

Fatigue, Physical Activity, and Quality of Life in Patients with Inflammatory Bowel Disease: A Cross-Sectional Study

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Purpose: The benefits of physical activity (PA) are widely recognized, but the intensity of PA in inflammatory bowel disease (IBD) patients with varying disease activity levels remains controversial. We aimed to investigate the relationship between PA levels, fatigue, and other health-related quality of life (QoL) in Chinese IBD patients.

Patients and Methods: The study is a cross-sectional investigation conducted at a comprehensive IBD diagnosis and treatment facility in East China, spanning from August 2022 to February 2023. A total of 245 participants were initially enrolled, and after excluding individuals with incomplete data about crucial exposure and outcome variables, the final sample size amounted to 237. Participants were provided with a questionnaire encompassing sociodemographic factors, clinical information, the International Physical Activity Questionnaire (IPAQ), the Multidimensional Fatigue Inventory (MFI-20), and the Inflammatory Bowel Disease Questionnaire (IBDQ). Correlation analysis was employed to assess the relationship between variables.

Results: A majority of participants (144) exhibited low levels of PA. Furthermore, 40.5% of all participants reported experiencing fatigue. Individuals with low levels of PA had an average MFI-20 score of 62.9 ± 16.0 . Correlation analysis showed that PA was significantly and negatively associated with fatigue ($r = -0.224$, $p < 0.001$). Additionally, PA was also negatively correlated with anxiety ($r = -0.150$, $p < 0.05$) and depression ($r = -0.242$, $p < 0.001$). On the other hand, PA was positively correlated with quality of life (QoL) ($r = 0.171$, $p < 0.01$). Furthermore, our analysis indicated that sleep disorders were positively associated with both anxiety ($r = 0.349$, $p < 0.01$) and depression ($r = 0.354$, $p < 0.001$).

Conclusion: The levels of PA are significantly low, and there is a high prevalence of fatigue among individuals with IBD. PA in IBD showed a strong negative correlation with fatigue and a strong positive correlation with quality of life.

Keywords: physical activity, inflammatory bowel disease, fatigue, quality of life

Introduction

Inflammatory bowel disease (IBD), namely Crohn's disease (CD) and ulcerative colitis (UC), refers to a group of chronic relapsing diseases of the gut that cannot be cured. In addition to intestinal symptoms, patients also experience psychosomatic symptoms such as fatigue,¹ anxiety or depression² and insomnia,³ which often cause them to be absent from their studies or workplaces.⁴ According to recent data, the global prevalence of IBD episodes has reached 6.8 million, with an upward trend over the past few decades,⁵ especially in the emerging industrialized countries of Asia,⁶ where the age of onset is gradually younger.⁷ Overall, it imposes a heavy economic burden on patients and the social healthcare system,⁸ and it has become a global public health problem.⁹

Apart from conventional medication, many IBD patients consult their healthcare providers for lifestyle recommendations in an effort to manage or potentially reverse their condition.¹⁰ Besides, the International Organization for Study of Inflammatory Bowel Disease states that it is particularly important to manage the disease through a healthy and active

lifestyle to achieve improvement in the physical and psychological symptoms of patients.¹¹ Among other chronic diseases, it is possible that exercise may have anti-inflammatory effects.¹² Fatigue is defined as a profound sensation of mental and/or physical exhaustion that persists even after periods of rest and sleep,^{13,14} and is frequently experienced by IBD patients, particularly in active enteritis. In chronic diseases, subclinical inflammation with elevated pro-inflammatory cytokines, such as interferon and TNF- α , has been proposed as the trigger for fatigue.¹⁵ Multiple studies have demonstrated the positive impact of exercise on fatigue in individuals with IBD.^{16–18} However, following an IBD diagnosis, patients tend to engage in significantly less physical activity (PA).¹⁹ Moreover, there is limited research on the intensity of PA and levels of fatigue in IBD patients with varying levels of disease activity,²⁰ and many controversial aspects still exist. Therefore, it is crucial to understand the relationship between the levels of PA, fatigue, and other health-related quality of life (QoL) in IBD patients.

This study aims to assess the levels of PA and fatigue in IBD patients, as well as to examine the correlation between varying levels of PA, fatigue, and other health-related QoL.

Materials and Methods

Study Design

The current study is a cross-sectional study performed at a nationwide IBD diagnosis and treatment center in East China, from August 2022 to February 2023. Those having an IBD diagnosis and who gave informed consent to participate in the study made up the study population. Participants had to be at least 18 years old. The Chinese IBD Diagnosis and Treatment Standards are the foundation for IBD diagnosis.²¹ Patients who could not understand or finish the survey were among the exclusion criteria. A total of 245 individuals were recruited in person by uniformly trained investigators using standardized language techniques. After excluding individuals with missing data on important exposure and outcome variables, the final sample size was 237. Subjects' demographic characteristics and clinical data such as gender, age, marital status, employment status, education, smoking status, health insurance, disease subtype, disease duration, IBD-related surgeries, disease activity (measured by the Mayo score for UC and the Crohn's disease activity index (CDAI) for CD), and medications were collected from the hospital information system.

Statement of Ethics

The research was conducted in compliance with the ethical guidelines outlined in the Declaration of Helsinki and received approval from the Ethics Committee of the Affiliated Hospital of Nanjing University of Chinese Medicine. Furthermore, informed consent was obtained from all participants involved in the study (2023NL-004-02).

Description of the Questionnaires and Outcomes

Each participant completed six effective questionnaires: International Physical Activity Questionnaire (IPAQ), the Multidimensional Fatigue Inventory (MFI-20), Fatigue Severity Scale (FSS), Pittsburgh Sleep Quality Index (PSQI), Hospital Anxiety and Depression Scale (HADS), and Inflammatory Bowel Disease Questionnaire (IBDQ).

The Chinese version of the IPAQ²² was used to assess PA levels, and we used a long scale to assess the amount of PA during the previous week. It is composed of 27 entries, and ultimately, the PA level of the individuals was categorized into three groups: high PA group, medium PA group, and low PA group. The unit of exercise is expressed using MET-min/week. The IPAQ has a specific scoring method and is not simply a value for calculating metabolic equivalents. For example, an individual will be categorized into the high PA group only when he or she meets one of the following conditions: the first, the number of days of high-intensity PA is greater than or equal to 3 days per week and the total PA level is greater than or equal to 1500 MET-min/week; and the second, the number of days of low-moderate-high-intensity PA is greater than or equal to 7 days per week, and the total PA level is greater than or equal to 3000 MET-min/week.

The MFI-20 is composed of 20 items divided into five domains. The scale assesses the impact of psychological and physiological factors on activity levels. Each item is scored 1–5 points from light to heavy,²³ with higher scores indicating higher fatigue. Tian and Hong translated MFI-20 into Chinese, and the Chinese version has high internal consistency, good scale correlation validity and sufficient construct validity.²⁴

Using the Chinese version of the validated FSS to evaluate the degree to which fatigue impairs function. The FSS consists of nine statements, with each statement rated on a scale ranging from “strongly disagree” to “strongly agree”. A score of 4 on the FSS indicates that fatigue has a significant impact on daily activities.²⁵

Sleep parameters were evaluated by collecting subjective reports using the Chinese-language version of the PSQI. The PSQI is a self-reported questionnaire consisting of seven components measured on a 0–3 interval scale. A higher score indicates worse sleep quality. With well-validated sensitivity, the score reaches 5 points or higher, the patient has obvious sleep disorders.²⁶

The HADS is a self-report tool that allows rapid screening of patients for emotional abnormalities. It consists of a validated 14-item self-report questionnaire, with seven items comprising the HADS-depression sub-scale (HDS) and seven items comprising the HADS-anxiety sub-scale (HAS).²⁷ Each item is scored on a scale of 0 to 3, resulting in a maximum sub-scale score of 21, where higher scores indicate a more severe condition. Based on the recommendations of the HADS designers,²⁸ we established a threshold of 11 for each sub-scale as a high score criterion.

The IBDQ is a 32-item self-management scale that assesses bowel-related experiences in the past two weeks. Each entry is scored on a scale of 1 to 7, with a score of 1 indicating the most frequent and/or severe symptoms and a score of 7 indicating the least frequent and/or severe symptoms. Finally, cumulative scores were calculated by summing all 32 items. The higher the total score, the more favorable the outcome.²⁹ This scale was designed for people with IBD and is one that has been validated to be sensitive to changes in disease activity.³⁰

Statistical Methods

Software such as GraphPad Prism 9.0, Origin 2021, Microsoft Excel and SPSS 22.0 were applied to extract and analyze the data. Qualitative data were presented as frequencies and percentages, while continuous variables were reported as mean \pm standard deviation (SD) or median (interquartile range). Statistical comparisons were performed using the Mann–Whitney *U*-test for continuous variables and the Pearson Chi-square test for categorical variables. The Spearman correlation method was used to establish the relationship between fatigue, QoL and PA. A *p*-value less than 0.05 was considered statistically significant.

Results

Participant Characteristics

A total of 237 participants who met the eligibility requirements were included in the study, with a mean age of 42.2 ± 15.6 (SD) years and a range of ages from 18 to 88 (Table 1). Of these participants, females made up 39.2% of the overall participant population. The interquartile range for the median number of years since diagnosis was 4 (2–7). The majority of participants (63.3%) had UC, and 34.6% of the patients were in remission. Based on the Mayo score, 15.3% of UC patients had an inactive disease, while 36.7%, 40.7%, and 7.3% had mildly, moderately, or highly active conditions, respectively. Approximately 43.9% of patients were undergoing biological treatment, while 165 patients (69.6%) were being treated with aminosalicylate. In terms of CD patients, the CDAI revealed that 32.1% had active disease and 67.8% were in clinical remission. Additionally, Table 1 provides details on past surgical procedures as well as current treatments.

IBD Patients' Physical Activity and Fatigue

There were 237 respondents completed the IPAQ, among whom, 18.1% were classified as high PA, 21.1% as moderate PA, and 60.8% as low PA. Among participants with low levels of PA, UC totaled 90, or 62.5%, and CD 54, or 37.5%. The percentages were identical for the other two categories, with UC at 62.0% for moderate PA and 67.4% for high PA; thus, CD was 38.0% and 32.6% for the populations with moderate and high PA levels, respectively (Table S1). In addition to the disease type, the level of disease activity was similar across PA intensity populations, with 37.5%, 30%, and 30.2% of patients in low, moderate, and high PA intensity populations in remission, respectively (Figure 1a). In the area of fatigue, overall, the mean overall fatigue MFI was 60.2 ± 16.1 . It was discovered that 40.5% of patients with IBD had fatigue, as measured by a general fatigue score of 12 or higher. The median and IQR of the five dimensions and the total score of fatigue are presented in Figure 1b. All of these scores were normally distributed.

Table 1 Demographic- and Disease-Related Characteristics of IBD Patients

Variables	UC(n=150)	CD(n=87)	All IBD(n=237)
Female, n(%)	63(42.0)	30(34.5)	93(39.2)
Age(years), Mean ± SD	45.9±15.1	36.0±14.5	42.2±15.6
BMI, n(%)			
Thinnish	18(12)	17(19.5)	35(14.8)
Normal	97(64.7)	62(71.3)	159(67.1)
Overweight	31(20.7)	6(6.9)	37(15.6)
Obesity	4(2.7)	2(2.3)	6(2.5)
Marital status, n(%)			
Unmarried	28(18.7)	30(34.5)	58(24.5)
Married	118(78.7)	57(65.5)	175(73.8)
Divorced or Death of a spouse	4(2.7)	–	4(1.7)
Employment status, n(%)			
Employed full-time	68(45.3)	40(46)	108(45.6)
Long-term sick leave	21(14)	9(10.3)	30(12.7)
Employed part-time	19(12.7)	21(24.1)	40(16.9)
Unemployed	2(1.3)	2(2.3)	4(1.7)
Retired	37(24.7)	10(11.5)	47(19.8)
Student	3(2)	5(5.7)	8(3.4)
Education, n(%)			
Primary school or below	14(9.3)	3(3.4)	17(7.2)
Junior high school	14(9.3)	8(9.2)	22(9.3)
Senior high school	47(31.3)	9(10.3)	56(23.6)
Junior college or Undergraduate	71(47.3)	66(75.9)	137(57.8)
Master's degree or above	4(2.7)	1(1.1)	5(2.1)
Smoking status, n(%)			
No	126(84.0)	75(86.2)	201(84.8)
Yes	6(4.0)	5(5.7)	11(4.6)
Ex	18(12.0)	7(8.0)	25(10.5)
Medical insurance, n(%)	142(94.7)	84(96.6)	226(95.4)
Disease duration(years), median (IQR)	4(2, 8.3)	2(1, 6)	4(2, 7)
IBD related surgery, n(%)	11(7.3)	31(35.6)	42(17.7)
Disease activity, n(%)			
Remission	23(15.3)	59(67.8)	82(34.6)
Mild activity	55(36.7)	21(24.1)	76(32.1)
Moderate activity	61(40.7)	7(8.0)	68(28.7)
Severe activity	11(7.3)	–	11(4.6)
Current medication, n(%)			
Aminosalicylates	139(92.7)	26(29.9)	165(69.6)
Corticosteroids	14(9.3)	2(2.3)	16(6.8)
Immunomodulators	2(1.3)	–	2(0.8)
Biologic therapies	35(23.3)	69(79.3)	104(43.9)
Nutrition therapies	43(28.7)	46(52.9)	89(37.6)
Laboratory parameters			
Hemoglobin(g/L), Mean ± SD	121.8±23.0	120.5±20.3	121.3±22.0
Albumin(g/L), Mean ± SD	39.6±5.5	38.2±5.3	39.0±5.5
Erythrocyte sedimentation rate(mm/h), median (IQR)	13(5.8, 24.8)	19(8, 38)	14(6, 30)
C reactive protein(mg/L), median (IQR)	3.4(1.9, 6.0)	5.8(2.6, 23.9)	3.8(2, 11.6)
Fecal calprotectin(μg/g), median (IQR)	581.4(115.1, 854.3)	515.3(99.3, 888.1)	556.1(108, 869.6)

Abbreviations: UC, Ulcerative colitis; CD, Crohn's disease; IBD, Inflammatory bowel disease; SD, standard deviation; BMI, body mass index; IQR, Interquartile range; PA, Physical activity.

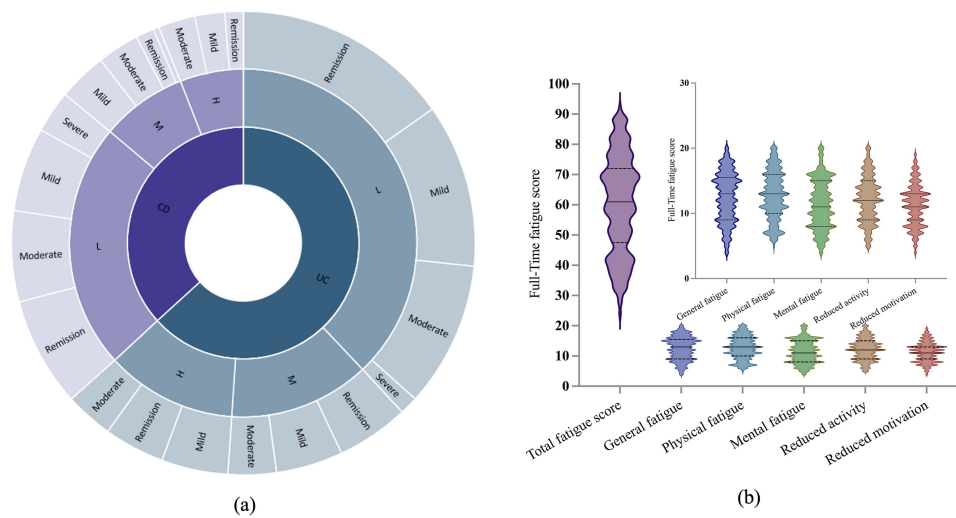


Figure 1 (a) Percentage relationship between physical activity level, disease type and disease activity level. (b) Fatigue in IBD patients as measured by MFI scales. **Notes:** The median is represented by the solid line, while the interquartile range is shown by the dotted line. The scores of the five subscales of the Multidimensional Fatigue Inventory (overall fatigue, physical weariness, reduced activity, reduced motivation, and mental fatigue) in patients with IBD are shown in the little insert inside the graphs (b). **Abbreviations:** L, Low physical activity; M, Moderate physical activity; H, High physical activity.

Other Outcomes in Patients with IBD with Different Levels of Activity

Regarding PA in patients with IBD, among all participants, 144 with low PA had an MFI score of 62.9 ± 16.0 ; 50 with moderate PA had an MFI score of 57.7 ± 15.3 ; and 43 with high-intensity PA had an MFI score of 53.7 ± 15.1 , with different mean fatigue values for different levels of PA ($p < 0.001$) (Figure 2). Further details on the scores of different physical activities for all outcomes are presented in Figure 2b.

Correlation

A significant negative correlation was observed between PA and fatigue ($r = -0.224$, $p < 0.001$). PA was found to have a negative correlation with anxiety and depression (PA and anxiety $r = -0.150$, $p < 0.05$; PA and depression $r = -0.242$, $p < 0.001$). On the other hand, PA was positively correlated with QoL ($r = 0.171$, $p < 0.01$). Additionally, anxiety and

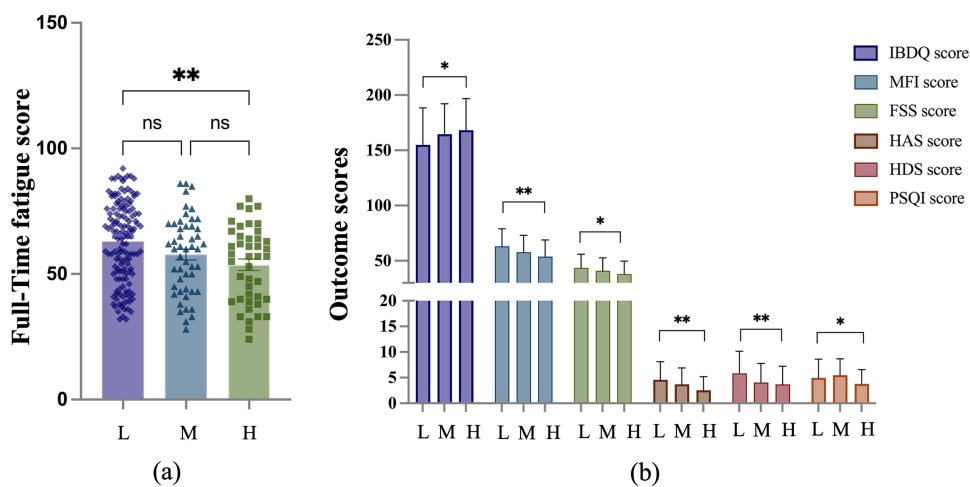


Figure 2 (a) Fatigue scores of people with different physical activity levels. (b) Outcome scores for people with different physical activity levels. **Notes:** (a) The full-time fatigue score is measured by MFI scales. Scatter representation of the distribution of the data. The p-values were calculated by the LSD test for independent samples, Bonferroni correction. (** $p < 0.001$; ns: non-significant). (b) Data are presented as median and range. Parametric and non-parametric tests are selected based on whether the data are homogeneous in variance and whether they conform to a normal distribution. (** $p < 0.001$; * $p < 0.05$). **Abbreviations:** L, Low physical activity; M, Moderate physical activity; H, High physical activity.

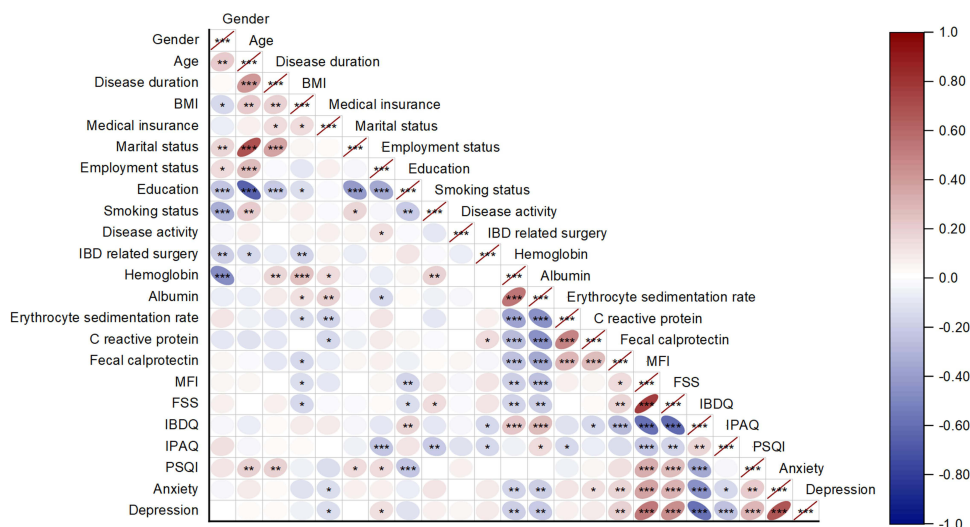


Figure 3 Correlation analysis of 23 factors.

Notes: Some factors have a negative correlation, represented by the color blue, while others have a positive correlation, represented by the color red. The greater the relevance, the darker the color. The greater the relevance, the greater the inclination. (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

depression were negatively correlated with QoL (anxiety and QoL $r = -0.649$, $p < 0.001$; depression and QoL $r = -0.684$, $p < 0.001$). Moreover, sleep disorders, anxiety and depression showed a positive correlation (anxiety and sleep disorders $r = 0.349$, $p < 0.01$; depression and sleep disorders $r = 0.354$, $p < 0.001$) (Figure 3 and Table S2).

Discussion

This cross-sectional study aimed to examine the levels of PA, the prevalence of fatigue, and the correlation between PA levels and fatigue in IBD patients in China. Among the 237 respondents, 60.8% had low levels of PA, and 40.5% reported experiencing fatigue. The study also found that PA in IBD patients was significantly and negatively associated with fatigue, and significantly and positively associated with QoL.

This study found that a majority of patients with IBD tend to engage in low levels of PA, even when their health condition is relatively stable. This could be attributed to the limitations imposed by the disease.³¹ Firstly, engaging in PA may trigger gastrointestinal symptoms such as bloating, nausea, the urge to defecate, or diarrhea, which are concerns for individuals with IBD.³² Secondly, impaired psychological well-being, including depressive symptoms, can act as a barrier to regular PA.³³ Anxiety and depression have been identified as limitations to PA in adults with IBD.³⁴ Additionally, common obstacles reported by patients with IBD include fatigue, pain, fecal urgency, and muscle weakness.^{35,36} Our study revealed that patients with CD and UC showed similar patterns of PA, and those in remission were more likely to engage in moderate and high-level PA. This finding is consistent with two previous studies involving a total of 780³⁷ and 312 participants,³⁸ respectively. Additionally, these studies suggest that engaging in PA during remission can help reduce the risk of disease recurrence.³⁸ However, a meta-analysis indicated that while PA had a significant protective effect on the subsequent development of CD, this effect was not observed in UC.³⁹ Consequently, it is essential to develop personalized PA recommendations for individuals with IBD, taking into account their specific disease type and activity level. Furthermore, it is crucial to evaluate the effectiveness of PA interventions in both remission and active disease states.

PA was found to have a significant negative effect on fatigue levels in patients ($r = -0.224$, $p < 0.001$), indicating that higher PA levels were associated with lower fatigue. These findings are consistent with other studies.⁴⁰ However, the majority of patients (81.9%) had low to moderate levels of PA, falling short of the weekly amount of PA recommended by the World Health Organization.⁴¹ In our survey, 75% of the patients considered fatigue as the main reason for limiting their PA. A study conducted in Malta revealed a significant decline in PA levels after IBD diagnosis, particularly in patients with UC, with fatigue identified as a major contributing factor.¹⁹ Interestingly, our study found that patients who

were more physically active experienced lower levels of fatigue. This association can be attributed to the link between fatigue and inflammation.⁴² Regular exercise induces cells to secrete anti-inflammatory factors such as IL-1ra⁴³ while inhibiting the production of inflammatory factors such as TNF- α . This process enhances myocyte insulin sensitivity, promotes glucose uptake,⁴⁴ improves muscle strength and endurance, and alleviates muscle fatigue. Additionally, it is known that disruption of the gut flora plays a role in the development of IBD, which is also associated with fatigue.⁴⁵ Regular and long-term exercise can improve the dysbiosis of gut microbiota, increase beneficial microbiota and enrich bacterial diversity,⁴⁶ thereby alleviating anxiety and depression, reducing fatigue and ultimately improving the QoL of patients by regulating the brain-gut axis.⁴⁷ Our findings suggest that fatigue management in patients with IBD can be achieved by recommending moderate PA and developing individualized exercise programs. Chronic disease management in patients with IBD can be achieved by recommending moderate PA and developing an individualized exercise program.

In addition, in the correlation analysis, we found that PA and anxiety-depression were negatively correlated (PA and anxiety $r = -0.150$, $p < 0.05$; PA and depression $r = -0.242$, $p < 0.001$), and depression, in particular, was strongly negatively correlated. This result is not merely the same as our research hypothesis, but also consistent with the results of other previous studies. In other words, PA has a positive impact on patients. In a randomized controlled trial of Crohn's patients, PA improved patients' mood.⁴⁸ In another study, patients reported that exercise made them energetic.⁴⁹ Furthermore, PA was positively correlated with QoL ($r = 0.171$, $p < 0.01$), and the higher the level of PA, the better the QoL. In a cross-sectional survey in the UK with the participation of 918 IBD patients, 72% reported that exercise improved their overall well-being, their QoL and also their sleep.⁵⁰ However, in our study, we found extremely weak correlations between PA and sleep. We believe that this may be connected with the fact that the subjects were mostly hospitalized and the hospital environment affected their level of PA and quality of sleep. As a result, we did not find the correlation between them. In summary, we still recommend moderate PA for patients to improve mood, sleep and QoL.⁵¹ Through a healthy lifestyle, we can promote patients' physical and mental symptoms, improve their QoL, and reduce the burden on individuals and even society.

Additionally, we analyzed the results of indicators other than PA and fatigue, such as anxiety, depression, QoL, and sleep quality, and explored the relationship between them. The results of this study suggested moderate negative correlations between depression and anxiety and QoL (anxiety and QoL $r = -0.649$, $p < 0.001$; depression and QoL $r = -0.684$, $p < 0.001$). This is consistent with the findings of Thomann.⁵² This may be explained by the fact that anxiety and depression can exacerbate symptoms such as intestinal permeability, flora imbalance, abdominal pain, and diarrhea.⁵³ Furthermore, negative evaluations of social function can also contribute to a decline in QoL. Cognitive behavioral therapy, mindfulness-based therapies (including meditation and yoga), and gut-directed hypnotherapy, have shown short-term improvements in QoL and reduction in depression.⁵⁴ Anxiety and depression and sleep quality also showed correlated results (anxiety and sleep quality $r = 0.349$, $p < 0.01$; depression and sleep quality $r = 0.354$, $p < 0.001$). These results are in line with earlier studies showing a connection between poor sleep quality and a range of mental health issues, such as anxiety and depression.⁵⁵ The association between anxiety, depression and sleep quality highlights the importance of psychological assessment in patients with IBD. Besides, a weak correlation between QoL and sleep quality was observed. Freeman's study reported an association between sleep quality and worsening of health-related QoL.⁵⁵ Scott's findings also suggested that sleep apnea and insomnia symptoms may, at least temporarily, increase the likelihood of poorer QoL.⁵⁶ Hence, addressing sleep disruptions holds the potential to improve future QoL outcomes.

Limitations

The empirical findings presented herein should be considered within the confines of certain limitations. Firstly, cross-sectional studies make it difficult to monitor changes over time. It can only provide weak evidence of an association between independent variables and outcomes. Secondly, this study was conducted in only one tertiary hospital in China, and the sample size was relatively limited. Thirdly, measurement tools such as dynamometers were not utilized to quantitatively assess parameters like muscle strength of patients in this study, potentially reducing the objectivity of the outcomes. Finally, the study did not take into account other variables, such as dietary habits. Future research will focus

on conducting multi-center, large-sample intervention studies that account for the disease characteristics of IBD and incorporate clinical laboratory examinations.

Conclusion

In conclusion, the levels of PA are remarkably low, and there is a high prevalence of fatigue in IBD patients. In the correlation analysis, PA was negatively associated with fatigue, anxiety, and depression, and positively associated with QoL. Based on our findings, we suggest that healthcare providers should consider factors such as disease activity, fatigue, and QoL when instructing IBD patients to engage in PA.

Abbreviations

UC, Ulcerative Colitis; CD, Crohn's Disease; IBD, Inflammatory Bowel Disease; QoL, Quality of Life; BMI, Body Mass Index; IQR, Interquartile Range; PA, Physical Activity; IPAQ, International Physical Activity Questionnaire, MFI, Multidimensional Fatigue Inventory; FSS, Fatigue Severity Scale; PSQI, Pittsburgh Sleep Quality Index; HADS, Hospital Anxiety and Depression Scale; HAS, The Hospital Anxiety and Depression Scale-anxiety sub-scale; HDS, The Hospital Anxiety and Depression Scale-depression sub-scale; IBDQ, Inflammatory Bowel Disease Questionnaire.

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Disclosure

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