

## Reply to the reviewers' comments

Dear Editor-in-Chief,

We thank you for your decision letter for our manuscript entitled “**Changing trends in the minimally invasive surgery for chronic pancreatitis**”. We have considered the reviewer's comments and provide below a point-by-point answer to each of them. Changes have been incorporated and highlighted in the revised manuscript. We are grateful to the reviewers for their comments which have helped us improve the manuscript. We hope that you will find this revised version suitable for publication in your esteemed journal.

With kind regards,

Authors

### Response to comments

#### Reviewer 1

1. **Abstract must include problem, objectives, your methodology and results achieved.**

As suggested by the reviewer, the abstract has been modified.

2. What is your major contribution in this field? Elaborate it in the conclusion section.

Authors have multiple publications in the field of chronic pancreatitis (PMID: 24817516, 33234753, 31825008, 34366610, 36601487). The publication that is relevant to the current review is Shukla A, Gnanasekaran S, Kalayarasan R, Pottakkat B. Early experience with robot-assisted Frey's procedure surgical outcome and technique: Indian perspective. J Minim Invasive Surg. 2022 Dec 15;25(4):145-151. doi: 10.7602/jmis.2022.25.4.145. PMID: 36601487. The appropriate publication of the authors has been added to the revised manuscript.

3. Write down the main problem in existing procedures at the end of the literature review?

The main problem with the existing procedures is they are primarily focused on pancreatic ductal and parenchymal decompression. However, it is well-documented that anatomical factors alone do not contribute to pancreatic pain in all patients. In a subgroup of CP patients, neurological pathways of pain play a dominant role, which the current surgical procedures do not address. It has been added in the revised manuscript

4. Following research need to be referenced in your manuscript:  
<https://onlinelibrary.wiley.com/doi/10.1002/jcp.27281>  
<https://pubmed.ncbi.nlm.nih.gov/35549629/>  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8966419/>

The appropriate references suggested by the reviewer have been added to the revised manuscript (Ref. 64)

5. Simplify your methodology.

The simplified methodology has been included in the abstract of the revised manuscript.

#### Reviewer 2

1. The manuscript is well organized and well written. The content is of interests for readers. One concern need to been addressed. MIS for chronic pancreatitis is technical demanding, it will be better when introducing the different operations or madality, addd the related clinical research or evidence.

We thank the reviewers for the positive comments. As suggested by the reviewer the related evidence when introducing different procedure has been added in the revised manuscript. As pain relief is the important outcome measure a column highlighting percentage of patients who had complete pain relief has been added in the revised tables 2 and 3.

#### Reviewer 3

1. The article describes the treatment history of chronic pancreatitis pain in detail, but does not describe the pain mechanism. One or two sentences can be used to properly describe the hypothesis of various pain mechanisms.

As suggested by the reviewer hypothesis of various pain mechanisms has been added to the revised manuscript.

“Pathogenesis of pain in chronic pancreatitis is multifactorial and includes anatomical and neuropathic factors. Anatomical alterations include ductal hypertension, raised pancreatic parenchymal pressure, acute inflammation, and pancreatic ischemia. The lack of correlation between pain severity and

anatomical changes suggests neurological factors' role. Neuropathophysiology of pain in chronic pancreatitis includes peripheral sensitization-induced pain, neuropathic remodeling, and central sensitization of pancreatic pain.”

2. Some parts of the article only describe the results of previous studies without mentioning detailed data. It is suggested to add data related to the conclusion.

The relevant data related to the previous studies have been added in the revised manuscript. As pain relief is the important outcome measure a column highlighting percentage of patients who had complete pain relief has been added in the revised tables 2 and 3.

#### Editors comments

1. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

As per the requirement, the pictures are provided in PowerPoint so that all graphs or arrows, or text portions can be reprocessed by the editor. And all the pictures included in the manuscript are original pictures of the authors.

2. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden

The tables were modified as per the instructions

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**Author contributions:**

Kalayarasan R and Shukla A did the literature search. Shukla A wrote the first draft of the review. Kalayarasan R conceptualized the work, supervised the writing, gave intellectual inputs, and critically revised the manuscript.

**Supportive foundations:** Nil

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**Acknowledgment:** Nil

## Changing trends in the minimally invasive surgery for chronic pancreatitis

### Abstract

Chronic pancreatitis is a debilitating pancreatic inflammatory disease characterized by intractable pain resulting in poor quality of life. Conventional management of pancreatic pain consists of a step-up approach with medications and lifestyle modifications followed by endoscopic intervention. Traditionally surgery is reserved for patients who do not improve with other interventions. However, recent studies suggest that early surgical intervention is more beneficial as it can mitigate the progression of the pathologic process and prevent loss of pancreatic function. Despite the widespread adoption of minimally invasive approaches in various gastrointestinal surgical disorders, minimally invasive surgery for chronic pancreatitis is slow to evolve. Technical difficulty due to severe inflammatory changes has been the major impediment to the widespread usage of minimally invasive surgery in chronic pancreatitis. With this background, the present review aimed to critically analyze the available evidence on the minimally invasive treatment of chronic pancreatitis. A PubMed search of all relevant articles was performed using the appropriate keywords, parentheses, and Boolean operators. Most initial laparoscopic series have reported the feasibility of lateral pancreaticojejunostomy, considered an adequate procedure only in a small proportion of patients. The pancreatic head is the pacemaker of pain, so adequate decompression is critical for long-term pain relief. Recent studies have documented the feasibility of minimally invasive duodenum-preserving pancreatic head resection. With improvements in laparoscopic instrumentation and technological advances, minimally invasive surgery for chronic pancreatitis is gaining momentum. However, more high-quality evidence is required to document the superiority of minimally invasive surgery for chronic pancreatitis.

**Key words:** Robotics; Laparoscopy; Surgery; Chronic pancreatitis; Pancreas; Pancreatitis

**Core tip:** Pain in chronic pancreatitis is a significant symptom that demands utmost attention as it compromises the quality of life and inherently risks narcotic addiction. Surgical management for chronic pancreatitis began with various open surgical drainage and resection procedures. Since pain is the primary indication for intervention, a minimally invasive approach is an attractive proposition in chronic pancreatitis. Despite the slow adoption of laparoscopic and robotic surgery in chronic pancreatitis, safety and feasibility have been documented in recent studies. The challenges and limitations highlighted in the present review could guide future research on minimally invasive surgery in chronic pancreatitis.

## **INTRODUCTION**

Chronic pancreatitis is a progressive pancreatic inflammatory disease that leads to fibrosis and parenchymal tissue loss resulting in impaired endocrine and exocrine function. While consumption of alcohol is the leading cause of chronic pancreatitis worldwide, idiopathic pancreatitis remains common in India and China[1,2]. The most common and dominant symptom of chronic pancreatitis is pain, which can be persistent, severe, or recurrent episodes with pain-free intervals significantly impacting the quality of life[2,3].

Traditionally, pain in chronic pancreatitis is managed initially with analgesics, pancreatic enzyme replacement therapy, and lifestyle modifications followed by endoscopic or surgical intervention. Almost half of the patients who do not respond to medical or endoscopic management are referred for surgical intervention[4]. The most common indication for surgery is intractable pain. Studies have reported that early surgical management has better outcomes than intervention in the advanced disease stage[3,5]. While the minimally invasive approach is widely used for various gastrointestinal and pancreatobiliary disorders, its application in chronic pancreatitis is disproportionately low. As chronic pancreatitis is a benign disorder with pain as the primary indication for intervention, a minimally invasive approach is an attractive proposition. The technical difficulty, combined with the potential for vascular injury and bleeding associated with pancreatic inflammation and fibrosis, is the primary reason for the slow adoption of minimally invasive techniques in chronic pancreatitis. However, recent studies have shown the feasibility of laparoscopic and robotic surgery for chronic pancreatitis. Also, with advancements in endoscopic treatment, there is a trend towards the less invasive treatment of chronic pancreatitis. The present review focuses on the challenges, evolution, and changing trends in the minimally invasive management of chronic pancreatitis.

## **SEARCH STRATEGY**

All the authors did a PubMed search of relevant articles. Further, the articles' reference lists were also searched for additional appropriate studies. The keywords and combinations included in the search were: "pancreatitis"; "chronic pancreatitis"; "idiopathic pancreatitis"; endoscopic management" and "chronic pancreatitis"; "Frey's procedure" and "Laparoscopic"; "Frey's procedure" and "robotic"; "Puestow procedure" and "Laparoscopic"; "Puestow procedure" and "robotic"; "Beger procedure" and "Laparoscopic"; "Beger procedure" and "robotic"; "chronic pancreatitis" and "total pancreatectomy" and "laparoscopic"; "chronic pancreatitis" and "total pancreatectomy" and "robotic". The search was limited to publications in English literature. All the authors agreed that the articles selected for review were relevant.

## ENDOSCOPIC MANAGEMENT OF CHRONIC PANCREATITIS

Endoscopic intervention is recommended as a minimally invasive alternative to surgery in patients who do not improve with medical management. The journey of stone removal from the pancreatic duct dates back to 1891 when Alfred Pearce Gould retrieved calculi from the Wirsung duct in a London hospital[6]. Berkeley G Moynihan performed transduodenal removal of pancreatic stones in 1902, followed by transpancreatic stone removal in 1908 by Mayo Robson. The development of the fiberoptic endoscope for diagnosis in 1958 by Basil Isaac Hirschowitz changed the trends of endoscopic management. William C Watson succeeded in developing the technique for papillotomy with an energy source leading to the endoscopic extraction of calculi and subsequent stent placement[7,8]. Pathogenesis of pain in chronic pancreatitis is multifactorial and includes anatomical and neuropathic factors. Anatomical alterations include ductal hypertension, raised pancreatic parenchymal pressure, acute inflammation, and pancreatic ischemia [9-11]. The lack of correlation between pain severity and anatomical changes suggests neurological factors' role. Neuropathophysiology of pain in chronic pancreatitis includes peripheral sensitization-induced pain, neuropathic remodeling, and central sensitization of pancreatic pain[10,11]. Endoscopic therapy aims to relieve pain by clearance of intraductal stones, thereby decompressing the pancreatic duct. Proponents of



endoscopic therapy suggest that patients with complete ductal clearance by endoscopic approach have shown similar pain relief compared to the surgical group[12]. At the same time, the ability to modify the disease progression and prevent loss of pancreatic function with early surgical intervention was proposed in favor of surgical management [13,14].

Traditionally chronic pancreatitis patients were managed initially with analgesics and pancreatic enzyme replacement therapy, followed by endoscopic intervention with or without extracorporeal shockwave therapy[15,16]. Patients with an inadequate clinical response following endoscopic treatment should be discussed in the multidisciplinary meeting and considered for surgical management[10,16]. The potential benefit of this approach is that surgery could be avoided in some patients with successful endoscopic management. However, various studies comparing the efficacy of endoscopic management with surgery have shown better pain control with the early surgical intervention[17-19]. Randomized trials comparing the endoscopic and surgical approaches have shown a better quality of life and pain relief in the surgical group, especially with early surgery[12,20,21](Table 1). Also, patients with inflammatory pancreatic head mass, distal pancreatic duct stricture, and extensive parenchyma calcifications of the pancreatic head might be difficult to treat by endoscopy. Despite the available evidence favoring surgical treatment, advancements in endoscopic lithotripsy techniques and extracorporeal shockwave lithotripsy (ESWL) are continuously improving the ductal clearance rate, and the endoscopic approach is helpful in a subset of chronic pancreatitis patients[16]. Patients with dominant stricture in the pancreatic head with upstream dilatation and those with intraductal calculi in the pancreatic head or proximal body are ideal candidates for endoscopic intervention.

### **Pancreatic lithotripsy**

Worldwide, ESWL is commonly used for pancreatic lithotripsy, especially in Asia and Europe. While recent advancements like intraductal endoscopic laser or electrohydraulic lithotripsy might improve ductal clearance, they are not widely available. Hence, most of the available data are for ESWL [22]. A meta-analysis of

various studies has reported a 70% stone clearance rate with ESWL[23]. With ESWL, stone clearance is more favorable for solitary calculus in the head of the pancreas. However, recurrence of stones after ESWL was seen in 14% to 23% of patients mandating further intervention[24]. ESWL is combined with pancreatic duct stenting in patients with associated pancreatic duct stricture[25]. European Society of Gastrointestinal Endoscopy (ESGE) recommends ESWL for the removal of radiopaque obstructive main pancreatic duct calculi greater than 5 mm found in the head or body of the pancreas and endoscopic retrograde cholangiopancreatography (ERCP) for main pancreatic duct calculi that are radiolucent or smaller than 5mm[26].

### **Endoscopic stenting**

Main pancreatic duct strictures are often seen in half of the chronic pancreatitis patients and are usually located in the pancreatic head region. The standard management of these strictures is balloon dilatation and placement of a temporary stent for at least a year[27]. Pain relief after a long-term follow-up of 5 years has been seen in almost half of patients after stent withdrawal[28,29]. However, stricture recurrence has been reported in up to 38% of patients after two years[28,30]. Complications related to stenting include stent migration and occlusion. Distal stent migration toward the pancreatic tail and proximal stent migration to the duodenum was reported in 7.5% and 5.2% of patients, respectively[31]. Stent migration can be prevented with large-winged or pigtail catheters[31,32]. The ESGE recommends managing painful pain pancreatic duct strictures with the help of a single 10 Fr stent for one uninterrupted year if symptoms improve after placement[26]. The stent should be exchanged based on symptoms or signs of stent dysfunction on imaging at at least six months intervals.

### **Endoscopic ultrasound-guided intervention**

Endoscopic ultrasound (EUS) guided drainage of the main pancreatic duct is used as a second-line procedure after the failure of ERCP. Despite high success rates of 68 to 75%, the complications like perforation, bleeding, and pancreatitis reported in 5 to 43% of patients were key drawbacks for EUS-guided drainage[33, 34]. Another EUS-guided procedure is the celiac plexus block, whereby a steroid with a local

anesthetic agent is injected at the celiac plexus to block the pancreatic nerve fibers. EUS-guided celiac plexus block is preferred over the traditional percutaneous method. However, despite the high technical success and short-term pain relief in 55%-70% of patients, long-term outcomes are discouraging[35-37].

## **SURGICAL MANAGEMENT OF CHRONIC PANCREATITIS**

### **Evolution of open surgical procedures**

The systemic reviews and meta-analyses of the available studies comparing surgical management with endoscopic intervention continue to support the superiority of surgical treatment in chronic pancreatitis [38-40]. The intriguing voyage of surgical management of chronic pancreatitis has witnessed a huge transformation from surgical decompression of the obstructed duct and denervation of the pancreas to pancreatic head resection, total pancreatectomy, and various other hybrid procedures. In 1911, Gothe Link, a gynecologist from Indiana, was the first to describe external tube drainage of the pancreatic duct for ductal calculi or stricture with good long-term pain relief[41]. Desjardins and Coffey, around similar times, proposed drainage of the pancreas using the intestine after conducting animal studies[42,43]. This empiricism was materialized by Duval and separately by Zollinger in 1954 by describing the first caudal end-to-end pancreaticojejunostomy using a Roux-en-Y jejunal loop for chronic pancreatitis[44,45]. Further, modification in the decompressive procedure was done by Puestow and Gillesby, in 1958, by invaginating caudal pancreaticojejunostomy after longitudinally opening the pancreatic duct from the body to the tail region of the pancreas[46]. Their procedure was further modified by Partington and Rochelle, in 1960, by creating side-to-side Roux-en-Y pancreaticojejunostomy, commonly called the Puestow procedure[47]. Though the Puestow procedure was considered standard drainage procedure for almost 40 years, the long-term benefits were not befitting. Despite short-term pain relief in 80% of patients, the pain recurred in 30% on long-term follow-up [48-51]. The foremost reason for recurrent pain was undealt nidus of inflammation and persistent ductal disease in the head of the pancreas. To tackle the head disease, German surgeon Hans Beger performed the first duodenum-preserving pancreatic head resection in 1971 and

reported postoperative outcomes of 52 patients in 1980[52]. In 1984, Warren described splenopancreatic flap, a denervation procedure for chronic pancreatitis[53]. However, the long-term results of this complex procedure were never published or replicated by other surgeons[9,53].

In 1987, Frey and Smith described a hybrid operation consisting of pancreatic head resection and longitudinal pancreaticojejunostomy, also known as Frey's procedure[54]. Izbicki et al. modified Frey's procedure by doing a more extensive excavation of the pancreatic head and duct and named it Hamburg modification[55]. Similarly, Gloor et al. from Berne modified the duodenum-preserving pancreatic head resection by omitting the challenging step of pancreatic neck transection[56]. To minimize the risk of penetrating the posterior pancreatic capsule, Frey and Akumra recommended limiting the posterior extent of head coring to the back wall of opened Wirsung and the uncinata duct, also known as modified Frey's procedure[57,58]. Sakata et al. described the minimum Frey procedure in which a small spindle-shaped anterior resection of the pancreatic head was performed and reported an equivalent outcome[59]. However, a retrospective study by Tan et al. reported superior long-term pain relief and quality of life with the original Frey's procedure compared to the modified Frey's[60]. A systematic review and meta-analysis of trials comparing various resectional and hybrid procedures reported similar postoperative pain relief. However, quality of life and other perioperative outcomes favor duodenum-preserving pancreatic head resection procedures[61].

### **The era of minimally invasive surgery**

There is a trend towards minimally invasive procedures for various surgical disorders, and the change is inevitable for chronic pancreatitis[62-64]. Though the surgical procedures described for chronic pancreatitis are complex and challenging due to inflamed gland they can be accomplished in selected patients[63-65]. In high-volume centers with expertise in advanced laparoscopic procedures, complex pancreatic procedures can be safely performed with comparable postoperative outcomes[63-69]. Also, with its ergonomic advantages, robotic surgery could

overcome some of the technical limitations of laparoscopic surgery and potentially widen the use of a minimally invasive approach in chronic pancreatitis[70,71].

### **Minimally invasive Puestow procedure**

Like open surgical procedures, minimally invasive surgery for chronic pancreatitis began with a modified Puestow procedure. Kurian and Gagner, in 1999, reported the first series of five patients who underwent a laparoscopic Puestow procedure[72]. Subsequently, two series with 17 and 12 patients were published from India[73,74]. The first small case series of 5 patients from the United Kingdom was published by Khaled et al. in 2014[75]. The feasibility and favorable short-term outcomes of the laparoscopic Puestow procedure were documented in multiple case series[76-81](Table 2). In most series, the procedure was performed with five laparoscopic trocars. The initial entry to the lesser sac and exposure of the anterior surface of the pancreas can be technically challenging in patients with recent or recurrent acute episodes of pancreatitis. Hence, those patients should be avoided during the early phase of the minimally invasive Puestow procedure. In most laparoscopic series, two to three gastric retraction sutures are used to lift the stomach away from the pancreas and improve exposure. Needle aspiration is commonly used to identify the pancreatic duct, and intraoperative ultrasound is helpful in patients with undilated duct[74]. Extraction of all intraductal calculi, especially those in the head and tail region, is critical for long-term pain relief. Sahoo et al. reported the usefulness of cystoscope and endoscopic basket in clearing residual intraductal stones [76]. Proficient intracorporeal suturing skill is critical to accomplish safe pancreaticojejunostomy. Kim et al. reported the benefits of using barbed sutures for laparoscopic pancreaticojejunostomy[77]. Bhandarwar et al. used endostaplers for laparoscopic pancreaticojejunostomy anastomosis with the anvil part placed within the pancreatic duct[78]. However, as highlighted by the authors, the technique was feasible only in seven out of 17 patients with pancreatic duct diameter of more than 10mm[78]. Alternatively, a robotic platform can minimize the challenges associated with intracorporeal suturing. After the initial case reports of the robotic Puestow procedure Kirks et al. documented its usefulness in a series of seven patients[83-87].

However, with the emerging evidence supporting some form of head resection to achieve long-term pain relief, the minimally invasive Puestow procedure is recommended only in a subset of chronic pancreatitis patients with an atrophic pancreas and dilated pancreatic duct with predominant intraductal calculi.

### **Minimally invasive Frey's procedure**

Frey's procedure is one of the most commonly performed surgeries for chronic pancreatitis. Pancreatic head coring is the technically challenging step of this hybrid procedure, especially during minimally invasive surgery. The first series of laparoscopic Frey's procedure was published by Tan et al. in 2015[88]. Subsequently, a small series of four patients reported the feasibility and short-term outcomes of laparoscopic Frey's procedure[89]. The largest published series to date had 15 patients in the laparoscopic Frey's group[90]. The relatively small number of studies with fewer patients highlight the technical challenges of laparoscopic Frey's procedure (Table 3). In open Frey's procedure, the surgeon's left hand, kept under the posterior surface of the pancreas head, guides the extent of posterior head coring. In the absence of a definite landmark, pancreatic head coring until the level of the posterior pancreatic capsule is challenging during laparoscopic surgery. Hence, in all the laparoscopic series, only modified Frey's procedure was performed using the main pancreatic duct as the landmark and coring to the posterior wall of the duct[88-90]. In the laparoscopic approach, ultrasonic shears and bipolar vessel sealing devices are commonly used for head coring. Lack of articulation and difficulty securing precise hemostatic sutures further increase the difficulty of laparoscopic pancreatic head coring, especially along uncinate ducts[90]. With its articulating instruments, the robotic platform could potentially overcome technical difficulties during head coring and pancreaticojejunostomy. Hamad et al. highlighted the usefulness of the robotic approach in bleeding control during head coring in their series of four patients[62]. However, similar to the laparoscopic approach, due to the lack of a definite landmark, coring was limited to the posterior wall of the duct in the robotic modified Frey's procedure (Fig. 1). The median operative time and blood loss were 372 minutes and 163 ml, respectively[62]. **Similarly Shukla et al. reported the feasibility of robot**

assisted Frey's procedure in nine patients with chronic pancreatitis [92]. Robotic approach is associated with less blood loss and shorter hospital stay compared to open Frey's procedure. The parenchyma posterior to the main pancreatic duct in the pancreatic head was preserved to prevent injury to the superior mesenteric vein[62,91]. Tile Pro technology in the robotic platform allows the surgeon to view ultrasound images in the console, thereby avoiding damage to the common bile duct and portal vein during dissection[62,92]. Bleeding is one of the common causes of conversion in minimally invasive Frey's procedure. Inflammatory pancreatic head mass and preoperative acute exacerbation of pancreatitis were identified as significant risk factors for intraoperative blood loss. Hence, minimally invasive Frey's procedure is recommended in patients with dilated pancreatic duct and enlarged pancreatic head on imaging without inflammatory mass, recent acute exacerbation, and pancreatitis-related complications.

### **Minimally invasive duodenum preserving pancreatic head resection**

In patients with inflammatory head mass, duodenum preserving pancreatic head resection (DPHR) is preferred over pancreatoduodenectomy because of favorable long-term outcomes. As previously highlighted, lack of definite landmarks precludes pancreatic head coring until the posterior pancreatic capsule in minimally invasive Frey's procedure. Minimally invasive duodenum-preserving pancreatic head resection could potentially overcome that limitation. After the initial case reports, Cai et al. documented the feasibility of laparoscopic DPHR procedure in 5 patients with chronic pancreatitis[93-95]. The mean operative time and hospital stay were 275 minutes and 11 days, respectively. One patient had grade B postoperative pancreatic fistula, and pancreaticojejunostomy anastomotic site bleed in one patient[95]. In laparoscopic DPHR after the pancreatic neck transection, the pancreatic head is retracted to identify the plane between the pancreatic parenchyma and posterior pancreatic capsule. As the dissection proceeds along the superior border of the pancreas, the bile duct should be identified and preserved. Identifying the intrapancreatic duct is a significant technical challenge with minimally invasive DPHR. Indocyanine green (ICG) fluorescence facilitates bile duct identification in the

triangle formed by the gastroduodenal artery, portal vein, and superior border of the pancreas (Fig. 2). Energy sources should be judiciously used around the bile duct to prevent thermal damage[96-98]. Also, ischemia of the bile duct can be prevented by preserving the posterosuperior pancreaticoduodenal artery, a proximal branch of the gastroduodenal artery, and preserving pancreatic tissue medial to the bile duct. To prevent duodenal ischemia and delayed gastric emptying, the pancreaticoduodenal arcade along the medial border of the duodenum should be preserved. Hong et al. reported the usefulness of ICG in assessing vascular arcade and identifying common bile duct in a series of 22 patients with different pancreatic pathology[96]. The mean operative time and blood loss of five patients with chronic pancreatitis included in their series were 264 minutes and 215 ml, respectively. The mean postoperative hospital stay was 7.5 days, and there was no conversion to open surgery or postoperative mortality [96].

Inflammation and tissue adhesion in chronic pancreatitis can distort the anatomy of pancreaticoduodenal vessels resulting in vascular injury and significant bleeding during DPHR. A 3D reconstruction of preoperative cross-sectional imaging could help to better understand the anatomy of pancreaticoduodenal vessels and the relationship of the intrapancreatic common bile duct. Also, 3D printing technology can be helpful for surgical training and preoperative planning in patients undergoing minimally invasive DPHR[96-98]. As with other minimally invasive procedures for chronic pancreatitis, a robotic platform could minimize the technical challenges associated with DPHR. Peng et al. first reported the feasibility of robotic DPHR[99]. However, in a recent series of 68 patients undergoing robotic DPHR for various pancreatic diseases, only three patients had chronic pancreatitis[100]. Different published series on minimally invasive DPHR highlight technical development and challenges of the procedure in chronic pancreatitis. Minimally invasive DPHR is the preferred procedure in patients with inflammatory head mass and those with enlarged pancreatic head and extensive parenchymal calcifications. However, if the inflammatory changes preclude the safe creation of a retropancreatic tunnel over the portal vein alternative surgical procedure should be considered.



## **Minimal invasive total pancreatectomy with or without islet cell autotransplantation**

Total pancreatectomy is primarily indicated in chronic pancreatitis patients with debilitating pain in whom all other measures are unsuccessful and those with recurrent acute pancreatitis[101]. However, total pancreatectomy should be combined with islet cell autotransplantation to minimize the risk of brittle diabetes. Some centers recommend total pancreatectomy early in the disease course before activation of neuropathic pain circuits, especially in patients with small duct disease or genetic etiology[101]. However, selecting suitable patients is critical as, despite islet cell autotransplantation, more than 50% of patients might require lifelong exogenous insulin. Literature on minimally invasive total pancreatectomy is sparse, with variations in technique[102-105]. Blair et al., in 2016, reported the feasibility and safety of laparoscopic total pancreatectomy with islet cell autotransplantation in 20 patients with chronic pancreatitis[104]. The mean operative time and hospital stay were 430 minutes and 11 days, respectively, with no postoperative mortality[104]. Similarly, Fan et al. reported the feasibility of laparoscopic total pancreatectomy with islet cell autotransplantation in 22 patients with two conversions[102]. In both the laparoscopic series, the pancreatic neck was transected, and two-stage retrieval was used, with the pancreatic head and body retrieved separately[102,104]. However, studies have shown the importance of preserving pancreatic arterial and venous flow until retrieval to reduce warm ischemia time during the pancreatic dissection phase and improve islet yield[106]. In the robotic series reported by Galvani et al. and Zureikat et al. the feasibility of total pancreatectomy without pancreatic neck transection and preserving vascular flow till the final step to reduce warm ischemia was documented[103,105]. Another technical challenge is dense retroperitoneal adhesions due to recurrent pancreatic inflammation. Although laparoscopic and robotic total pancreatectomy with islet autotransplantation is safe and feasible, appropriate patient selection is critical for deriving the benefit of a minimally invasive approach.

## **Challenges and future perspectives**

The available evidence suggests that minimally invasive surgery for chronic pancreatitis is feasible in selected patients. However, the poor quality of available evidence precludes definite conclusions. Also, the surgeon should adhere to surgery principles for chronic pancreatitis, irrespective of the approach. As the pancreatic head is the pacemaker of pain in most patients, adequate resection and decompression of the pancreatic head are critical. However, most of the reported series on minimally invasive approaches for chronic pancreatitis have focused on the feasibility of lateral pancreaticojejunostomy or modified Frey's procedure which may be appropriate only in a minority of chronic pancreatitis patients. Recent series have shown the feasibility of minimally invasive duodenal preserving pancreas head resection, which may be the ideal procedure for most chronic pancreatitis patients. However, a minimally invasive approach is feasible only in patients without extensive inflammatory adhesions or recent acute exacerbation. Preoperative cross-sectional imaging and biochemical parameters like serum amylase and lipase are not sensitive to predict inflammatory changes. Also, studies evaluating the predictive value of markers of systemic inflammation like white blood cell count, IL-6, and C reactive protein yielded disappointing results[88]. Future studies should focus on identifying reliable markers that can accurately predict ongoing pancreatic inflammation, thereby aiding patient selection for a minimally invasive approach. With recent evidence supporting early surgical intervention before the development of extensive fibrosis or local complications, more patients may be suitable for minimally invasive surgery. Also, the main problem with the existing procedures is they are primarily focused on pancreatic ductal and parenchymal decompression. However, it is well-documented that anatomical factors alone do not contribute to pancreatic pain in all patients. In a subgroup of chronic pancreatitis patients, neurological pathways of pain play a dominant role, which is not addressed by the commonly performed surgical procedures. Also, future studies should compare laparoscopic and robotic procedures for chronic pancreatitis to document the advantages of the robotic platform.

## CONCLUSION

As pain is the primary indication for intervention in chronic pancreatitis use of a minimally invasive approach is an attractive proposition. However, due to technical challenges, both endoscopic intervention and minimally invasive surgery for chronic pancreatitis have lagged compared to other benign gastrointestinal disorders. With improvements in laparoscopic instrumentation and technological advances like indocyanine green fluorescence, minimally invasive surgery for chronic pancreatitis is gaining momentum. Also, with its distinct advantages, the robotic platform can widen the adoption of minimally invasive surgery in chronic pancreatitis. However, well-designed trials with long-term follow-ups are required to document the superiority of minimally invasive surgery for chronic pancreatitis.

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## Figure legends

Figure 1. Robotic modified Frey's procedure. A) pancreatic head coring is done till the level of the posterior wall of the pancreatic duct (marked with star). The bile duct can be seen on the medial wall of the cored-out tissue (arrow). B) Indocyanine green fluorescence demonstrates the bile duct on the medial wall of the cored-out tissue.

Figure 2. Robotic duodenum preserving pancreatic head resection. A) Dissection of the pancreatic parenchyma from the posterior pancreatic capsule. B) Identification of the common bile duct in the triangle formed by the gastroduodenal artery, superior border of the pancreas, and portal vein. C) Pancreatic duct (arrow) divided at its junction with the bile duct. D) Post pancreatic head resection, indocyanine green fluorescence demonstrates bile duct.



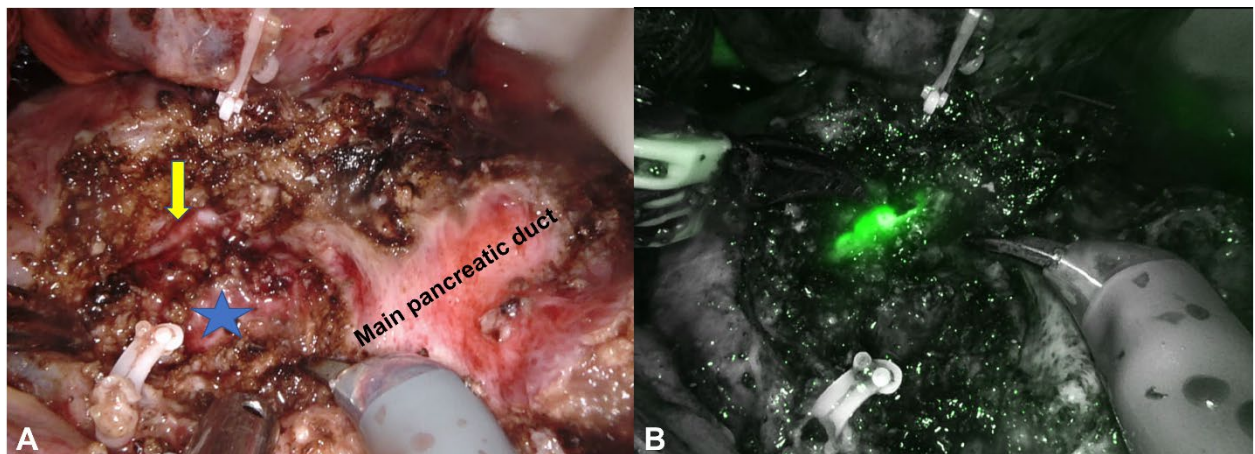


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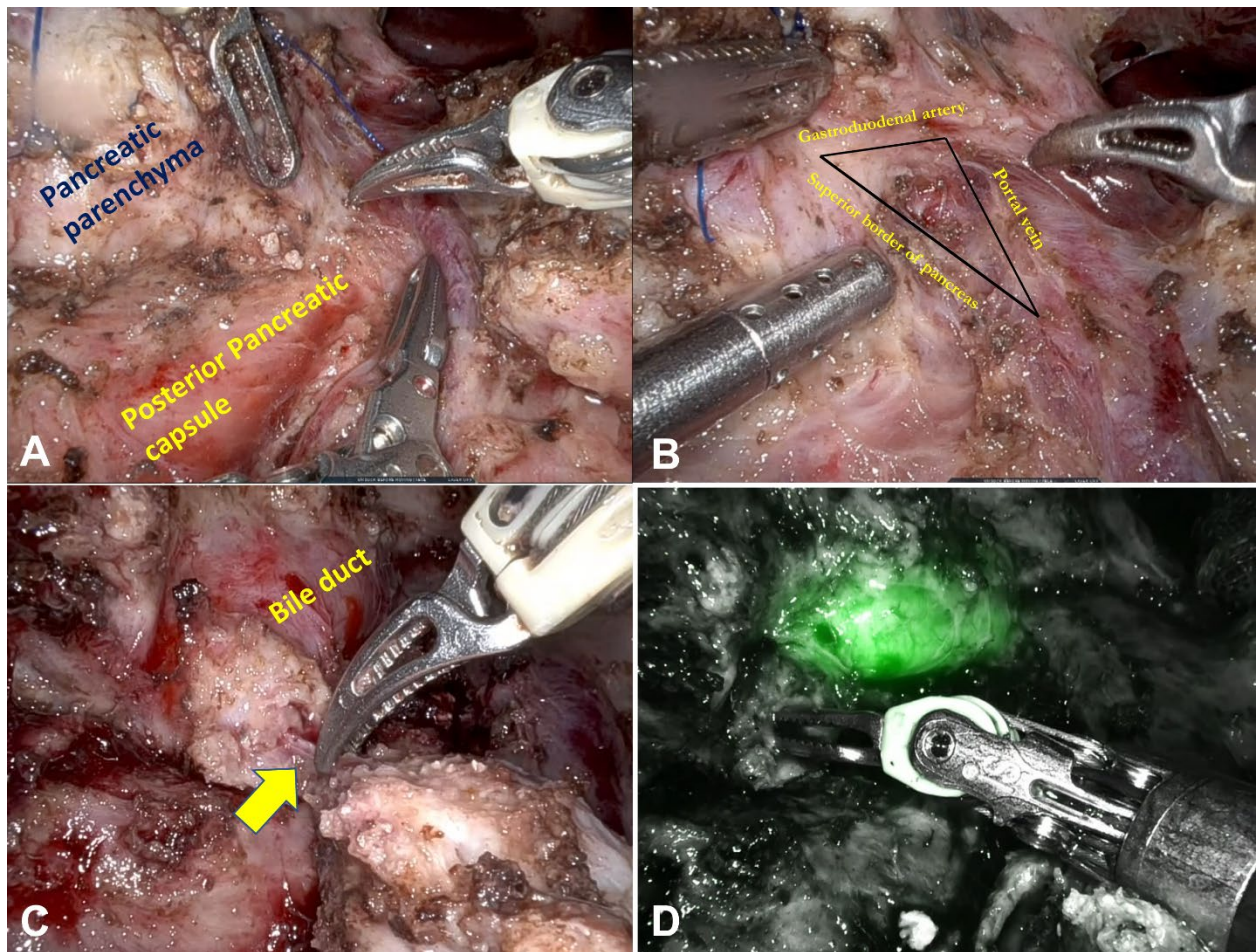


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## Abbreviations

1. Extracorporeal shockwave lithotripsy (ESWL)
2. European Society of Gastrointestinal Endoscopy (ESGE)
3. Endoscopic retrograde cholangiopancreatography (ERCP)
4. Endoscopic ultrasound (EUS)
5. Duodenum preserving pancreatic head resection (DPHR)

Table 1. Studies comparing endoscopic and surgical management of chronic pancreatitis

Authors	Country	No of patients (n), Surgery/ Endoscopy	Complete and partial pain relief (%), Surgery/Endoscopy	Complication (%), Surgery/ Endoscopy	Mortality (n), Surgery/ Endoscopy	Follow up (months)  Surgery/ Endoscopy
Dite et al, 2003 <sup>[12]</sup>	Czech Republic	36/36	86/61	Not reported	0/0	60
Cahen et al, 2011 <sup>[20]</sup>	Netherlands	16/15	80/38	0/25	0/1	79
Hong et al, 2011 <sup>[19]</sup>	China	27/35	77/47	14/22	1/0	60
Kawashima et al, 2018 <sup>[17]</sup>	Japan	41/10	100/100	20/27	0/0	-
Jiang et al, 2018 <sup>[18]</sup>	China	40/46	83/80	26/8	0/0	63.5/57.3
Issa et al, 2020 <sup>[21]</sup>	Netherlands	44/44	58/39	27/25	0/0	18

Table 2. Studies on laparoscopic Puestow procedure

Authors (year)	Country	No of patients (n)	Mean operative time (minutes)	Mean hospital stay (days)	Conversion (n)	Mortality	Follow up, (months)	Complete pain relief (%)
Kurian et al, 1999 <sup>[72]</sup>	USA	5	240	3-7	Nil	Nil	30	80
Tantia et al, 2004 <sup>[73]</sup>	India	17	277	5.2	4	Nil	12	82.3
Palanivelu et al, 2006 <sup>[74]</sup>	India	12	172	5	Nil	Nil	52.8	83.3
Khaled et al,2014 <sup>[75]</sup>	United Kingdom	6	278	7	Not reported	Nil	14.2	66.7
Sahoo et al, 2014 <sup>[76]</sup>	India	12	265.5	5.8	Nil	Nil	16.5	100 (follow up reported for 8 patients) 100
Kim Hong, et al, 2015 <sup>[77]</sup>	Korea	11	200	7	Nil	Nil	21	
Bhandarwar, et al, 2018 <sup>[78]</sup>	India	28	189.7	5.8	4	Nil	12	87.5
Rege et al, 2019 <sup>[79]</sup>	India	32	131.2	5.2	1	Nil	14.2	75
Javed et al, 2020 <sup>[80]</sup>	India	41	180	5	excluded	Nil	43.6	91
Nag et al, 2022 <sup>[81]</sup>	India	33	300	7	Nil	Nil	25	71

Table 3. Studies on laparoscopic Frey's procedure

Authors (year)	Country	Patients (n)	Mean operative time (minutes)	Mean hospital stay (days)	Conversion (n)	Mortality	Follow up (months)	Complete and partial pain relief
Tan et al, 2015 <sup>[88]</sup>	China	9	323	7	2	Nil	3	Not reported
Kilburn et al, 2016 <sup>[89]</sup>	Australia	4	130	7	Nil	Nil	26	100%
Senthilnathan et al, 2019 <sup>[90]</sup>	India	15	271	6.4	10 out of 57 patients in different arms	Nil	60	88%