ORIGINAL ARTICLE

Observational Study

Simple pain measures reveal psycho-social pathology in patients with Crohn's disease

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Abstract

AIM
To determine whether pain has psycho-social associations in adult Crohn's disease (CD) patients.

METHODS
Patients completed demographics, disease status, Patient Harvey-Bradshaw Index (P-HBI), Short Form Health Survey (SF-36), Short Inflammatory Bowel Disease Questionnaire (SIBDQ), and five socio-psychological questionnaires: Brief Symptom Inventory, Brief COPE Inventory, Family Assessment Device, Satisfaction with Life Scale, and Work Productivity and Activity Impairment Questionnaire. Pain sub-scales in P-HBI, SF-36 and SIBDQ measures were recoded into 4 identical scores for univariate and multinomial logistic regression analysis of associations with psycho-social variables.

RESULTS

The cohort comprised 594 patients, mean age 38.6 ± 14.8 years, women 52.5%, P-HBI 5.76 ± 5.15. P-HBI, SF-36 and SIBDQ broadly agreed in their assessment of pain intensity. More severe pain was significantly associated with female gender, low socio-economic status, unemployment, Israeli birth and smoking. Higher pain scores correlated positively with psychological stress, dysfunctional coping strategies, poor family relationships, absenteeism, presenteeism, productivity loss and activity impairment and all WPAI sub-scores. Patients exhibiting greater satisfaction with life had less pain. The regression showed increasing odds ratios for psychological stress (lowest 2.26, highest 12.17) and female gender (highest 3.19) with increasing pain. Internet-recruited patients were sicker and differed from hardcopy questionnaire patients in their associations with pain.

CONCLUSION

Pain measures in P-HBI, SF-36 and SIBDQ correlate with psycho-social pathology in CD. Physicians should be aware also of these relationships in approaching CD patients with pain.

Key words: Crohn's disease; Psycho-social pathology; Pain

Core tip: Pain is a very important symptom in patients with Crohn's disease. Pain level and frequency are measurable with a series of simple questionnaires. We show that pain has demographic associations concerning gender, economic status, birthplace and smoking, as well as psycho-social associations such as disease coping strategies, family support, satisfaction with life, absenteeism and presenteeism related to the workplace, and leisure activity. Understanding these relationships will assist physicians in their approach to patients with pain.

INTRODUCTION

Crohn's disease (CD) is an idiopathic inflammatory condition of the gastrointestinal tract, most commonly affecting the small and large intestines, and causing diarrhea, pain, malaise, weight loss and anemia. Abdominal pain is the commonest form of pain in patients with CD. It constitutes a major diagnostic criterion of CD in epidemiological studies and the first therapeutic target in CD patient management[1-5]. Over 50% of adult patients with active CD reported having abdominal pain[6,7]. Interestingly, pain is also present when CD is not active. Pain was present in 20% to 50% of patients in clinical remission[1,8,9]. It has been suggested that in these cases the pain results from persistent peripheral sensitization after the acute CD episode has passed, and that this hypersensitivity is augmented by psychological stressors[10]. Concern about pain was reported to be higher in some countries than others; it is reportedly higher in patients in Israel compared to some other countries[11]. Up to a third of patients need to take analgesics for abdominal pain[9]. Medical cannabis is increasingly used to relieve abdominal pain in CD[12]. It was shown that dependence on medication for pain was associated with poorer health status[13]. Pain results in impaired socio-psychological functioning and a reduced quality of life[9,14]. Abdominal pain in CD is associated with depression and increased anxiety[15,16].

The above-quoted studies indicate that while the intensity of pain in CD is a consequence of the pathology of the disease, it is related also to the psychological functioning of these individuals in response to illness-induced stress, and may be moderated by the coping mechanisms used by patients to deal with their illness, and perhaps by demographic variables. These important relationships are as yet poorly understood, and further knowledge in this area may contribute to improving the treatment of these patients. We aimed to investigate the relationship of pain to psychological functioning and disease-coping in the broad spectrum of CD patients of different demographic status. We report here the results of our study performed in a country-wide large non-selected community cohort of CD patients.

MATERIALS AND METHODS

Patients

Consecutive adult (age 18 years and over) patients consenting to take part in an ongoing socio-economic study of CD in the Israeli adult patient population were studied using self-report questionnaires. Patients were eligible to participate whatever the duration or severity of their illness, and irrespective of their past and present treatments and surgery (if any). There were two methods of patient recruitment. Most patients (70%) were recruited on a consecutive basis when presenting for follow-up or acute non-hospitalized care at the out-patient Gastroenterology Departments of five participating university-affiliated tertiary care hospitals in Israel. These patients met the standard criteria for diagnosis as CD (ECCO), and were given the option of completing the questionnaires on paper or on the internet in their own time at home. The other patients were canvassed on the website of "The Israel Foundation for

Crohn's Disease and Ulcerative Colitis" and completed the questionnaires on-line. It was assumed that these patients would have established CD. Physicians and nurses did not assist in completing the questionnaires. All questionnaires were in the public domain and were made available in their validated Hebrew translations. Knowledge of Hebrew was a condition for inclusion in the study. Charts of hospital-recruited patients were checked to uncover any psychological or psychiatric disease, but this information could not be ascertained for patients recruited by the internet.

Study design

This was a cross-sectional study with data collection from July 2013 to June 2016. Patients reported socio-demographic and medical characteristics including gender, year and place of birth, education, economic status, marital status and number of children, religion and religiosity, current and past smoking habits, disease duration, current medications, anytime surgery for CD, and hospitalizations for CD in the past year. Data concerning co-morbidities were collectible from most patients attending at the hospitals. Patients completed the Patient Harvey-Bradshaw Index (P-HBI), Short Form Health Survey (SF-36) and Short Inflammatory Bowel Disease Questionnaire (SIBDQ), all of which include questions about pain. In addition, patients completed five socio-psychological questionnaires: Brief Symptom Inventory (BSI), Brief COPE Inventory (COPE), Family Assessment Device (FAD), Satisfaction with Life Scale (SWLS) and Work Productivity and Activity Impairment Questionnaire (WPAI).

P-HBI[17]: This clinical measure of the severity of disease was specifically designed for patients with CD. It consists of 4 items reflecting the previous day's symptoms and signs of CD; the question regarding the physician's assessment of the possible presence of an abdominal mass in the original HBI is removed in the P-HBI, making the questionnaire suitable for completion by the patients themselves. A total score < 5 indicates disease remission, 5-7 mild disease, 8-16 moderate disease, and > 16 severe disease.

SF-36[18]: This generic health-related quality of life measure is comprised of 36 items divided into eight domains, which in turn are grouped as Physical Health Summary Score (physical functioning, role-physical, bodily pain, general health) and Mental Health Summary Score (vitality, role-emotional, social functioning, mental health). Responses refer to the past four weeks. The range of the Physical or Mental Health Summary Score is 0-100. A higher score represents a better quality of life. The Hebrew version has been validated[19].

SIBDQ[20]: Is an inflammatory bowel disease-specific

health-related quality of life tool measuring physical, social, and emotional status. It consists of 10 items: each item refers to the last two weeks, and is rated on a 7 degree scale (1 = all the time, 7 = never). The total score is in the range from 10-70. A higher value indicates a better quality of life. A validated Hebrew version was used[21].

BSI[22]: This instrument is a measure of psychological stress in the past month. It consists of 53-items that assess nine symptomatic dimensions (depression, somatization, obsession-compulsive, interpersonal sensitivity, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism) on a 0-4 scale; a higher score implies more psychological distress. The General Severity Index (GSI) yields a useful global summary score called the GSI with range 0-4. In non-patient normal individuals the GSI was reported as 0.30 ± 0.31. The Hebrew version was validated[23].

Brief COPE Inventory[24]: This measure comprises 28 items; each item is rated on a 4 degree scale (1 = I do not do it at all, 4 = I do it very much). Items are grouped to yield 14 coping subscales that are grouped into 3 strategies: emotion-focused (emotional support use, positive reframing, humor, acceptance, religion), problem-focused (active coping, instrumental support use, planning), and dysfunctional coping (self-distraction, denial, substance use, behavioral disengagement, venting, self-blame). A greater score indicates more use of that coping strategy. The Brief COPE presents the present condition of the subject. We used the validated version in Hebrew[25].

FAD[26]: This is a scale that measures the level of perceptions of family functioning and communication. It consists of 12 items; each item can be rated on a 4 degree scale (1 = strongly agree, 4 = not agree at all). A higher value indicates a worse family functioning. This measure has a Cronbach's Alpha = 0.89. It has been validated in Hebrew[27].

SWLS[28]: This instrument measures the individual's level of satisfaction with life at that moment in time. It includes five questions (q): "q1, my life is close to ideal; q2, conditions of my life are excellent; q3, I am satisfied with my life; q4, I have gotten the important things I want in life; q5, if I could live my life over, I would change almost nothing." Each question is rated on a 7-point scale (1 = not agree at all with the item, 7 = strongly agree). The possible range of this scale is from 1-7 per question. The summary score has a range of 5-35, with a higher value indicating a higher level of satisfaction with life. Cronbach's alpha was 0.89. This measure has been validated in Hebrew[29].

WPAI[30]: This measure evaluates the effect of disease on the patient's ability to work and to perform regular

Table 1 Details of pain questions and scoring[1]

Questionnaire	Question about pain	Score in questionnaire	Recoded score
Patient Harvey-Bradshaw Index	Did you have abdominal pains yesterday?	0 None	0
		1 Mild	1
		2 Moderate	2
		3 Severe	3
MOS Short-Form Survey Instrument	How much bodily pain have you had during the past 4 wk?	1 None	0
		2 Very Mild	0
		3 Mild	1
		4 Moderate	1
		5 Severe	2
		6 Very Severe	3
Short Inflammatory Bowel Disease Questionnaire	How often during the past 2 wk have you been troubled by pain in the abdomen?	1 All of the time	3
		2 Most of the time	2
		3 A good bit of the time	2
		4 Some of the time	1
		5 A little of the time	1
		6 Hardly any of the time	0
		7 None of the time	0

[1]Pain questions in the three questionnaires with original scoring, and the recoded scores used in the analysis.

activities in the past 7 d (not including the present day). This instrument yields 4 scores: absenteeism (work time missed due to disease), presenteeism (impairment while working, *i.e.*, reduced on-the-job effectiveness due to disease) work productivity loss (overall work impairment, *i.e.*, the sum of absenteeism plus presenteeism) and activity impairment (degree that disease impairs regular activities). Scores are expressed as percentages. Higher scores indicate greater impairment at work or when performing activities. The Hebrew version of this measure was accessed from the internet[31].

Statistical analysis
All data from the questionnaires were pooled in a single database. The questions relating to pain were question 2 in P-HBI, question 4 in SIBDQ and question 21 in SF-36. These questions emphasized different aspects of pain and differed by the time period under review and the possible responses. Patients whose data were deemed eligible for analysis were required to have filled in all 3 questions patients; with any missing values were excluded. Based on the frequency of patients' responses to these questions, 4 sub-scores (no pain, mild pain, moderate pain, severe pain) were formulated for each pain scale and used in the analysis (Table 1). Results are expressed as means (± SD), and medians (IQR) where the data distribution was skewed. Univariate analysis was used to show the significance of associations of pain with demographic and socio-psychological variables. We used the Mann-Whitney test, Kruskal-Wallis test, *t*-test, and Spearman correlations to test the significance of associations depending on the type of distribution of the data. A multinomial logistic regression was used to examine the associations between the level of pain (in the three

scales) and those demographic and socio-psychological variables that were significant on univariate analysis. Each pain questionnaire was examined separately, and the "no pain" state was the reference category. The model controlled for age, education, economic status and family status. Statistical significance was set at $P < 0.05$. Since the analysis revealed large differences between patients filling in the questionnaires by internet or hardcopy, these results are shown separately.

Ethical considerations
The study was approved by the Ethics Committees of all participating hospitals and the patients recruited at these hospitals signed an approved informed consent form. Patients recruited *via* the website were deemed to have consented to participate in the study when they completed the questionnaires electronically. The consent form contained a description of the study, its aims and scope. A similar explanation was posted on the website. All data were treated anonymously.

RESULTS
Patients
The total cohort comprised 594 patients with mean age (± SD) 38.6 ± 14.8 years, and 57.6% were women. Duration of disease was 11.05 ± 8.73 years in the entire cohort; 10.8% of patients reported a disease duration of 2 years or less. The P-HBI was 5.76 ± 5.15; 44.6% of the patients were in remission and 55.4% had various grades of active disease. Further demographic data of the cohort are given in Table 2. Very few patients (< 5%) were found to have mild psychological comorbidities and they were included in the analysis since this did not impact on the outcome of the study. In the entire cohort 45.1% of patients were on biologic medication. These patients reported more pain by the P-HBI ($P = 0.03$) compared with those not on biologic medication. However, there were no differences in respect of the level or frequency of pain by SF-36 or SIBDQ.

We compared the patients who completed the questionnaires by internet or as hardcopy (Table 2). Internet patients had a lower economic status, higher disease activity level by P-HBI score and worse quality of life compared to the hardcopy patients.

Questionnaires
Results of the socio-psychological questionnaires appear in Table 3. In the total cohort the SF-36 summary scores were: physical 42.09 ± 10.76, and mental 41.99 ± 11.33. The SIBDQ total score was 46.33 ± 13.83. Half the patients reported their economic status as moderate. The mean score for satisfaction with life was moderate at 22.06 ± 7.64. The GSI mean score of 0.98 ± 0.75 indicated a mild psychological distress level in the cohort, but the FAD mean score of 1.81 ± 0.55 revealed moderate disturbance of family

Table 2 Demographic parameters and disease characteristics of the Crohn's disease cohort

Patient characteristic	Total cohort *n* = 594	Internet questionnaire *n* = 370	Hardcopy questionnaire *n* = 224	*P* value[1]
Age (yr)				0.151
mean ± SD	38.56 ± 14.06	36.99 ± 12.65	39.48 ± 14.77	
Median (min-max) (IQR)	35 (18-79) (28-47)	35 (18-72) (26 -44)	35 (19-79) (28-49)	
Education (yr)				0.043
mean ± SD	14.81 ± 2.93	15.05 ± 2.65	14.66 ± 3.08	
Disease duration (yr)				0.234
mean ± SD	11.05 ± 8.73	10.39 ± 8.23	11.45 ± 9.00	
Median (min-max) (IQR)	10 (0-47) (4-15.5)	10 (0-41) (3-16)	10 (0-47) (5-15)	
Female gender	57.6%	59.78%	56.90%	0.521
Married/living together	58.6%	57.01%	60.16%	0.452
Economic status				
Good	29.8%	25.45%	33.15%	0.040
Moderate	49.8%	57.27%	46.58%	
Poor	18.9%	17.27%	20.27%	
Current cigarette smoking	18.9%	16.97%	21.55%	0.183
Biologic medication	45.1%	44.64%	45.41%	0.856
Surgery, ever	33.3%	32.59%	33.78%	0.765
Hospitalization in past year	25.3%	26.79%	24.32%	0.503
Patient Harvey-Bradshaw Index (P-HBI)	5.76 ± 5.15	6.70 ± 5.69	5.32 ± 4.83	0.002
P-HBI sub-groups				
Disease remission (score < 5)	44.60%	66 (40.00%)	199 (55.74%)	0.003
Mild disease (score 5-7)	20.00%	47 (28.48%)	72 (20.17%)	
Moderate disease (score 8-16)	19.40%	40 (24.24%)	75 (21.01%)	
Severe disease (score > 16)	3.90%	12 (7.27%)	11 (3.08%)	

[1]Statistical differences between internet and hardcopy source of questionnaires.

Table 3 Scores of the social questionnaires of the Crohn's disease cohort

Variables	Total cohort mean ± SD Median (min-max) (IQR)	Internet Questionnaire mean ± SD Median (min-max) (IQR)	Hardcopy Questionnaire mean ± SD Median (min-max) (IQR)	*P* value[1]
MOS Short-Form Survey Instrument				
Physical health	42.09 ± 10.76	40.88 ± 10.41	42.72 ± 10.90	0.041
Mental health	41.99 ± 11.33	39.23 ± 11.36	43.42 ± 11.05	< 0.001
Short Inflammatory Bowel Disease Questionnaire, total score	46.33 ± 13.83	42.02 ± 13.38	48.84 ± 13.48	< 0.001
SWLS	22.06 ± 7.64	20.81 ± 7.92	22.82 ± 7.37	0.004
	23 (5-35) (16-28)	21.0 (5-35) (15-27)	24.0 (5-35) (17-29)	
GSI	0.98 ± 0.75	1.11 ± 0.80	0.90 ± 0.70	0.002
	0.79 (0-3.92) (0.38-1.47)	0.9 (0.0-3.9) (0.4-1.6)	0.7 (0.0-3.2) (0.4-1.3)	
FAD	1.81 ± 0.55	1.90 ± 0.56	1.75 ± 0.53	0.001
	1.75 (1.0-4.0) (1.33-2.17)	1.9 (1.0-4.0) (1.4-2.3)	1.7 (1.0-4.0) (1.3-2.1)	
COPE: Emotion-focused strategies	24.23 ± 5.88	24.50 ± 5.77	24.07 ± 5.94	0.340
	24.5 (3-40) (20-29)	25 (6-39) (20-29)	24 (3-40) (20-28)	
COPE: Problem-focused strategies	16.10 ± 4.74	16.82 ± 4.51	15.67 ± 4.83	0.004
	16 (3-24) (13-20)	17 (4-24) (14-20)	16 (3-24) (12-19)	
COPE: Dysfunctional Strategies	22.28 ± 5.93	23.41 ± 5.86	21.60 ± 5.87	0.000
	22 (6-42) (18-26)	23 (8-41) (20-27)	21 (6-42) (17-25)	
WPAI: Absenteeism (%)	8.81 ± 19.26	11.12 ± 20.77	7.36 ± 18.16	0.021
	0 (0-100) (0-8.35)	0 (0-100.0) (0-15.2)	0 (0-100) (0-1.6)	
WPAI: Presenteeism (%)	29.16 ± 30.20	31.52 ± 30.44	27.54 ± 30.00	0.119
	20 (0-100) (0-50)	20 (0-100.0) (10.0-55.0)	20.0 (0-100) (0-50)	
WPAI: Work productivity loss (%)	29.19 ± 30.38	33.60 ± 31.57	26.50 ± 29.38	0.025
	20 (0-100) (0-50)	21.2 (0-100) (10-60)	20.0 (0-100) (0-40.7)	
WPAI: Activity impairment (%)	33.92 ± 30.61	37.60 ± 30.86	31.74 ± 30.30	0.021
	30 (0-100) (10-60)	30 (0-100) (10-60)	20.0 (0-100) (0-50)	

[1]Statistical differences between internet and hardcopy source of questionnaires. SWLS: Satisfaction with Life Scale; GSI: Global Severity Index; FAD: McMaster Family Assessment Device; COPE: Brief Cope Inventory; WPAI: Work Productivity and Activity Impairment Questionnaire.

functioning. Patients made greater use of emotion-focused and dysfunctional coping strategies compared with problem-focused strategies. Concerning the work productivity of the patients, 8.81% reported absenteeism from work and 29.19% reported loss of productivity while at work. Nearly 30% of patients reported
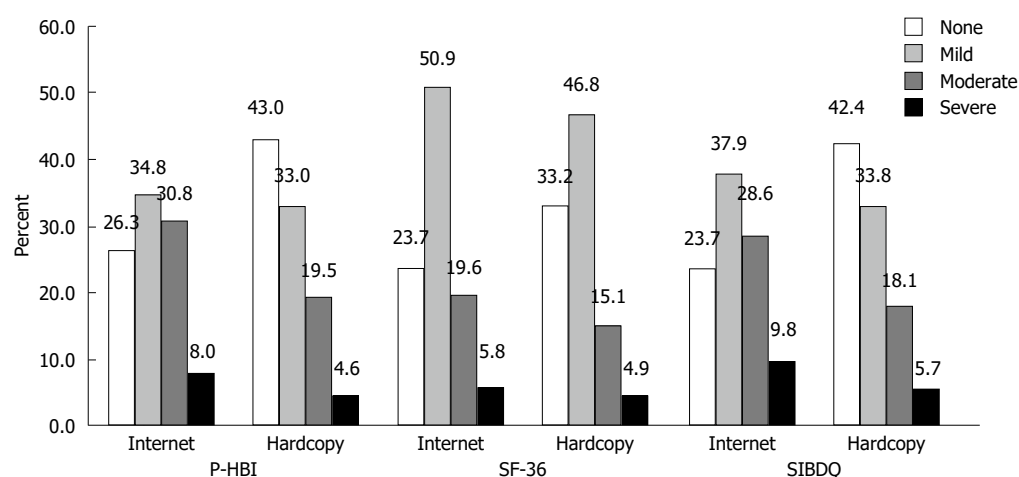
Figure 1 Responses to the pain questions by the Patient Harvey-Bradshaw Index, Short Form Health Survey and Short Inflammatory Bowel Disease Questionnaire, for patients completing the questionnaires by internet or hardcopy. Patient Harvey-Bradshaw Index (P-HBI) and Short Form Health Survey (SF-36) measure pain intensity whereas Short Inflammatory Bowel Disease Questionnaire (SIBDQ) measures pain frequency. *P* values for differences in responses to the pain questions are: by P-HBI *P* < 0.001, by SF-36 *P* = 0.081, by SIBDQ *P* < 0.001.

overall work impairment, and one third of the patients responded that their disease impaired regular daily activities. The data shown separately for internet and hardcopy patients also appear in Table 3. Significant differences between these groups are noted for quality of life measures, SWLS, GSI, FAD, problem-focused coping, dysfunctional coping, and three of the WPAI measures. Internet patients had lower quality and satisfaction of life scores and more psychological stress compared with hardcopy patients. Internet patients also reported having more problems with family support. Furthermore, internet patients made greater use of problem-focused and dysfunctional coping than hardcopy patients. The internet patients had more absenteeism from work, were less productive and had more activity impairment compared with hardcopy patients.

The mean scores (± SD) of the pain questions in the three questionnaires were the following: P-HBI 0.99 ± 0.92, SF-36 52.79 ± 28.44, and SIBDQ 4.46 ± 1.82. The median scores (IQR) of the pain questions were: P-HBI 1 (0-2), SF-36 40 (40-80), and SIBDQ 5 (3-6), respectively. The distribution of the patients' responses to the pain questions (Figure 1) indicated that the responses to P-HBI and SIBDQ were in close agreement, whereas the responses to SF-36 revealed relatively more patients reporting mild pain. Internet patients reported more pain intensity or frequency compared with hardcopy patients with respect to the pain scores by P-HBI and SIBDQ; the differences were statistically significant (both *P* < 0.001). Demographic variables associated significantly with the degree of reported pain by all three pain measures are shown in Table 4. By the P-HBI measure, females had more frequent moderate and severe pain than males (33.7% *vs* 24.2%, *P* = 0.005). Likewise, the P-HBI showed significantly more frequent moderate and severe pain in patient with poorer economic status, birthplace in

Israel and not working. By the SF-36 pain measure, a similar result was noted for female gender, poorer economic status, Asia-Africa birthplace and not working. Again, by the SIBDQ pain measure, more frequent moderate and severe pain was noted for poor economic status, birthplace in Israel, current smoker and not working. In Tables 5 and 6 these data are shown separately for the internet and hardcopy patients. It will be noted that the statistically significant differences occur more in the hardcopy part of the cohort.

Pain measures
The results of the five socio-psychological measures were examined in relation to the results of the pain measures (Table 7). More intense pain (moderate and severe pain rather than no pain or mild pain) by P-HBI was noted for GSI, emotion-focused coping strategies, dysfunctional coping strategies, FAD, and all four WPAI analyses. For SF-36 the variables significantly associated with more intense pain were GSI, problem-focused strategies, dysfunctional coping strategies, FAD, and all four WPAI analyses. For the SIBDQ pain measure the significant associations with more intense pain were noted for GSI, dysfunctional coping strategies, FAD, and again all four WPAI analyses. On the other hand, a greater satisfaction with life score was significantly associated with less pain by P-HBI, SF-36 and SIBDQ pain measures (all *P* < 0.0001). The differences described here in the total cohort occurred in both the hardcopy and internet patients (Tables 8 and 9).

Regression analysis
A multinomial logistic regression analysis of demographic and social variables and intensity of pain was carried out. The results of the internet and hardcopy patients are shown separately in Table 10, which is designed in particular to show the differences between

Table 4 Comparison of demographic variables with the pain measures in the whole cohort *n* (%)

Variables	P-HBI					SF-36					SIBDQ				
	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value
Education (yr)	15.1 ± 2.9	14.7 ± 2.8	14.8 ± 3.1	13.5 ± 3.1	0.017	14.8 ± 2.7	15.0 ± 2.7	14.6 ± 3.8	14.3 ± 3.1	0.463	15.1 ± 3.0	14.9 ± 2.8	14.7 ± 3.0	13.3 ± 2.5	0.001
Gender					0.005					< 0.001					0.054
Female	100 (32.1)	107 (34.3)	87 (27.9)	18 (5.8)		74 (23.7)	156 (50.0)	62 (19.9)	20 (6.4)		103 (33.0)	105 (33.7)	81 (26.0)	23 (7.4)	
Male	103 (45.4)	69 (30.4)	40 (17.6)	15 (6.6)		88 (38.8)	106 (46.7)	25 (11.0)	8 (3.5)		96 (42.3)	76 (33.5)	39 (17.2)	16 (7.0)	
Economic status					< 0.001					< 0.001					< 0.001
Poor	22 (19.6)	36 (32.1)	40 (35.7)	14 (12.5)		11 (9.8)	57 (50.9)	33 (29.5)	11 (9.8)		17 (15.2)	36 (32.1)	38 (33.9)	21 (18.8)	
Moderate	105 (35.5)	110 (37.2)	65 (22.0)	16 (5.4)		96 (32.4)	150 (50.7)	39 (13.2)	11 (3.7)		112 (37.8)	104 (35.1)	64 (21.6)	16 (5.4)	
Good	88 (49.7)	49 (27.7)	35 (19.8)	5 (2.8)		66 (37.3)	78 (44.1)	25 (14.1)	8 (4.5)		79 (44.6)	66 (37.3)	26 (14.7)	6 (3.4)	
Birthplace					0.048					0.015					0.013
Western	19 (76.0)	3 (12.0)	2 (8.0)	1 (4.0)		12 (48.0)	9 (36.0)	1 (4.0)	3 (12.0)		19 (76.0)	4 (16.0)	1 (4.0)	1 (4.0)	
Asia-Africa	14 (43.8)	12 (37.5)	5 (15.6)	1 (3.1)		7 (21.9)	16 (50.0)	9 (28.1)	0 (0)		13 (40.6)	13 (40.6)	6 (18.8)	0 (0.0)	
FSU	15 (44.1)	15 (44.1)	3 (8.8)	1 (2.9)		14 (41.2)	19 (55.9)	0 (0.0)	1 (2.9)		20 (58.8)	9 (26.5)	4 (11.8)	1 (2.9)	
Israel	111 (39.9)	92 (33.1)	61 (21.9)	14 (5.0)		90 (32.4)	128 (46.0)	46 (16.5)	14 (5.0)		105 (37.8)	98 (35.3)	56 (20.1)	19 (6.8)	
Current smoker					0.052					0.170					< 0.001
No	175 (38.5)	152 (33.5)	104 (22.9)	23 (5.1)		140 (30.8)	220 (48.5)	75 (16.5)	19 (4.2)		172 (37.9)	156 (34.4)	102 (22.5)	24 (5.3)	
Yes	29 (25.9)	41 (36.6)	32 (28.6)	10 (8.9)		29 (25.9)	52 (46.4)	21 (18.8)	10 (8.9)		26 (23.2)	43 (38.4)	25 (22.3)	18 (16.1)	
Working					< 0.001					< 0.001					< 0.001
No	61 (32.8)	51 (27.4)	51 (27.4)	23 (12.4)		40 (21.5)	86 (46.2)	45 (24.2)	15 (8.1)		60 (32.3)	53 (28.5)	50 (26.9)	23 (12.4)	
Yes	152 (39.9)	140 (36.7)	77 (20.2)	12 (3.1)		130 (34.1)	183 (48.0)	52 (13.6)	16 (4.2)		147 (38.6)	143 (37.5)	74 (19.4)	17 (4.5)	

P-HBI and SF-36 measure pain intensity whereas SIBDQ measures pain frequency. Data are mean ± SD or *n* (%). P-HBI: Patient Harvey-Bradshaw Index; SF-36: Short Form Health Survey; SIBDQ: Short Inflammatory Bowel Disease Questionnaire.

these patient groups with regard to the magnitude of the associations. The association was significant for GSI with all three pain measures and for all three results of pain in hardcopy patients, while for internet patients the associations were significant with all measures except mild pain by P-HBI and SF-36. Furthermore, there was a progressive increase in the odds ratio with increasing intensity of pain in all three measures for the internet and hardcopy patients. Female gender too demonstrated a significant association with SF-36 for moderate and severe intensities of pain, likewise with an increasing odds ratio, only for the hardcopy patients. For the P-HBI and SIBDQ measures, however, the regression with female gender was significant only for mild pain by both P-HBI (OR = 1.07) and SF-36 (OR = 1.07), and for moderate pain by SIBDQ (OR = 1.10), for hardcopy patients. Problem-focused coping in hardcopy patients was associated with all levels of pain by P-HBI. Internet patients did not demonstrate any association of dysfunctional coping strategies was significant for mild pain by P-HBI (OR = 1.07) and SF-36 (OR = 1.07), and for moderate pain by SIBDQ (OR = 1.10), for hardcopy patients. Problem-focused coping in hardcopy patients was associated with all levels of pain by P-HBI. Internet patients did not demonstrate any association of pain and coping strategies at the 5% statistical level, and few associations at the 10% level.

DISCUSSION

We have shown in the present study, carried out in a large cohort of CD patients with disease duration of 11 years, that the severity of pain as measured by the questions from the P-HBI, SF-36 and SIBDQ has significant associations with demographic and psycho-social measures. Patients with more intense pain tended to be females, poorer, unemployed, more stressed, less satisfied with life, and Israeli-born rather than immigrants. The pain questions from P-HBI, SF-36 and SIBDQ showed good general agreement in many of these associations. Internet patients had more active disease and lower scores for lower quality of life, and differed in their correlations with pain compared with the hardcopy patients.

Table 5 Comparison of demographic variables with the pain measures - Internet _n_ (%)

Variables	P-HBI					SF-36					SIBDQ				
	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value
Education (yr)	15.2 ± 2.5	15.1 ± 2.5	15.0 ± 2.7	14.4 ± 3.4	0.758	14.9 ± 2.7	15.2 ± 2.3	15.1 ± 2.9	13.8 ± 4.2	0.397	15.1 ± 2.9	15.5 ± 2.4	14.9 ± 2.6	13.6 ± 2.8	0.033
Gender															
Female	28 (54.9)	37 (62.7)	37 (63.8)	8 (50.0)	0.628	18 (41.9)	62 (65.3)	23 (63.9)	7 (70.0)	0.055	26 (55.3)	37 (60.7)	38 (65.5)	9 (50.0)	0.589
Male	23 (45.1)	22 (37.3)	21 (36.2)	8 (50.0)		25 (58.1)	33 (34.7)	13 (36.1)	3 (30.0)		21 (44.7)	24 (39.3)	20 (34.5)	9 (50.0)	
Economic status					0.003					0.001					< 0.001
Bad	4 (6.9)	12 (16.0)	16 (23.2)	6 (33.3)		2 (3.9)	18 (15.9)	12 (27.9)	6 (46.2)		2 (3.8)	13 (15.5)	12 (19.4)	11 (50.0)	
Medium	25 (43.1)	13 (17.3)	15 (21.7)	3 (16.7)		21 (41.2)	24 (21.2)	8 (18.6)	3 (23.1)		19 (36.5)	23 (27.4)	11 (17.7)	3 (13.6)	
Good	29 (50.0)	50 (66.7)	38 (55.1)	9 (50.0)		28 (54.9)	71 (62.8)	23 (53.5)	4 (30.8)		31 (59.6)	48 (57.1)	39 (62.9)	8 (36.4)	
Current Smoker					0.175					0.821					0.353
Not Smoking	52 (91.2)	62 (81.6)	53 (76.8)	14 (87.5)		44 (84.6)	95 (84.1)	33 (80.5)	9 (75.0)		46 (90.2)	70 (83.3)	49 (79.0)	16 (76.2)	
Smoking	5 (8.8)	14 (18.4)	16 (23.2)	2 (12.5)		8 (15.4)	18 (15.9)	8 (19.5)	3 (25.0)		5 (9.8)	14 (16.7)	13 (21.0)	5 (23.8)	
Working					0.093					0.044					0.033
Not Working	13 (24.1)	21 (29.6)	17 (29.8)	10 (55.6)		8 (17.0)	31 (31.3)	15 (36.6)	7 (53.8)		13 (26.0)	18 (24.3)	19 (33.3)	11 (57.9)	
Working	41 (75.9)	50 (70.4)	40 (70.2)	8 (44.4)		39 (83.0)	68 (68.7)	26 (63.4)	6 (46.2)		37 (74.0)	56 (75.7)	38 (66.7)	8 (42.1)	

P-HBI and SF-36 measure pain intensity whereas SIBDQ measures pain frequency. Data are mean ± SD or _n_ (%). P-HBI: Patient Harvey-Bradshaw Index; SF-36: Short Form Health Survey; SIBDQ: Short Inflammatory Bowel Disease Questionnaire.

Table 6 Comparison of demographic variables with the pain measures - Hardcopy _n_ (%)

Variables	P-HBI					SF-36					SIBDQ				
	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value
Education (yr)	15.1 ± 3.0	14.5 ± 2.9	14.5 ± 3.3	12.5 ± 2.4	0.002	14.7 ± 2.7	14.8 ± 3.0	14.3 ± 4.4	14.6 ± 2.0	0.411	15.1 ± 3.1	14.5 ± 3.0	14.5 ± 3.3	12.9 ± 2.2	0.004
Gender															
Female	72 (47.4)	70 (59.8)	50 (72.5)	10 (58.8)	0.005	56 (47.1)	94 (56.3)	39 (76.5)	13 (72.2)	0.002	77 (50.7)	68 (56.7)	43 (69.4)	14 (66.7)	0.067
Male	80 (52.6)	47 (40.2)	19 (27.5)	7 (41.2)		63 (52.9)	73 (43.7)	12 (23.5)	5 (27.8)		75 (49.3)	52 (43.3)	19 (30.6)	7 (33.3)	
Economic status					< 0.001					< 0.001					< 0.001
Bad	18 (11.5)	24 (20.0)	24 (33.8)	8 (47.1)		9 (7.4)	39 (22.7)	21 (38.9)	5 (29.4)		15 (9.6)	23 (18.9)	26 (39.4)	10 (47.6)	
Medium	76 (48.4)	60 (50.0)	27 (38.0)	7 (41.2)		68 (55.7)	79 (45.9)	16 (29.6)	7 (41.2)		81 (51.9)	56 (45.9)	25 (37.9)	8 (38.1)	
Good	63 (40.1)	36 (30.0)	20 (28.2)	2 (11.8)		45 (36.9)	54 (31.4)	17 (31.5)	5 (29.4)		60 (38.5)	43 (35.2)	15 (22.7)	3 (14.3)	
Current Smoker					0.026					0.178					< 0.001
Not Smoking	123 (83.7)	90 (76.9)	51 (76.1)	9 (52.9)		96 (82.1)	125 (78.6)	42 (76.4)	10 (58.8)		126 (85.7)	86 (74.8)	53 (81.5)	8 (38.1)	
Smoking	24 (16.3)	27 (23.1)	16 (23.9)	8 (47.1)		21 (17.9)	34 (21.4)	13 (23.6)	7 (41.2)		21 (14.3)	29 (25.2)	12 (18.5)	13 (61.9)	
Working					< 0.001					0.003					0.007
Not Working	48 (30.2)	30 (25.0)	34 (47.9)	13 (76.5)		32 (26.0)	55 (32.4)	30 (53.6)	8 (44.4)		47 (29.9)	35 (28.7)	31 (46.3)	12 (57.1)	
Working	111 (69.8)	90 (75.0)	37 (52.1)	4 (23.5)		91 (74.0)	115 (67.6)	26 (46.4)	10 (55.6)		110 (70.1)	87 (71.3)	36 (53.7)	9 (42.9)	

P-HBI and SF-36 measure pain intensity whereas SIBDQ measures pain frequency. Data are mean ± SD or _n_ (%). P-HBI: Patient Harvey-Bradshaw Index; SF-36: Short Form Health Survey; SIBDQ: Short Inflammatory Bowel Disease Questionnaire.

Table 7 Comparison of social questionnaires with the pain measures in the whole cohort

Variables	P-HBI					SF-36					SIBDQ				
	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value
GSI	0.6 ± 0.5	1.0 ± 0.6	1.3 ± 0.8	1.8 ± 1.0	< 0.001	0.6 ± 0.5	1.0 ± 0.7	1.4 ± 0.8	1.6 ± 0.9	< 0.001	0.6 ± 0.5	1.0 ± 0.7	1.3 ± 0.7	1.8 ± 0.9	< 0.001
COPE: Emotion-focused Strategies	23.4 ± 5.9	24.7 ± 5.7	25.0 ± 5.8	24.2 ± 7.1	0.045	23.4 ± 5.9	24.6 ± 5.9	24.2 ± 5.7	26.0 ± 5.8	0.154	23.6 ± 5.9	24.8 ± 5.7	24.8 ± 5.5	23.0 ± 7.3	0.059
COPE: Problem-focused Strategies	15.6 ± 4.9	16.1 ± 4.7	16.8 ± 4.4	16.6 ± 4.9	0.249	15.4 ± 5.1	16.1 ± 4.5	16.5 ± 4.5	18.2 ± 4.3	0.042	15.6 ± 5.1	16.2 ± 4.7	17.0 ± 4.1	15.4 ± 4.6	0.067
COPE: Dysfunctional Strategies	20.0 ± 5.5	22.9 ± 5.5	24.0 ± 5.8	25.6 ± 6.6	< 0.001	20.0 ± 5.7	22.7 ± 5.7	24.0 ± 5.9	25.9 ± 5.5	< 0.001	19.9 ± 5.4	22.8 ± 5.4	24.5 ± 6.0	24.6 ± 6.9	< 0.001
FAD	1.7 ± 0.5	1.8 ± 0.6	1.9 ± 0.5	2.1 ± 0.7	0.003	1.7 ± 0.6	1.8 ± 0.5	1.9 ± 0.5	1.8 ± 0.7	0.081	1.7 ± 0.5	1.9 ± 0.5	1.8 ± 0.6	2.0 ± 0.7	< 0.001
SWLS	24.3 ± 6.6	22.0 ± 7.7	19.9 ± 7.5	17.7 ± 9.8	< 0.001	24.5 ± 6.7	22.3 ± 7.1	18.4 ± 8.4	17.9 ± 9.1	< 0.001	24.8 ± 6.4	22.2 ± 7.3	19.2 ± 7.4	16.9 ± 9.8	< 0.001
WPAI: Absenteeism	3.9 ± 11.9	5.9 ± 12.4	18.2 ± 27.2	43.4 ± 37.6	< 0.001	2.8 ± 10.6	8.3 ± 18.6	21.3 ± 25.2	29.4 ± 35.0	< 0.001	1.8 ± 5.5	7.8 ± 18.3	19.1 ± 22.7	38.5 ± 42.2	< 0.001
WPAI: Presenteeism	14.6 ± 22.8	29.9 ± 28.0	44.4 ± 29.7	77.1 ± 26.4	< 0.001	13.0 ± 20.7	29.2 ± 26.1	55.0 ± 32.9	70.7 ± 34.1	< 0.001	10.6 ± 18.2	31.6 ± 27.5	48.2 ± 29.4	69.0 ± 31.1	< 0.001
WPAI: Work productivity loss	15.7 ± 23.3	29.5 ± 26.9	46.4 ± 32.4	80.6 ± 27.1	< 0.001	13.7 ± 20.9	30.0 ± 27.0	58.6 ± 33.2	65.3 ± 35.5	< 0.001	10.2 ± 15.9	32.7 ± 27.9	52.2 ± 30.9	66.6 ± 34.7	< 0.001
WPAI: Activity Impairment	17.1 ± 23.6	32.9 ± 26.4	51.1 ± 27.9	78.3 ± 23.5	< 0.001	14.3 ± 22.0	33.4 ± 25.4	59.8 ± 27.8	76.1 ± 28.8	< 0.001	12.3 ± 19.6	34.9 ± 25.4	52.7 ± 26.2	78.9 ± 24.1	< 0.001

P-HBI and SF-36 measure pain intensity whereas SIBDQ measures pain frequency. Data are mean ± SD. P-HBI: Patient Harvey-Bradshaw Index; SF-36: Short Form Health Survey; SIBDQ: Short Inflammatory Bowel Disease Questionnaire; GSI: Global Severity Index; COPE: Brief Cope Inventory; FAD: McMaster Family Assessment Device; SWLS: Satisfaction with Life Scale; WPAI: Work Productivity and Activity Impairment Questionnaire.

Table 8 Comparison of social questionnaires with the pain measures - Internet

Variables	P-HBI					SF-36					SIBDQ				
	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value
GSI	0.7 ± 0.7	1.0 ± 0.7	1.3 ± 0.8	2.1 ± 0.9	< 0.001	0.7 ± 0.7	1.0 ± 0.7	1.5 ± 0.7	1.9 ± 1.1	< 0.001	0.7 ± 0.6	1.0 ± 0.7	1.4 ± 0.7	1.9 ± 1.0	< 0.001
COPE: Emotion-focused Strategies	23.4 ± 6.1	24.8 ± 5.5	25.5 ± 5.6	23.2 ± 6.3	0.158	23.5 ± 6.1	24.8 ± 6.0	24.7 ± 4.6	25.5 ± 5.7	0.655	24.4 ± 5.6	24.3 ± 5.8	25.2 ± 5.7	23.4 ± 6.5	0.525
COPE: Problem-focused Strategies	15.7 ± 4.8	16.8 ± 4.5	17.5 ± 4.0	18.3 ± 4.8	0.096	15.8 ± 5.1	16.7 ± 4.4	17.5 ± 4.0	19.7 ± 4.1	0.051	16.1 ± 4.5	16.7 ± 4.8	17.7 ± 3.8	16.6 ± 5.0	0.384
COPE: Dysfunctional Strategies	20.8 ± 5.8	23.4 ± 5.8	24.4 ± 5.2	27.7 ± 5.4	< 0.001	20.9 ± 5.7	23.2 ± 5.8	25.4 ± 4.9	27.8 ± 5.5	< 0.001	20.9 ± 5.4	22.8 ± 5.5	24.8 ± 5.8	27.4 ± 5.6	< 0.001
FAD	1.8 ± 0.6	1.9 ± 0.5	1.9 ± 0.5	2.2 ± 0.7	0.116	1.8 ± 0.6	1.9 ± 0.5	2.0 ± 0.5	2.1 ± 0.8	0.264	1.8 ± 0.6	1.9 ± 0.5	2.0 ± 0.6	2.1 ± 0.7	0.074
SWLS	24.1 ± 7.7	20.8 ± 7.6	19.4 ± 7.3	15.5 ± 8.5	< 0.001	24.8 ± 7.7	21.2 ± 6.7	16.1 ± 7.6	16.8 ± 10.4	< 0.001	24.1 ± 7.7	21.3 ± 7.3	18.6 ± 7.3	17.2 ± 9.5	< 0.001
WPAI: Absenteeism	5.2 ± 12.1	6.9 ± 12.8	17.3 ± 25.2	38.1 ± 40.7	0.002	3.4 ± 9.7	11.3 ± 21.7	17.1 ± 21.5	46.3 ± 35.8	< 0.001	1.6 ± 4.9	9.1 ± 18.5	18.9 ± 21.1	35.4 ± 50.3	< 0.001
WPAI: Presenteeism	15.2 ± 25.8	27.1 ± 26.2	43.2 ± 26.7	76.7 ± 29.6	< 0.001	12.7 ± 17.9	31.5 ± 27.8	51.4 ± 32.1	80.0 ± 24.5	< 0.001	9.1 ± 13.9	31.4 ± 29.9	44.6 ± 26.4	68.0 ± 35.8	< 0.001
WPAI: Work productivity loss	18.0 ± 26.1	29.2 ± 26.7	47.3 ± 30.3	78.2 ± 32.2	< 0.001	15.5 ± 20.6	32.6 ± 29.3	59.3 ± 32.0	78.5 ± 17.5	< 0.001	9.5 ± 14.4	32.6 ± 29.4	52.2 ± 28.9	62.1 ± 42.4	< 0.001
WPAI: Activity Impairment	16.5 ± 23.1	34.2 ± 26.2	48.6 ± 27.0	80.6 ± 25.7	< 0.001	16.3 ± 21.9	34.2 ± 26.0	62.8 ± 25.4	88.0 ± 18.7	< 0.001	11.5 ± 16.4	34.2 ± 25.6	48.6 ± 25.9	82.5 ± 24.5	< 0.001

P-HBI and SF-36 measure pain intensity whereas SIBDQ measures pain frequency. Data are mean ± SD. P-HBI: Patient Harvey-Bradshaw Index; SF-36: Short Form Health Survey; SIBDQ: Short Inflammatory Bowel Disease Questionnaire; GSI: Global Severity Index; COPE: Brief Cope Inventory; FAD: McMaster Family Assessment Device; SWLS: Satisfaction with Life Scale; WPAI: Work Productivity and Activity Impairment Questionnaire.

Pain

Pain is an important symptom in CD patients and features prominently in Patient Reported Outcome scales like the Crohn's Disease Activity Index (CDAI) and the P-HBI, as well as the health-related quality of life measures SIBDQ and SF-36. While measurement of pain by the patient's subjective response to 4 questions as in the CDAI and the P-HBI has been disputed as to its reliability, it nevertheless remains a widely accepted practice and its brevity makes it quite acceptable to patients. P-HBI and SIBDQ both ask about abdominal pain, which is the commonest form of pain in CD patients, present in about 70% of women and 65% of men[8,32]. SF-36 however enquires about bodily pain, which would include in particular rheumatological pain that is present in 30%-40% of CD patients, particularly in women[8,32]. The recall period of the P-HBI is just one day, adding to its reliability. For the SIBDQ and SF-36 the recall period is longer, 2 and 4 wk respectively. This longer recall period may explain

Table 9 Comparison of social questionnaires with the pain measures - Hardcopy

Variables	P-HBI					SF-36					SIBDQ				
	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value	No pain	Mild pain	Moderate pain	Severe pain	P value
GSI	0.6 ± 0.5	1.0 ± 0.6	1.4 ± 0.7	1.6 ± 1.0	< 0.001	0.5 ± 0.5	1.0 ± 0.7	1.3 ± 0.8	1.4 ± 0.7	< 0.001	0.5 ± 0.5	1.0 ± 0.6	1.3 ± 0.8	1.7 ± 0.8	< 0.001
COPE: Emotion-focused Strategies	23.4 ± 5.8	24.6 ± 5.8	24.5 ± 6.0	25.3 ± 7.9	0.234	23.4 ± 5.9	24.4 ± 5.8	23.8 ± 6.4	26.3 ± 6.0	0.302	23.3 ± 6.0	25.1 ± 5.6	24.4 ± 5.3	22.5 ± 8.3	0.076
COPE: Problem-focused Strategies	15.6 ± 5.0	15.6 ± 4.8	16.1 ± 4.7	14.6 ± 4.4	0.725	15.2 ± 5.2	15.8 ± 4.6	15.8 ± 4.8	17.1 ± 4.3	0.642	15.4 ± 5.3	15.8 ± 4.6	16.4 ± 4.3	14.0 ± 3.8	0.192
COPE: Dysfunctional Strategies	19.8 ± 5.4	22.6 ± 5.3	23.5 ± 6.4	23.1 ± 7.2	< 0.001	19.7 ± 5.7	22.3 ± 5.5	22.9 ± 6.3	24.5 ± 5.1	< 0.001	19.6 ± 5.4	22.8 ± 5.3	24.1 ± 6.3	21.5 ± 7.0	< 0.001
FAD	1.7 ± 0.5	1.8 ± 0.6	1.8 ± 0.5	1.9 ± 0.7	0.088	1.7 ± 0.5	1.8 ± 0.5	1.8 ± 0.6	1.6 ± 0.5	0.224	1.7 ± 0.5	1.8 ± 0.5	1.7 ± 0.5	1.9 ± 0.6	0.016
SWLS	24.4 ± 6.1	22.7 ± 7.6	20.3 ± 7.7	20.2 ± 10.8	0.003	24.4 ± 6.3	23.0 ± 7.2	20.1 ± 8.6	18.6 ± 8.2	0.002	25.1 ± 5.8	22.7 ± 7.4	19.8 ± 7.5	16.5 ± 10.3	< 0.001
WPAI: Absenteeism	3.4 ± 11.9	5.3 ± 12.2	19.2 ± 29.5	57.8 ± 29.1	< 0.001	2.5 ± 11.0	6.4 ± 16.0	25.6 ± 28.4	19.7 ± 33.1	< 0.001	1.8 ± 5.8	6.8 ± 18.3	19.4 ± 24.8	41.1 ± 37.8	< 0.001
WPAI: Presenteeism	14.4 ± 21.4	31.5 ± 29.1	46.0 ± 33.5	78.0 ± 22.8	< 0.001	13.2 ± 22.2	27.5 ± 24.6	58.3 ± 33.8	64.4 ± 39.4	< 0.001	11.2 ± 19.7	31.7 ± 25.8	53.0 ± 32.6	70.0 ± 27.5	< 0.001
WPAI: Work productivity loss	14.8 ± 22.2	29.7 ± 27.2	45.5 ± 34.9	86.1 ± 11.3	< 0.001	12.9 ± 21.2	28.3 ± 25.4	58.0 ± 34.9	57.7 ± 41.9	< 0.001	10.4 ± 16.4	32.7 ± 27.0	52.3 ± 33.7	70.5 ± 29.6	< 0.001
WPAI: Activity Impairment	17.3 ± 23.9	32.1 ± 26.6	53.5 ± 28.6	75.7 ± 21.4	< 0.001	13.4 ± 22.1	32.8 ± 25.1	57.6 ± 29.4	69.4 ± 31.7	< 0.001	12.6 ± 20.6	35.5 ± 25.4	56.3 ± 26.2	75.0 ± 23.8	< 0.001

P-HBI and SF-36 measure pain intensity whereas SIBDQ measures pain frequency. Data are mean ± SD. GSI: Global Severity Index; COPE: Brief Cope Inventory; FAD: McMaster Family Assessment Device; SWLS: Satisfaction with Life Scale; WPAI: Work Productivity and Activity Impairment Questionnaire.

Table 10 Multinomial logistic regression analysis, stratified by source of questionnaire, of General Severity Index, gender, the three coping strategies and the intensity of pain[1]

Characteristic	No pain	Mild pain		Moderate pain		Severe pain	
		Internet OR (P value)	Hardcopy OR (P value)	Internet OR (P value)	Hardcopy OR (P value)	Internet OR (P value)	Hardcopy OR (P value)
Pain by HBI							
GSI	Ref.	1.74 (0.14)	2.67 (< 0.001)	2.89 (0.01)	6.13 (< 0.001)	8.51 (< 0.001)	11.66 (< 0.001)
Gender (female)	Ref.	1.11 (0.80)	1.63 (0.07)	1.03 (0.95)	3.43 (0.00)	0.76 (0.69)	2.43 (0.14)
Emotion-focused	Ref.	1.01 (0.81)	1.04 (0.21)	1.04 (0.35)	1.06 (0.15)	0.96 (0.56)	1.15 (0.03)
Problem-focused	Ref.	1.04 (0.53)	0.91 (0.02)	1.05 (0.44)	0.91 (0.04)	1.14 (0.19)	0.79 (< 0.001)
Dysfunctional	Ref.	1.04 (0.49)	1.07 (0.04)	1.02 (0.67)	1.04 (0.30)	1.02 (0.76)	1.01 (0.90)
Pain by SF36							
GSI	Ref.	2.05 (0.07)	3.22 (< 0.001)	5.87 (< 0.001)	6.20 (< 0.001)	10.12 (< 0.001)	6.69 (< 0.001)
Gender (female)	Ref.	2.22 (0.05)	1.42 (0.18)	2.41 (0.09)	4.29 (< 0.001)	3.60 (0.15)	3.82 (0.03)
Emotion-focused	Ref.	1.01 (0.86)	1.01 (0.76)	1.02 (0.71)	1.04 (0.42)	1.02 (0.81)	1.06 (0.35)
Problem-focused	Ref.	1.05 (0.47)	0.96 (0.32)	1.11 (0.16)	0.96 (0.39)	1.23 (0.10)	0.97 (0.74)
Dysfunctional	Ref.	1.05 (0.38)	1.07 (0.05)	0.98 (0.77)	1.05 (0.28)	1.03 (0.73)	1.07 (0.23)
Pain by SIBDQ							
GSI	Ref.	2.39 (0.03)	4.04 (< 0.001)	5.57 (< 0.001)	5.53 (< 0.001)	6.20 (< 0.001)	19.91 (< 0.001)
Gender (female)	Ref.	1.16 (0.72)	1.21 (0.50)	1.43 (0.44)	1.93 (0.07)	0.73 (0.62)	3.06 (0.08)
Emotion-focused	Ref.	0.97 (0.49)	1.06 (0.09)	0.98 (0.72)	1.01 (0.88)	0.97 (0.62)	1.10 (0.14)
Problem-focused	Ref.	1.04 (0.52)	0.91 (0.01)	1.08 (0.23)	0.96 (0.41)	0.88 (0.21)	0.79 (< 0.001)
Dysfunctional	Ref.	1.01 (0.91)	1.06 (0.06)	1.00 (0.99)	1.10 (0.01)	1.11 (0.14)	0.99 (0.83)

[1]Statistical differences from the reference value (No pain) are shown. GSI: General Severity Index.

why more patients reported mild pain intensity with SF-36 compared with the other measures. It is also possible that our method of recoding the 6 items in SF-36 to 4 scores corresponding to the questions of P-HBI may account for some of this difference. On the other hand, we recoded the SIBDQ as well, from 7 items to 4 scores, and still its agreement with P-HBI was very good. Thus, the longer recall period may be the explanation: that patients tend to become accustomed to pain over time and discount its intensity. In all, we showed that the combined use of the pain questions from all 3 measures was a useful tool to assess the severity of pain in this CD cohort. The use of the pain questions from the Harvey-Bradshaw Index (similar to P-HBI with an additional question regarding the presence or absence of an abdominal mass) and the SIBDQ was previously reported in a study of opiate use in CD patients in the United States, but no attempt was made to standardize these respective scores[33].

Pain in CD is treated with a variety of analgesics including nonsteroidal anti-inflammatory drugs, opiates and more recently cannabis preparations[12,33,34]. Pain in CD patients is reported as often being undertreated, as was found in a recent large Swiss study[8]. Treatment of pain is often neglected in the patient whose disease is controlled. Unfortunately the ethical limitations of our protocol did not allow of investigation of pain treatments in the cohort.

Predictors of pain

Predictors of abdominal pain in CD have been little investigated. In a pediatric CD cohort in the United States it was shown by multivariate analysis that pain was predicted by depression, weight loss and abdominal tenderness[14]. However, this cohort was composed entirely of subjects suffering from depression, which is known to exacerbate symptoms like pain in chronic illnesses[35]. In a Scandinavian study performed on distressed adults with CD, use of the SF-36 measure revealed that personality impacted on the pain subscale[36]. These two studies did not relate to patients without diagnosed confounding conditions. Our study is the first detailed attempt to our knowledge to unravel the factors that are associated with increased severity of pain in CD patients without psychological or psychiatric comorbidities. By using a self-selected large community cohort presenting all stages of the disease course we were able to investigate patients who are representative of the average patients attending outpatient facilities for on-going medical care. By using a broad spectrum of psycho-social questionnaires we were able to relate the measures of psychological stress, coping strategies, family functioning, satisfaction with life, and functioning at work and at leisure to the intensity of pain captured by the three pain questions. In the univariate analysis, working patients reported less intense pain than those unemployed, and in fact close to 40% of workers had no pain at

all. Consistent with this finding, patients with a poorer economic status reported more pain by all three pain measures. Patients with a higher level of satisfaction with life score experienced significantly less pain. In the multinomial logistic regression analysis, stress as measured by the GSI was the variable most related to pain, with the odds ratio increasing progressively as the pain intensity rose. Gender behaved in a fairly similar fashion, with females having more intense pain than males, but with lower odds ratios. These observations show convincingly that the level of stress experienced by patients, as well as gender issues, requires careful clinical consideration in CD cases presenting with pain. It is well known that current smokers have a worse course of CD than non-smokers[37]. Our study adds to this knowledge by the new finding that current smokers experience significantly more pain than non-smokers.

It is well documented that CD patients are less productive than healthy controls and have more periods off work[38]. The literature on this topic has focused in general on the role of medical treatments, particularly the more successful biologic therapy, as well as abdominal surgery in improving the ability of these patients to work. The present study is the first documentation of the association of pain with both work impairment and a lower socioeconomic state. Women are reported to have more severe CD than men[39]. Women with CD also have a reduced quality of life compared with men[40]. Our study however is the first to explore the differences in pain severity and the impact of pain on several psycho-social variables. In healthy individuals and patients with CD there are no gender differences in satisfaction with life[41,42]. The present study indicates that patients with a greater satisfaction of life are healthier, with less pain.

Pain and coping measures

Coping with chronic diseases is an important mental resource to improve patients' well-being, but the variety of measures has resulted in a plethora of concepts regarding coping strategies[43]. We studied disease-coping strategies in relationship to pain using the COPE instrument, which clearly separates emotion-focused, problem-focused and dysfunctional coping strategies and avoids any overlap of component questions[24]. By univariate analysis we found that the dysfunctional coping strategy was significantly correlated with the intensity of pain in all three pain measures. This is not surprising, since this is in fact a negative coping mechanism which does not promote better control of the disease. In the regression analysis we found that dysfunctional coping was associated with mild or moderate pain by all three pain measures. The positively-orientated coping strategies, emotion-focused and problem-focused, showed few correlations with pain intensity. This is contrary to what we expected and the matter requires further investigation. Nevertheless,

these findings regarding coping mechanisms present a message for clinicians treating patients with pain: namely, that prompt referral to a psychologist versed in these matters may assist CD patients to cope correctly with their illness and may actually lead to reduction of their pain level, particularly when dysfunctional coping strategies are identified and averted.

The strengths of our study include the use of a large representative cohort and a series of well-accepted psycho-social instruments. The consistencies of the three pain questions demonstrate the validity of this method of assessing pain. One limitation was the use of recall tools, although a recent publication regarding patients with inflammatory bowel disease did find that patient recall was quite adequate for research purposes[44]. The lack of access to detailed clinical material was another limitation. Thus, we could not relate our findings to specific phenotypes of CD by the Montreal classification, nor were we able to document any treatments given for pain and relate them to our research. Furthermore, we could not determine the direction of the reported associations because of the cross-sectional design of our study. Future work should thus include long-term follow up of patients and knowledge of their phenotypic classification and analgesic medication. Moreover, an interventional program will be required to evaluate whether medical and psychological therapy can alleviate pain and its associations in these patients.

In conclusion, the pain questions in the P-HBI, SF-36 and SIBDQ, although differing in their focus, were related a variety of psycho-social pathologies in our CD cohorts. These are associations or correlations and of course cannot imply causality in a cross-sectional study. We suggest that clinicians apply these three simple questions in the busy clinic setting to determine the severity of pain even in those patients who appear to be in remission. In fact, patients could fill in this information in two or three minutes while waiting to be seen. This simple strategy may identify patients in need of psychological treatment.

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COMMENTS

Background

Pain is a very prominent symptom in Crohn's disease (CD), and often is very disabling for patients and requires specific medication. Since patients with CD have socio-psychological disturbances, the authors wished to examine whether these have any associations with pain. Authors wished to determine if knowledge of such associations could be useful to the physicians who manage such patients.

Research frontiers

Intensive perusal of the literature indicated that subject matter of this article has not been researched previously.

Innovations and breakthroughs

Authors found that the pain questions forming part of three commonly used questionnaires in the clinical assessment of these patients were associated with demographic, social and psychological characteristics in these patients.

Applications

The authors suggest that the findings in this study serve as a guide in the clinical and psychological assessment of patients with Crohn's disease.

Terminology

The research makes use of a variety of questionnaires which are well known in psychology but are less familiar to physicians. These are described in detail in the methods section of the paper.

Peer-review

The reviewers of this paper have emphasized that pain is only one of several symptoms in these patients, that socio-demographics impact on this symptom, that patients filling in questionnaires by hardcopy or the internet might represent subsets of patients with important social and disease characteristics, that the use of questionnaires in translation requires validation, that medication type could influence the pain symptom and needs to be considered.

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