Pancreatology 14 (2014) 497–502

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Original article

Pain severity reduces life quality in chronic pancreatitis: Implications for design of future outcome trials

Søren Schou Olesen [a, *], Jacob Juel [a], Anders Klitgaard Nielsen [b], Jens Brøndum Frøkjær [b], Oliver H.G. Wilder-Smith [c, d], Asbjørn Mohr Drewes [a, d]

[a] Mech-Sense, Department of Gastroenterology & Hepatology, Aalborg University Hospital, Denmark
[b] Mech-Sense, Department of Radiology, Aalborg University Hospital, Denmark
[c] Pain and Nociception Neuroscience Research Group, Department of Anaesthesiology, Pain and Palliative Care, Radboud University Medical Centre, The Netherlands
[d] Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Aalborg University, Denmark

ARTICLE INFO

Article history:
Available online 7 October 2014

Keywords:
Chronic pancreatitis
Pain severity
Pain time pattern
Quality of life
Complications
Symptoms

ABSTRACT

Background/objectives: Chronic pancreatitis (CP) is a disabling disease characterised by abdominal pain, and various pancreatic and extra-pancreatic complications. We investigated the interactions between pain characteristics (i.e. pain severity and its pattern in time), complications, and quality of life (QOL) in patients with CP.

Methods: This was a cross-sectional study of 106 patients with CP conducted at two North European tertiary medical centres. Detailed information on clinical patient characteristics was obtained from interviews and through review of the individual patient records. Pain severity scores and pain pattern time profiles were extracted from the modified brief pain inventory short form and correlated to QOL as assessed by the EORTC QLQ-C30 questionnaire. Interactions with exocrine and endocrine pancreatic insufficiency, as well as pancreatic and extra-pancreatic complications were analysed using regression models.

Results: Pain was the most prominent symptom in our cohort and its severity was significantly correlated with EORTC global health status ($r = -0.46$; $P < 0.001$) and most functional and symptom subscales. In contrast the patterns of pain in time were not associated with any of the life quality subscales. When controlling for interactions from exocrine and endocrine pancreatic insufficiency no effect modifications were evident ($P = 0.72$ and $P = 0.85$ respectively), while the presence of pancreatic and extra-pancreatic complications was associated with an almost 15% decrease in life quality ($P = 0.004$).

Conclusions: Pain severity and disease related complications significantly reduce life quality in patients with CP. This information is important in order to design more accurate and clinical meaningful endpoints in future outcome trials.

Introduction

Chronic pancreatitis (CP) is a disabling disease with a dramatic impact on quality of life (QOL) and a significant cost due to health resource utilisation [1,2]. The underlying pathology is a process of continuing inflammation leading to irreversible pancreatic damage, concomitant functional impairment and ultimately endocrine (i.e. diabetes) and exocrine pancreatic insufficiency [3]. Although symptoms associated with pancreatic insufficiency may account for some of the symptom burden in CP, upper abdominal pain is the most prominent symptom and present in 80–90 % of patients during their disease course [4]. Also, a number of pancreatic and extra-pancreatic complications including pseudocysts, bile duct obstruction, duodenal obstruction and splenic vein thrombosis have been associated with pain and may further compromise the wellbeing of patients with CP [5].

Previous studies have documented a decreased QOL in patients with CP, but the association to symptom type and burden remains controversial. Accordingly, Mullady and co-workers found a significant association between pain pattern in time (i.e. constant vs. intermittent pain) and QOL in a large North American cohort, while

* Corresponding author. Mech-Sense, Department of Gastroenterology & Hepatology, Aalborg University Hospital, Mølleparkvej 4, 9000 Aalborg, Denmark. Tel.: +45 99326243; fax: +45 99326507.
E-mail addresses: soren.s.olesen@gmail.com, sso@mech-sense.com (S.S. Olesen).

http://dx.doi.org/10.1016/j.pan.2014.09.009

pain severity did not influence QOL [6]. In contrast, pain severity was significantly correlated to QOL in a study from Poland [1]. Furthermore, the association of QOL and symptoms of pancreatic dysfunction as well as pancreatic and extra-pancreatic complications have not been clearly established. Taken together more research is needed in this area in order to better understand the complex interplay of symptoms, complications and QOL in CP. This information is also crucial to design more accurate and clinically meaningful endpoints in future outcome trials [7].

In the present study we investigated the association between pain symptoms, complications and QOL in a well-characterised North European population with CP. We hypothesised that an increased pain symptom burden and more complications would significantly decrease QOL. The primary aims of the study were: 1) to investigate the association between pain symptoms (i.e. pain severity and pain pattern in time) and QOL, 2) to examine putative interactions with exocrine and endocrine pancreatic insufficiency, as well as pancreatic and extra-pancreatic complications (i.e. pseudocysts, bile duct obstruction, duodenal obstruction and splenic vein thrombosis). In addition, we explored any associations of QOL to lifestyle factors (i.e. smoking and drinking habits) and duration of CP.

Methods

This study was a cross-sectional study conducted at two tertiary referral hospitals in the Netherlands and Denmark. The ethical Committees in both countries approved the study, and all patients provided written informed consent. The diagnosis of CP was based on The Mayo Clinic diagnostic criteria [8]. We included findings of ductal pathology from magnetic resonance cholangiopancreaticography (MRCP) in addition to endoscopic retrograde cholangiopancreaticography (ERCP) since MRCP is the preferred diagnostic modality to characterise ductal pathology nowadays and has replaced the role of ERCP as a diagnostic test [9]. Information on patient demographics, aetiology and duration of CP, Body Mass Index (BMI), diabetes, complications to CP (i.e. pseudocysts, bile duct obstruction, duodenal obstruction and splenic vein thrombosis), and the use of pain medications were obtained from clinical interviews in the outpatient clinics of our institutions and through review of the individual patient records. The TIGAR-O risk factor classification system was used to categorise patients according to the risk factor most strongly associated with pancreatitis [10]. For example, a person with recurrent acute pancreatitis due to excess alcohol consumption were categorised under “toxic-metabolic” predisposition rather than “recurrent and severe acute pancreatitis” predisposition. The faecal elastase-1 concentration test, 72-h fecal fat collection and the ^{13}C-mixed triglyceride breath test were used to diagnose pancreatic exocrine insufficiency according to the preferred local clinical practice.

Subjects were stratified into 5 categories by mean reported alcohol consumption using definitions similar to the National Health Interview Survey [11]. Drinking categories included abstainers (no alcohol use), light drinkers ($\leq$0.5 drinks per day or $\leq$3 drinks per week), moderate drinkers (>0.5 to 1 drink per day or 4 to 7 drinks per week for women; >0.5 to 2 drinks per day or 4 to 14 drinks per week for men), heavy drinkers (>1 to <5 drinks per day or 8 to 34 drinks per week for women; >2 to <5 drinks per day or 15 to 34 drinks per week for men), and very heavy drinkers (>5 drinks per day or >35 drinks per week for both sexes). Tobacco use was stratified by number of cigarette packs per day as suggested by the North American Pancreatitis Study-2 consortium [6].

The European organization for research and treatment of cancer quality of life questionnaire (EORTC QLQ-C30) was used to evaluate QOL [12,13]. The EORTC QLQ-C30 is composed of single-item measures and multi-item scales with scores ranging from 0 to 100 after linear transformation of the raw score. A high score for a functional scale represents a high level of functioning, as does a high score for the global health status, while a high score for the symptom scale represents a high level of symptomatology.

Pain scores were measured using the modified brief pain inventory short form (m-BPIsf) [14]. This 14-item questionnaire is designed to captures two dimensions of pain: pain severity and its interference with daily activities. Based on a 0 to 10 visual analogue scale pain severity was measured as the arithmetic mean of the current pain experience (i.e. “pain right now”) and the average, worst and least pain during the previous seven days. In addition, these four pain severity items were used to construct the pain time pattern as illustrated in Fig. 1. The pain interference score was calculated as the arithmetic mean of the following seven pain interference items using the same 0 to 10 visual analogue scale as for the pain severity score: 1) general activity, 2) mood, 3) walking ability, 4) work ability, 5) relations with other people, 6) sleep, and 7) enjoyment of life.

Statistical analysis

All data are presented as mean ± SD unless otherwise indicated. The associations between EORTC QLQ-C30 subscales and items, pain severity, and clinical and demographic variables were analysed by a two-step procedure. First, putative associations were explored by ANOVAs (categorical variables, i.e. pain time pattern, drinking and smoking categories) and Pearson's product–moment correlation coefficients (continuous variables, i.e. pain severity and duration of CP). Tukey–Kramer pairwise comparisons were used for post-hoc analysis. Second, linear regression models were fitted for significant associations from the primary analysis (i.e. life quality vs. pain severity). The following factors were considered as co-variables in the regression model to adjust for potential confounding: i) diabetes, ii) exocrine pancreatic insufficiency, and iii) pancreatic and extra-pancreatic complications. All reported *P*-values were two sided and a *P*-value <0.05 was considered as an indication of statistical significance. For the primary analysis an adjusted *P*-value $\leq$0.001 was used to account for multiple comparisons [15].

Results

A total of 106 patients with CP were enrolled in the study. Seventy-five patients (71%) had parenchymal calcifications and 74 patients (71%) had ductal pathology, while histology was available in 8 patients (8%). Baseline demographics and clinical characteristics are reported in Table 1. The patients had a mean age of 57.6 ± 10.6 years and 73 (70%) were men.

Constant pain with intermittent pain attacks was the most prevalent pain time pattern (51%), followed by constant pain (32%)

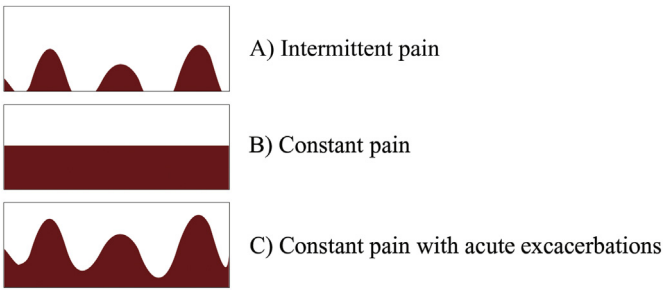

Fig. 1. Temporal pain pattern profiles of chronic pancreatitis patients.