Observational Studies

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Criterion validity and discriminatory ability of the central sensitization inventory short form in individuals with inflammatory bowel diseases

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Abstract

Objectives: Increased symptoms related to central sensitization have previously been reported in inflammatory bowel disease (IBD) patients, identified by the original central sensitization inventory (CSI-25). However, the recently developed CSI short form (CSI-9) may be more clinically useful. The aim of the present study was to evaluate the performance of CSI-9 compared to the original CSI-25 in individuals with IBD. Study objectives were to investigate the criterion validity of the CSI-9 to the CSI-25, assess individual association of the CSI measures with clinical features of IBD and pain presentations, and to establish disease-specific CSI-9 and CSI-25 cut-off scores for discriminating the presence of self-reported pain in individuals with IBD.

Methods: Cross-sectional online survey was performed on adults with IBD exploring self-reported demographics, comorbidity, and clinical IBD and pain features. Criterion validity of the CSI-9 was investigated using intraclass correlation coefficient $(ICC)_{3,1}$. Area under the receiver operating characteristic curve (AUC-ROC) analysis was conducted to investigate the discriminative ability of both versions of CSI.

Results: Of the 320 participants, 260 reported the presence of abdominal and/or musculoskeletal pain. CSI-9 and CSI-25 demonstrated substantial agreement ($ICC_{3,1}$=0.64, 95% CI [0.58, 0.69]). AUC (95% CI) indicated that CSI-9 (0.788 (0.725, 0.851), p<0.001) and CSI-25 (0.808 (0.750, 0.867), p<0.001) were able to adequately discriminate the presence of pain using cut-offs scores of ≥17 (CSI-9) and ≥40 (CSI-25). Abdominal pain severity was the only feature to differ in significant association to CSI-25 (p=0.002) compared to CSI-9 (p=0.236). All other features demonstrated significant associations to both CSI versions, except age (p=0.291 and 0.643) and IBD subtype (p=0.115 and 0.675).

Conclusions: This is the first study to explore and validate the use of CSI-9 in IBD patients. Results demonstrated concurrent validity of the CSI-9 to CSI-25, with similar significant association to multiple patient features, and a suggested cut-off value of 17 on CSI-9 to screen for individuals with pain experiences. Study findings suggest that CSI-9 is suitable to use as a brief tool in IBD patients.

Keywords: central sensitization; inflammatory bowel disease; musculoskeletal pain.

Introduction

Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, are chronic inflammatory conditions of the gastrointestinal tract [1–4]. Pain is reported in over 70% of individuals with IBD, where the most common complaints relate to abdominal and musculoskeletal (MSK) pain experiences [5–9]. Although acute abdominal pain is a common consequence of active IBD and structural changes, such as strictures, current literature reports abdominal pain experiences in the absence of such factors, suggestive of mechanisms of central sensitization [10, 11]. Our previous investigations exploring persistent MSK pain in IBD demonstrated worse pain experiences in individuals with greater symptoms related to central sensitization [12, 13].

Central sensitization has been proposed as a phenomenon that involves hypersensitivity of the central nervous system [14–17], which may lead to worse pain experiences seen in multiple patient populations, including low back pain, osteoarthritis, and rheumatoid arthritis [18–20]. The

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mechanisms of central sensitization are believed to be responsible for the overlapping clinical features of central sensitivity syndromes, including irritable bowel syndrome, fibromyalgia, and temporomandibular joint disorder [21, 22]. It has been proposed that the symptoms common to these syndromes, including fatigue, sleep disturbances, and cognitive symptoms, can be considered not as belonging to individual disorders, but as different manifestations of primary central sensitization mechanisms [22]. This viewpoint informed the development of symptomatic screening tools, such as the central sensitization inventory (CSI), to broadly assess and quantify the degree of presenting symptomatology, in order to identify potential contributions from mechanisms of central sensitization [22].

The original CSI is a 25-item tool used to investigate an array of common symptoms associated with central sensitivity syndromes, within the domains of physical, emotional distress, headache/jaw, and urological features [22]. Higher CSI-25 scores indicate increased symptomology, with a benchmark score (≥40) suggesting the likely presence of one or more central sensitivity syndromes [22, 23]. Additionally, total CSI-25 scores have demonstrated the ability to distinguish between patients with chronic MSK pain and healthy controls [23, 24]. Similarly, higher CSI-25 scores have demonstrated association with worse pain-related outcomes [24, 25], as well as poor long-term postoperative outcomes [26, 27].

We previously utilized CSI-25 as a screening tool for central sensitization symptomology in patients with IBD, where worse pain experiences were associated with higher CSI scores [12, 13]. Like many chronic conditions, pain management has been identified as a top challenge and priority in IBD research, indicated by both clinicians and patients [28–30]. As such, linking the presence of pain with a profile of symptomology related to central sensitization may provide clinicians with useful information regarding the potential presence of central mechanisms. Similarly, CSI may represent a useful tool for prospectively monitoring patients' risk for developing persistent pain, as well as responses to treatment.

Although CSI-25 has previously been used in IBD research, a potential limitation relates to the inclusion of items exploring symptoms commonly seen in IBD patients consequent of underlying disease processes and inflammation, such as bowel and skin problems [31]. CSI-25 does not differentiate whether positive scoring of these items is related to symptoms of central sensitization or are a consequence of active IBD. Recently, a 9-item short form of the CSI (CSI-9) was developed as a quick and clinically useful screening tool to reduce patient burden in both clinical and research environments [32]. Interestingly, the items which potentially overlap between common symptoms of IBD and those of central sensitization have been excluded in the CSI-9, suggesting that CSI-9 may be more useful to explore central sensitization symptoms in IBD patients.

As previously noted, the CSI-25 benchmark score (≥40) was validated to identify the presence of central sensitivity syndromes [22, 23], and previously demonstrated correlation to chronic MSK pain and worse pain experiences [33]. However, targeted investigations in specialized populations, such as migraine [34], fibromyalgia, and other MSK pain experiences [35], have demonstrated unique CSI-25 cut-off scores to discriminate conditions and/or pain presentations in these populations. Similarly, IBD-specific cut-off values for CSI could provide clinicians with a tool which highlight symptoms that may persist and contribute to possible central sensitization mechanisms alongside pain presentations, thereby triggering targeted management pathways. Therefore, investigation of appropriate cut-off values for both CSI-25 and CSI-9 are needed to better understand the use of CSI tools in IBD patients.

The aim of the present study was to evaluate the performance of CSI-9 compared to the original CSI-25 in individuals with IBD. Study objectives were to investigate the criterion validity of the CSI-9 to the CSI-25, assess individual association of the CSI measures with clinical features of IBD and pain presentations, and to establish disease-specific CSI-9 and CSI-25 cut-off scores for discriminating the presence of self-reported pain (i.e. abdominal and MSK) in individuals with IBD. We hypothesized that CSI-9 would demonstrate acceptable validity with similar association to participant features as the CSI-25.

Methods

Research design

The current study is a sub-analysis derived from data collected as part of a primary cross-sectional online survey of individuals with IBD [36]. Ethical approval for the primary study was granted by the University of Otago Human Ethics Committee (Health) (approval number – H17/095), in accordance with the Declaration of Helsinki.

Study participants

Individuals with a self-reported IBD diagnosis, aged 18 years and older were invited to participate in an online survey through Crohn's and Colitis New Zealand Charitable Trust (CCNZ) email database and additional social media outlets associated with: IBD research groups, New Zealand health forums, patient support groups, and practitioner resource groups. Investigation of self-reported medical history demonstrated that IBD patients are able to accurately report (κ=0.96–0.97) their medical history regarding type of disease through

online investigations [37, 38]. CCNZ is a national organization that offers support, advice, and information to individuals suffering from IBD. All participants were provided with detailed information related to the study and signed a consent form to participate. Individuals were excluded if they reported any of the following: pregnancy, nerve injuries, neurological conditions (e.g., stroke, multiple sclerosis, peripheral neuropathy, and Parkinson's disease), and surgery within the last 3 months.

Demographics and comorbidity

Participant demographics included: age, gender, and ethnicity. Comorbidities assessed in the present study included health conditions identified on the Self-Administered Comorbidity Questionnaire [39], extra-intestinal manifestation checklist [40], and conditions identified on part B of the CSI.

CSI measures

Participants were asked to complete the original CSI-25. Part A of the CSI-25 evaluates features across an array of somatic and emotional symptoms, with each item scored on a Likert scale of 0–4, and overall scoring ranging from 0 to 100 [41]. Higher scores indicate increased symptomology related to mechanisms of central sensitization, with scores ≥40 indicating the likely presence of central sensitivity syndromes [22, 23]. The use of CSI-25 as a measure of symptoms related to central sensitization has been previously validated (AUC=0.86, Sensitivity=81%, Specificity=75%) in a large population with central sensitivity syndromes [22, 23].

The CSI-9 short form was developed using Rasch analysis and demonstrated good internal consistency (Cronbach's alpha=0.80) and test-retest reliability (intraclass correlation coefficient $(ICC)_{3,1}$=0.79) in patients with MSK pain disorders and health individuals [32]. In the present sub-analysis, item responses for the CSI-9 were extracted from the CSI-25 completed by the study participants. Overall scoring for the CSI-9 ranges from 0 to 36, with scores ≥ 20 previously demonstrating the ability to discriminate the presence of painful MSK conditions [35].

IBD features

IBD features evaluated in the present study included: IBD subtype, IBD activity, and health-related quality of life. IBD activity was evaluated using the patient Harvey Bradshaw Index (P-HBI) for Crohn's disease and patient Simple Clinical Colitis Activity Index (P-SCCAI) for ulcerative colitis. The P-HBI correlates highly with the clinician administered HBI, with moderate to large agreement between clinicians and patients, and significant positive predictive value (96%) for identifying disease remission [42]. Similarly, the patient administered SCCAI (P-SCCAI) demonstrated substantial agreement (87%, κ=0.66) with the clinician administered SCCAI [43]. Both P-SCCAI and P-HBI identify disease remission as scores of ≤4 [43, 44].

Health-related quality of life was assessed through the validated Short IBD Questionnaire (SIBDQ) [45, 46]. SIBDQ demonstrated significant retest reliability (ICC=0.65, Cronbach's α=0.78) with ability to detect clinically meaningful changes in health-related quality of life through the assessment of five heath dimensions (bowel symptoms, systemic symptoms, functional impairment, social impairment, and emotional function) [45]. SIBDQ scoring is interpreted as poor (10–29), moderate (30–49), and optimal (50–70) [45, 46].

Pain features

Pain features evaluated in the present study included: MSK pain (location, severity, and interference), as well as abdominal pain (severity). Regional (n=47) MSK pain location and distribution was identified by participants using a body diagram developed by recommendations from current literature regarding MSK conditions in IBD [6, 9] and investigations for the reliability of pain drawing [47]. If multiple painful regions were identified, participants were asked to nominate their 'main area of pain'. MSK pain severity was recorded relative to regions identified as the individual's 'main area of pain' using an 11-point numeric rating scale (NRS) (0 indicating 'no pain', 10 indicating 'worst pain') [48]. Participants were asked to consider their MSK pain and indicate: "*How strong was the STRONGEST pain during the past 4 weeks?*" Similarly, abdominal pain severity was evaluated using an 11-point numeric rating scale [48]. Participants were asked to consider the last 7 days and indicate: "*How would you rate your abdominal pain on average?*"

MSK pain interference was evaluated through Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference 4a short form [49]. PROMIS short forms, developed by the National Institutes of Health, have undergone extensive qualitative expert and patient review, as well as quantitative analysis of data collected on general populations and clinical samples [49]. Scoring of PROMIS short forms identify findings as: mild (50–59), moderate (60–69), or severe (≥70) [49].

Statistical analysis

Essential dataset for the present study was identified as completion of all items included in the CSI-25. Scatterplots, Q-Q plots, and histograms were used to examine data distribution. The $ICC_{3,1}$ with the 95% confidence interval (CI) was calculated to investigate the criterion validity of CSI-9 to CSI-25. $ICC_{3,1}$ values 0–0.40 were considered to indicate fair agreement between the CSI tools, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.81–1.00 almost perfect agreement [50].

Spearman rank-order correlations were used to examine the relationships between both versions of the CSI and clinical features (i.e., MSK pain severity, MSK pain interference, abdominal pain severity, IBD activity, SIBDQ, and total comorbidity scores). The following criteria were used to interpret the strength of association between variables of interest [51, 52]: very weak (<0.19), weak (0.20–0.30), moderate (0.30–0.50), strong (0.50–0.79), and very strong (≥0.80).

Area under the receiver operating characteristic curve (AUC-ROC) analysis was conducted to explore the ability of CSI-9 and CSI-25 to discriminate participants with self-reported pain (i.e. MSK and/or abdominal) [53]. Interpretation of the AUC ranges from 0.5 (no ability to discriminate between subject groups) to 1.0 (perfectly discriminates between subject groups), with a general satisfactory level of 0.7 [54]. Additionally, the maximum Youden Index (sensitivity + specificity – 1) was used to identify the optimal cut-off scores for discriminating participants with self-reported pain [53].

Subsequently, participants were divided into two groups (i.e., high symptom group vs. low symptom group) determined by the

identified cut-off scores for both CSI-25 and CSI-9. Mann-Whitney U and chi-square tests were used to investigate any differences in the clinical features between the high and low groups for each CSI tool. Statistical analyses were conducted using the open-source R statistical software and SPSS version 26.0 (IBM Corp., Armonk, NY, U.S.A.). The significance level was set at $p<0.05$ for all statistical analyses.

Results

A total of 370 individuals with IBD volunteered to participate in the online survey. Eleven respondents were excluded due to minimum age requirements. Thirty-nine respondents were excluded due to incomplete essential datasets. The mean (SD) age of the remaining 320 respondents was 43.86 (14.76) years, with 80% (n=256) of participants identifying as female, 19% (n=62) as male, and 1% (n=2) as gender diverse. Study participants identified with the following ethnic groups: New Zealand European (n=286), Maori (n=19), Indian (n=5), Australian (n=5), North American (n=4), Fijian (n=3), South African (n=2), and other European (n=14).

IBD features

Summary results for the outcome measures utilized in the present study are presented in Table 1. Of the 320 participants, 208 (65%) reported IBD subtype as Crohn's disease, 102 (32%) reported ulcerative colitis, and 10 (3%) reported indeterminate colitis. Of the participants who reported Crohn's disease (n=208), five indicated the presence of an ileostomy and therefore were unable to utilize the patient Harvey Bradshaw Index (P-HBI), which requires evaluation of bowel habits not assessable in patients with intestinal stomas. Consequently, assessment of IBD activity is reported for the remaining n=315 participants.

Pain features

Of the included participants, 81% (n=260) reported the presence of abdominal and/or MSK pain. Of these participants, 14% (n=37) reported the presence of only abdominal pain, 33% (n=86) reported the presence of only MSK pain, and 53% (n=137) reported the presence of both abdominal and MSK pain. Of the MSK regions identified as painful by study participants, the low back was overall the most frequently reported painful region (n=135, 60%) and was also identified most frequently as the 'main area of pain' (n=42, 18%).

Table 1: Summary of study outcome measures.

Outcome measure	Range	Mean, SD
CSI-25	3–85	44.56 (15.03)
CSI-9	1–34	20.05 (6.13)
Active IBD (yes, n [%])[a]		183 (58)
SIBDQ	21–67	46.45 (9.66)
Total comorbidity scores	0–11	3.07 (2.06)
Abdominal pain severity (n=174)	0–9	4.42 (2.31)
Musculoskeletal pain (n=223)		
Severity (strongest)	0–10	6.93 (2.17)
Interference	41.60–75.60	58.61 (7.33)

SD, standard deviation; CSI-25, original 25-item central sensitization inventory; CSI-9, 9-item central sensitization inventory; IBD, inflammatory bowel disease; SIBDQ, short inflammatory bowel disease questionnaire. [a]Harvey Bradshaw Index (Crohn's disease) and Simple Clinical Colitis Activity Index (ulcerative colitis).

Criterion validity

The CSI-9 demonstrated significant association with CSI-25 (*rho*=0.89, $p<0.001$). The $ICC_{3,1}$ between CSI-9 and CSI-25 was 0.64 (95% confidence interval, 0.58–0.69), suggesting substantial agreement.

Correlation to clinical features

The CSI-9 and CSI-25 demonstrated significant correlation with all the observed clinical features (Table 2). Of these features, CSI-9 and CSI-25 demonstrated the strongest association with SIBDQ (*rho*=−0.58 and −0.65, respectively, $p<0.001$), indicating that poor health-related quality of life was associated with higher CSI scores on both scales. Similarly, higher CSI-9 and CSI-25 scores demonstrated moderate association with increased IBD activity scores (*rho*=0.43 and 0.49, $p<0.001$), greater total comorbidity scores (*rho*=0.39 and 0.46, $p<0.001$), greater MSK pain interference (*rho*=0.40 and 0.45, $p<0.001$), and worse MSK pain severity (*rho*=0.33 and 0.35, $p<0.001$). Higher CSI-9 and CSI-25 scores demonstrated weak association with worse abdominal pain severity (*rho*=0.19 and 0.27, $p<0.001$).

Discriminate analysis

ROC analysis (Figure 1) and AUC (95% CI) indicated that CSI-9 (0.788 (0.725, 0.851), $p<0.001$) and CSI-25 (0.808 (0.750, 0.867), $p<0.001$) were able to adequately

Table 2: Rank-order correlation of clinical features to the original and short form of the central sensitization inventory (n=320).

Clinical feature	CSI-9 (*Rho*)	CSI-25 (*Rho*)
IBD activity	0.43*	0.49*
SIBDQ	−0.58*	−0.65*
Comorbidity	0.39*	0.46*
Musculoskeletal pain severity	0.33*	0.35*
Musculoskeletal pain interference	0.40*	0.45*
Abdominal pain severity	0.19*	0.27*

CSI-9, 9-item central sensitization inventory; CSI-25, original 25-item central sensitization inventory; IBD, inflammatory bowel disease; SIBDQ, short inflammatory bowel disease questionnaire. *Significant at p<0.001.

discriminate between participants with and without pain. The maximum Youden Index suggests that the optimal cut-off score to discriminate individuals with self-reported abdominal and/or MSK pain is ≥17 for CSI-9 and ≥40 for CSI-25 (Table 3). A cut-off value of 17 for CSI-9 represented a sensitivity and specificity of 83.5 and 61.7%, respectively, whereas a cut-off of 40 for the CSI-25 demonstrated a sensitivity and specificity of 73.5 and 76.7%, respectively.

Table 3: Central sensitization inventory original and short form cut-off scores for discriminating the presence of self-reported pain experiences in patients with IBD.

Version	Cut-off score	Sn, %[a]	Sp, %[b]	YI	AUC (95% CI)
CSI-9	15	88.8	48.3	0.372	0.788
					(0.725, 0.851)*
	16	86.5	56.7	0.432	
	17	**83.5**	**61.7**	**0.451**	
	18	78.5	65.0	0.435	
	19	71.9	70.0	0.419	
	20	66.2	73.3	0.395	
CSI-25	37	77.7	61.7	0.394	0.808
					(0.750, 0.867)*
	38	75.8	68.3	0.441	
	39	75.0	73.3	0.483	
	40	**73.5**	**76.7**	**0.501**	
	41	70.4	78.3	0.487	
	42	67.7	80.0	0.477	

Bold font represents cut-off values indicated by the highest Youden's Index. IBD, Inflammatory bowel disease; Sn, sensitivity; Sp, Specificity; YI, Youden's Index; AUC, area under the curve; CI, confidence interval; CSI, central sensitization inventory. *Significant at p<0.001. [a]Sensitivity: the proportion of actual positive results that were correctly identified. [b]Specificity: the proportion of negative results that were correctly identified.

Between-group comparison

Comparison of participant features between the high and low groups for both CSI measures are presented in Table 4. Of the examined features, abdominal pain severity was significantly different between high/low groups for the CSI-25 (p=0.002) but did not demonstrate a significant difference between the CSI-9 high/low groups (p=0.236). All the remaining features demonstrated significant between group differences for both CSI-9 and CSI-25, with the exception of age (p=0.291 and 0.643, respectively) and IBD subtype (p=0.115 and 0.675, respectively).

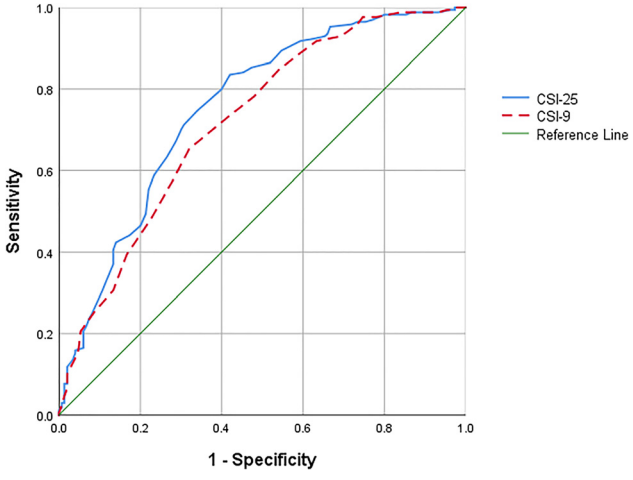

Figure 1: Receiver operating characteristic curve analyses for the 9-item central sensitization inventory (CSI-9) and the original 25-item CSI (CSI-25) to discriminate the presence of self-reported pain in individuals with IBD.

Discussion

The purpose of this study was to evaluate the performance of the CSI-9 compared to the original CSI-25 in individuals with IBD. This study found a substantial agreement between the CSI measures ($ICC_{3,1}$=0.64) in this population, with similar associations to multiple participant features and unique cut-off values for discriminating the presence of self-reported pain. These results are similar to previous investigation of the psychometric properties of the CSI-9 in individuals with MSK pain (n=505), where the $ICC_{3,1}$ between CSI-25 and CSI-9 was 0.69 (95% CI, 0.64–0.73) [32].

Similarly, study results support previous reports which have demonstrated that associations with clinical features did not differ significantly between the two versions of CSI [32, 35]. In the present study, associations between CSI-25 and CSI-9 to SIBDQ (*rho*=−0.65 and −0.58, p<0.001) and

Table 4: Comparison of participant features between the CSI-9 and CSI-25 high symptom and low symptom groups based on cut-off scores to discriminate self-reported pain among individuals with IBD.

Feature	CSI-9			CSI-25		
	Low (<17) (n=80)	High (≥17) (n=240)	p	Low (<40) (n=115)	High (≥40) (n=205)	p
Gender (female, n [%])	52 (65)	204 (85)	0.001[a,*]	79 (69)	177 (86)	0.001[a,*]
Age (mean, SD)	46.2 (17.5)	43.3 (13.5)	0.291[b]	45.0 (16.8)	43.5 (13.2)	0.643[b]
IBD subtype (yes, n [%])			0.115[a]			0.675[a]
Crohn's disease	45 (56)	163 (68)		72 (63)	136 (66)	
Ulcerative colitis	33 (41)	69 (29)		40 (35)	62 (30)	
Indeterminate colitis	2 (3)	8 (3)		3 (2)	7 (4)	
Comorbidity count (mean, SD)	1.9 (1.5)	3.5 (2.1)	<0.001[b,*]	2.0 (1.7)	3.7 (2.0)	<0.001[b,*]
IBD activity (yes, n [%])	28 (35)	160 (67)	<0.001[a,*]	40 (35)	148 (72)	<0.001[a,*]
SIBDQ (mean, SD)	54.0 (7.6)	43.9 (8.9)	<0.001[b,*]	53.0 (7.0)	42.8 (9.0)	<0.001[b,*]
Abdominal pain (n, %)			<0.001[a,*]			<0.001[a,*]
Yes	24 (30)	150 (63)		38 (33)	136 (66)	
No	56 (70)	90 (37)		77 (67)	69 (34)	
Abdominal pain severity (mean, SD)	3.8 (3.0)	4.5 (2.2)	0.236[b]	3.4 (2.6)	4.7 (2.1)	0.002[b,*]
MSK pain (n, %)			<0.001[a,*]			<0.001[a,*]
Yes	33 (41)	190 (79)		52 (45)	171 (83)	
No	47 (59)	50 (21)		63 (55)	34 (17)	
MSK pain interference (mean, SD)	53.9 (8.6)	59.4 (6.8)	<0.001[b,*]	54.3 (7.7)	59.9 (6.7)	<0.001[b,*]
MSK pain severity (mean, SD)	5.4 (3.0)	7.2 (1.9)	0.002[b,*]	5.7 (2.5)	7.3 (1.9)	<0.001[b,*]
Pain type (n, %)			<0.001[a,*]			<0.001[a,*]
None	37 (46)	23 (10)		46 (40)	14 (7)	
Abdominal only	10 (12)	27 (11)		17 (15)	20 (10)	
MSK only	19 (24)	67 (28)		31 (27)	55 (27)	
Abdominal and MSK	14 (18)	123 (51)		21 (18)	116 (56)	

CSI, central sensitization inventory; IBD, inflammatory bowel disease; SIBDQ, short inflammatory bowel disease questionnaire; SD, standard deviation; MSK, musculoskeletal. *Significant at p<0.05. [a]Chi-squared. [b]Mann–Whitney U.

abdominal pain severity (*rho*=0.27 and 0.19, respectively, p<0.001) represent the greatest differences between the CSI tools in their strength of association with clinical features. SIBDQ assesses numerous consequences of IBD on an individual's quality of life, including bowel and systemic symptoms [45]. As previously indicated, some of the items omitted from the CSI-9 also examine symptoms commonly seen in IBD patients as a consequence of disease processes [31]. As such, the removal of these items may explain the weaker association between the CSI-9 and SIBDQ scores compared to the original CSI-25.

Current study results suggest that abdominal pain severity in patients with IBD is poorly associated with both CSI tools. Conversely, MSK pain experiences (i.e., severity and interference) demonstrated moderate associations with the CSI tools. This difference between pain severity correlations suggests that abdominal pain severity may be less related to central sensitization symptomology, and thus likely to be related to other constructs (i.e., structural disease processes). However, it is important to note that associations in the present study do not account for influences from factors which have previously demonstrated independent association with CSI and pain severity scores, such as sex [32, 41], comorbidity count [41], and IBD activity scores [13]. As such, it is unclear whether accounting for these additional factors would result in stronger observed associations between abdominal pain severity and CSI scoring.

In the present study, AUC results suggest that CSI-9 and CSI-25 are able to adequately discriminate the presence of self-reported pain in individuals with IBD, using cut-off values of 17 and 40, respectively. However, although the sensitivity and specificity of the CSI-25 cut-off point were relatively similar (i.e., 73.5 and 76.7%, respectively), the cut-off for CSI-9 demonstrated a greater difference (i.e., 83.5 and 61.7%, respectively). This suggests that although CSI-9 was able to more accurately identify participants with self-reported pain compared to the CSI-25, it was less accurate in correctly identifying the absence of pain. As such, although CSI-9 may be useful as

an initial screening tool to identify IBD patients with an increased likelihood of having pain, positive findings should prompt further confirmatory investigations.

Current results demonstrate significant differences between high and low symptom groups for both CSI versions with regards to correlations with multiple participant features. Generally speaking, participants in the high CSI groups were more likely to be female and found to have worse health-related quality of life, greater comorbidity, and worse pain experiences. Although there were more female participants (n=256, 80%) in the present study, these results are similar to previous reports in multiple painful MSK conditions, suggesting that CSI may be capturing a similar construct in individuals with IBD [22, 23, 55, 56]. However, future research should utilize gender matched investigations to confirm study findings. Finally, with the exception of abdominal pain severity, all study features trended in a very similar manner across both CSI versions. This suggest that the items omitted in the CSI-9 may have little if any impact in determining the profile of the high/low symptom groups in individuals with IBD.

As previously stated, abdominal pain is considered a primary symptom of active IBD processes. Therefore, it is unsurprising that the percentage of participants with abdominal pain across the groups were very similar to those who met criteria for active IBD, with a similar trend seen in both CSI versions (Table 4). Additionally, although abdominal pain severity was not found to be significantly different between the CSI-9 groups, the interpretation of the severity values seen in the CSI-25 groups vs. those of CSI-9 are unlikely to be clinically meaningful.

This is the first study to explore and validate the use of CSI-9 in individuals with IBD. Study findings report notable similarities between associations of multiple participant features and both CSI tools. Consequently, study results suggests that the CSI-9 is suitable to use as a brief tool in patients with IBD, with suggested cut-off value of 17 to screen for individuals with pain (i.e., abdominal and/or MSK). However, the use of CSI-9 to monitor patients' response to treatments and/or the development of chronic pain is still unknown. Therefore, future research should explore the use of continuous CSI-9 scoring as a clinical tool to prospectively identify patients at-risk of developing chronic pain and/or to monitor treatment responses. Additionally, future research exploring the relationship between other IBD clinical features and both CSI versions may provide greater depth of understanding of current study findings and for the use of these measures in this population. The present study included an online survey precluding the ability to utilize clinical assessments in study participants, which may have strengthened study findings. CSI-9 in the present study was extracted from one administration of the original CSI-25. Future research investigating independent administration of CSI-9 would allow for more definitive conclusions regarding its performance in individuals with IBD when compared to the CSI-25.

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