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Type of pain, pain-associated complications, quality of life, disability and resource utilisation in chronic pancreatitis: a prospective cohort study

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Abstract

Objective—To compare patients with chronic pancreatitis (CP) with constant pain patterns to patients with CP with intermittent pain patterns.

Methods—This was a prospective cohort study conducted at 20 tertiary medical centers in the USA comprising 540 subjects with CP. Patients with CP were asked to identify their pain from five pain patterns (A—E) defined by the temporal nature (intermittent or constant) and the severity of the pain (mild, moderate or severe). Pain pattern types were compared with respect to a variety of demographic, quality of life (QOL) and clinical parameters. Rates of disability were the primary outcome. Secondary outcomes included: use of pain medications, days lost from school or work, hospitalisations (preceding year and lifetime) and QOL as measured using the Short Form-12 (SF-12) questionnaire.

Results—Of the 540 CP patients, 414 patients (77%) self-identified with a particular pain pattern and were analysed. Patients with constant pain, regardless of severity, had higher rates of disability, hospitalisation and pain medication use than patients with intermittent pain. Patients with constant pain had lower QOL (by SF-12) compared with patients who had intermittent pain. Additionally, patients with constant pain were more likely to have alcohol as the aetiology for their pancreatitis. There was no association between the duration of the disease and the quality or severity of the pain.

Conclusions—This is the largest study ever conducted of pain in CP. These findings suggest that the temporal nature of pain is a more important determinant of health-related QOL and healthcare utilisation than pain severity. In contrast to previous studies, the pain associated with CP was not found to change in quality over time. These results have important implications for improving our understanding of the mechanisms underlying pain in CP and for the goals of future treatments and interventions.

INTRODUCTION

Pain represents the most common and difficult to control feature of chronic pancreatitis (CP); resulting in an inordinate degree of disability and an estimated annual cost in the USA in excess of US $638 million.[1,2] The manifestation of pain in individuals is highly variable, with some patients experiencing continuous pain of varying severity while others experience pain which is only intermittent or a background level of continuous pain coupled with intermittent flares in pain severity The pathophysiology of pain in CP is complex and poorly understood and no intervention or treatment provides complete relief of pain in all patients, with some interventions carrying the potential for harm.[3–6] Most studies of therapeutic interventions in CP (eg, coeliac plexus block, Puestow procedures or pancreatic enzyme supplements) have measured reductions in pain severity as a primary outcome to determine response. Studies of this design are based on the assumption that pain severity impacts functioning and quality of life (QOL). There have been no studies to date which have examined the effect of temporal pain patterns on QOL, rates of disability and healthcare utilisation.

In the current study we examine the effect of constant versus intermittent pain patterns and compare these results with those in patients with mild to moderate versus severe pain

patterns. We hypothesised that the temporal pattern of pain (constant vs intermittent) rather than severity (mild to moderate vs severe) would have a more profound effect on outcomes and that patients with constant (rather than intermittent) pain patterns would have significantly poorer QOL and increased levels of disability healthcare utilisation and pain medication use.

METHODS

Study design and aims

We hypothesised that the chronicity of pain (constant vs intermittent) rather than the severity (mild, moderate or severe) was a more significant determinant of QOL and resource utilisation in patients with painful CP. The aim of our study was to compare resource utilisation, disability and QOL among patients with CP who were experiencing differing types of abdominal pain, specifically mild to moderate pain versus severe pain and constant versus intermittent abdominal pain. Data for this study were derived from the North American Pancreatitis Study-2 (NAPS2).[7] NAPS2 was a multicentre prospective study conducted from 2000 to 2006 involving 20 centres across the USA which collected standardised data and blood from patients with acute recurrent pancreatitis and CP. Only data pertaining to patients with CP (n=540) were used for this analysis. CP was defined by predetermined imaging criteria (primarily endoscopic retrograde cholangiopancreatography (ERCP; note that ERCP was not required for eligibility and was not performed solely for the purpose of diagnosis or study enrolment) or CT) or histology. The detailed study protocol and methodology have been previously published.[7] The study was approved by the Institutional Review Board at each participating centre, and all subjects provided written informed consent prior to enrolment.

Assessment of pain, resource utilisation and QOL

Patients were asked to assess the type and severity of their pain based on recommendations of the American Gastroenterological Association technical review of the topic.[8] Specifically subjects were asked if they had pain and, if so, what type of pain they experienced. A multiple choice question (table 1) was used to classify the pattern (intermittent vs chronic) and severity (mild to moderate vs severe) of pain.[9] Effects of pain on daily function were assessed by recording the number of days (work or school) missed in the previous month due to pain, and whether they were on disability benefit or unemployed because of pain. The health survey Short Form-12 (SF-12) was used to assess QOL. The SF-12 is a validated QOL questionnaire that was derived from the SF-36[10,11] and has been used in a variety of chronic conditions to measure functioning and symptoms including pain.[12–14] The SF-12 is composed of 12 questions which measure eight different domains. The scores are weighted averages of the physical and mental components of the 12 questions comprising the SF-12 instrument for measuring QOL. The scores are transformed to produce a normally distributed population score with a mean of 50 and an SD of 10. Each SF-12 scale is standardised using a z-score transformation using the SF-12 scale means and SDs from the 1998 general US population. Simply put, a score <50 shows that health status is below average. The questionnaire used in NAPS2 also captured detailed data on patient

demographics, aetiology of pancreatitis, alcohol and tobacco use, frequency of hospitalisations due to pancreatitis and the use of pain medications.

Statistical analysis

To examine the relationship between pain pattern and outcomes of interest, patients in each of the five pain pattern categories were combined in the following manner: first, patients with intermittent pain patterns (A+C) were combined and compared with patients with constant (B+D+E) pain patterns. Secondly patients with only mild to moderate pain (A+B) were compared with patients with any component of severe pain (C+D+E). Finally the five pain patterns were individually compared with one another.

Descriptive analyses are presented as proportions for categorical data and as mean±SD or median and IQR for continuous data where appropriate. In order to control for skewed data, the following continuous data were re-organised by category: days of school/work lost per month (none, 1–5, 6–9 and ≥10), hospitalisations in the last year related to pancreatitis pain (none, 1–2 and ≥3) and hospitalisations over their entire lifetime related to pancreatitis pain (≤2, 3–5, 6–9 and ≥10). Categorical data were compared using χ^2 tests. Continuous data were analysed using Student t test or Mann–Whitney, as appropriate. Associations between the duration of the CP pain and the frequency (intermittent vs constant) and intensity (mild to moderate vs severe) of the pain were determined using Spearman's rank correlation coefficient (r_s). All p values <0.05 were considered significant. Data analysis was performed using SPSS version 14 (SPSS, Chicago, Illinois, USA) and the R Project software (http://www.r-project.org).

RESULTS

A total of 540 patients with CP were enrolled in NAPS2. Among the 540 patients with CP, a self-reported pain pattern was available in 414 patients. The baseline demographic and clinical characteristics for these patients, overall as well as according to pain pattern, are outlined in table 2. Overall, patients had a mean age of 48.9 (±15.4) years and were predominantly white (83.3%) with a normal or low body mass index (BMI; 58.9%). Approximately two-thirds (268/414) of patients with CP reported a history of acute pancreatitis. According to the treating physician's designation, alcohol was considered the sole cause or a significant contributor in 189 (45.7%) patients. Only 17 patients (4.1%) were reported to have autoimmune pancreatitis as an aetiology or risk factor in their disease.

In the overall cohort (414 patients), almost half (47.3%) of the patients used pain medication on a regular basis for abdominal pain due to pancreatitis. Patients were hospitalised a median of 1 time (IQR 0, 3) within the year preceding enrolment and a median of 5 times (IQR 2, 12) over their lifetime. When specifically queried on disability benefit, 399 out of 414 patients provided a response. Of these, >25% (123/399) of the patients were on disability benefit. Among patients who acknowledged ever drinking alcohol, two-thirds (63%) of patients reported current drinking at the time of study enrolment. Most light and moderate drinkers continued to drink at low levels, while fewer than half of heavy (16%) or very heavy (45%) drinkers reported drinking >2 drinks on a drinking day at the time of study enrolment. The distribution of current drinking and drinking patterns were generally similar

based on individual pain patterns, severity of pain or whether the pain was intermittent or constant. The majority of patients acknowledged current (47%) or past (23%) tobacco use, with an average of a pack per day use. When we examined the association between the length of symptoms and pain pattern, we found that the duration of the disease did not correlate with either the frequency (intermittent vs constant) or the severity of the pain (r_s=0.017, p=0.725 for frequency and r_s=0.073, p=0.142 for severity).

The most common pain pattern was type ‘D’ (n=158), a pattern characterised by constant mild pain with superimposed episodes of severe pain. The next most common pattern was type ‘C’ (n=128), characterised by a generally pain-free existence with episodes of severe pain. There were no statistically significant differences in age, race, BMI, or history of acute pancreatitis between pain groups. Patients with ‘E’ type pain (constant, unchanging, severe pain) were significantly less likely to be regular users of alcohol than patients with ‘B’ type pain (constant, mild to moderate pain; 65% vs 87%, p=0.04).

Pain pattern groups were then combined to produce an ‘intermittent’ pain group (A+C, n=186) and a ‘constant’ pain group (B+D+E, n=228). Patients with intermittent pain tended to be older (mean age 50.6 years vs 47.6 years, p=0.049) (table 3) while patients with constant pain were more likely to have alcohol as the sole aetiology or risk factor for CP (according to physician diagnosis) than patients with intermittent pain (50% vs 40%, p=0.01). There was no difference in race, BMI, family history of pancreatic cancer, or personal history of acute pancreatitis in patients with intermittent patterns of pain compared with those with constant pain patterns. Patients with intermittent pain patterns were more likely to ‘abstain’ from alcohol use than patients with constant pain patterns (25.9% vs 20.6%, p=0.04). Conversely, patients with constant pain patterns were more likely to acknowledge very heavy (average weekly alcohol ≥35 drinks) alcohol use during the period of maximum drinking in their life (31.1% vs 19.5%, p=0.002). Patients with constant pain were more likely to be current (rather than past or never) smokers than patients with an intermittent pattern of pain (OR 1.67 (95% CI 1.1 to 2.5)). Regardless of severity, patients with CP and constant pain were more than four times more likely to be on chronic pain medication than patients with CP and intermittent abdominal pain (OR 4.4 (95% CI 2.8 to 6.8)). Furthermore, patients with constant pain were more than twice as likely to be disabled as patients with intermittent pain (42.1% vs 17.5%, OR 3.2 (95% CI 2.0 to 5.1)). Patients with intermittent pain patterns were twice as likely not to miss any days of work or school compared with their constant pain counterparts (60.4% vs 29.9%, OR 2.02 (95% CI 1.4 to 2.8)) (figure 1A). Among patients not on disability benefit (constant pain 125/216 (57.9%) vs intermittent pain 151/283 (82.5%)), patients with constant pain were more likely to miss ≥5 days of work or school per month than patients with intermittent pain (89/125 (71%) vs 56/151 (37%), p<0.001).

More than 90% (376/414) of patients had been hospitalised on at least one occasion in their lifetime for pain related to CP. Patients with intermittent pain were more likely to have no hospitalisations for pancreatic pain in the preceding year (χ^2=6.2, p=0.004) while those with constant pain were more likely to have been hospitalised ≥10 times in the last year (χ^2=8.8, p=0.001) (figure 2A). Similarly, patients with intermittent pain were more likely to have ≤2 hospitalisations over their entire lifetime for pain related to their CP (χ^2=16.0, p<0.001),

while those with constant pain patterns were more likely to have ≥10 hospitalisations (χ^2=19.8, p=0.00001) (figure 3A).

Pain patterns were then combined into a mild to moderate pain group (A+B) and a severe pain group (C+D+E). In contrast to the differences seen when constant pain patterns were compared with intermittent pain patterns, there were no statistically significant differences seen when patients with mild to moderate pain (A+B) were compared with patients with severe pain (C+D+E) in any of the comparisons noted in table 3. Specifically, patients with CP and severe pain were no more likely to be smokers or to use alcohol regularly, to be on chronic pain medication or to be disabled by their pain than patients with mild to moderate degrees of pain. Although patients with mild to moderate degrees of pain severity were more likely to have missed no days of school or work due to their pain compared with patients with severe pain (χ^2=6.6, p=0.005), there were no significant differences associated with severe pain and missed days of school or work (figure 1B). Similarly, although patients with mild to moderate pain were more likely to have no hospitalisations in the last year and ≤2 hospitalisations over their lifetime for pancreatic pain (χ^2= 10.0 and 5.8, p=0.001 and 0.006, respectively), there were no significant differences associated with severe pain and hospitalisations in the last year (figure 2B) or lifetime hospitalisations (figure 3B).

Participants in the NAPS2 study completed the standardised and validated quality of life survey SF-12. For each of the patients, the SF-12 scores were calculated both for a physical component summary (PCS) and a mental component summary (MCS) using the scoring method provided in the SF-12 version 2 reference manual[15] In general, higher scores correlate with greater well-being and functioning. Overall, there were no differences in PCS or MCS scores between individual pain patterns (figure 4A). Patients with intermittent patterns of pain (A+C) had significantly higher scores for both the mental (mean MCS score 47.6±9.9 vs 39.9±11.7, p<0.001) and the physical (mean PCS score 42.2±10.7 vs 33.3±10, p<0.001) component scores than patients with constant pain patterns (B+D+E) (figure 4B). In contrast, there was a less impressive difference between PCS scores when comparing patients with mild to moderate pain with those with severe pain (mean PCS score 39.8±10.7 vs 36.7±11.3, p=0.02) and no differences in MCS scores when comparing groups by severity (mean MCS score 43.5±11.2 vs 43.4±11.7, p=0.93)(figure 4C).

A post hoc stratified analysis was conducted to examine differences which might be present among various subpopulations. When data were stratified by gender, we found that both female and male patients with constant pain patterns (B+D+E) were more likely to use pain medications regularly, be on disability benefit, have a greater number of days lost per month (work or school) as well as hospitalisations in the past year and over their lifetimes than male or female patients with intermittent (A+C) pain patterns. When we stratified by smoking status and gender, we found that female patients but not male patients who had never smoked were more likely to have intermittent rather than constant pain (p=0.002) while those females who were current smokers were more likely to have constant pain than those who did not (p=0.012).

To determine the possible effect of aetiology on pain patterns, we stratified the data by cause of CP as determined by the treating physician. Using this approach, we found that patients

who were disabled were more likely to have alcohol as the aetiology for their CP than non-alcohol causes ($p<0.001$). However, regardless of the aetiology of the CP, patients with constant pain were more likely to be disabled than patients with intermittent patterns of pain ($p<0.001$). This finding therefore supports an independent effect of pain pattern on disability. Among patients in whom alcohol was considered the primary or contributing cause of CP, patients with constant pain patterns were more likely to be current smokers than those with intermittent pain ($p= 0.026$). Conversely, among patients who had a non-alcohol cause for CP, constant pain patterns were not significantly more common among current smokers compared with never smokers ($p=0.672$).

DISCUSSION

Pain and an individual's experience of pain are perhaps the most complex and poorly understood phenomena in medicine today. When treatments are ineffective in relieving pain, patients are left with feelings of hopelessness and isolation.[16] Pain is the hallmark symptom of CP, occurring in up to 90% of patients, and is the inciting symptom for admission in 93% of cases.[1718] Because of the prevalence of pain and its associated costs, both tangible and intangible, a significant proportion of treatments have been directed at reducing or eliminating it, and these have had mixed results. Moreover, most interventional and therapeutic studies are conducted in patients with constant and severe pain rather than intermittent or mild to moderate pain, and it is not surprising that no treatments to date result in uniform improvement in all patients.[19–24]

Historically, clinical trials in patients with CP have measured outcomes based on a reduction of pain severity without regard for an individual's pain frequency, although there are a few notable exceptions.[2526] These approaches have been based on the presumption that pain severity rather than frequency has a greater impact on QOL and functioning. In the current study, we examined the effects of pain on QOL and healthcare utilisation in patients with intermittent versus constant pain patterns. We showed that patients with constant pain, regardless of severity, had higher rates of disability, hospitalisation and pain medication use than patients with intermittent pain and that patients with constant pain had lower QOL (by SF-12) compared with patients with intermittent pain. In contrast, patients with severe pain failed to show greater rates of disability, hospitalisation or chronic use of pain medications compared with patients with mild to moderate degrees of pain. There have been no studies which have examined the correlation between pain patterns and QOL, healthcare utilisation or disability in patients with CP.

The concept that pain patterns might influence QOL and response to treatment is relatively unstudied. In one study of 193 patients with myofascial pain syndrome, patients with constant pain were more likely to fail treatment with trigger point injections than patients with an intermittent pattern of pain.[27] In a recent study, the effect of pain pattern on treatment response was examined in 95 patients undergoing microvascular decompression for trigeminal neuralgia. Patients with intermittent pain patterns were more likely to experience complete pain relief following surgery than those with a constant pain pattern (60% vs 25%, $p=0.003$).[28] In other disease paradigms, pain severity rather than frequency seems to play a significantly greater role in functioning and resource utilisation.[29]

In a longitudinal study of 124 patients with alcoholic CP, Ammann *et al* examined the relationship between pain pattern, aetiology of pain and response to treatment.[930] Type A pain was defined as intermittent pain episodes with intervening pain-free periods, while type B pain was characterised by prolonged periods of persistent (daily) pain. In this series, B-type pain was seen in late-stage disease and was associated with disease-related complications (eg, pseudocyst or stricture formation) which responded to surgical intervention. This study did not examine differences between the two pain patterns in quality of life, healthcare utilisation or narcotic use. In contrast to this study, we found no correlation between the duration of the disease and either pain severity or pain frequency.

A longstanding and controversial issue is whether the pain in CP improves with progressive pancreatic insufficiency (so-called 'burn out'). In one study, Ammann *et al* studied 245 patients with CP for a mean of 10 years and found that the pain of the majority of patients improved over time, particularly in those with alcoholic calcific CP.[17] In contrast to the Ammann data, Lankisch and colleagues followed 335 patients with painful CP for >10 years and found that the majority did not experience spontaneous pain relief with progressive pancreatic insufficiency.[31] This same group also found that the majority of patients with both alcoholic and non-alcoholic CP continued to have pain at a mean follow-up of 10 years.[32] Our data are consistent with those of the Lankisch group and conclusively demonstrate that disease duration does not correlate with pain severity or frequency. Additionally, in light of recent data supporting central mechanisms of pain in CP, it is likely that persistent CP pain is largely independent of pancreatic fibrosis and progressive pancreatic insufficiency.[33] In other words, progressive pancreatic atrophy and insufficiency should not impact pain since the origin of the pain is no longer at the level of the pancreas. That CP pain does not seem to improve over time has important implications in the counselling and treatment of patients. Patients should not be told that their pain is likely to improve over time and it is quite possible that earlier and more aggressive treatment of pain may prevent or delay the central remodelling associated with intractable symptoms.

A surprisingly high proportion (63%) of patients with CP in our study who self-reported ever drinking acknowledged ongoing use of alcohol. In agreement with studies by Ammann and others, we have found that continued use of alcohol has no influence on pain severity.[934] This is the first study to show that heavy alcohol use is associated with constant pain patterns while intermittent pain patterns are associated with abstinence from alcohol. An alternative explanation to a cause–effect relationship is that patients with intermittent patterns of pain have the opportunity to experiment with alcohol's effects on their symptoms and, through this, learn that the alcohol exacerbates their symptoms and therefore avoid alcohol use, while patients with constant pain patterns are unable to perceive differences in their pain when actively consuming alcohol, thereby never ceasing to use it.

Our study has several limitations, many of which are associated with study design (cross-sectional survey study), and include recall, selection, coding and response bias. Response bias refers to study participants who fail to provide a response to one or more questions. If non-responders differ from responders in important factors, these missing data may have a significant impact on the conclusions of the research. In our study, almost a quarter (126/540) of the patients surveyed did not endorse a pain pattern although many still

provided responses to questions dealing with the impact of their pain on functioning, medication use and overall QOL. In order to determine how these missing data might have affected the findings of the study, we examined patient characteristics in all patients who had not designated a pain pattern, but who did have a physician-designated pain pattern (n=61/126, 48%). Patients who did not designate a pain pattern were more likely to have mild to moderate, intermittent pain (according to physician designation) than constant pain of any severity. Overall, these patients were less likely to: (1) use pain medications regularly and (2) be on disability benefits. They were more likely to: (1) have no hospitalisations in the preceding year; (2) have fewer hospitalisations in their lifetime; and (3) have higher PCS and MCS scores on the SF-12 test. Given these findings, we would predict that if these missing data were available, the conclusions of the study would be further supported rather than negated.

The fact that a significant number of patients failed to select or designate a pain pattern may be due to a lack of appropriate response categories. In other words, none of the five pain categories accurately described the patient's individual perception of pain. Previous studies on the validity of survey instruments to assess pain have suggested that those with >5 possible responses are more likely to be accurate than those with ≤5 responses.[3536] Another potential bias is the limitation of a single measure in accurately estimating the effects of pain on outcomes and it is intuitive that multiple measurements over a longer time course would reduce errors in estimates of pain magnitude and effects.[37]

An overwhelming majority of clinical trials in CP have focused on the reduction of pain severity without regard to frequency (often ignoring this factor altogether) and none has shown consistent and reliable improvement in patients' symptoms. A plea for standardisation in pain assessment and comparisons between patients with uniform patterns of pain was made >10 years ago and continues still today.[38–40] Our study is the first to show that patients who experience constant rather than intermittent patterns of pain have significantly poorer QOL and greater rates of disability and resource utilisation. In contrast, pain severity appeared to have little or no effect on these important end points. The lack of an effect based on severity is perhaps even more surprising and unexpected than the differences seen between intermittent and constant pain patterns. The explanation for the lack of a difference between pain severity patterns may lie in the arbitrary and ambiguous nature of mild, moderate or severe pain as well as the diverse experience of pain within and between individual patients. What might be perceived as 'moderate' pain by one person might be considered 'severe' pain by the next. Patients might experience one pain pattern for weeks or months and then change to a different pain pattern. This in turn would lead to heterogeneity within these groups and dilution of any differences which might exist. In contrast, the difference between 'constant' and 'intermittent' is much more distinct and easily defined. Taken together, the results of this study suggest that the assessment of pain frequency and the accurate identification of pain patterns will be pertinent to understanding results of future research. The findings also imply that interventions which provide a remission from pain might be more effective than those which only decrease pain severity. Future studies of the NAPS2 database analysing the effect of pain pattern on response to various treatments are planned and should provide further direction to the care of these complex patients.

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Significance of this study

What is already known about this subject?

- Pain is a pervasive and difficult to treat symptom of chronic pancreatitis.
- Interventions to treat pain in patients with chronic pancreatitis have had inconsistent results.
- Patterns of pain differ among patients and little is known about the effects of varied pain patterns on quality of life and resource utilisation.

What are the new findings?

- Patients who experience constant rather than intermittent patterns of pain have significantly poorer QOL and greater rates of disability and resource utilisation.
- In contrast, patients with severe pain are no more likely to be disabled or to utilise healthcare resources than patients with mild to moderate pain.
- There was no association between the duration of chronic pancreatitis and the quality or frequency of pain.

How might it impact on clinical practice in the foreseeable future?

- The results of this study suggest that the assessment of pain frequency and the accurate identification of pain patterns will be pertinent to understanding results of future research.
- These findings also imply that interventions which provide a remission from pain might be more beneficial than those which only decrease pain severity.

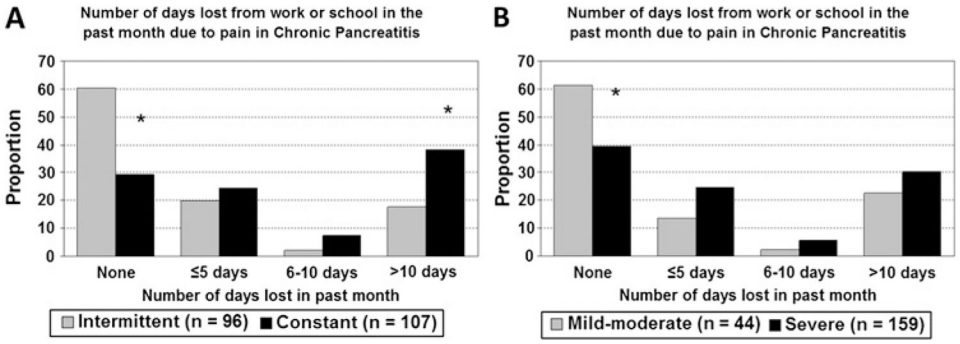

Figure 1.

Days lost per month from work or school by temporal classification (intermittent vs chronic) (A) and by severity (mild to moderate vs severe) (B).

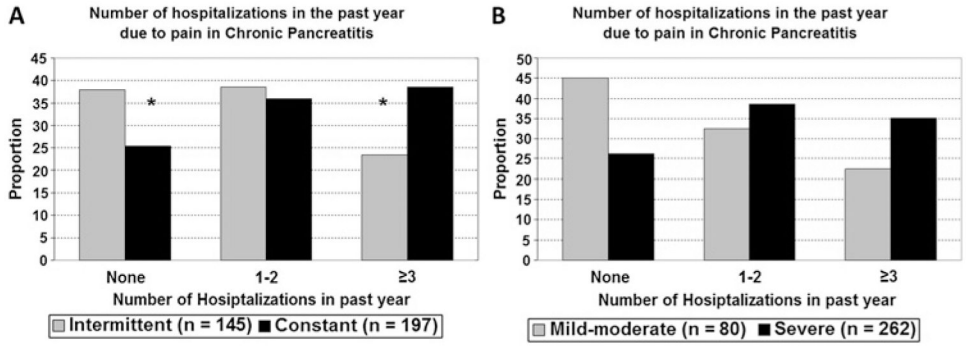

Figure 2.

Hospitalisations in the last year by temporal classification (intermittent vs chronic) (A) and by severity (mild to moderate vs severe) (B).

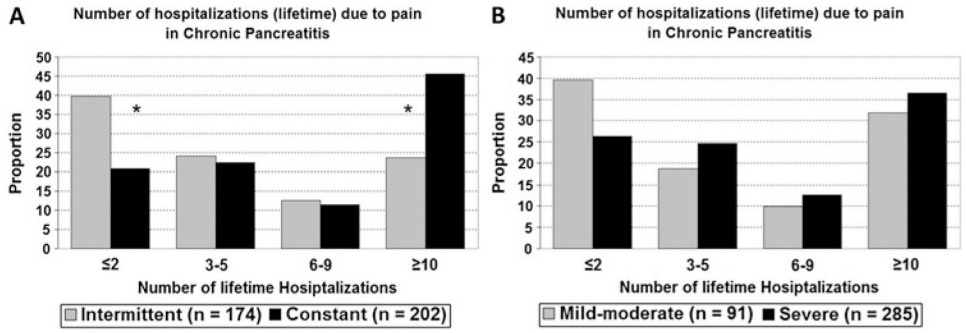

Figure 3.

Hospitalisations over the entire lifetime by temporal classification (intermittent vs chronic) (A) and by severity (mild to moderate vs severe) (B).

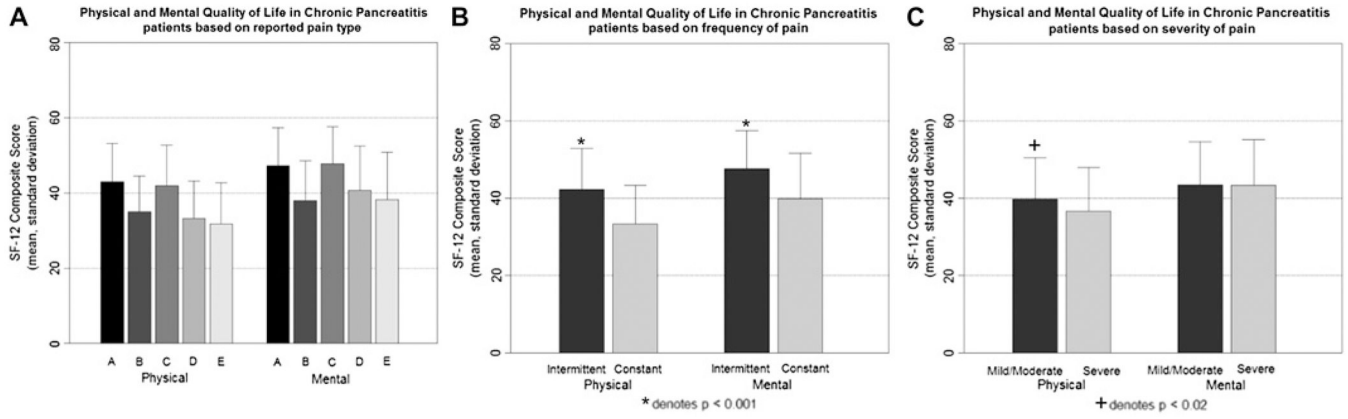

Figure 4.

Short Form-12 (SF-12) composite score (physical functioning (PCS) and mental functioning (MCS)) by individual pain pattern (A), by temporal pattern (B) and by pain severity (C). Higher scores are associated with greater well-being and better functioning.

Table 1

Pain patterns

Pattern	Definition
A	Episodes of mild to moderate pain, usually controlled by medication
B	Constant mild to moderate pain usually controlled by medication
C	Usually pain free with episodes of severe pain
D	Constant mild pain plus episodes of severe pain
E	Constant severe pain that does not change

Possible choices for self-designation of pain experienced by participants of the NAPS2 study. Patients were asked to select the pattern that most closely described the pain they experienced related to underlying pancreatitis.

Table 2

Demographic and clinical characteristics by pain pattern in patients with chronic pancreatitis in the NAPS2 study

		Pain pattern				
Variable	**All patients**	**A**	**B**	**C**	**D**	**E**
Number (%)	414 (100)	58 (14.0)	38 (9.2)	128 (30.9)	158 (38.2)	32 (7.7)
Gender						
Male	205 (49.5)	31 (53.4%)	21 (55.3%)	67 (52.3%)	72 (45.6%)	14 (43.8%)
Age (mean±SD)	48.9±15.4	51.7±15.6	47.7±12.7	50.2±17.7	47.8±14.1	46.5±14.1
Race						
White	344 (83.3)	48 (84.2)	28 (73.7)	112 (87.5)	132 (83.5)	24 (75.0)
Black	50 (12.1)	7 (12.3)	9 (23.7)	12 (9.4)	15 (9.5)	7 (21.9)
Others or mixed	19 (4.6)	2 (3.5)	1 (2.6)	4 (3.1)	11 (7.0)	1 (3.1)
Body mass index (current)						
Normal or low	239 (58.9)	33 (56.9)	17 (47.2)	76 (60.8)	94 (60.3)	19 (61.3)
Overweight	120 (29.6)	18 (31.0)	16 (44.4)	34 (27.2)	45 (28.8)	7 (22.6)
Obese	47 (11.6)	7 (12.1)	3 (8.3)	15 (12.0)	17 (10.9)	5 (16.1)
Drinking category (%)						
Abstainer	95 (23.0)	11 (19.0)	5 (13.2)	37 (29.1)	31 (19.6)	11 (34.4)
Light	79 (19.1)	16 (27.6)	8 (21.1)	22 (17.3)	33 (20.9)	0 (0.0)
Moderate	84 (20.3)	16 (27.6)	4 (10.5)	27 (21.3)	34 (21.5)	3 (9.4)
Heavy	48 (11.6)	5 (8.6)	4 (10.5)	15 (11.8)	18 (11.4)	6 (18.8)
Very heavy	107 (25.9)	10 (17.2)	17 (44.7)	26 (20.5)	42 (26.6)	12 (37.5)
Smoking (%)						
Never	120 (29.1)	17 (29.8)	7 (18.4)	48 (37.8)	41 (25.9)	7 (21.9)
Past	96 (23.3)	17 (29.8)	11 (28.9)	27 (21.3)	34 (21.5)	7 (21.9)
Current	196 (47.6)	23 (40.4)	20 (52.6)	52 (40.9)	83 (52.5)	18 (56.3)
Amount of smoking (%)						
Never	120 (29.9)	17 (30.9)	7 (18.4)	48 (38.7)	41 (26.6)	7 (23.3)
<1 packs/day	116 (28.9)	13 (23.6)	17 (44.7)	32 (25.8)	47 (30.5)	7 (23.3)
≥1 packs/day	165 (41.1)	25 (45.5)	14 (36.8)	44 (35.5)	66 (42.9)	16 (53.3)
Acute pancreatitis ever (%)						

		Pain pattern				
Variable	**All patients**	**A**	**B**	**C**	**D**	**E**
Yes	268 (65.2)	32 (57.1)	26 (68.4)	90 (70.3)	100 (63.7)	20 (62.5)
No	73 (17.8)	13 (23.2)	4 (10.5)	16 (12.5)	35 (22.3)	5 (15.6)
Unclear	70 (17.0)	11 (19.6)	8 (21.1)	22 (17.2)	22 (14.0)	7 (21.9)
Alcohol diagnosis by physicians*						
Yes (%)	189 (45.7)	20 (34.5)	21 (55.3)	55 (43)	75 (47.5)	18 (56.3)
Regular use of pain medication (%) (n=330)						
Yes	156 (47.3)	13 (26.0)	23 (76.7)	24 (20.7)	79 (71.8)	17 (70.8)
No	174 (52.7)	37 (74.0)	7 (23.3)	92 (79.3)	31 (28.2)	7 (29.2)
Disability (%) (n=399)						
Yes	123 (30.8)	8 (14.0)	15 (42.9)	24 (19.0)	58 (38.2)	18 (62.1)
No	276 (69.2)	49 (86.0)	20 (57.1)	102 (81.0)	94 (61.8)	11 (37.9)

*Alcohol considered as a working diagnosis or risk factor with or without other diagnoses.

Table 3

Demographic and clinical characteristics by pain pattern; intermittent versus chronic and mild to moderate versus severe

	Pain pattern			Pain pattern		
Variable	**Intermittent**	**Constant**	**p Value**	**Mild to moderate**	**Severe**	**p Value**
Number (%)	186 (44.9)	228 (55.1)		96 (23.2)	318 (76.8)	
Gender						
Male	98 (52.7)	107 (46.9)	0.28	52 (54.2)	153 (48.1)	0.35
Age at enrolment (mean±SD)	50.6±17.1	47.6±13.8	0.05	50.1±14.6	48.6±15.7	0.38
Race (%) (n=413)						
White	160 (86.5)	184 (80.7)	0.26	76 (80.0)	268 (84.3)	0.22
Black	19 (10.3)	31 (13.6)		16 (16.8)	34 (10.7)	
Others or mixed	6 (3.2)	13 (5.7)		3 (3.2)	16 (5.0)	
Body mass index (n=406)						
Normal or low	109 (59.6)	130 (58.3)	0.95	50 (53.2)	189 (60.6)	0.45
Overweight	52 (28.4)	68 (30.5)		34 (36.2)	86 (27.6)	
Obese	22 (12.0)	25 (11.2)		10 (10.6)	37 (11.9)	
Drinking category (%) (n = 413)						
Abstainer	48 (25.9)	47 (20.6)	0.01	16 (16.7)	79 (24.9)	0.50
Light	38 (20.5)	41 (18.0)		24 (25.0)	55 (17.4)	
Moderate	43 (23.2)	41 (18.0)		20 (20.8)	64 (20.2)	
Heavy	20 (10.8)	28 (12.3)		9 (9.4)	39 (12.3)	
Very heavy	36 (19.5)	71 (31.1)		27 (28.1)	80 (25.2)	
Smoking (%) (n = 412)						
Never	65 (35.3)	55 (24.1)	0.02	24 (25.3)	96 (30.3)	0.25
Past	44 (23.9)	52 (22.8)		28 (29.5)	68 (21.5)	
Current	75 (40.8)	121 (53.1)		43 (45.3)	153 (48.3)	
Amount of smoking (%) (n=401)						
Never	65 (36.3)	55 (24.8)	0.05	24 (25.8)	96 (31.2)	0.52
<1 packs/day	45 (25.1)	71 (32.0)		30 (32.3)	86 (27.9)	
≥1 packs/day	69 (38.5)	96 (43.2)		39 (41.9)	126 (40.9)	
Acute pancreatitis ever (%) (n=411)						

Variable	Pain pattern		p Value	Pain pattern		p Value
	Intermittent	Constant		Mild to moderate	Severe	
Yes	122 (66.3)	146 (64.3)	0.62	58 (61.7)	210 (66.2)	0.62
No	29 (15.8)	44 (19.4)		17 (18.1)	56 (17.7)	
Unclear	33 (17.9)	37 (16.3)		19 (20.2)	51 (16.1)	
Regular use of pain medication (%) (n=330)						
Yes	37 (22.3)	119 (72.6)	<0.001	36 (45.0)	120 (48.0)	0.73
No	129 (77.7)	45 (27.4)		44 (55.0)	130 (52.0)	
Disability (%) (n=399)						
Yes	32 (17.5)	91 (42.1)	<0.001	23 (25.0)	100 (32.6)	0.21
No	151 (82.5)	125 (57.9)		69 (75.0)	207 (67.4)	