Patil did the statistical analysis and contributed in the writing manuscript; Awanish Tewary contributed in writing manuscript and data collection; Aakash Roy did critical review of manuscript and contributed in statistical analysis; MK Goenka contributed in designing research, did the critical review, and contributed in statistical analysis. All authors have read and approved the final manuscript.

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**Conflict of Interest**

None.

**References**


