



## Non-pharmacological pain palliation methods in chronic pancreatitis

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### Abstract

Chronic pancreatitis (CP) is a condition characterized by persistent and often severe pain resulting from the inflammatory disease of the pancreas. While pharmacological treatments play a significant role in palliative pain management, some patients require non-pharmacological methods. This review article focuses on non-pharmacological approaches used to alleviate pain in CP. The article examines non-pharmacological palliation options, including surgery, endoscopic approaches, neurostimulation techniques, acupuncture, and other alternative medicine methods. The effectiveness of each method is evaluated, taking into consideration patient compliance and side effects. Additionally, this article emphasizes the importance of personalized pain management in CP and underscores the need for a multidisciplinary approach. It aims to summarize the existing knowledge on the use of non-pharmacological palliation methods to improve the quality of life for patients with CP.

**Key Words:** Chronic pancreatitis; Pain; Surgery; Endoscopy

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**Core Tip:** The management of chronic pancreatitis (CP) involves careful planning of surgical interventions to prevent pain from becoming chronic and autonomous, potentially leading to opioid dependency. Early surgery, within the first three years of symptom onset, is associated with better outcomes. Surgical procedures aim to address pancreatic and bile duct obstructions and can be drainage or resection-based, depending on the patient's condition. Minimally invasive and endoscopic options are also available. A multidisciplinary approach, including interventions like celiac plexus blocking, percutaneous nerve stimulation, and acupuncture, can be considered, although further research is needed to confirm their effectiveness. Decision-making should involve input from healthcare providers to determine the most suitable treatment for each CP patient. Additionally, for calcified CP with strictures and calculi, extracorporeal shock-wave lithotripsy is a potential option, with the type and timing of endoscopic treatment tailored to the patient's needs.

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## INTRODUCTION

Chronic pancreatitis (CP) is a chronic inflammatory disease with a variety of etiologies that are impacted by regional and sociocultural variables. It results in the progressive destruction of pancreatic tissue and the development of fibrous scarring. The clinical diagnosis of CP often relies on a combination of clinical symptoms, medical history, imaging studies, and pancreatic function tests. A definitive diagnosis of CP is typically established through a detailed evaluation of these factors. The incidence and prevalence of CP vary by area, with rates ranging from 5 to 15 cases per 100000 people and a prevalence of 40 to 120 cases per 100000, assuming a 20-year median survival time. In recent years, these figures have risen significantly in Asian countries[1,2].

Chronic alcohol drinking is the leading cause of CP, accounting for over 70% of all cases. A consistent alcohol intake of 70 g or more per day for at least 12 mo is usually necessary to develop CP. Tobacco use is both a risk factor and an independent risk factor for CP[3,4].

Pathophysiologically, CP causes fibrosclerotic change of pancreatic tissue, which is frequently accompanied by calcifications. The persistent and gradual loss of functional pancreatic tissue is caused by local fibro-inflammatory and neuroimmunologic alterations. Initially, these alterations largely impair exocrine function, resulting in symptoms such as steatorrhea, weight loss, maldigestion, and vitamin deficiencies. Endocrine failure may occur later in the disease's course, resulting in symptoms and problems associated with diabetes mellitus[2,4].

In virtually all CP patients, pain is a major and clinically important symptom. Pain in CP is caused by immunologic and neurological alterations that result in changes in peripheral nerve diameter, density, and function, which correspond with pain severity with time. Pain is first created on a peripheral level, but due to neuronal plasticity and memory function in the peripheral and central nervous systems, it transforms into a stimulus-independent pain experience approximating autonomous pain. As a result of cerebral cortical remodelling, this neuronal plasticity eventually leads to permanent alterations in pain perception. Many CP patients, particularly those in severe stages, develop opiate addiction and suffer substantial impairment as a result of persistent pain[2,5].

The goal of therapy is to relieve pain, improve healing, preserve quality of life (QOL), and address postoperative requirements. Initial management comprises lifestyle changes, dietary optimization, risk factor reduction by abstinence from alcohol, and tobacco and smoking cessation. Analgesics, neuromodulators, antioxidants, pancreatic enzyme replacement for insufficiency, and diabetes control are all part of supportive medical therapy[6].

The "fourth" level of the WHO pain management ladder incorporates interventional pain treatment techniques. Endoscopic ultrasound (EUS)-guided plexus block, splanchnic nerve block, spinal cord stimulation, transcranial magnetic stimulation, and acupuncture are examples of these interventions. According to current United European Gastroenterology guidelines, following therapies may be useful in some instances of CP. However, it is vital to highlight that these treatments will only be available to a small percentage of patients, usually after all other therapeutic choices have been explored[7,8].

## PAIN ASSESSMENT

In the field of pancreatology, the assessment of outcomes in patients with CP presents a challenge due to a lack of standardization in measurement tools[9]. Several quality of life assessments were used, including the Short Form 36 Health Survey, Short Form 12 Health Survey, Functional Assessment of Chronic Illness Therapy Pancreatic Disease subscale, and the European Organization for Research and Treatment of Cancer QLQ-C30. Recently, a disease-specific module known as QLQ-PAN28 (CP) was created and validated, augmenting the QLQ-C30's reliability and validity data for CP patients[10].

The complex character of chronic pain makes pain evaluation challenging in CP patients. Pain intensity has been measured using unidimensional scales such as the visual analog scale (VAS) and numeric rating scales. VAS, a 10-cm line with "anchor" words at both ends, and numeric rating scales (0 to 10) have both been employed, with VAS being more accurate and sensitive in detecting chronic pain[11]. To capture the complexities of chronic pain, multidimensional instruments such as the McGill Pain Questionnaire have been developed. The McGill Pain Questionnaire is well-known for its accuracy in measuring multiple aspects of pain, distinguishing between individuals with different chronic pain syndromes, and identifying therapy effects. It has mostly been employed in the assessment of chronic noncancer pain, although its application in CP investigations is limited. It has the benefit of measuring several dimensions of pain, but it can be complicated, and a shorter variant is not accessible in as many languages. Only one research documented its usage in CP, and no meaningful impact was seen[12,13].

In conclusion, measuring outcomes in CP patients presents complications due to a lack of standardized assessment instruments. QOL scales such as the QLQ-C30, as well as disease-specific modules, are being created and validated. Pain evaluation methods differ, with VAS being the most commonly utilized in CP studies, whereas the multidimensional McGill Pain Questionnaire provides useful insights but is less commonly used in CP research. The intricacy of CP pain undermines the validity of pain alleviation ratings even further[12]. Overall, more standardization and research are required to improve outcome evaluation in CP patients.

## SURGICAL INTERVENTION

Surgery in CP patients should be planned carefully to prevent missing the phase when pain becomes permanent and autonomous, resulting in continuous pain creation independent of stimuli. It is critical to prioritize pain treatment in order to avoid chronic opiate use and dependency[2]. Because the WHO pain medicine concept already includes regular opioid prescription in the second stage, treating CP-related symptoms and morphological alterations is critical[14]. The optimal timing for surgical intervention depends on various patient and disease-related factors. In contrast, prolonged disease duration and regular narcotic use may lead to recurrent pain even after surgery, often attributed to sensitization of central pain pathways. Surgery initiated within three years of symptom onset usually results in better pain management and preservation of pancreatic function. Enables a complete study of the efficacy of endoscopic treatment without creating persistent opioid dependency[2].

### *Surgical procedures*

The primary goal of CP surgery is to clear the pancreatic and, if required, bile duct obstructions. This may entail the removal of fibrotic and calcified tissue that is causing the blockage[15].

As a result, there are two types of surgical treatment methods to consider: Drainage operations and resection treatments. Traditionally, the pancreatic head has been thought to be the primary cause of pain in the majority of CP patients[2]. Surgery for CP has progressed from drainage procedures with a one-third relapse rate to approaches based on the "pacemaker theory," which suggests that the pancreatic head is a key contributor to the pain process in CP and supports the use of resection and hybrid procedures[2,14].

In the setting of a normal pancreatic head, drainage methods are used, with a dilated pancreatic duct having the Puestow operation or its Partington and Rochelle modification and a non-dilated pancreatic duct receiving the Izbicki treatment[16]. Pancreaticoduodenectomy (PD) or pylorus-preserving pancreaticoduodenectomy (PPPD) is performed on patients who have a suspicious pancreatic head mass. Patients with a pancreatic head mass who have no or low suspicion of cancer undergo duodenum-preserving pancreatic head resection (DPPHR) in one of two ways, depending on intraoperative results[17].

Because of the high prevalence of recurring pain, drainage treatments have historically been supplanted by resection and hybrid procedures. PD, especially pylorus-preserving PD, and DPPHR are now the most often performed procedures in the treatment of CP[4]. Both are quite effective in relieving pain and maintaining pancreatic endocrine function. DPPHR had less short-term morbidity and greater exocrine function than PD. Long-term consequences, however, are identical[13].

Beger and Frey's techniques within DPPHR have not revealed substantial short- or long-term differences in terms of results. However, the Berne approach is simpler and faster to do, with a shorter hospital stay, than the Beger surgery, but the long-term consequences are the same. A recent multi-center randomized controlled study with a two-year follow-up found no difference in partial pancreatectomy that included PPPD and conventional PD against DPPHR, including its many versions such as Beger, Frey, and Berne[16]. However, most evidence support DPPHR in terms of lower morbidity, higher QOL, less pancreatic endocrine dysfunction, and similarly effective pain management when compared to PD and PPPD, making DPPHR and its variants the surgery of choice for CP. There is no randomized controlled trial that compares complete pancreatectomy islet autotransplantation to the other procedures utilized in the setting of CP. The surgical competence provided to patients through this vast range of surgical procedures differs between physicians and facilities[4].

Surgery for CP can be performed using minimally invasive procedures such as laparoscopic and robotic techniques. Although standard resections such as partial pancreatoduodenectomy and distal pancreatectomy are performed similarly to other causes, the inflammatory alterations and portal hypertension associated with CP might offer difficulties. Patients who require drainage operations such as pseudocyst-jejunostomy or lateral pancreatojejunostomy may benefit from minimally invasive resections. Robotic techniques have been used in several CP-specific resections, such as DPPHR. While these findings suggest the viability of minimally invasive surgery in CP, no randomized controlled trials have been

conducted, and any benefits over routine open surgery remain speculative[2,18,19]. Total pancreatectomy with islet autotransplantation in small duct disease has shown promising results[6].

## ENDOSCOPIC INTERVENTIONS

Endoscopic therapy has traditionally been used first in clinical practice because to its less intrusive and outpatient character, as well as the perceived reduced risk compared to surgery. Furthermore, some clinical recommendations support endoscopic treatment as the main option for CP-related symptomatic pancreatic duct blockage[20]. While endoscopy is a viable alternative to surgery for those who are not surgical candidates or prefer a less invasive approach, endoscopists must emphasize the evidence supporting surgery as well as the logistical challenges associated with the need for endoscopic retrograde cholangiopancreatography (ERCPs). Endoscopic pancreatic duct stenting can provide symptomatic relief in patients with CP, particularly those with painful strictures or obstructions in the pancreatic duct. It is important to note that this procedure is part of a multidisciplinary approach to the management of CP, which may also involve lifestyle modifications, medications, and, in severe cases, surgical intervention. Individual treatment plans should be tailored to the patient's specific needs and the stage of the disease. Given the decision's complexity, shared decision-making should ideally involve all care providers, including surgeons, endoscopists, gastroenterologists, primary care physicians, and psychologists, in order to provide patients with a well-rounded presentation of the evidence and allow them to make an informed decision[20,21]. During an 18-mo follow-up, the ESCAPE study, a Dutch multicenter randomized trial including 88 patients with a dilated main pancreatic duct (MPD), found that early surgery resulted in greater rates of complete or partial pain alleviation (58% *vs* 39%) compared to endotherapy[22]. These findings are consistent with the findings of two prior randomized controlled studies conducted in the Czech Republic and the Netherlands. In recent years, there have been advancements in endoscopic procedures for patients with CP, particularly when conventional ERCP proves challenging due to anatomical variations or strictures. EUS-guided pancreatic duct drainage, also known as EUS-PDD, is an emerging technique that offers an alternative approach to address pancreatic duct obstruction and pain relief[23]. Although these trials have inherent limitations in addressing this complicated problem, the aggregate findings indicate early surgery as the recommended way to relieving pain in obstructive CP *vs* endoscopic decompression[24,25].

## CELIAC PLEXUS BLOCKING

Celiac plexus blocking is another pain therapy approach that is commonly used, despite the lack of data to support its effectiveness. There are no sham-controlled studies, raising the possibility that the reported benefits are just the natural course of disease that would have happened in the absence of intervention. Pain treatment is typically best handled in a multidisciplinary environment involving gastroenterologists and surgeons due to the multiple patient and disease-related elements involved[26]. EUS-guided celiac plexus block is reserved in selected patients to treat debilitating pain[6].

## ACUPUNCTURE AND PERCUTANEOUS ELECTRIC NERVE STIMULATION

Percutaneous nerve stimulation (PNS) involves the use of implanted subcutaneous electrodes to electrically stimulate specific nerve trunks[12]. The gate control hypothesis of pain, proposed by Melzack and Wall[27] in 1965, is one of the most commonly accepted explanations for how the PNS works. According to this idea, pain nerve fibers of varying diameters operate as "gates" for various forms of sensory input. It claims that pain perception can be minimized by delivering competitive non-painful stimulation *via* bigger fiber neurons to block the gates associated with small-fiber discomfort. It is feasible to close these gates by activating A fibers in the same nerve area as C fibers, effectively stopping the passage of pain signals[27]. As a result, non-painful stimulation of the peripheral nerve region reduces pain signals. Several different hypotheses have been developed, many of which investigate how the PNS may cause changes in various neuromodulators[28]. While the exact mechanism of PNS remains unknown, its potential benefits have been recognized for some time[12].

Percutaneous electric nerve stimulation is a viable treatment option for CP pain. While further study is needed to confirm its efficacy, PNS has the potential to give considerable relief for CP patients suffering from chronic and terrible pain. Collaboration among healthcare experts, including gastroenterologists and pain specialists, is critical to ensure patients receive complete care. Physicians should consider addressing PNS as a potential pain treatment option with CP patients who have not received acceptable relief from standard therapies. A thorough evaluation, tailored treatment strategies, and close monitoring can improve the results of PNS therapy for CP-related pain[29].

Acupuncture is a complementary therapy that holds promise in the management of CP pain. While further research is needed to establish its efficacy definitively, acupuncture can be considered as an adjunctive approach in the overall care of CP patients. Physicians should explore considering acupuncture as a treatment option with CP patients, particularly those who are experiencing inadequate pain management with conventional techniques, and collaborate with experienced acupuncturists to give the most complete care[30].

**Table 1** Table provides an overview of various treatment methods for chronic pancreatitis, summarizing key points for each approach

Treatment method	Key points
Surgical intervention	Careful planning to prevent permanent and autonomous pain Priority on pain treatment to avoid chronic opioid use Optimal timing depends on patient and disease factors. Early surgery may result in greater pain alleviation
Surgical procedures	Goal: Clear pancreatic and bile duct obstructions Two types: Drainage operations and resection treatments Evolution from drainage to resection and hybrid procedures
Minimally invasive procedures	Laparoscopic and robotic techniques as options Robotic techniques lack conclusive evidence over open surgery
Endoscopic interventions	Endoscopic therapy as a first, less intrusive option Pancreatic duct stenting for relief in CP with strictures
Celiac plexus blocking	Commonly used for pain therapy, but effectiveness data lacking Endoscopic ultrasound-guided celiac plexus block reserved for selected cases
Acupuncture and PNS	PNS a viable treatment for CP pain Acupuncture shows promise as a complementary therapy. Further research needed
ESWL	ESWL alone or with ERCP based on individual characteristics Endoscopic treatment recommended post-ESWL in specific cases

PNS: Percutaneous electric nerve stimulation; ESWL: Extracorporeal Shock-Wave Lithotripsy; ERCP: Endoscopic retrograde cholangiopancreatography; CP: Chronic pancreatitis.

## EXTRACORPOREAL SHOCK-WAVE LITHOTRIPSY

Clinical trials have taken a variety of ways to treating people with painful calcified CP. While some studies recommend a combination of extracorporeal shock-wave lithotripsy (ESWL) and ERCP for greater ductal clearance and pain reduction, others believe that ESWL alone may be adequate. Individual characteristics, such as the existence of strictures and calculi in the MPD, may influence the decision between these procedures[31,32].

When strictures and calculi coexist, both ERCP and ESWL are frequently required. The timing of ERCP after ESWL is debatable, with some recommending at least two days to account for probable reactive edema in the MPD or adjacent tissues[33].

Endoscopic treatment following ESWL is currently recommended by the European Society of Gastrointestinal Endoscopy for patients who do not have spontaneous stone removal after satisfactory ESWL fragmentation and those with MPD strictures. The therapy should be chosen based on the unique patient's situation[34]. Treatment methods are summarized Table 1.

## CONCLUSION

In conclusion, CP is a challenging condition primarily caused by chronic alcohol consumption, often accompanied by tobacco use. Pain is a significant symptom in CP and necessitates effective management.

Therapeutic approaches range from lifestyle changes and medical interventions to interventional procedures. Surgery is most effective when performed early in the disease course. Assessing CP outcomes is complicated due to a lack of standardized measurement tools, making it essential to further research in this area. Endoscopic therapies and minimally invasive surgeries are recommended as initial approaches, with shared decision-making among healthcare providers for patient-specific care. Complementary therapies, like acupuncture and PNS, offer potential relief for CP-related pain. Extracorporeal shock-wave lithotripsy is effective in managing calcific pancreatitis, especially when patient selection and personalized care are prioritized.

In summary, CP management is multifaceted and patient-specific, requiring a collaborative approach to improve patients' QOL and pain management outcomes.



## FOOTNOTES

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