

Pain in chronic pancreatitis: What can we do today?

Margherita Binetti, Valeria Tonini

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Margherita Binetti, Valeria Tonini, Department of Medical and Surgical Science, University of Bologna, Alma mater Studiorum, Bologna 40138, Italy

Corresponding author: Valeria Tonini, MD, Academic Research, Doctor, Researcher, Surgeon, Surgical Oncologist, Department of Medical and Surgical Science, University of Bologna, Via Massarenti 9, Bologna 40138, Italy. valeria.tonini@unibo.it

Abstract

The aim of this study is to illustrate the complexity of pain management in chronic pancreatitis (CP). In this context, pain represents the most common and debilitating symptom, and it deeply affects patient's quality of life. Multiple rating scales (unidimensional, bidimensional and multidimensional) have been proposed to quantify CP pain. However, it represents the result of complex mechanisms, involving genetic, neuropathic and neurogenic factors. Considering all these aspects, the treatment should be discussed in a multidisciplinary setting and it should be approached in a stepwise manner. First, a lifestyle change is recommended and nonsteroidal anti-inflammatory drugs represent the gold standard among medical treatments for CP patients. The second step, after medical approach, is endoscopic therapy, especially for complicated CP. In case of failure, tailored surgery represents the third step and decompressive or resection procedures can be chosen. In conclusion, CP pain's management is challenging considering all these complex aspects and the lack of international protocols.

Key Words: Chronic pancreatitis; Pain; Multifactorial mechanism; Stepwise approach; Endoscopic treatment; Early surgery

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Core Tip: The aim of this review is to analyse and discuss treatment options in chronic pancreatitis management. Lifestyle change represents the starting point in uncomplicated chronic pancreatitis (CP). Medical treatment should be the first considered in a stepwise approach. The use of nonsteroidal anti-inflammatory drugs is the gold standard, but opioids, antioxidants, neuromodulators have important roles as well. Endoscopic retrograde cholangiopancreatography, extracorporeal shock wave lithotripsy with or without endoscopy, sphincterotomy with stent placement or transgastric drainage can be chosen in complicated CP patients with obstructions or pseudocysts. A decompressive or resection operation can be chosen in surgical treatment. In conclusion, CP pain management is an ongoing challenge because of lack of international consensus on protocols. Nowadays, a tailored step-up treatment discussed in a multidisciplinary setting is considered the best approach.

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INTRODUCTION

Chronic pancreatitis (CP) is a progressive pancreatic disorder characterized by inflammation and fibrosis. The incidence and prevalence of CP remain low. The incidence is estimated about 4-12 per 100000 persons/year; while the prevalence is about 37-42 per 100000 persons/year. Abdominal pain represents its most disabling manifestation, and its prevalence in CP is about 80% of patients; painless pancreatitis only presents in 10%-20% of cases. In painless CP steatorrhea, malabsorption and endocrine dysfunction often develop[1].

In addition, acute and chronic pancreatitis represents a leading cause of hospital admissions[1]. Both genetic and environmental factors contribute to CP[2]. CP risk factors are summarised by the TIGAR-O acronym: *T* = Toxic (alcohol abuse, tobacco smoking, medications or toxins), *I* = Idiopathic (not associated with any known gene), *G* = Gene Mutation (complex genetics or modifying genes, ex. PRSS1, CFTR, SPINK1), *A* = Autoimmune (steroid responsive chronic pancreatitis), *R* = Recurrent (CP due to vascular diseases and post-irradiation damage), *O* = Obstructive (CP associated with pancreas divisum, Sphincter of Oddi disorder and duct obstruction)[3] and the M-ANNHEIM acronym includes: Alcohol and nicotine consumption, nutritional and hereditary factors, Efferent duct, Immunological, Miscellaneous and rare metabolic factors[4].

CP generally occurs together with mid-epigastric abdominal pain associated with nausea and vomiting[5]. In fact, abdominal pain represents the most frequent and debilitating symptom of chronic pancreatitis[6], and up to the 80% of patients with CP present recurrent episodes[2]. It is usually described starting in the epigastric zone with radiation to the back but may present variability[7]. The possible complete resolution of pain after the ongoing loss of pancreatic exocrine function remains a controversial topic[5]. CP presence could be associated to new onset diabetes (20%), steatorrhea (19%) and weight loss (16%) in painless patients[8]. CP patients can experience increased pain after eating, potentially leading to poor nutrition intake[9]. According to a recent review by Lukic *et al*[10] "chronic" abdominal pain persists for more than 3 mo.

Pain in CP has both somatic and visceral components. The afferent nerves of viscera terminate at various levels of the spinal cord, leading to a diffuse pain feeling. Part of the nerve projections involve sympathetic fibres, leading to nausea, diarrhoea and early satiety[11]. Considering CP clinical presentation, pain represents the most debilitating factor[3]. It has a great effect on quality of life (QoL). Pain severity can present as mild-moderate (18%) or severe (67%), and pain frequency can be intermittent (32%) or constant (53%)[2]. The aim of this study is to illustrate the complexity of pain management in CP. The underlying mechanisms of pain have been analysed, both in neuropathic and nociceptive components. The genetic role has been also described. After CP pain diagnosis, some unidimensional, bidimensional or multidimensional scales may be used to quantify the chronic pain. International guidelines have not been published yet. However, medical treatment is recommended as a first approach. In case of failure, endoscopic options can be tested. Surgical options should be chosen only in case of medical and endoscopic failure.

DIAGNOSIS

The diagnosis of CP remains a clinical challenge[12]. According to the United European Gastroenterology evidence-based Guidelines about CP diagnosis, endoscopic ultrasonography (US) recruits the highest possible number of patients, while endoscopic retrograde cholangiopancreatography (ERCP) and transabdominal US have the highest and lowest sensitivity, respectively[12].

Different scales can be used for pain assessment. The Numerical Pain Rating Scale is a one-dimensional rating scale and it is widely recommended, but multidimensional ones such as the Brief Pain Inventory and the McGill Pain Questionnaire are preferred[12]. General pain assessment tools can differentiate between[13]: Unidimensional tools: Pain visual analogue scale (VAS), pain numerical rating scale, pain intensity categories (mild, moderate, severe), pain improvement/relief categories, pain pattern (constant/intermittent), postprandial pain (yes/no or intensity); Bidimensional tools: Daily pain duration median pain VAS, number of days with pain median pain VAS, number of hours of pain median pain VAS, degree of frequency median pain VAS, pain frequency pain severity; Multidimensional tools:

McGill Pain Questionnaire (full and short-form), PainDetect Questionnaire, pain score (intensity, frequency and consequences of pain). Some specific pain assessment tools in CP are reported: Izbicki pain score, Ammann (Type A&B), Type A-E, Group 1e3 pain patterns, QLQ-PAN28[13].

PAIN MECHANISMS

The mechanism of CP abdominal pain is complex. Although pancreatic damage represents a fundamental component, it also involves both nociceptive function and central pain perception[14,15].

Regarding pancreatic damage, acinar cell injury and pancreatic duct obstruction cause parenchymal ischemia, which is the base of abdominal pain in CP. This local ischemia induces inflammation that causes nociceptive stimulation of peripancreatic nerves. Repetitive stimulations can lead to permanent changes in spinal cord and cerebral cortex[7].

Nociceptive pain occurs after primary afferent neuron activation due to chemical or mechanical stimuli[16,17]. The exact nature of factors that actually activate intrapancreatic nociceptors is still unknown[18].

Neuropathy is an important component of CP pain. The continuous sensitization of central nociceptive receptors may result in a self-perpetuating pain state, which is independent from peripheral input[19]. Intrapancreatic nerves both increase in size (neural hypertrophy) and in number (neural invasion)[20].

In 2010, some authors analysed cortical reorganization in CP patients. They showed prolonged latencies of evoked potentials in the frontal region and in insular dipole localization. These findings showed that prolonged pain in CP patients leads to central reorganization[21]. The constant stimulation of afferent pathways leads to neuroplastic changes in the central nervous system (CNS) with overactivity of pain-related structures in a chronic activation setting. Various CNS areas are involved, such as the medial thalamus, the somatosensory cortex, the parietoinsular cortical regions and limbic areas[22].

Some biochemical studies have analysed specific molecules implicated in CP pain mechanisms. According to some authors, pancreatic nociceptor involvement with an increased excitability seems to be related to K⁺ current downregulation. TRPV1, nerve growth factor and protease activated receptor 2 seem to be involved[23]. Biochemical and histopathological characteristics in CP patients are similar to those observed in patients with other nerve fibre lesions[24]. Compared to healthy controls, CP patients also have increased glutamate/creatinine (glu/cre) levels in the anterior cingulate cortex, while they have reduced N-acetylaspartate/creatinine (NAA/cre) levels[25]. These mechanisms have been revealed by cerebral spectroscopy.

Chronic pancreatitis' genetic profile has also been analysed. It plays an important role in pain perception and tolerance. Serum levels of transforming growth factor beta 1 seem to be higher in patients with nociceptive pain, while GP130 seems to be marker for neuropathic pain[26]. Some studies also suggest a role for neuromodulator drugs in the treatment of pain based on genetic susceptibility[27].

Over the years, many different theories have been proposed about the origin of pain in CP. It represents a multifactorial process. "Pancreatic duct hypertension" is considered one of the most accredited theories[28]. A direct relationship between pain and duct hypertension was first described by White *et al*[29]. It has been reproduced by infusing saline infusion with ductal pressure exceeding 25 mmHg.

In addition to histological changes, there are also CP-related functional changes[30], including maldigestion, diarrhea, weight loss and diabetes mellitus following islet-cell dysfunction[28].

CURRENT GUIDELINES

The official guidelines for CP pain treatment have been prepared following CP clinical and diagnostic criteria revisions. The first guideline was created in 2009[31] and the second one in 2015[32]. The third edition was published in 2022, "Evidence-based clinical practice guidelines for chronic pancreatitis"[33], after the redefinition of CP as a pathogenic fibro-inflammatory syndrome.

The guidelines for pain management of pain in chronic pancreatitis (2017) contain recommendations from the Working Group for the International Consensus Guidelines for Chronic Pancreatitis in collaboration with the International Association of Pancreatology, American Pancreatic Association, Japan Pancreas Society and European Pancreatic Club[6].

The European Society for Gastrointestinal Endoscopy Guidelines recommend, in case of obstruction of pancreas head or body, endoscopic therapy with Extracorporeal shock wave lithotripsy with or without endoscopy (ESWL) as first treatment, followed by re-evaluation 6-8 wk later[34].

However, absolute indications about CP treatment are missing due to the lack of standardized protocols. International guidelines recognise a lack of international consensus about diagnostic tools and validated assessment in CP pain management.

PAIN MANAGEMENT IN CHRONIC PANCREATITIS

Abdominal pain is a complex symptom and requires a tailored treatment[7]. Traditional pain management starts with lifestyle changes, such as cessation of both smoking and alcohol consumption[5,35]. According to 2017 guidelines abstinence from smoking has a weak recommendation, while abstinence from alcohol has a moderate recommendation

[6]. Correct treatment of CP pain involves either anatomic and neurologic contribution to pain[7].

The World Health Organization recommends a stepwise approach[4]. To examine CP pain management, it is useful to differentiate: CP Simple abdominal pain/back pain management; Complicated CP management: pancreatic pseudocyst, internal pancreatic fistula, biliary stenosis (Figure 1).

PAIN TREATMENT IN CHRONIC PANCREATITIS

Abdominal or back pain are the most frequent presentation in uncomplicated CP.

Medical

Medical therapies are recommended for patients without pancreatic duct obstruction, with a lower severity of pain[7] according to a “pain relief ladder” principle, as proposed by the World Health Organization[19].

A stepwise CP pain management approach begins with acetaminophen and non-steroidal anti-inflammatory drugs, followed by low potency and longer acting opioids[4].

Medical therapies

Acetaminophen: For many authors it is the first choice[36]. However, according to other authors, Paracetamol is safe but does not result in satisfactory pain relief[37].

Nonsteroidal anti-inflammatory drugs: According to the majority of authors, nonsteroidal anti-inflammatory drugs (NSAIDs) represent the first choice for analgesia in CP pain control. Only few studies evaluated the efficacy of various analgesics[38].

Opioids: Opioid analgesics are additive therapy in case of persistent or increasing pain. In this context, opioid use disorder is a risk. The careful selection of CP patients who would benefit from opioid therapy and predicting the risk of potential misuse should be applied[36]. According to Ratnayake *et al*[39], spinal cord stimulation is effective on reducing CP pain and has a potential effective role in reducing opioid use.

Antioxidants: Many antioxidants including vitamin A, C, E, selenium and methionine have been proven. The goal of antioxidant use is to decrease ‘ischemia-induced inflammation’, which could represent a peri-pancreatic nerve stimulus [4]. A sufficient dose of antioxidants should be recommended. However, according to some other authors, antioxidants are not related to better CP pain control[6,40]. A recent study concludes that a combination of antioxidants and Pregabalin significantly reduces CP pain[41].

Neuromodulators: Pregabalin, gabapentin, tricyclic antidepressants: Pregabalin was shown to reduce daily pain scores compared to placebo in a randomized study[7]. Considering 64 enrolled total patients, 36% of Pregabalin-treated patients against 24% Placebo-treated patients reported pain relief[15]. According to Cochrane Library, short-term use of Pregabalin decreases pain scores and opiate use but increases adverse events compared to placebo[42].

Pancreatic enzyme replacement therapy: Exogenous enzyme therapy may decrease enzyme secretion and improve malabsorption in patients with exocrine insufficiency. In addition, it is a non-invasive therapy with no adverse effects [43]. However, according to the most recent CP management guidelines, pancreatic enzyme replacement therapy (PERT) is not recommended but is useful for some abdominal symptoms, such as abdominal distension and flatulence in pancreatic exocrine dysfunction[33]. Decreased pancreatic secretion can be used if symptoms persist[44]. In regard to PERT therapy, doses of 1000 USP units of lipase × kg of patient body weight are advised to achieve nutritional parameter improvement[44].

Endoscopic or surgical therapy requires careful patient detection, especially regarding pancreatic anatomy. Patients with pancreatic duct dilatation may benefit from endoscopic or surgical therapies[45]. Therefore, patients may be classified as patients with structural abnormalities (called big-duct disease) and patients without anatomical abnormalities (also called as small-duct disease or minimal change CP)[45].

Endoscopic treatment

The advantages of endotherapy have been largely reported. In fact, endoscopic interventions can be repeated, if required, keeping surgical option valid[46]. International Guidelines[6] recommend ESWL as a safe and effective procedure for uncomplicated painful CP.

Endoscopic complications are divided into early and late complications. Early complications include cholangitis (especially related to sphincterotomy’s procedure), pseudocyst infection or pancreatic duct damage[46]. However, endoscopic therapy for CP appears to be a safe and effective option[47]. In the last decade, endoscopic-ultrasound (EUS) guided celiac plexus neurolysis role has been redefined, rediscussing both the technique and patient selection[48].

Surgical treatment

Surgical treatment is recommended for patients when endoscopic treatment has failed for pain relief[33]. Some authors tried to prepare a classification system to establish an international system of pain and QoL surveillance (M-ANNHEIM score)[19].

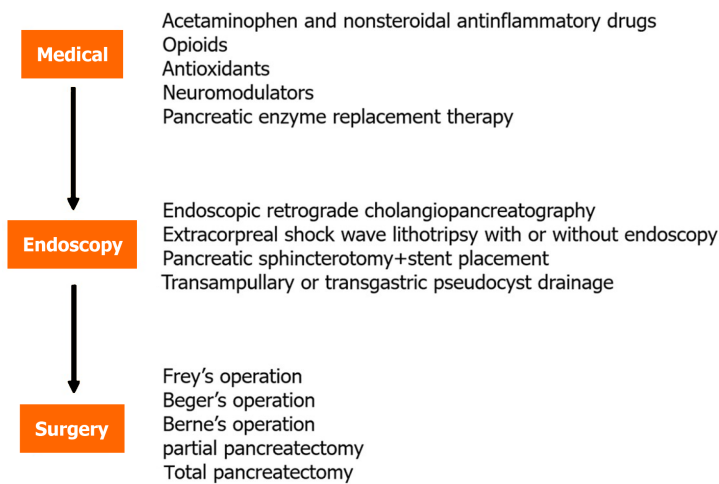


Figure 1 Chronic pancreatitis pain treatment options.

A recent randomized clinical trial (ESCAPE trial) showed that surgical treatment could be more effective than endoscopic first approach for mid-term and long-term pain relief[49]. In this study, a later pancreaticjejunostomy according to Partington and Rochelle is recommended in patients with non-enlarged pancreatic head (< 4 cm). On the other hand, a resection with duodenum preserving is performed for patients with enlarged pancreatic head (> 4 cm)[49].

According to Ratnayake *et al*[50], the Frey procedure is considered the best surgical treatment considering post-operative QoL improvement. It is also considered the procedure with lower complications considering POPF (post-operative pancreatic fistula) and PEI (post-operative exocrine insufficiency).

PAIN TREATMENT COMPLICATED CHRONIC PANCREATITIS

Some important complications may occur in CP

Pancreatic pseudocyst: 20%-40% of CP cases present with pseudocyst. The exact pathogenesis is still unknown. The blockage of the main pancreatic duct and ongoing pancreatic secretion seems to lead to pseudocyst formation[51].

Internal pancreatic fistula: A pancreatic fistula may present both in chronic and acute pancreatitis. It may occur as an asymptomatic cyst or sepsis from infected fluid collection. Minor leaks could be treated in a conservative way. In other cases, an interventional radiologist, skilled endoscopist or a surgeon should be involved[52].

Biliary stenosis: Progressive and irreversible fibrosis of the pancreatic parenchyma in CP leads to benign biliary strictures. In this context, first line therapy is interventional endoscopy with stenting[53].

Pseudoaneurysm: Pseudoaneurysm is a rare complication of CP due to the erosion of peripancreatic vessels by lipolytic and proteolytic enzymes. CP pseudoaneurysms are more common in patients with alcohol abuse[54].

Endoscopic treatment

The aim of an endoscopic approach is to remove obstructing pancreatic obstacles. Endoscopy strategies can achieve therapeutic benefits related to pancreatic outflow obstruction relief to alleviate pain[44]. Significant pain relief can be obtained when ductal irregularities are corrected, stones are extracted and strictures eliminated[44].

All endoscopic interventions are performed by expert endoscopists under consciousness sedation. Some strategies are:

ERCP: Patients with stones and ductal strictures can benefit from drainage procedures[2]. However, ductal stones or strictures often occur in the late stages of disease[45]. They are common both in alcoholic and hereditary pancreatitis. A dilatation with stenting procedure is required or a removal of main duct stones could be chosen in patients with non-enlarged pancreatic head (< 4 cm).

ESWL: It is indicated for disintegrated stones in main pancreatic duct, which are impossible to remove with other endoscopic therapies[19].

According to the 2017 Guidelines[6], ESWL for pancreatic stones is only recommended for ductal stones of 2-5 mm calcified or radiolucent stones. The SCHOKE (Extracorporeal Shock Wave Lithotripsy and Endotherapy for Pain in Chronic Pancreatitis) trial is a randomized controlled trial that demonstrated the effectiveness of external lithotripsy in pancreatic duct decompression and pain relief[55].

Pancreatic sphincterotomy and stent placement for pain relief: An important topic is the role of pancreatic duct stenting in CP. Nowadays, the "on demand stent replacement" instead of "intervals stent replacement" is preferred. The first choice might provide good palliation in CP pain[56].

Transampullary or transgastric drainage of pseudocyst: Pseudocyst drainage should be restricted to patients with important sequelae, such as infection, early satiety and weight loss. According to recent literature, endoscopic pseudocyst treatment has lower mortality and higher success rate than a surgical approach[47]. Both transpapillary and transmural approaches can be used. An EUS-guided transmural approach is preferred for large pseudocysts (d > 5 cm)[47].

All procedures have been studied in adult CP patients and no prospective or randomized controlled trials about CP endoscopic therapy in children have been published[57].

Surgical treatment

Pain represents the most common indication for operative CP management[4]. Some authors consider early surgery as the best choice. According to these authors an early surgical intervention is associated with improved pain control[58]. A proposed cutoff of early surgery is 26.5 mo from symptom onset.

A surgical approach should be suggested: (1) In the 1st 2/3 years after clinical symptoms onset; (2) For patients with five or less endoscopic procedures; and (3) For patients without opioid medical treatment.

Generally, the surgical procedures for pain treatment in CP patients can be divided in: Decompressive procedures, focused on ductal hypertension; Resection procedures, focused on inflammatory masses/stones in the pancreas head. The pancreatic head is the most innervated part of the organ. In this context, surgical removal of pancreatic head results in outflow amelioration. The removal of the inflamed pancreatic head leads to pain relief because it removes the enlarged nerves and improves outflow obstruction[30]. In regard to pancreatic resections, there are many options. The classic Whipple operation or pylorus sparing sacrifices extensive pancreatic resection. Limited pancreatic head resection is involved in Beger's operation and a more extensive drainage procedure is done in Frey operation, combining a longitudinal incision of pancreatic duct and excavation. The Berne procedure (a modified Beger procedure) does not include pancreatic head detachment[59].

In 2022, Waage *et al*[60] generated a CP surgical treatment algorithm considering firstly the presence of pancreatic duct dilatation. DPPHR (duodenum-preserving pancreatic head resection) is necessary in the case of pancreatic duct dilatation with pancreatic head pseudotumor or parenchymal calcification. Among DPPHR, the Frey's procedure is preferred. A pancreatic-jejunostomy is chosen in case of pancreatic duct dilatation but in the absence of pseudotumor/parenchymal calcification[61]. On the other hand, total pancreatectomy procedure is achieved in small duct disease. Distal pancreatectomy with or without splenectomy is indicated for CP tail pathology[60].

According to Skube *et al*[62], Frey's procedure is indicated for patients with main pancreatic duct dilatation and pancreatic head disease. On the other hand, Beger and Berne modification are indicated in patients with pancreatic head or duodenum and/or common bile duct disease involvement.

DISCUSSION

Chronic pancreatitis represents a leading cause of hospitalization. One of the most important and common symptoms related to CP is pain[63]. It usually involves the upper abdomen, often radiating to the back and worsened by meals[16, 28].

According to some authors, pain level is also related to CP etiology[28]. In alcohol-induced CP, pain is a constant symptom, while in "senile" or delayed-onset CP, the painless course is more frequent (50%). According to Amman *et al* [64], two different patterns are recognised: Type A: Characterised by recurrent episodes of abdominal pain; Type B: Characterised by prolonged or persistent pain.

Type A is characterised by short periods of pain and long pain-free intervals. Patients with type A pain are managed medically. On the other hand, type B has been hypothesised to be due to local complications, needing surgical intervention to achieve pain relief[65]. Completely painless chronic pancreatitis is a very rare form of CP[8].

However, according to a recent study by Kempeneers *et al*[66], the continuous and intermittent pain patterns in CP seem not to be two different pathophysiological entities. In fact, no differences in imaging and disease duration have been highlighted. According to the same study, different sub-patterns can be identified in the continuous: Persistent pain with slight fluctuation, persistent pain with pain attacks and pain attacks with pain between them. All of these different pain patterns can be mixed with each other.

At the beginning of 2000, CP mechanisms have been largely analysed and two different theories have been proposed: The neurogenic theory and the intraductal/intraparenchymal hypertension theory. According to the first one, CP is generated by a result of increased pressures, like in compartment syndrome. While, according to the second one, pain is generated by noxious substances on peripancreatic nerves[67]. However, nowadays, the complexity of CP is well recognised.

The most important effect of pain is the worsening of QoL. Psychiatric comorbidities are prevalent in CP patients. The effect of anxiety seems to be mediated *via* pain, while depression is independently related to QoL[68,69].

Pain has a central role in CP treatment[70]. An increasing number of studies elucidated the efficacy of a mechanism-based-treatment with specific analgesic protocol[71].

The optimal management of CP involves several specialties and, similar to cancer patients, may benefit from a multidisciplinary team[60,72].

In the past, many different surgical approaches to CP pain treatments have been proposed, such as the DuVal procedure, involving pancreatic tail resection with splenectomy followed by pancreatic jejunostomy, in order to improve retrograde drainage and pain[4]. However, a conservative step-up approach is currently considered the gold standard [73].

Alcohol and smoking cessation is suggested and a low-fat diets is also useful[37]. The medical treatment is considered the first approach[74]. The “three-step ladder” is largely adopted in this context. The first medical step is NSAID use. Opioid analgesics are commonly used, but they cannot be used for long-term treatment protocols, because of dependence risk and complications[37]. A combined antioxidant therapy seems to be safe and effective in CP pain relief[75].

A non-conservative approach is then attempted in case of conservative treatment failure. Endoscopy is considered a good alternative to surgery since the early years of 2000[76]. During the last 2 decades, the advancement of pancreatic endotherapy has given a significant contribution to the management of pancreatic pain.

In CP, main pancreatic duct obstruction caused by stricture or stones or by a combination of both requires interventional endoscopy or surgical approach[56]. These interventions and decreasing intraductal pancreatic pressure, can provide pain relief[77]. Pain represents the most common indication for operative CP management[4].

Among endoscopic therapies, an ERCP including dilatation with stenting procedure is required. An expertise endoscopist is recommended[2]. In case of big stones with diameter greater than 2-5 mm, the ESWL approach can be chosen. ERCP and ESWL both have great results in pain relief[19].

On the other hand, the surgical approach involves decompressive or resection procedures. The first ones focus on ductal hypertension, while the second ones focus on inflammatory masses/stones. Among surgical procedures, the Frey operation combines a longitudinal incision of pancreatic duct and parenchyma excavation, the Beger procedure is a limited pancreatic head resection, while Berne modification procedure involves a more limited pancreatic head resection [62]. In case of intraductal papillary mucinous neoplasm or suspected malignancy, a partial pancreatectomy is indicated. In the case of intractable disease, hereditary pancreatitis or small duct disease a total pancreatectomy should be necessary [62].

Some observational studies have suggested that the early surgery could reduce a disease progression, preserving pancreatic function[49].

An important challenge is the difficulty to compare different treatment efficacies in pain relief because of the lack of an international scale for pain comparison[11]. However, the Pancreatitis-Quantitative Sensory Testing consortium is working on meta-analysis comparing endoscopic and surgical treatments[17].

A recent systematic review including only randomized clinical trials comparing short-term and long-term outcomes showed superior results in surgical interventions compared to endoscopic ones. The number of complications is similar in both groups[77]. However, no definitive or international consensus has been achieved.

The new frontiers of interests in CP pain treatment have been reported in an article by Maydeo *et al*[78]. Being less invasive with acceptable complications, they prefer endoscopic approaches as first treatment. They also consider endotherapy the best in cost-effectiveness, because of biodegradable stents that reduce overall cost.

CONCLUSION

In conclusion, CP pain management is an ongoing challenge. Many different mechanisms are involved in CP pain onset. A tailored treatment for each patient allows for faster and effective pain control. Much progress has been made in CP pain comprehension and treatment, but the lack of international treatment protocols remains a major problem[79]. Nowadays, a step-up tailored treatment discussed in a multidisciplinary setting is considered the gold standard.

FOOTNOTES

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Country/Territory of origin: Italy

ORCID number: Margherita Binetti 0000-0003-2630-5884; Valeria Tonini 0000-0003-3130-2928.

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