Prospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
50(5) 1–10

DOI: 10.1177/03000605221098868
journals.sagepub.com/home/imr
SAGE

Evaluation of health-related quality of life and influencing factors in patients with Crohn disease

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Abstract

Objective: We assessed levels of anxiety and depression in patients with Crohn disease (CD) to identify predictors of health-related quality of life (HRQOL).

Methods: In this case-control study, we enrolled 50 adult patients with CD and 50 matched, healthy controls. All participants completed self-administered questionnaires including the Self-rating Anxiety Scale (SAS), Self-rating Depression Scale (SDS), Short Form-36 Health Survey (SF-36), and Short Inflammatory Bowel Disease Questionnaire (IBDQ, patients only). We analyzed the relationship between HRQOL and influencing factors.

Results: Mean total scores on the SAS, SDS, and SF-36 were significantly different between patients and controls. IBDQ scores among patients in the active phase of CD were significantly lower than those in remission phase. SF-36 scores were significantly lower in patients with CD compared with healthy controls. SF-36 scores among patients with active CD were significantly lower than scores among those in remission, and SF-36 scores in patients without complications were significantly higher than in those with complications. SF-36 scores in patients with good nutritional status were also significantly higher than scores in malnourished patients with CD.

Conclusions: Depression, anxiety, disease activity, complications, and nutritional status were predictive factors of decreased HRQOL in patients with CD.

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Keywords
Crohn disease, health-related quality of life, short form-36 health survey, active disease, complication, nutritional status

Date received: 1 February 2022; accepted: 19 April 2022

Introduction

Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn disease (CD), has a nonspecific etiology and the incidence and prevalence of IBD are increasing.[1] To date, there is no definite cure for CD, and treatment is concentrated on managing the inflammatory response and maintaining remission with a focus on maintenance therapy.[2]

Psychological effects from CD and medications are experienced by many patients. Anxiety disorders and depression can have a profound effect on quality of life (QOL), including the ability to work and maintain a family life. There is no doubt that stress is a triggering and exacerbating factor connected with the course and symptoms of CD.[3] Although an annual increase in the number of patients with CD had been documented in China, very few studies have focused on both health-related quality of life (HRQOL) and psychological symptoms in these patients.

CD involves a chronic progressive process that is characterized by intermittent recurrence. Disease activity influences a number of mechanisms, including metabolic disturbances associated with chronic inflammation, protein-losing enteropathy, chronic blood loss, and malabsorption, as well as side effects of medication.[4] Higher CD disease activity increases the likelihood that patients will have poorer QOL and advancing malnutrition.[5] Many of these patients have severe forms of gastrointestinal (GI) and systemic illness, and some patients experience a series of complications. These outcomes can temporarily or permanently lower patients' HRQOL.[6]

The Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) are self-report questionnaires used to assess disease symptoms, severity, and clinical status.[7,8] HRQOL is defined as a multidimensional concept that is used to assess health-related physical, emotional, and social functions.[9] Patients with CD have higher rates of depression and may have higher rates of other anxiety-related disorders.[10]

In this study, we investigated depression and anxiety levels as well as HRQOL among patients with CD to identify predictive risk factors of decreased HRQOL in these patients.

Methods

Patients

In this case-control study, we recruited patients with CD from the First Hospital of Soochow University between January 2019 and December 2020. The diagnostic criteria for all patients were those set out in the 2007 guidelines of the Chinese Medical Association "The Specification Consensus for Right Diagnosis and Treatment of Inflammatory Bowel Disease in China."[11] In our patients, CD was classified as active disease or remission according to the CD Activity Index (CDAI). Healthy volunteers without a family history of IBD or related diseases were also recruited from the First People's Hospital of Soochow University during the same period and included as normal controls.

An anonymous, self-administered questionnaire was sent to all participants via an Internet platform.

The Ethics Committee of the First Hospital of Soochow University approved the study protocol. The patients participating in the study provided written formed consent. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[12]

Clinical features of patients

A demographic survey was used to collect information on sex, age, marital status (married, unmarried or divorced), education level (middle school or below, college degree or above), medical insurance (none or residents' basic health insurance), use of biologic therapy (yes or no), surgery (yes or no), and disease status (active or remission). The criteria used for clinical disease activity were those stipulated in the CDAI.[13] The Patient-Generated Subjective Global Assessment (PG-SGA) incorporates a numerical score as well as a global rating of nutritional status (well-nourished, malnourished or severely malnourished). Patients were scored and categorized as follows: 0–1, no nutritional intervention required at present; 2–3, educational intervention by a dietitian or clinician for symptom management; 4–8, intervention by a dietitian indicated with physician consultation; and $\geq$9, critical need for dietary intervention and symptom management.[14] For each component of the PG-SGA, 0–4 points are awarded according to the impact of symptoms on nutritional status. The higher the score, the greater the risk of malnutrition.

Emotional status

Patients' anxiety levels were judged using the Self-rating Anxiety Scale (SAS) and depression was estimated using the Self-rating Depression Scale (SDS). In both scales, scores for each item range from 1 to 4. The scores for each scale were multiplied by 1.25. A score of 50 or more on the SAS indicates anxiety, and a score of more than 53 on the SDS indicates sustained depression. Higher scores on these scales are related to a greater likelihood of psychological morbidity.

Health-related quality of life (HRQOL)

The 10-item Inflammatory Bowel Disease Questionnaire (IBDQ) has been applied effectively in patients with IBD.[15] The IBDQ includes physical, social, emotional, and systemic domains. The questionnaire is graded on a scale from 1 to 7 (severe to no problem at all, respectively). Total scores range from 10 (poor) to 70 (best).

The Medical Outcomes Study Questionnaire Short Form 36, or Short Form-36 Health Survey (SF-36), address general health parameters and is designed for the evaluation of general populations and for health policies.[16] The SF-36 is also applied in clinical practice and research related to certain diseases. The SF-36 includes 36 items in two dimensions, the physical component summary (PCS) and mental component summary (MCS). The PCS comprises four subscales: physical function (PF), role limitations owing to physical health (RP), bodily pain (BP), and general health perceptions (GH). The MCS also comprises four subscales: vitality (VT), social functioning (SF), role limitations owing to emotional problems (RE), and mental health (MH). Scores range from 0 to 100 for each subscale in both dimensions, with higher scores indicating better health.

Statistical analysis

All demographic, clinical, physical, and psychological variables were included in

descriptive analyses. Categorical variables are reported as frequency (percentage), and continuous variables are reported as mean ± standard deviation or standard error. The Student *t* test was used to compare differences in the SAS, SDS, IBDQ, and SF-36 scores between two groups. For demographic and clinical variables in patients with CD, we used multiple regression analyses to identify the determinants of HRQOL. We used IBM SPSS version 19.0 to analyze all data (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

Fifty adult patients with CD, and 50 matched healthy controls were enrolled in this study. Fifty adult patients with CD (14 male and 36 female patients, age 14–60 years), and 50 matched healthy controls (19 male and 31 female patients, age 15–57 years), were enrolled in this study. General demographic information of the included patients with CD are summarized in Table 1, according to the Montreal revision (2005) of the Vienna classification, which is considered the international standard of subtyping in CD. Overall, 26 (52%) patients were less than age 16 years, 20 (40%) were between age 17 and 40 years, and 4 (8%) were more 40 years old. The region of involvement was the terminal ileum in 28 (56%) patients, colon in 19 (38%) patients, and ileocolon in 3 (6%) patients. As for the behavior of CD, 8 (16%) patients were classified as having non-stricturing non-penetrating disease (designated as B1), 39 (78%) as having stricturing disease (B2), and 3 (6%) patients as having penetrating disease (B3). The occurrence of perianal fistulae and abscesses is considered a "modifier," denoted with a "P" (for perianal) added to B1, B2 or B3.

Table 1. Montreal phenotype classification in patients with CD.

Montreal phenotype classification	n (%)
Age (A), y	
A1 (≤16)	26 (52%)
A2 (17–40)	20 (40%)
A3 (>40)	4 (8%)
Location (L)	
L1: terminal ileum	28 (56%)
L2: colon	19 (38%)
L3: ileocolon	3 (6%)
L4: upper GI	0 (0%)
L1 + L4: terminal ileum + upper GI	0 (0%)
L2 + L4: colon + upper GI	0 (0%)
L3 + L4: ileocolon + upper GI	0 (0%)
L4: upper GI only	0 (0%)
Behavior (B)	
B1: non-stricturing, non-penetrating	8 (16%)
B2: stricturing	39 (78%)
B3: penetrating	3 (6%)
Occurrence of perianal fistulae and abscesses (P)	
B1P: non-stricturing, non-penetrating with perianal fistulae and abscesses	4 (8%)
B2P: stricturing with perianal fistulae and abscesses	2 (4%)
B3P: penetrating with perianal fistulae and abscesses	2 (4%)

CD, Crohn disease; GI, gastrointestinal.

A total of 4 (8%) patients were classified as B1P, 2 (4%) as B2P, and 2 (4%) as B3P.

SAS and SDS in patients with CD

In our study, both the mean SAS score (38.78 ± 6.4) and mean SDS score (47.08 ± 9.5) among patients with CD was found to be significantly higher than scores ($SAS = 34.57 \pm 6.7$, $SDS = 43.23 \pm 8.7$) among control participants ($p < 0.05$) (Figure 1).

HRQOL in patients with CD

In patients with CD, mean IBDQ scores in the active phase of disease were lower than those in the remission phase (Table 2). Mean physical symptoms scores were

49.50 ± 7.62 and 60.12 ± 4.01 among patients in active phase and those in remission phase, respectively. Mean systemic symptom scores in these groups were 23.92 ± 5.07 and 26.24 ± 3.97, and mean emotional function scores were 57.13 ± 15.62 and 67.34 ± 15.17, respectively. Mean respective social function scores were 22.15 ± 9.08 and 25.44 ± 2.03.

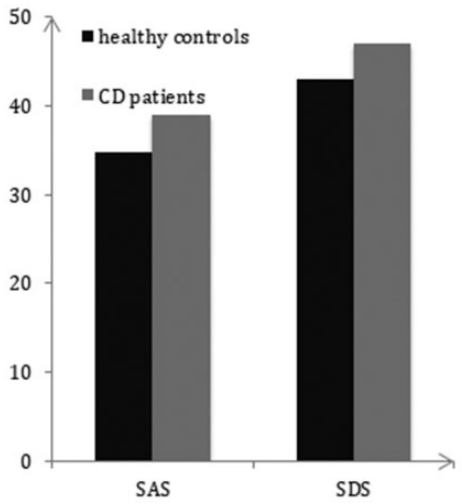

Figure 1. SAS and SDS total scores between patients with CD and healthy controls (mean ± standard error).
*$p < 0.05$ indicates a significant difference between patients with CD and healthy controls.
SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale.

These scores demonstrated significantly lower HRQOL among patients with active disease than among patients in remission ($p < 0.05$). The total SF-36 score was significantly different between patients with CD and healthy controls ($p < 0.05$). Comparing each subscale, scores for PF, RP, and MH differed between patients with active disease and those in remission ($p < 0.05$). PF, RF, BP, RE and MH scores in patients with complications were significantly lower than those in patients with no complications. Subscale scores of GH and VT were relatively lower for malnourished patients than for well-nourished ones ($p < 0.05$) (Table 3 and Figure 2).

Mean SF-36 domain scores of patients with CD and different clinical factors

As shown in Table 4, we conducted multivariate regression analyses to assess the relationship between IBDQ domains and general characteristics of patients with CD. We found a significant correlation between IBDQ domains and disease activity status, as well as nutritional risk ($p < 0.05$). No significant correlations were found between IBDQ domains and sex, age, marital status, educational background, medical insurance, use of biologics, and surgery ($p > 0.05$).

Table 2. IBDQ scores according to disease activity indices.

	Crohn disease (N = 50)		
IBDQ domain	Active * (n = 33)	Remission (n = 17)	P‡
Physical symptoms	49.50 ± 7.62	60.12 ± 4.01	$p < 0.05$
Systemic symptoms	23.92 ± 5.07	26.24 ± 3.97	$p < 0.05$
Emotional function	57.13 ± 15.62	67.34 ± 15.17	$p < 0.05$
Social function	22.15 ± 9.08	25.44 ± 2.03	$p < 0.05$

*Disease activity assessed using the Crohn Disease Activity Index.
‡Student *t* test.
Values in the table are mean ± standard error.
IBDQ, Inflammatory Bowel Disease Questionnaire.

Table 3. SF-36 domain scores in patients according to clinical factors.

	Clinical stage		Clinical features		Nutritional status	
Domain	Active	Remission	Complications	No complications	Well-nourished	Malnourished
PF	60.02 ± 20.12	73.81 ± 20.12*	61.27 ± 23.08	70.79 ± 23.08#	80.23 ± 30.11	76.32 ± 21.07
RP	31.59 ± 40.72	56.37 ± 42.34*	30.26 ± 33.15	48.34 ± 46.89#	48.337 ± 21.07	39.45 ± 37.30
BP	67.69 ± 24.21	74.21 ± 22.14	66.12 ± 21.09	81.14 ± 23.09#	72.43 ± 27.318	71.10 ± 26.00
GH	40.02 ± 21.34	46.62 ± 21.49	43.69 ± 21.91	50.47 ± 18.28	50.63 ± 23.21@	38.01 ± 18.53
VT	52.83 ± 17.83	60.51 ± 17.79	59.83 ± 16.43	63.01 ± 18.66	70.23 ± 18.80@	50.26 ± 17.28
SF	75.49 ± 24.07	80.62 ± 24.97	82.75 ± 23.43	86.17 ± 25.27	90.39 ± 20.02	87.06 ± 20.33
RE	38.56 ± 41.13	42.02 ± 42.65	24.43 ± 44.37	58.52 ± 39.09#	60.65 ± 45.00	55.04 ± 44.21
MH	63.32 ± 11.71	80.03 ± 14.64*	57.27 ± 12.25	75.24 ± 17.01#	76.30 ± 21.13	72.15 ± 17.57

Notes: Versus active, $p \leq 0.05$; versus complications, $p \leq 0.05$; versus well-nourished, $p \leq 0.05$.
Values in the table are mean ± standard error.
SF-36, Short Form-36 Health Survey; PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health.

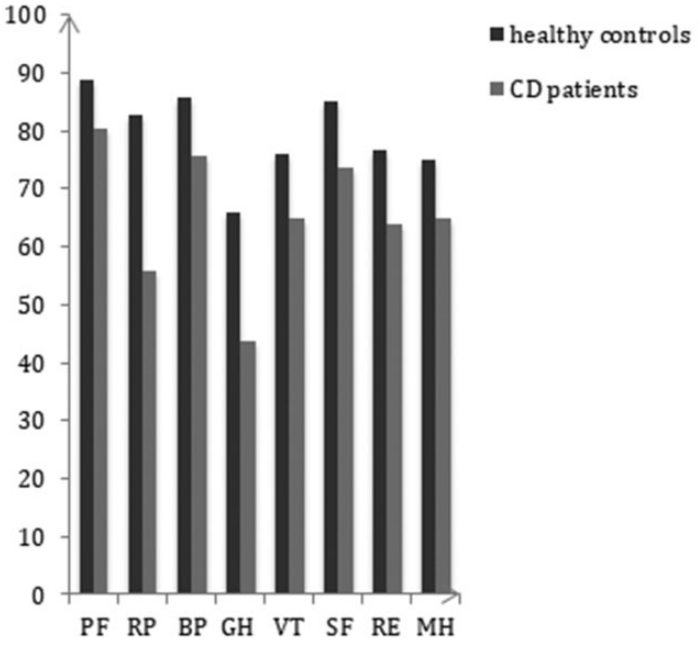

Figure 2. SF-36 summary scores and subscale scores between patients with CD and healthy controls (mean ± standard error).
*$p < 0.05$ indicates a significant difference between patients with CD and healthy controls.
CD, Crohn disease; SF-36, Short Form-36 Health Survey; PF, physical functioning; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health.

Discussion

The relationship between psychiatric symptoms and the GI environment are well studied in various GI disorders. In comparison with healthy controls, more severe symptoms of depression and anxiety are

Table 4. Multivariate regression analyses of the relationship between HRQOL and predictor variables.

	IBDQ scores (mean ± SE)	*t*	P
Sex		1.045	>0.05
Male	161.67 ± 33.1		
Female	157.67 ± 34.2		
Age, y		0.837	>0.05
<35	158.07 ± 36.4		
≥35	162.53 ± 30.6		
Marital status		0.840	>0.05
Married	157.71 ± 34.9		
Unmarried or divorced	161.03 ± 32.4		
Educational level		0.127	>0.05
Middle school or below	155.71 ± 33.1		
College degree or above	160.53 ± 31.7		
Medical insurance		0.713	>0.05
No insurance	157.03 ± 31.9		
Residents' basic health insurance	163.81 ± 30.5		
Use of biologic therapy		0.306	>0.05
Yes	156.09 ± 31.2		
No	161.23 ± 34.7		
Surgery		0.997	>0.05
Yes	153.09 ± 32.5		
No	160.19 ± 31.4		
Disease status		2.357	<0.05
Active	154.83 ± 27.5		
Remission	187.14 ± 30.1		
Nutritional risk		2.171	<0.05
Yes	153.26 ± 31.1		
No	185.01 ± 29.7		

IBDQ, Inflammatory Bowel Disease Questionnaire; HRQOL, health-related quality of life.

reported among individuals with non-erosive reflux disease, irritable bowel syndrome, and functional dyspepsia.[17] Patients with IBD may have a higher lifetime rate of depression and anxiety disorders.[10]

In the current study, we investigated the status of patients with CD in terms of psychological characteristics and HRQOL levels. Our evaluation of patients' SAS and SDS scores showed that patients with CD exhibited more severe symptoms of anxiety and depression. Our findings are generally in accordance with those of other studies. Kim et al. revealed that the prevalence rates of depression and anxiety decreased during periods of IBD remission to 33% and 27%, respectively.[18] The evidence suggests a possible cyclical relationship in CD whereby GI symptoms increase an individual's risk for worsening mood symptoms, which subsequently increase their risk for worsening physical symptoms.

The IBDQ is a commonly used tool for the assessment of QOL in patients with CD.[19] An association between clinical symptoms and QOL is reasonable and has been previously confirmed in web-based surveys by Kappelman et al. and Long et al. using the IBDQ.[20,21] We found that all IBDQ subscale scores were significantly lower in the active-phase group than those

among patients in remission. We found statistically significant differences between active phase and remission phase in scores related to GI symptoms, systemic symptoms, emotional function, and social function. The main intestinal complications of CD include acute inflammation of the intestines, ulcers, obstruction, and perforation. Many studies have revealed that mood dysfunction and psychological stress can trigger relapses in IBD.[22–24] Among patients with CD, anxiety is associated with mood, stress, abdominal pain, and lower socioeconomic status.[25] Patients with poor coping skills or little social support, as well as those with certain personality traits such as neuroticism, may be predisposed to feeling frustrated or sad and to avoiding social interactions.

Clinical observations have indicated that stressful experiences can adversely influence the course of CD. The notion of perceived stress involves an individual's subjective perception of and emotional response to stress. Stress is a triggering and exacerbating factor connected with the course and symptoms of IBD.[26] A negative relationship between psychological stress and the development of IBD has been found. [27] Together with patients' awareness that they have an incurable disease that has an uncertain course and prognosis as well concerns about the need for surgery or increased risk of developing carcinoma, these factors are likely to lead to anxiety and depression in patients with IBD.[28]

CD can negatively affect QOL owing to depression and anxiety as well as social isolation and altered self-image.[29] Our findings support the strong discriminating capability of the IBDQ in assessing clinical symptoms, with a strong correlation between symptom scores and each score on the SF-36. In our study, patients with CD had lower SF-36 scores than scores in healthy controls. A bidirectional relationship exists between psychological comorbidity and CD, with each producing an effect on the course of the other.[24] Hence, social and psychological support and interventions should be provided earlier in patients diagnosed with CD and should be included in further investigations.

Our findings are in line with those of other studies showing that active disease is a typical risk factor for poor QOL in patients with IBD and that QOL among patients in remission is better than that among individuals with active disease.[30] There are few reports in China evaluating the correlation of HRQOL with the clinical status of CD. Our data showed that disease activity, having complications, and malnourishment were correlated with lower HRQOL. Our research results showed that disease activity was an independent predictive factor for impaired HRQOL, with patients who had active CD showing significantly lower SF-36 mean scores (PE, RP, MH) than those in remission. Patients with more complications, such as perianal abscess and fistula formation, had lower HRQOL (PF, RP, BP, RE, and MH scores) than those without complication.

In one study, malnourished patients were more likely than well-nourished patients to be underweight and to have more active flare-ups and more IBD-related hospital admissions over the preceding 12 months.[31] Malnourished patients have greater unintentional weight loss, a pronounced reduction in food intake, and more GI-related symptoms, including diarrhea, which could be the result of disease activity, surgery, or medications. In all SF-36 domains, clinically malnourished patients with CD had lower HRQOL (GH and VT scores), which is likely to have an impact on the progression of clinical symptoms, such as unintentional weight loss, abdominal pain, and diarrhea. Hence, nutritional support could be an appropriate therapy for malnourished patients with CD.

Multivariate regression analyses also showed that disease activity and nutritional status were correlated with HRQOL. There was no correlation with sex, age, marital status, educational level, or biologic therapy, in line with the findings of other studies.[32]

There are some limitations in our research. First, the number of patients with CD enrolled in our study was small. Second, very few of our patients were using biologic therapy; therefore, we could not effectively assess whether this was an independent risk factor of poor HRQOL. Hence, studies including larger samples from multiple centers and follow-up visits are needed in future investigations.

Conclusion

Depression and anxiety significantly influence HRQOL in patients with CD. We identified depression, anxiety, disease activity, complications, and malnourished status as predictive factors of decreased HRQOL in these patients.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The authors received financial support for the research, authorship, and/or publication of this article from the Clinical Immunology Key Laboratory Open Research Project of Jiangsu Province (KJS2110) and Suzhou Science & Technology plan project (SYS201747).

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