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## Review Article

## Pain assessment in chronic pancreatitis: A comparative review of methods

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## ABSTRACT

**Background:** Patients with chronic pancreatitis (CP) frequently report chronic abdominal pain that adversely impacts their quality of life. Assessment of pain in CP is required for clinical management and clinical studies. International consensus guidelines recognized a lack of specific and validated pain assessment tools for CP. Therefore, the aim of this systematic review is to identify and compare all clinical studies that assessed pain in the context of a treatment for pain in CP.

**Methods:** A systematic literature search was performed in PubMed, Cochrane Library and Ovid MEDLINE. The search identified all intervention studies for pain in CP and the pain assessment tools used based on pre-defined inclusion and exclusion criteria.

**Results:** Of 341 articles identified, 137 studies were included. Pain assessment tools were both general and CP-specific. The latter were used in only 22 (16%) studies. Despite recommendations the aspects of pain assessed were limited and variable between tools. Validation of these tools in CP patients was limited to quality of life measures. None of the pain assessment tools evaluated duration of pain and postprandial pain.

**Conclusions:** There are no published pain assessment tools for CP that includes all relevant aspects of pain. There is the need to develop a comprehensive and validated pain assessment tool for patients with CP to standardised pain assessment, identify likely underlying pain mechanisms, help select appropriate treatments, report outcomes from interventions, improve clinical communication and aid the allocation of patients to clinical trials.

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## 1. Introduction

Chronic pancreatitis (CP) is a disease characterized by progressive inflammation and scarring of the pancreas that commonly presents as chronic abdominal pain that is disabling, difficult to treat and may have a negative impact on the quality of life. Other complications of CP include diabetes, pancreatic exocrine insufficiency leading to malnutrition, weight loss and osteoporosis and psychosocial effects [1–5]. There are different patterns and aspects to chronic pancreatitis pain that reflect one or more pain mechanisms. These include mechanical, inflammatory, malabsorptive and neurogenic pain mechanisms [4,6]. There are also different

treatments for pain in CP, including analgesics, enzymes, antioxidants, nutrition, radiotherapy, neuroablation, as well as endoscopic and surgical treatments [7–12]. The selection of treatments and their efficacy might be related to pain mechanisms, as well as other factors, and these require further study. The outcomes from the treatments for CP are often difficult to predict and disappointing, with patients continuing to have severe pain and a poor quality of life [13].

Many studies relating to the treatment of pain in CP are bedevilled by inadequate pain assessment, the primary endpoint. International consensus guidelines [2–4,14,15] variably recommend assessing pain duration, intensity, character, frequency, pattern, narcotic use and quality of life (QOL). It is also important to assess for chronic pain syndrome or hyperalgesia [16]. The international guidelines recommended using a variety of pain assessment methods, both general and CP-specific. These pain assessment methods evaluate a variety of different aspects of pain that might reflect different pain mechanisms and the likely efficacy

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of different treatments.

A formal comparative evaluation of the different pain assessment tools is required to determine whether they are fit for purpose, in the light of the diverse pain mechanisms and treatment alternatives. The longitudinal management of individual patients and the research of patient groups with CP requires a pain assessment tool that is accurate, reliable and easy to use, but also one that takes into account all recommended aspects of pain in order to best facilitate the identification of patients with different pain mechanisms and to help select the most effective treatment(s). The aim of this systematic review is to identify and compare all clinical studies that report interventions for pain in CP and to evaluate the aspects of pain included in the pain assessment tools. The hypothesis is that current pain assessment tools do not take into account all relevant aspects of pain and as a result there is significant room to improve on the assessment of pain for clinical management and to perform further research studies.

## 2. Methods

A list of all possible interventions for pain in CP was obtained from the British Medical Journal (BMJ) Best Practice [17] and review papers [7–12]. MeSH terms of the treatments were searched in PubMed and a search strategy developed. The purpose was to identify all intervention studies for pain in patients with CP and to identify the methods used for pain assessment. A systematic literature search was then conducted in PubMed, the Cochrane Library and Ovid MEDLINE for the period 1 January 1950 to 31 March 2016. The search strategy used was:

("Pancreatitis, Chronic" [Mesh] AND "Pain" [Mesh] AND (((((((((((((((((((Diet therapy [Subheading]) OR "Alcohol abstinence" [Mesh]) OR "Smoking cessation" [Mesh]) OR "Analgesia" [Mesh]) OR "Pancreatic Extracts" [Mesh]) OR "pregabalin" [Supplementary Concept]) OR "Octreotide" [Mesh]) OR "Antioxidants" [Mesh]) OR "loxiglumide" [Supplementary Concept]) OR "Sphincterotomy, Endoscopic" [Mesh]) OR ("Stents" [Mesh] AND "Pancreatic Ducts" [Mesh]) OR "Lithotripsy" [Mesh]) OR ("Decompression, Surgical" [Mesh] AND "Pancreatic Pseudocyst" [Mesh]) OR ("Choledochostomy" [Mesh] AND "Anastomosis, Roux-en-Y" [Mesh]) OR "Choledochostomy" [Mesh]) OR ("Pancreatic Ducts" [Mesh] AND "Decompression, Surgical" [Mesh]) OR "Pancreaticoduodenectomy" [Mesh]) OR ("Pylorus" [Mesh] AND "Organ Sparing Treatments" [Mesh] AND "Pancreaticoduodenectomy" [Mesh]) OR "Pancreatectomy" [Mesh]) OR ("Celiac Plexus" [Mesh] AND "Anaesthetics, Local" [Mesh]) OR "Thoracoscopy" [Mesh] AND "splanchnicectomy")) OR "Transcranial Magnetic Stimulation" [Mesh]) OR "Radiotherapy, Image-Guided" [Mesh]) OR ("Biliary Tract" [Mesh] AND "Stents" [Mesh]))

The inclusion criteria were: (1) human studies, (2) studies describing how pain was assessed in patients with CP, (3) studies that reported interventions for pain in CP and subsequent outcomes of treatment on pain, and (4) studies limited to the English language. The exclusion criteria were: (1) studies that had patients with autoimmune pancreatitis and hepatopancreatobiliary malignancy, (2) Review papers, (3) on going studies, (4) long-term follow up of previous studies, and (5) duplicate cohorts of patients. A secondary search was performed from the reference list of relevant studies and reviews for articles not identified by the primary search strategy.

Data was extracted from the included studies on the method of pain assessment, the specific aspects of pain assessed, intervention(s) used to treat pain and the outcomes of the interventions on pain.

The pain assessment tools identified from the literature were compared against the 8 aspects of pain that were considered

important for pain evaluation in chronic pancreatitis as recommended by the American Gastroenterological Association (AGA) (Table 4) [14]. Eight additional aspects of pain were included, having been identified from the studies included in this review [18–20] and from international consensus guidelines [4]. These additional aspects include the description of pain, location of pain, radiation of pain, triggers/exacerbators of pain, relieving factors of pain, postprandial pain, symptoms associated with pain, and impact of pain on mental health.

## 3. Results

The search yielded 341 potentially eligible studies, of which 137 studies met the inclusion criteria (Fig. 1). Of the 137 studies, 37 (27%) were randomised controlled trials (RCTs). The types of interventions for pain are outlined in Table 1. The majority of interventions were surgical (64/137, 47% or which 6 were RCT's) consisting of decompression of the pancreatic duct, pancreatic resection or a combination of both. The next most common intervention were endoscopic (28/137, 20%, of which 2 were RCTs) consisting of clearing the pancreatic duct via lithotripsy or endoscopic stone removal, stricture dilation, stenting or a combination. Of the remaining RCTs in the included studies, 9 investigated analgesic drugs and 7 neuroablative procedures.

The general pain assessment tools summarised in Table 2. These tools were developed for other painful conditions and not validated in CP. For example, the McGill Pain Questionnaire (MPQ) [22] and Pain Detect Questionnaire (PDQ) [23] were validated in arthritis and lower back pain, respectively. The general assessment tools are grouped into: (i) unidimensional tools that assess one aspect of pain, of which the pain visual analogue scale (VAS) was the most common; (ii) bidimensional tools, which combine two aspects of pain; (iii) multidimensional tools that assess more than two aspects of pain; and (iv) impact of pain tools that evaluate QOL, level of disability and effects of pain on mental and emotional states. Of these general pain assessment tools, only the Medical Outcomes Study Short Form-36 Health Survey (SF-36) and Short Form-12 Health Survey (SF-12) have been validated in CP [24–26].

Each included study used at least one of these general pain assessment tools to evaluate pain in CP patients. There was no association between the characteristics of the study (e.g. type of intervention, study design, patient population and study duration) and the general pain assessment tools selected. For instance, one RCT compared the frequency of abdominal pain as the only pain assessment tool in patients receiving organ-preserving pancreatic head resection or pylorus-preserving pancreaticoduodenectomy [27]. In contrast, another RCT that evaluated the efficacy of Pregabalin used a pain VAS, Brief Pain Inventory (BPI) questionnaire and PDQ to assess pain before and after intervention [18].

The CP-specific pain assessment tools were used in 22 studies (Table 3), 7 (32%) of which were RCTs. The Izbicki pain score, used by 13 (59%) studies, focused on common aspects of pain including intensity, frequency, analgesic use and inability to work. These aspects of pain are assigned a score based on a pre-determined scale. The average of the four variables gave the final pain score, where a higher score signified worse pain. The other three tools, Ammann (used in 5 studies), Type A-E and Group 1–3 pain patterns (used in 1 study each) were developed to classify the common pain patterns in CP. These broadly refer to constant pain, intermittent pain attacks or a mixture of both with varying intensities. The Quality of life Questionnaire-Pancreatic Modification (QLQ-PAN28) (9%) was developed to complement the European Organisation for Research and Treatment of Cancer QOL questionnaire (EORTC QLQ-C30) to measure CP-specific QOL. None of these CP-specific pain assessment tools have had psychometric evaluation except the EORTC

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