

Management of Fatigue in Inflammatory Bowel Disease: A Narrative Review

Dan-Dan Wang^{1,2}, Shi-Guang Ren^{1,2}, Rui Hu^{1,2}, Hui-Lan Zhai¹, Fen Xie¹, Lu Jiang¹, Wen-Lei Huang³, Xue-Qin Li³

¹Department of Gastroenterology, the 2nd Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi Province, 330006, People's Republic of China; ²School of Nursing, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi Province, 330006, People's Republic of China; ³Nursing Department, the 2nd Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi Province, 330006, People's Republic of China

Correspondence: Xue-Qin Li, Nursing Department, the 2nd Affiliated Hospital, Jiangxi Medical College, Nanchang University, No. 1 of Minde Road, Donghu District, Nanchang, 330006, People's Republic of China, Tel +86 13870892330, Email xueqinlidlrxq@outlook.com

Abstract: Inflammatory bowel disease (IBD) encompasses chronic inflammatory conditions of the digestive tract, including Crohn's disease and ulcerative colitis. Fatigue is one of the common and important extraintestinal symptoms in IBD patients, which significantly affects the patient's ability to work, daily life, social activities, emotional state, and cognitive function. Although the impact of fatigue on patients' quality of life cannot be ignored, medical professionals still have limited knowledge of its concepts, assessment tools, influencing factors, and non-pharmacological interventions, which may lead to neglect and inadequate management of the symptoms. The purpose of this article is to review the definition and epidemiological characteristics of IBD-related fatigue and to discuss the application of four commonly used fatigue assessment tools in patients with IBD. In addition, we will analyze the multiple factors that affect fatigue in IBD patients from three levels: physiological, psychological, and sociodemographic. Finally, we will assess the effectiveness of different non-pharmacological interventions in alleviating fatigue in people with IBD and make corresponding clinical recommendations.

Keywords: inflammatory bowel disease, fatigue, assessment tools, influencing factors, non-pharmacological interventions, review

Introduction

Inflammatory bowel disease (IBD) is a chronic, nonspecific, recurrent inflammatory disorder of the gastrointestinal tract, primarily consisting of Crohn's disease (CD) and ulcerative colitis (UC).¹ In China, the number of IBD patients increased by 911,000 between 1991 and 2019.² Fatigue is one of the most frequent self-reported symptoms in patients with IBD,³ with up to 80% of patients experiencing fatigue in the active phases of the disease and 40% to 50% of patients continuing to be affected even in remission.⁴ Fatigue is associated with impaired health-related quality of life, as well as decreased physical functioning, mood disorders, and low productivity.^{5–7}

Despite the widespread prevalence and significant debilitating consequences, fatigue in patients with IBD is often underrecognized in clinical practice, and its treatment and management remain suboptimal.⁸ It is important to fully understand the symptoms and factors influencing fatigue in patients with IBD to develop effective and targeted nursing interventions. In this article, the factors influencing fatigue in patients with IBD and current assessment tools are reviewed, and non-pharmacological nursing interventions for fatigue are summarized to provide a reference for improving the quality of life for patients with IBD and promoting clinical nursing practices.

The Concept and Epidemiology of Fatigue in Inflammatory Bowel Disease

In their seminal paper, Ream and Richardson⁹ analyzed the concept of 'fatigue' in 1996, and they described it as a subjective, unpleasant symptom that incorporates a general feeling from tiredness to exhaustion that interferes with an individual's living ability. Since fatigue encompasses multiple dimensions such as physiology, psychology, and sociology, it

is an extremely complex phenomenon that may not be fully described with a simple definition. In 2007, Markowitz et al¹⁰ proposed that fatigue consists of three components: (1) physical fatigue, which impairs the ability to perform certain activities; (2) emotional fatigue, characterized by low interest, mood swings, or decreased participation in daily activities; (3) psychological fatigue, which involves difficulty in concentrating, memory loss, and emotional instability.

Due to the multidimensionality, subjectivity, and non-specificity of fatigue, there is still no standardized definition of IBD-related fatigue in China and other countries worldwide. Currently, IBD-related fatigue is generally understood within the context of chronic illness fatigue as “extreme and persistent tiredness, weakness, or exhaustion”, which may be physical, mental, or both, and is not easily resolved by sleep or rest.¹¹

Several studies have shown that fatigue is prevalent in patients with IBD, and its prevalence varies by region and patient population. In Europe and the United States, epidemiological studies on fatigue are relatively abundant. In a multicenter survey of France, Germany, Italy, Spain, the United Kingdom, and the United States,¹² fatigue was reported in 22.6% (239/1057) of patients with UC and 26.0% (320/1228) of patients with CD. In a survey conducted in the United Kingdom, fatigue was reported in 30% of 8486 patients with IBD.¹³ In a survey in France and Belgium, fatigue was reported in 54.1% of 1704 patients, and the prevalence of fatigue was found to be significantly higher in patients with active disease than in patients in remission (64.9 versus 44.7%).¹⁴ As the incidence of IBD in Asia continues to increase year by year,¹⁵ there is a gradual increase in related studies. A study in India found that 55.9% of 202 patients with IBD reported fatigue¹⁶. China has the highest prevalence of IBD in Asia,¹⁷ but there are relatively few studies on fatigue in IBD patients. Scholars surveyed 311 IBD patients in China, and the results showed that the prevalence of fatigue was 60.77%, of which the fatigue rate was as high as 71.88% in patients with active disease and 49.01% in patients in remission.¹⁸ Studies around the world have shown that fatigue is a common and serious problem in IBD patients, and more attention and management of fatigue in IBD patients need to be strengthened to improve the quality of life of patients.

Assessment Tools for Fatigue in Patients With Inflammatory Bowel Disease

Multidimensional Fatigue Inventory (MFI-20)

The Multidimensional Fatigue Inventory (MFI-20) is an assessment tool developed by Dutch scholar Smets et al¹⁹ in 1995. The scale measures the fatigue level of cancer and chronic fatigue patients individuals in the past two weeks and comprises the following five dimensions: general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation. Studies have shown that if using both the general and physical fatigue dimensions together does not provide additional information, the two dimensions can be combined. The MFI-20 consists of 20 items, each dimension consists of 4 items, and is scored on a scale of 1 to 5, with 1 being “not at all compliant” and 5 being “completely compliant”. Fatigue-related items are scored in the forward direction, while non-fatigue-related items are scored in the opposite direction, with a total score of 20~100 points, and the higher the score, the more severe the fatigue. Specific fatigue levels are: mild fatigue (20–40 points), moderate fatigue (40–60 points), and severe fatigue (60–100 points). The MFI-20 performed well on internal consistency, with Cronbach’s α coefficient of 0.84. Due to its short and practical entries, the MFI-20 has been translated into many languages and has been used in fatigue assessment in a variety of populations in several countries such as France, Poland, Lithuania, Turkey, China, and others.^{20–24}

The MFI-20 is one of the commonly used scales to assess fatigue in patients with IBD. However, most of the existing studies have not been systematically psychometric validated,^{25–27} and only Jelsness-Jørgensen et al²⁸ tested 410 patients with IBD in Norway, and the results showed that Cronbach’s α coefficient was ≥ 0.70 in all dimensions except for the “motivation reduction” dimension, and the test-retest reliability was good. Therefore, it is suggested that the reliability and validity of the MFI-20 scale should be verified according to local culture and population characteristics in future fatigue studies of IBD patients. At the same time, healthcare workers should focus on the evaluation of interventions based on the results of the MFI-20 to explore effective strategies to improve fatigue in patients with IBD.

Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F)

The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) was a scale developed by Yellen et al²⁹ in 1997 and was originally used to evaluate the level of self-reported fatigue in patients with cancer-related anemia over the past week, and its effects on physical, psychological, and social aspects. The FACIT-F contains 13 items, of which 5 items assess fatigue experience and 8 items assess the impact of fatigue on daily activities. All items are scored on a 5-point Likert scale with options ranging from “not at all (0)” to “very much (4)”, with a total score ranging from 0 to 52, with higher scores indicating less fatigue. In cancer patients, FACIT-F has a Cronbach’s α coefficient of 0.93 to 0.95, showing strong internal consistency. The scale is available for download <https://www.facit.org/measures/FACIT-F>.

While FACIT-F was originally developed for the cancer patient population, it has also been validated for use in other patient populations, including rheumatoid arthritis, Parkinson’s disease, multiple sclerosis, and IBD.^{30–33} In patients with IBD, FACIT-F has shown strong internal consistency, with Cronbach’s α coefficients ranging from 0.86 to 0.88 and 0.94 to 0.96 in patients with CD and UC, respectively.³³ A 7 to 10 point increase or 4 to 9 points in the FACIT-F total score was found to be clinically meaningful in patients with moderately to severely active CD and UC.³³ Recently, another study noted a cut-off of 6 to 9 points for change in FACIT-F scores in patients with moderately to severely active CD.³⁴ This threshold for score changes helps clinicians assess the effectiveness of fatigue treatment and guide clinical practice. However, no studies have been conducted in patients with quiescent or mild IBD.

The concise format of the FACIT-F scale allows for a quick assessment of the fatigue levels of patients using a few items and is suitable for the initial fatigue screening in large samples. In addition, the FACIT-F score can be converted to a Patient-Reported Outcomes Measurement Information System (PROMIS) score, enabling the comparison of fatigue levels of patients with IBD with those of the general population and other patients with chronic illnesses. However, as a one-dimensional fatigue assessment tool, FACIT-F has limitations in qualitatively and quantitatively assessing patients’ fatigue experience, and cannot deeply explore the mechanisms that lead to fatigue in individual patients.

Inflammatory Bowel Disease Fatigue Scale (IBD-F)

The Inflammatory Bowel Disease Fatigue Scale (IBD-F) was developed by British scholar Czubier-Dochan et al³⁵ in 2014 specifically to assess fatigue in patients with IBD. It assesses fatigue over the past two weeks and is divided into three subscales: IBD-F1, consisting of 5 items to assess the severity and frequency of fatigue; IBD-F2, consisting of 30 items to assess the impact of fatigue on daily life; and IBD-F3, consisting of 5 open-ended questions to explore additional conditions related to fatigue. All subscales are scored on a scale of 0 to 4, with the IBD-F3 not included in the total score. The IBD-F1 options range from “no fatigue (0)” to “severe fatigue (4)”, with a total score of 0–20 points, and the higher the score, the more severe the fatigue of the patient; The IBD-F2 options range from “no time (0)” to “all time (4)”, with a total score of 0–120 points, with higher scores indicating greater impact of fatigue on daily life. The Cronbach’s α coefficients for IBD-F1 and IBD-F2 were 0.91 and 0.98, respectively, and the intra-group correlation coefficients were 0.74 and 0.83, indicating that the scale has good reliability and validity and can accurately reflect the severity of fatigue in IBD patients and its impact on their personal lives.³⁵

Studies have shown that IBD patients are more likely to use the IBD-F scale than the MFI-20 because it is a more realistic reflection of their experience of fatigue.³⁵ In addition, the open-ended questions of the IBD-F3 help healthcare workers identify other contributing factors and develop priority solutions. At present, the scale has been translated into multiple languages and used in countries such as Greece, Brazil, Poland, China, and the Netherlands,^{36–41} and has shown good internal consistency and reproducibility. However, the scale was not developed with a cut-off value for fatigue defined. Lage et al⁴⁰ suggested that the cut-off value for IBD-F1 to distinguish between significant and non-significant fatigue was 11, while Varbobitis et al³⁶ suggested 7.5 as the cut-off value. These differences may be due to differences in the reference standard for fatigue scores, the study area, and the population. In the future, the unification of the reference standard of fatigue scores, the expansion of the study area, and the inclusion of more IBD patients will help to determine the global IBD-F cut-off value, and provide more accurate standards for the fatigue management of IBD patients.

Patient-Reported Outcomes Measurement Information Systems-Fatigue Short Form Scale (PROMIS-Fatigue SF Scale)

The Patient-Reported Outcomes Measurement Information Systems (PROMIS) is an international standardized measurement tool developed by the National Institutes of Health in 2004, which can be applied to different types of people under different conditions and environments^{42,43}. PROMIS has developed a library of many items, including physical functioning, pain, social functioning, and fatigue, among others. The system has three different measurement forms, namely static short form, dynamic computerized adaptive testing (CAT), and feature set short form (Profile). The short table is composed of entries in the project library that are based on the hierarchical order of the project response theory and the CAT test that are performed more frequently. Each item bank developed by PROMIS has corresponding short forms. In the PROMIS-Fatigue Scale item bank, there are short forms such as 4a, 6a, and 7a, which are used to assess an individual's fatigue experience over the past week and the impact of fatigue on daily activities. The PROMIS-Fatigue Scale item is rated on a 5-scale Likert scale from “not at all (1)” to “very much (5)”, with higher scores indicating higher levels of fatigue.⁴⁴

At present, the application of PROMIS-Fatigue SF in patients with IBD is limited. American scholar Feagan et al have conducted a relevant study on patients with moderate to severe active IBD, and the results show that PROMIS-Fatigue SF-7a Scale has good efficacy and reliability.⁴⁵ They noted that when the scale total score is reduced by more than 7 points, it can be considered a threshold for clinically meaningful improvement in fatigue. Therefore, the research team recommends this scale as an assessment tool for the effectiveness of fatigue treatment. However, given the wide variety of PROMIS-Fatigue SF, further validation is needed to determine which scale is most useful in assessing fatigue in patients with IBD. Compared to traditional fatigue assessment tools, the PROMIS-Fatigue SF is short, easy to fill out, and has been translated into multiple languages (see <http://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis/available-translations> for details). These tools are free to use, but commercial users are required to obtain permission to use, reproduce, or distribute them. In addition, PROMIS provides a unified set of metrics, which facilitates the comparison and analysis of data from different countries and regions in fatigue-related studies, and lays the foundation for research collaboration on a global scale.

Influencing Factors of Fatigue in Patients With IBD

Physiological Factors

Disease Activity

The correlation between fatigue and disease activity in patients with IBD remains inconclusive. Lee et al⁴⁶ found a significant correlation between fatigue symptoms and disease activity of IBD in a study on 177 patients with IBD, suggesting that fatigue may be directly influenced by the inflammatory process. However, a multicenter prospective study conducted in Spain showed that depression, anxiety, sleep deprivation, and extraintestinal manifestations were all associated with fatigue, but disease activity was not significantly relevant.⁴⁷ The study relied primarily on the Harvey-Bradshaw index to assess disease activity, which is based on factors such as abdominal pain, abdominal mass, and arthralgia but does not consider objective indicators of active disease, such as C-reactive protein (CRP) and fecal calprotectin (FC), among others.

To address these limitations, more comprehensive and objective assessment indicators, including endoscopic scores, CPR, FC, and so on, were used in a study conducted in Norway, and the results indicated that fatigue was associated with disease activity in patients with UC, but this association could not be established in patients with CD.⁴⁸ Therefore, the complex relationship between fatigue and disease activity needs to be examined in greater detail, especially in different types of IBD, such as UC and CD. Future studies that involve the use of more comprehensive, objective, and uniform assessment indicators have to be taken up to obtain more credible conclusions.

Inflammation

The pathogenesis of fatigue in patients with IBD remains unclear, but inflammation appears to play an important role in the onset and development of fatigue. Cytokines released during inflammation can activate the brain-gut axis, particularly

the hypothalamic-pituitary-adrenal (HPA) axis, which is the core stress response pathway. The activation of this axis promotes the release of cortisol from the adrenal glands—a process implicated in the occurrence of fatigue.⁴⁹

In one study, it was found that patients with IBD who reported fatigue had higher levels of memory T cells and neutrophils, but lower levels of monocytes, as compared to IBD patients without fatigue.⁵⁰ In addition, inflammatory cytokines such as tumor necrosis factor α (TNF- α), interferon γ (IFN- γ), and interleukin (IL)-12 were also significantly increased in the fatigue group, while interleukin-6 (IL-6) was decreased, suggesting that inflammation plays an important role in the pathogenesis of fatigue. However, Borren et al⁵¹ did not find an association between inflammatory cytokines and fatigue. Therefore, more research is required to clarify the relationship between fatigue and inflammation in patients with IBD.

Anemia

Anemia is one of the most common non-intestinal complications of IBD, primarily due to iron deficiency, with vitamin B12 or folate deficiency also contributing to the condition.⁵² The incidence of anemia among patients with IBD varies widely, ranging from 13.6% to 63.5%.^{3,52,53} Anemia has been shown to be associated with fatigue in patients with IBD.⁵² However, Uhlir et al³ found that fatigue occurred in both anemic (62.3%) and non-anemic patients (63.9%).

To further explore the association between anemia and fatigue, Bergamaschi et al⁵⁴ monitored the hemoglobin concentrations in IBD patients with anemia over 24 weeks of follow-up and found that hemoglobin concentrations were significantly correlated with fatigue symptoms in both active and remission stages of the disease. However, since the main objective of their study was to analyze the factors influencing anemia, the impact of anemia on fatigue was a secondary objective, and the results warrant further validation.

Although more evidence is needed to conclusively support the association between anemia and fatigue, given the high prevalence of anemia in patients with IBD, active screening for anemia in patients complaining of fatigue and offering timely treatment is recommended. Addressing anemia could be crucial in improving the fatigue status of such patients.

Psychological and Sleep-Related Factors

Psychological Factors

IBD is a long-term chronic disease, and patients often experience anxiety, depression, and other psychological disorders. The incidence of anxiety and depression in patients with IBD was found to be much higher than that in the general population, reaching 38.1% and 24.2%, respectively.⁵⁵ Depression and anxiety have been shown to be predictors of fatigue in patients with IBD.¹⁸

However, Pal et al¹⁶ suggested that while depression could predict fatigue in patients with IBD, anxiety did not. Feng et al²⁷ did not find a link between depression and fatigue, suggesting that fatigue might be a potentially undetected symptom of depression. Bernstein et al⁵⁶ conducted a three-year prospective study in Canada to further explore the predictors of fatigue over time. Their results showed that anxiety and depression could predict fatigue over time. Anxiety, depression, and fatigue involve multiple dimensions, including physiological, psychological, and social factors. Therefore, anxiety and depression may be both the cause and the result of fatigue, creating a dynamic, bi-directional relationship. Therefore, the provision of interventions targeting emotional and psychological factors by medical professionals could reduce the burden of fatigue, and at the same time, the interventions addressing fatigue could reduce emotional and psychological problems.

Sleep-Related Factors

One of the predictors of fatigue in patients with IBD is sleep quality, and patients with IBD have been found to have poorer quality of sleep compared with healthy individuals.⁵⁷ Sleep deprivation is strongly linked to reduced immune system function, increasing the risk of disease recurrence among sleep-deprived patients with IBD.⁵⁸ It has also been proposed that the exacerbation of intestinal symptoms may prevent patients with IBD from entering the restorative deep sleep stage, thereby reducing sleep quality and causing fatigue.²⁶ Additionally, persistent pain may also impact the patient's energy levels, leading to fatigue.⁵⁹

Although the exact pathogenesis of fatigue is unknown, a strong link between sleep quality and fatigue in patients with IBD is evident. Therefore, in clinical practice, healthcare professionals should pay close attention to patients with

IBD who complain of poor quality of sleep or sleep disorders and those who use sleep aids. Identifying and analyzing the causes or factors influencing poor sleep quality are essential to implementing targeted interventions to improve sleep quality and reduce the incidence of fatigue among patients with IBD.

Sociodemographic Factors

Fatigue in patients with IBD may also be influenced by sociodemographic factors such as age, gender, education level, and economic status. Previous studies^{3,14} have shown that as patients with IBD age, there is a gradual decline in their body functions and daily activities, and they are more prone to fatigue, making age a potential predictor of fatigue in this population. However, a recent study⁶⁰ has shown a lower prevalence of fatigue in older patients compared with younger patients with IBD, which may be related to differences in coping strategies, lifestyles, and work and family responsibilities in older adults.

In addition, female patients have been found to have higher levels of fatigue than male patients,^{12,14} but the reasons for this difference are not well understood. A probable reason could be that female patients are prone to experiencing a more diverse range of emotions, may tend to be more reactive and sensitive, have more family responsibilities, and experience greater emotional stress.

There is still a lack of strong evidence on the effects of other demographic factors, such as the patient's education level, economic status, occupational environment, disease course, and medication, on fatigue in patients with IBD. The impact of these factors on IBD-related fatigue needs to be verified in further research.

Non-Pharmacological Interventions for Fatigue in Patients With IBD

IBD is a chronic disease in which patients experience symptoms of fatigue for a long time. Currently, there are no specific drugs recommended for the prevention and treatment of fatigue in patients with IBD. Moreover, the efficacy of pharmacological treatments for fatigue is limited and often associated with side effects. Therefore, non-pharmacological interventions play a crucial role for managing fatigue in patients with IBD.

Psychological Interventions

Psychological interventions commonly used for managing fatigue in patients with IBD in China and other countries mainly include cognitive behavioral therapy (CBT), mindfulness training, and problem-solving therapy. Among these, CBT is considered to be the most effective psychological intervention.⁶¹ CBT was originally developed for the treatment of mood disorders and is mainly used to change patients' negative cognitions and improve their coping behaviors.

In 2019, Artom et al⁶² developed a CBT handbook specifically to address fatigue in IBD patients based on the CBT manual for fatigue management in patients with multiple sclerosis developed by van Kessel et al.⁶³ The handbook included a contents page, an introduction section with instructions for participants, eight topic-specific sessions, and homework task sheets. The sessions covered the following topics: an explanation of fatigue in IBD; CBT for IBD-related fatigue; activity scheduling; improving sleep; understanding IBD symptoms; changing one's thinking; managing stress, determining a sense of control and coping with emotions; social support; and preparation for the future. The feasibility and potential efficacy of CBT for fatigue treatment in patients with IBD was preliminarily assessed. This intervention lasted for eight weeks, during which the patient was required to have one 60-minute and seven 30-minute conference calls with the CBT therapist, with the specific agenda agreed upon between the therapist and the patient. The researchers found that patients experienced an improvement in fatigue and quality of life after the end of the intervention, and this improvement persisted during the 12-month follow-up period after the end of the intervention. The study was only a small-sample, single-center study with high requirements for patient compliance and therapists. Therefore, large randomized controlled trials are needed for future studies to verify their efficacy. At the same time, it is also necessary to consider the duration of the intervention, the economic cost, and the training of CBT therapists.

In addition, acceptance and commitment therapy (ACT) has also been shown to play a positive role in improving fatigue symptoms in patients with chronic diseases.⁶⁴ Promoting and evaluating the efficacy of ACT for fatigue in patients with IBD could be a valuable area for future research.

Exercise Intervention

Patients with IBD generally get inadequate exercise, with an online survey conducted in the United Kingdom showing that 50% and 33% of patients with IBD described their exercise levels as “minimal” or “inactive”, respectively. In their systematic review, Davis et al⁶¹ found that exercise played an important role in improving fatigue, anxiety, depression, as well as sleep quality in patients with IBD. Although the exact physiological mechanisms involved are not clearly understood, it is hypothesized that exercise can reduce inflammation levels and improve muscle condition in patients.

Patients with IBD can indulge in various forms of exercise such as aerobic, resistance, or a combination of aerobic and resistance exercises. Tailoring exercise prescriptions with respect to the principle, type, frequency, duration, and intensity of exercise to meet individual health conditions and preferences is crucial. Resistance exercise, or resistance exercise combined with aerobic exercise, is considered a rather safe exercise for patients with IBD.⁶⁵

The choice of intensity of exercise must also be considered carefully. Exercise intensity determines whether an exercise prescription is safe and effective, as excessive exercise may potentially lead to exacerbation of the disease. Tew et al⁶⁶ compared the impact of high-intensity interval training and moderate-intensity continuous training in patients with IBD and found an improvement in the maximal oxygen consumption of patients in the exercise group as compared with the control group, especially after high-intensity interval exercise, and their fatigue and quality of life also improved. In addition, they also found that moderate-to-high-intensity exercise did not exacerbate disease activity or gastrointestinal damage in patients with IBD. Despite these findings, the comparative efficacy of the two exercise interventions remains inconclusive and warrants further investigation.

At present, there is no agreed-upon optimal exercise prescription for patients with IBD. Further large-scale, multi-center, randomized trials are needed in the future to develop guidelines for optimal exercise prescription for adults with IBD.

Physical Interventions

Electroacupuncture

The main mechanism of action in electroacupuncture involves modulating the immune response. Specifically, it has been found to reduce the expression of pro-inflammatory cytokines, such as IL-1 β , IL-6, and TNF- α , while increasing the expression of anti-inflammatory cytokines.⁶⁷ Therefore, electroacupuncture may have a positive effect on fatigue symptoms in patients with IBD through immunomodulatory pathways. Horta et al⁶⁸ found that patients with IBD reported improvement in fatigue after eight weeks of electroacupuncture, but the efficacy of electroacupuncture needs to be verified further. This is because the fatigue status of both the electroacupuncture group and the sham electroacupuncture group was improved compared to the control group. However, efficacy between the two groups did not reach a statistically significant difference. This result may suggest that the improvement in electroacupuncture is due in part to the placebo effect, or it may imply a lack of specificity for the therapeutic effect, ie, it may not be as effective as sham electroacupuncture. Therefore, more scientific evidence is needed to support the therapeutic effect of electroacupuncture on fatigue.

In summary, although electroacupuncture has shown potential in modulating immune responses and providing a new approach for the treatment of fatigue in patients with IBD, its specific efficacy, long-term effects, and differentiation from placebo effects still need to be verified by larger-scale and more rigorous clinical studies.

Light Therapy

Light therapy is a non-invasive method that involves exposing the patient to specific wavelengths of light to simulate natural light, thereby regulating the biological clock and influencing the patient's mental and physiological state. This has been commonly used in the treatment of various sleep disorders.⁶⁹ In recent years, it has been used in the treatment of other health problems and has shown initial potential in relieving fatigue, depression, and pain in patients with IBD.

Ewais et al⁷⁰ developed a protocol to study the effects of a 10-week photobiomodulation intervention in 28 young patients with IBD on fatigue, pain, and depression. While their findings have not yet been published, this is the first study exploring the use of light therapy specifically for patients with IBD. The potential of light therapy as a new intervention for the treatment of fatigue in patients with IBD is promising but still needs further investigation with respect to the

specific mechanisms involved and its efficacy. The current evidence is insufficient to draw definitive conclusions about its efficacy and safety. Therefore, medical professionals should exercise caution when choosing these therapies, ensuring that treatment decisions are guided by the most recent research findings and clinical experience.

Conclusion

Fatigue significantly impacts the academic, personal, and professional lives of patients with IBD. At present, there is no consensus on the most effective tool for assessing fatigue in this population. Nevertheless, it is crucial for medical professionals to recognize the importance of addressing fatigue symptoms in patients with IBD and take timely measures that consider both alleviating and exacerbating factors to effectively intervene and manage fatigue. While there is a growing body of research on non-pharmacological interventions for managing fatigue in IBD patients, the evidence remains limited. Future research should focus on prospective studies comparing various non-pharmacological intervention methods to provide a sound theoretical foundation for the formulation of scientific and standardized fatigue management programs. Additionally, clinical nurses should play an active role in providing relevant fatigue-related information to patients and caregivers. Enhancing awareness about fatigue, offering coping strategies, and encouraging patients to proactively manage fatigue symptoms can improve their quality of life.

In order to more effectively manage fatigue in patients with IBD, a structured approach is recommended to integrate fatigue management into routine clinical practice. First, the development of clinical guidelines specifically for fatigue in IBD patients to standardize and standardize the fatigue management process will provide medical staff with clear operating specifications and assessment tools to ensure that each patient can receive individualized and comprehensive management. Secondly, it is essential to provide professional training to medical staff to improve their ability to recognize and cope with patient fatigue, such as through regular training workshops, simulation exercises and case discussions, to enhance their professionalism and clinical skills. Finally, it is also key to increase patient education and participation to encourage patients to be actively involved in their own management process. Awareness and self-efficacy of patients about the disease and its management can be improved through the development of creative and interactive educational materials, as well as the organization of counselling, support groups and self-management groups. Through these measures, people with IBD can be better supported to cope with fatigue, which in turn improves their quality of life.

Abbreviations

ACT, acceptance and commitment therapy; IBD, inflammatory bowel disease; CD, Crohn's disease; UC, Ulcerative colitis; MFI-20, Multiple fatigue inventory; FACIT-F, Functional assessment of chronic illness therapy-fatigue; IBD-F, Inflammatory bowel disease fatigue scale; PROMIS-Fatigue SF Scale, Patient-Reported Outcomes Measurement Information Systems–Fatigue Short Form scale; CRP, C-reactive protein; FC, Faecal Calprotectin; HPA, Hypothalamic Pituitary Adrenal; TNF- α , Tumor Necrosis Factor- α ; IFN- γ , Interferon- γ ; IL-12, Interleukin-12; CBT, Cognitive Behavioral Therapy; IL-1 β , Interleukin-1 β ; IL-6, Interleukin-6.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

This study is a literature review and does not require the informed consent of patients, and does not require ethical approval.

Consent for Publication

Not applicable.

Acknowledgments

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

Funding

(1) Jiangxi Province Graduate Student Innovation Fund Project in 2023 (No. YC2023-S199); (2) Jiangxi Provincial Health Commission Science and Technology Project (No. 202410256).

Disclosure

The authors declare that they have no competing interests in this work.

References

1. Akutko K, Stawarski A. Probiotics, prebiotics and synbiotics in inflammatory bowel diseases. *J Clin Med*. 2021;10(11):2466. doi:10.3390/jcm10112466
2. Shao B, Yang W, Cao Q. Landscape and predictions of inflammatory bowel disease in China: china will enter the compounding prevalence stage around 2030. *Front Public Health*. 2022;10:1032679. doi:10.3389/fpubh.2022.1032679
3. Uhlir V, Stallmach A, Grunert PC. Fatigue in patients with inflammatory bowel disease-strongly influenced by depression and not identifiable through laboratory testing: a cross-sectional survey study. *BMC Gastroenterol*. 2023;23(1). doi:10.1186/s12876-023-02906-0
4. Borren NZ, Long MD, Sandler RS, et al. Longitudinal trajectory of fatigue in patients with inflammatory bowel disease: a prospective study. *Inflamm Bowel Dis*. 2021;27(11):1740–1746. doi:10.1093/ibd/izaa338
5. Feagins LA, Moore PC, Crabtree MM, et al. Impact of fatigue on work productivity and activity impairment and health care utilization in patients with inflammatory bowel disease. *AM J GASTROENTEROL*. 2022;117(10):S639–S640.
6. Pekow J. Fatigue in inflammatory bowel disease: a common complaint with few answers. *GASTROENTEROLOGY*. 2022;163(5):1164–1165. doi:10.1053/j.gastro.2022.08.050
7. Stroie T, Preda C, Istratescu D, et al. Anxiety and depression in patients with inactive inflammatory bowel disease The role of fatigue and health-related quality of life. *MED*. 2023;102(19):e33713. doi:10.1097/MD.00000000000033713
8. Czuber-Dochan W, Norton C, Bredin F, et al. Healthcare professionals' perceptions of fatigue experienced by people with IBD. *J Crohns Colitis*. 2014;8(8):835–844. doi:10.1016/j.crohns.2014.01.004
9. Ream E, Richardson A. Fatigue: a concept analysis. *Int J Nurs Stud*. 1996;33(5):519–529. doi:10.1016/0020-7489(96)00004-1
10. Markowitz AJ, Rabow MW. Palliative management of fatigue at the close of life: "it feels like my body is just worn out". *JAMA*. 2007;298(2):217. doi:10.1001/jama.298.2.217
11. Czuber-Dochan W, Dibley LB, Terry H, et al. The experience of fatigue in people with inflammatory bowel disease: an exploratory study. *J Adv Nurs*. 2013;69(9):1987–1999. doi:10.1111/jan.12060
12. Regueiro M, Hunter T, Lukanova R, et al. Burden of fatigue among patients with ulcerative colitis and crohn's disease: results from a global survey of patients and gastroenterologists. *ADV THER*. 2023;40(2):474–488. doi:10.1007/s12325-022-02364-2
13. Norton C, Hart A, Miller L, et al. The relationship between fatigue, pain and urgency in 8486 people with inflammatory bowel disease: a survey. *GUT*. 2023;72(SUPPL_2):A109.
14. Amiot A, Chaibi S, Bouhnik Y, et al. Prevalence and determinants of fatigue in patients with IBD: a cross-sectional survey from the GETAID. *J Crohns Colitis*. 2023;17(9):1418–1425. doi:10.1093/ecco-jcc/jjad060
15. Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet*. 2017;390(10114):2769–2778. doi:10.1016/S0140-6736(17)32448-0
16. Pal P, Banerjee R, Vijayalaxmi P, et al. Depression and active disease are the major risk factors for fatigue and sleep disturbance in inflammatory bowel disease with consequent poor quality of life: analysis of the interplay between psychosocial factors from the developing world. *Indian J Gastroenterol*. 2024;43(1):226–236. doi:10.1007/s12664-023-01462-5
17. Ng SC, Tang W, Ching JY, et al. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-Pacific Crohn's and colitis epidemiology study. *Gastroenterology*. 2013;145(1):158–165. doi:10.1053/j.gastro.2013.04.007
18. Gong S, Fan Y, Lv B, et al. Fatigue in patients with inflammatory bowel disease in Eastern China. *World J Gastroenterol*. 2021;27(11):1076–1089. doi:10.3748/wjg.v27.i11.1076
19. Smets EM, Garssen B, Bonke B, et al. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *J Psychosom Res*. 1995;39(3):315–325. doi:10.1016/0022-3999(94)00125-0
20. Gentile S, Delarozziere JC, Favre F, et al. Validation of the French 'multidimensional fatigue inventory' (MFI 20). *Eur J Cancer Care (Engl)*. 2003;12(1):58–64. doi:10.1046/j.1365-2354.2003.00295.x
21. Buss T, Kruk A, Wisniewski P, et al. Psychometric properties of the polish version of the multidimensional fatigue inventory-20 in cancer patients. *J Pain Symptom Manage*. 2014;48(4):730–737. doi:10.1016/j.jpainsymman.2013.11.015
22. Gecaite-Stonciene J, Bunevicius A, Burkauskas J, et al. Validation of the multidimensional fatigue inventory with coronary artery disease patients. *Int J Environ Res Public Health*. 2020;17(21):8003. doi:10.3390/ijerph17218003
23. Basoglu F, Oncu J, Kuran B, et al. The reliability and validity of The Turkish version of multidimensional fatigue inventory-20 for the evaluation of different dimensions of fatigue in patients with fibromyalgia. *Turk J Phys Med Rehabil*. 2020;66(4):436–443. doi:10.5606/tftrd.2021.5781
24. Chuang LL, Chuang YF, Hsu MJ, et al. Validity and reliability of the traditional Chinese version of the multidimensional fatigue inventory in general population. *PLoS One*. 2018;13(5):e189850. doi:10.1371/journal.pone.0189850

25. Artom M, Czuber-Dochan W, Sturt J, et al. The contribution of clinical and psychosocial factors to fatigue in 182 patients with inflammatory bowel disease: a cross-sectional study. *Aliment Pharmacol Ther.* 2017;45(3):403–416. doi:10.1111/apt.13870
26. Borren NZ, Tan W, Colizzo FP, et al. Longitudinal trajectory of fatigue with initiation of biologic therapy in inflammatory bowel diseases: a prospective cohort study. *J Crohns Colitis.* 2020;14(3):309–315. doi:10.1093/ecco-jcc/jjz148
27. Xu F, Hu J, Yang Q, et al. Prevalence and factors associated with fatigue in patients with ulcerative colitis in China: a cross-sectional study. *BMC Gastroenterol.* 2022;22(1):281. doi:10.1186/s12876-022-02357-z
28. Jelsness-Jorgensen L, Moum B, Grimstad T, et al. The multidimensional fatigue inventory (MFI-20): psychometrical testing in a Norwegian sample of inflammatory bowel disease (IBD) patients. *Scand J Gastroenterol.* 2022;57(6):683–689. doi:10.1080/00365521.2022.2029939
29. Yellen SB, Cella DF, Webster K, et al. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage.* 1997;13(2):63–74. doi:10.1016/S0885-3924(96)00274-6
30. Cella D, Yount S, Sorensen M, et al. Validation of the functional assessment of chronic illness therapy fatigue scale relative to other instrumentation in patients with rheumatoid arthritis. *J Rheumatol.* 2005;32(5):811–819.
31. Hagell P, Hoglund A, Reimer J, et al. Measuring fatigue in Parkinson's disease: a psychometric study of two brief generic fatigue questionnaires. *J Pain Symptom Manage.* 2006;32(5):420–432. doi:10.1016/j.jpainsymman.2006.05.021
32. Delgado-Alvarez A, Matias-Guiu JA, Delgado-Alonso C, et al. Validation of Two New Scales for the Assessment of Fatigue in Multiple Sclerosis: F-2-MS and FACIT-F. Vol. 63. *Mult Scler Relat Disord*; 2022:103826
33. Loftus EVJ, Ananthakrishnan AN, Lee W, et al. Content validity and psychometric evaluation of the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) in patients with Crohn's disease and ulcerative colitis. *PharmacoEconomics - Open.* 2023;7(5):823–840. doi:10.1007/s41669-023-00419-w
34. Regueiro M, Su S, Vadhariya A, et al. Psychometric evaluation of the Functional Assessment of chronic illness therapy-fatigue (FACIT-Fatigue) in adults with moderately to severely active Crohn's disease. *Qual Life Res.* 2024;34(2):509–521. doi:10.1007/s11136-024-03829-3
35. Czuber-Dochan W, Norton C, Bassett P, et al. Development and psychometric testing of inflammatory bowel disease fatigue (IBD-F) patient self-assessment scale. *J Crohns Colitis.* 2014;8(11):1398–1406. doi:10.1016/j.crohns.2014.04.013
36. Varbobitis I, Kokkotis G, Gizis M, et al. The IBD-F patient self-assessment scale accurately depicts the level of fatigue and predicts a negative effect on the quality of life of patients with IBD in clinical remission. *Inflamm Bowel Dis.* 2021;27(6):826–835. doi:10.1093/ibd/izaa201
37. Liebert A, Wilenska A, Czuber-Dochan W, et al. Translation and validation of the inflammatory bowel disease fatigue (IBD-F) patient self-assessment questionnaire. *Prz Gastroenterol.* 2021;16(2):136–143. doi:10.5114/pg.2021.106665
38. Hatamnejad MR, Shirvani M, Pourhoseingholi MA, et al. Translation and cross-cultural adaptation of the Persian version of inflammatory bowel disease-fatigue (IBD-F) self-assessment questionnaire. *PLoS One.* 2023;18(7):e288592. doi:10.1371/journal.pone.0288592
39. Stoker A, Gruters A, Loon M, et al. Translation, validation and psychometric properties of the Dutch version of the Inflammatory Bowel Disease-Fatigue (IBD-F) self-assessment scale. *J Patient Rep Outcomes.* 2023;7(1):108. doi:10.1186/s41687-023-00642-3
40. Lage AC, Oliveira CC, Batalha A, et al. The inflammatory bowel disease-fatigue patient self-assessment scale: translation, cross-cultural adaptation and psychometric properties of the Brazilian Version (IBD-F BRAZIL). *Arq Gastroenterol.* 2020;57(1):50–63. doi:10.1590/s0004-2803.202000000-10
41. Scholz K, Thomann AK, Teich N, et al. Validation of the German Inflammatory Bowel Disease Fatigue (IBD-F) Questionnaire. *Z Gastroenterol.* 2023;61(2):164–171. doi:10.1055/a-1797-2688
42. Junghaenel DU, Christodoulou C, Lai JS, et al. Demographic correlates of fatigue in the US general population: results from the patient-reported outcomes measurement information system (PROMIS) initiative. *J Psychosom Res.* 2011;71(3):117–123. doi:10.1016/j.jpsychores.2011.04.007
43. Cella D, Yount S, Rothrock N, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. *Med Care.* 2007;45(5 Suppl 1):S3–S11. doi:10.1097/01.mlr.0000258615.42478.55
44. National Institutes of Health. PROMIS. [EB/OL] (2023-03-27). Available from: https://www.healthmeasures.net/index.php?option=com_content&view=category&layout=blog&id=147&Itemid=806.html. Accessed February 28, 2025.
45. Feagan BG, Sandborn WJ, Sands BE, et al. Qualitative and psychometric evaluation of the PROMIS-Fatigue SF-7a scale to assess fatigue in patients with moderately to severely active inflammatory bowel disease. *J Patient-Reported Outcomes.* 2023;7(1):115. doi:10.1186/s41687-023-00645-0
46. Lee HH, Gweon TG, Kang SG, et al. Assessment of fatigue and associated factors in patients with inflammatory bowel disease: a questionnaire-based study. *J Clin Med.* 2023;12(9). doi:10.3390/jcm12093116
47. Chavarria C, Casanova MJ, Chaparro M, et al. Prevalence and factors associated with fatigue in patients with inflammatory bowel disease: a multicentre study. *J Crohns Colitis.* 2019;13(8):996–1002. doi:10.1093/ecco-jcc/jjz024
48. Holten K, Bernklev T, Opheim R, et al. Fatigue in patients with newly diagnosed inflammatory bowel disease: results from a prospective inception cohort, the IBSEN III Study. *J Crohns Colitis.* 2023;17(11):1781–1790. doi:10.1093/ecco-jcc/jjad094
49. Kuwahara A, Matsuda K, Kuwahara Y, et al. Microbiota-gut-brain axis: enteroendocrine cells and the enteric nervous system form an interface between the microbiota and the central nervous system. *Biomed Res.* 2020;41(5):199–216. doi:10.2220/biomedres.41.199
50. Vogelaar L, de Haar C, Aerts BR, et al. Fatigue in patients with inflammatory bowel disease is associated with distinct differences in immune parameters. *Clin Exp Gastroenterol.* 2017;10:83–90. doi:10.2147/CEG.S123942
51. Borren NZ, Plichta D, Joshi AD, et al. Alterations in fecal microbiomes and serum metabolomes of fatigued patients with quiescent inflammatory bowel diseases. *Clin Gastroenterol Hepatol.* 2021;19(3):519–527. doi:10.1016/j.cgh.2020.03.013
52. Bergamaschi G, Castiglione F, D'Inca R, et al. Prevalence, pathogenesis and management of anemia in inflammatory bowel disease: an IG-IBD multicenter, prospective, and observational study. *INFLAMM BOWEL DIS.* 2023;29(1):76–84. doi:10.1093/ibd/izac054
53. Xue M, Chen J, Zheng W, et al. Clinical characteristics and quality of life in patients with inflammatory bowel disease-associated anemia in Southeast China. *Eur J Gastroenterol Hepatol.* 2023;35(3):275–284. doi:10.1097/MEG.0000000000002511
54. Bergamaschi G, Castiglione F, D'Inca R, et al.; Follow-up evaluation and management of anemia in inflammatory bowel disease: A study by the Italian Group for Inflammatory Bowel Diseases (IG-IBD). Digestive and liver disease: Official J Italian Soc Gastroenterol Italian Assoc Study of the Liver. 2024; 56(9):1483–1489.
55. Barberio B, Zamani M, Black CJ, et al. Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol.* 2021;6(5):359–370. doi:10.1016/S2468-1253(21)00014-5

56. Bernstein CN, Fisk JD, Dolovich C, et al. Understanding predictors of fatigue over time in persons with inflammatory bowel disease: the importance of depressive and anxiety symptoms. *Am J Gastroenterol*. 2024;119(5):922–929. doi:10.14309/ajg.0000000000002630
57. Guadagnoli L, Horrigan J, Walentyńczak M, et al. Sleep quality drives next day pain and fatigue in adults with inflammatory bowel disease: a short report. *J Crohn's Colitis*. 2024;18(1):171–174. doi:10.1093/ecco-jcc/jjad128
58. Canakis A, Qazi T. Sleep and Fatigue in IBD: an Unrecognized but Important Extra-intestinal Manifestation. *Curr Gastroenterol Rep*. 2020;22(2):8. doi:10.1007/s11894-020-0746-x
59. Jelsness-Jorgensen LP, Bernklev T, Henriksen M, et al. Chronic fatigue is more prevalent in patients with inflammatory bowel disease than in healthy controls. *Inflamm Bowel Dis*. 2011;17(7):1564–1572. doi:10.1002/ibd.21530
60. Fons AB, Asscher VER, Stuyt RJL, et al. Deficits in geriatric assessment are important in relation to fatigue in older patients with inflammatory bowel disease. *Digest Liver Dis*. 2024;56(9):1490–1496. doi:10.1016/j.dld.2024.01.196
61. Davis SP, Crane PB, Bolin LP, et al. An integrative review of physical activity in adults with inflammatory bowel disease. *Intest Res*. 2022;20(1):43–52. doi:10.5217/ir.2020.00049
62. Artom M, Czuber-Dochan W, Sturt J, et al. Cognitive-behavioural therapy for the management of inflammatory bowel disease-fatigue: a feasibility randomised controlled trial. *Pilot Feasibility Stud*. 2019;5:145.
63. van Kessel K, Moss-Morris R, Willoughby E, et al. A randomized controlled trial of cognitive behavior therapy for multiple sclerosis fatigue. *Psychosom Med*. 2008;70(2):205–213. doi:10.1097/PSY.0b013e3181643065
64. Maunick B, Skvarc D, Olive L, et al. Effects of acceptance and commitment therapy on fatigue for patients with cancer and other chronic health conditions: a systematic review and meta-analysis. *J PSYCHOSOMATIC RES*. 2023;171: 111366.
65. van Erp LW, Roosenboom B, Komdeur P, et al. Improvement of fatigue and quality of life in patients with quiescent inflammatory bowel disease following a personalized exercise program. *Dig Dis Sci*. 2021;66(2):597–604. doi:10.1007/s10620-020-06222-5
66. Tew GA, Leighton D, Carpenter R, et al. High-intensity interval training and moderate-intensity continuous training in adults with Crohn's disease: a pilot randomised controlled trial. *BMC Gastroenterol*. 2019;19(1):19. doi:10.1186/s12876-019-0936-x
67. Wu HG, Liu HR, Tan LY, et al. Electroacupuncture and moxibustion promote neutrophil apoptosis and improve ulcerative colitis in rats. *Dig Dis Sci*. 2007;52(2):379–384. doi:10.1007/s10620-006-9561-y
68. Horta D, Lira A, Sanchez-Lloansi M, et al. A prospective pilot randomized study: electroacupuncture vs. sham procedure for the treatment of fatigue in patients with quiescent inflammatory bowel disease. *Inflamm Bowel Dis*. 2020;26(3):484–492. doi:10.1093/ibd/izz091
69. Tan J, Cheng LJ, Chan EY, et al. Light therapy for sleep disturbances in older adults with dementia: a systematic review, meta-analysis and meta-regression. *Sleep Med*. 2022;90:153–166. doi:10.1016/j.sleep.2022.01.013
70. Ewais T, Begun J, Laakso E. Protocol for a single-arm feasibility study of photobiomodulation for fatigue, depression, and pain in inflammatory bowel disease. *Biomedicine*. 2023;11(8):2179. doi:10.3390/biomedicine11082179

International Journal of General Medicine

Publish your work in this journal

The International Journal of General Medicine is an international, peer-reviewed open-access journal that focuses on general and internal medicine, pathogenesis, epidemiology, diagnosis, monitoring and treatment protocols. The journal is characterized by the rapid reporting of reviews, original research and clinical studies across all disease areas. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/international-journal-of-general-medicine-journal>

Dovepress
Taylor & Francis Group