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Observational Study

Fatigue in patients with inflammatory bowel disease in Eastern China

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Abstract

BACKGROUND

Fatigue is a very common but relatively neglected problem in patients with inflammatory bowel disease (IBD). The prevalence rate of IBD in China is the highest in Asia, but there is little research on fatigue in patients with IBD. Neither the relationship between fatigue and quality of life (QoL) nor the relationship between fatigue and work productivity (WP) in Chinese IBD patients has been reported.

AIM

To investigate the prevalence of fatigue related to IBD in Eastern China, to identify the risk factors associated with fatigue, to assess the impact of fatigue on QoL, and to evaluate the relationship between fatigue and WP.

METHODS

A cross-sectional study was conducted in a Regional Tertiary IBD Diagnostic and Treatment Center in Eastern China. Clinical data of patients were collected, and disease activity was evaluated. Blood samples were analyzed to assess anemia, albumin, and inflammation. Fatigue was assessed using the multidimensional fatigue inventory. QoL and WP were measured using the short inflammatory bowel disease questionnaire and the work productivity and activity impairment general health questionnaire, respectively. The patients also completed assessments of depression (Patient Health Questionnaire-9) and anxiety (Generalized Anxiety Disorder 7-item Scale).

RESULTS

A total of 311 IBD patients, comprising 168 Crohn's disease patients and 143

guardian, provided informed written consent prior to study enrollment.

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ulcerative colitis patients, were enrolled. The prevalence of fatigue in patients with IBD was 60.77%. In a univariate logistic regression analysis, factors such as disease activity, depression, anxiety, anemia, and IBD-related surgery were individually related to a significantly increased risk of fatigue in IBD patients. Multivariate logistic regression analysis indicated that depression [odds ratio (OR) = 8.078, 95% confidence interval (CI): 4.113-15.865], anxiety (OR = 2.373, 95% CI: 1.100-5.119), anemia (OR = 2.498, 95% CI: 1.290-4.834), and IBD-related surgery (OR = 2.035, 95% CI: 1.084-3.819) were related to fatigue in IBD patients. There was a negative correlation between fatigue and QoL ($r = -0.831$; $P < 0.0001$) but a positive correlation between fatigue and WP loss.

CONCLUSION

The prevalence of fatigue in IBD patients in Eastern China is remarkably high even in clinical remission. Factors such as depression, anxiety, anemia, and IBD-related surgery are major risk factors for fatigue in IBD patients. In addition, fatigue has a negative impact on QoL and is positively correlated with WP loss.

Key Words: Inflammatory bowel disease; Fatigue; Quality of life; Work productivity; Risk factors; Eastern China

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Core Tip: Fatigue is a highly prevalent and burdensome symptom in patients with inflammatory bowel disease (IBD), with an important impact on quality of life and (indirect) health expenditures. The prevalence rate of IBD in China is the highest in Asia, but there is little research on fatigue in patients with IBD. In addition, the relationships of fatigue with quality of life and work productivity in Chinese IBD patients have not been reported.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic, nonspecific inflammation of the gastrointestinal tract with an unknown etiology that can be classified as ulcerative colitis (UC) and Crohn's disease (CD)^[1]. IBD has a high prevalence in young adults and is characterized by a long course, high recurrence rate, and severe complications (such as toxic megacolon, intestinal perforation, intestinal obstruction, intestinal bleeding, and cancer)^[2]. Mucus-bloody stools, diarrhea, abdominal pain, weight loss, and anemia are the main clinical manifestations of IBD^[3], which seriously impact the quality of life (QoL) of patients and increase the financial burden.

Fatigue is expressed as an overwhelming experience of mental and/or physical exhaustion that affects daily living and is unrelieved by rest or sleep^[4,5]. Studies in several countries have shown that fatigue is common in patients with IBD^[6-10]. Some studies have found that fatigue is associated with active enteritis^[11], especially with mucosal healing in patients with IBD^[12]. In addition, fatigue also has a negative psychological impact on patients with IBD, exacerbating clinical symptoms and promoting disease progression^[13]. Even as a result of fatigue, IBD patients have to adjust their daily activities and work, and some even choose to resign, which seriously affects their QoL^[14] and increases their financial burden^[15]. Fatigue is a very common but relatively neglected problem in IBD patients, especially in China. The prevalence rate of IBD in China is the highest in Asia^[16], but there is little research on fatigue in patients with IBD. In addition, the relationship between fatigue and QoL and work productivity (WP) in Chinese IBD patients has not been reported.

In this study, we aimed to investigate the prevalence and risk factors for fatigue in patients with IBD in Eastern China through a cross-sectional study. We also

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determined the relationships between fatigue and QoL and WP to evaluate the impact of fatigue on IBD patients in Eastern China.

MATERIALS AND METHODS

Study population

This cross-sectional study was conducted at the First Affiliated Hospital of Zhejiang Chinese Medical University, a Regional Tertiary IBD Diagnostic and Treatment Center in Eastern China, from February 2018 to August 2020. The inclusion criteria were a confirmed diagnosis of IBD and signed informed consent. The diagnostic criteria for IBD were based on the Chinese consensus on the diagnosis and treatment of IBD^[17]. The exclusion criteria were the inability to understand or complete the questionnaires, refusal to give written informed consent before participation, and concomitant diseases with fatigue as the main symptoms, such as cancer, heart disease, or liver cirrhosis. This study was registered at the Chinese Clinical Trials Registry (ChiCTR1900025890).

Ethics

This study was approved by the ethics committee of the First Affiliated Hospital of Zhejiang Chinese Medical University, and informed consent was obtained from all participants. Patients under the age of 16 were admitted to our study with consent from their parents or guardians.

Clinical and sociodemographic data

The demographic characteristics of the patients were collected, including age, sex, body mass index (BMI), course of the disease, current smoking habits, IBD-related surgery (such as colectomies, other bowel surgery, and perianal surgery), disease activity, type of IBD, location of disease, and current medications. Blood samples were collected (within one week before and after completion of the questionnaires) and analyzed for hemoglobin, albumin, and erythrocyte sedimentation rate.

Definitions

Disease activity and severity were assessed using the following clinical indices: Harvey-Bradshaw activity index^[18] was used for CD. Mayo score and Truelove and Witts criteria^[19] were used for UC. Anemia was defined as hemoglobin < 130 g/L for males and < 120 g/L for females. Hypoalbuminemia was defined as albumin < 35 g/L. BMI was based on the Chinese criteria of weight for adults^[20]. Underweight was defined as BMI < 18.5 kg/m²; normal weight was defined as 18.5 kg/m² ≤ BMI < 24.0 kg/m²; overweight was defined as 24.0 kg/m² ≤ BMI < 28.0 kg/m²; and obesity was defined as BMI ≥ 28.0 kg/m².

The significance level of coefficients is indicated only when they reach the 0.001 criterion. The following cutoffs were used to define the magnitude of the correlation coefficients: < 0.25, low correlation; 0.25 to 0.5, fair correlation; 0.5 to 0.75, moderate-to-good correlation; and > 0.75, good-to-excellent correlation^[21].

Questionnaires

Fatigue was analyzed using the multidimensional fatigue inventory (MFI; ranging from 20 to 100, with higher scores indicating more severe fatigue). This questionnaire, previously validated in Chinese and for IBD patients^[22], comprises 20 items divided into five subscales: General fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue^[23]. The definition of fatigue was complicated by a lack of clear cutoff scores. Several studies have found that scales of general fatigue are more psychometrically useful than the use of numerical rating scales, so the MFI of general fatigue can be called "fatigue"^[24-26]. Combining the values reported in a domestic study^[27] and foreign studies^[28-30] on the MFI, fatigue was defined as general fatigue score ≥ 12.

Depression was analyzed using the Patient Health Questionnaire-9 (PHQ-9), which has been validated in Chinese IBD patients^[31]. The PHQ-9 scores each of the 9 DSM-IV criteria on a scale ranging from "0" (not at all) to "3" (nearly every day). The total PHQ-9 score that categorizes depression is as follows: Nondepression as 0 ≤ PHQ-9 ≤ 4, mild depression as 5 ≤ PHQ-9 ≤ 9, moderate depression as 10 ≤ PHQ-9 ≤ 14, moderate-to-severe depression as 15 ≤ PHQ-9 ≤ 19, and severe depression as 20 ≤ PHQ-9 ≤ 27^[32].

The generalized anxiety disorder 7-item scale was completed to measure symptoms

of anxiety and has been validated in Chinese patients with IBD^[31]. The generalized anxiety disorder 7-item scale is a 7-item self-report instrument that is scaled from 0–3 (not at all, several days, more than half the days, and nearly every day), with total scores ranging from 0 to 21, and it is interpreted as follows: The absence of anxiety (0–4), mild anxiety (5–9), moderate anxiety (10–14), and severe anxiety (15–21)^[31].

The Short Inflammatory Bowel Disease Questionnaire (SIBDQ) was used to assess IBD-specific QoL^[34]. The SIBDQ includes 10 items, each with a score from 1 (worst) to 7 (best), with the total score ranging from 10 to 70 (the higher the score, the better the QoL). Furthermore, the SIBDQ has four domains: Bowel symptoms, systemic symptoms, emotional function, and social function.

The work productivity and activity impairment general health questionnaire^[35] measures time missed from work and work impairment because of IBD in the past week. The work productivity and activity impairment general health questionnaire includes four items: Work time missed (absenteeism), impaired productivity at work (presenteeism), overall work impairment (OWI; combined absenteeism and presenteeism), and impairment in non-work-related activities due to health problems (activity impairment). Absenteeism was calculated as [hours missed due to health problems / (hours missed due to health problems + hours worked)] × 100; presenteeism was calculated as (degree health affected productivity while working / 10) × 100; OWI was calculated as absenteeism + [(1-absenteeism) × presenteeism]; and (4) daily activity impairment was calculated as (degree of health affected daily activities / 10) × 100.

Statistical analysis

Quantitative variables are expressed as the mean ± SD or as medians and interquartile range (IQR), and qualitative variables are expressed as frequencies and percentages. After transforming fatigue from a quantitative to a qualitative variable (with/without fatigue), logistic regression analyses were performed. Variables with $P < 0.05$ in the univariate analysis were included in the multivariate analysis, and the results are expressed as odds ratios (ORs) with their corresponding 95% confidence intervals (CIs). Correlations between fatigue and QoL and WP were measured with Spearman's rank correlation coefficient. Statistical analyses were performed using Statistic Package for Social Science 24 (Statistic Package for Social Science Inc., Chicago, IL, United States), and $P < 0.05$ was considered statistically significant.

RESULTS

IBD patients' demographic and clinical characteristics

A total of 311 IBD patients, including 168 CD and 143 UC patients, were enrolled in this study. The participants had a median age of 42 (IQR: 31–53) years. Most of the participants had health insurance (90.35%, $n = 281$) and were married (74.28%, $n = 231$). There were 212 (68.17%) patients who had a job, of whom 208 (66.88%) were working full-time. Regarding the duration of disease, the participants reported a median of 5 (IQR: 2–12) years. A total of 51.45% of IBD patients were in the active phase of the disease, and 32.80% of participants had IBD-related surgery. The demographic and clinical characteristics of IBD patients are summarized in [Table 1](#).

Prevalence and score of fatigue in patients with IBD

The prevalence of fatigue in patients with IBD was 60.77%, including 71.88% in patients with active IBD and 49.01% in patients in remission. The median fatigue total score was 43 (IQR: 33–59) in IBD patients, and the median general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation scores were 12 (IQR: 9–15), 8 (IQR: 6–12), 9 (IQR: 6–12), 7 (IQR: 4–9), and 7 (IQR: 4–12), respectively ([Figure 1](#)).

Factors associated with fatigue

The univariate analysis showed that disease activity ($P < 0.001$, OR = 2.659; 95%CI: 1.663–4.253), depression ($P < 0.001$, OR = 13.722; 95%CI: 7.608–24.749), anxiety ($P < 0.001$, OR = 8.134; 95%CI: 4.351–15.204), anemia ($P < 0.001$, OR = 3.792; 95%CI: 2.232–6.440), and IBD-related surgery ($P < 0.05$, OR = 1.654; 95%CI: 1.004–2.727) were associated with the presence of fatigue ([Figure 2A](#)).

Multivariate logistic regression analysis indicated that depression ($P < 0.001$, OR = 8.078, 95%CI: 4.113–15.865), anxiety ($P = 0.028$, OR = 2.373, 95%CI: 1.100–5.119), anemia ($P = 0.007$, OR = 2.498, 95%CI: 1.290–4.834), and IBD-related surgery ($P = 0.027$, OR =

Table 1 Demographic and clinical characteristics of inflammatory bowel disease patients

	CD (n = 168)	UC (n = 143)
Age, yr, median (IQR)	39 (IQR: 28-52.75)	45 (IQR: 33-54)
Gender, n (%)		
Female	71 (42.26)	64 (44.76)
Male	97 (57.74)	79 (55.24)
BMI, n (%)		
Normal	94 (55.95)	81 (56.64)
Thinnish	60 (35.71)	37 (25.88)
Overweight	11 (6.55)	25 (17.48)
Obesity	3 (1.79)	0 (0)
Marital status, n (%)		
Unmarried	58 (34.52)	14 (9.79)
Married	105 (62.50)	126 (88.11)
Divorced	3 (1.79)	3 (2.10)
Death of a spouse	2 (1.19)	0 (0)
Employment status, n (%)		
No work	16 (9.52)	13 (9.09)
Full time	117 (69.64)	91 (63.64)
Retired	15 (8.93)	35 (24.48)
Long-term sick leave	1 (0.60)	3 (2.10)
Students	19 (11.31)	1 (0.69)
Medical insurance, n (%)		
Yes	151 (89.88)	130 (90.91)
No	17 (10.12)	13 (9.09)
Education, n (%)		
Primary school or below	14 (8.33)	20 (13.99)
Junior high school	34 (20.24)	36 (25.17)
Senior high school	32 (19.05)	41 (28.67)
Junior college or Undergraduate	81 (48.21)	42 (29.37)
Master degree or above	7 (4.17)	4 (2.80)
Montreal classification, n (%)		
L1 ileal	38 (22.62)	
L2 colonic	14 (8.33)	
L3 ileocolonic	72 (42.86)	
L4 upper gastrointestinal tract	11 (6.55)	
L1 + L4	13 (7.74)	
L3 + L4	20 (11.90)	
E1 proctitis		37 (25.88)
E2 left-sided UC		40 (27.97)
E3 extensive UC		66 (46.15)
Disease activity: n (%)		
Remission	100 (59.52)	51 (35.66)

Mild activity	26 (15.48)	43 (30.07)
Moderate activity	31 (18.45)	37 (25.88)
Severe activity	11 (6.55)	12 (8.39)
Duration of disease, yr, median (IQR)	5.50 (IQR, 2-11)	5 (IQR, 2.3-13)
Current medication, <i>n</i> (%)		
5-ASA	19 (11.31)	88 (61.54)
IS	42 (25)	30 (20.98)
5-ASA + IS	22 (13.09)	8 (5.59)
Biological preparation	45 (26.79)	5 (3.50)
Biological preparation + IS	34 (20.24)	8 (5.59)
Other	6 (3.57)	4 (2.80)
IBD related surgery, <i>n</i> (%)		
No	80 (47.62)	129 (90.21)
Yes	88 (52.38)	14 (9.79)

CD: Crohn's disease; UC: Ulcerative colitis; IBD: Inflammatory bowel disease; 5-ASA: 5-aminosalicylic acid; IQR: Interquartile range; IS: Immunosuppressant.

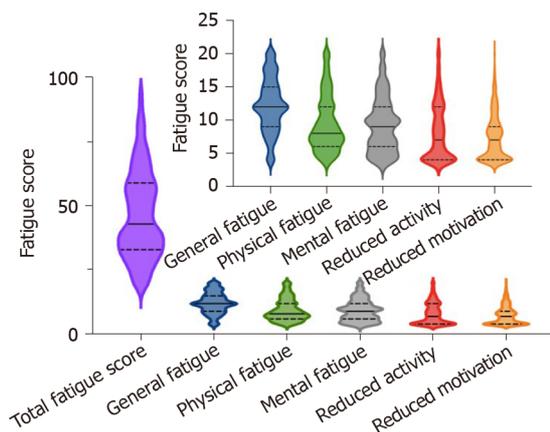


Figure 1 Fatigue score in the inflammatory bowel disease patients. The solid line indicates the median, and the dotted line indicates the interquartile range. The small insert within the graphs in Figure 1 enlarges the scores of the five subscales of multidimensional fatigue inventory (general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue) in the inflammatory bowel disease patients.

2.035, 95%CI: 1.084-3.819) were related to fatigue in IBD patients (Figure 2B).

Fatigue and QoL

The median QoL total score was 53 (IQR: 44-62), and the median scores of bowel symptoms, social function, emotional function, and systemic symptoms were 17 (IQR: 13-20), 12 (IQR: 9-13), 9 (IQR: 6-12), 15 (IQR: 11-19), and 11 (IQR: 10-13), respectively (Figure 3). Fatigue was negatively correlated with QoL ($r = -0.831$; $P < 0.0001$), particularly with emotional function ($r = -0.721$; $P < 0.0001$) (Figure 4A). Further analysis revealed that general fatigue ($r = -0.785$; $P < 0.0001$) showed a good-to-excellent correlation with negative QoL, and reduced activity ($r = -0.731$; $P < 0.0001$) and psychological fatigue ($r = -0.704$; $P < 0.0001$) showed a moderate-to-good correlation with negative QoL (Figure 4B).

Fatigue and WP

There were 208 (66.88%) patients who were working full-time, and their prevalence of fatigue was 58.65%. Further analysis found that their median total fatigue score was 41 (IQR: 32.25-58), with median general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation scores of 12 (IQR: 9-15), 9 (IQR: 7-12), 9 (IQR: 6-11), 6

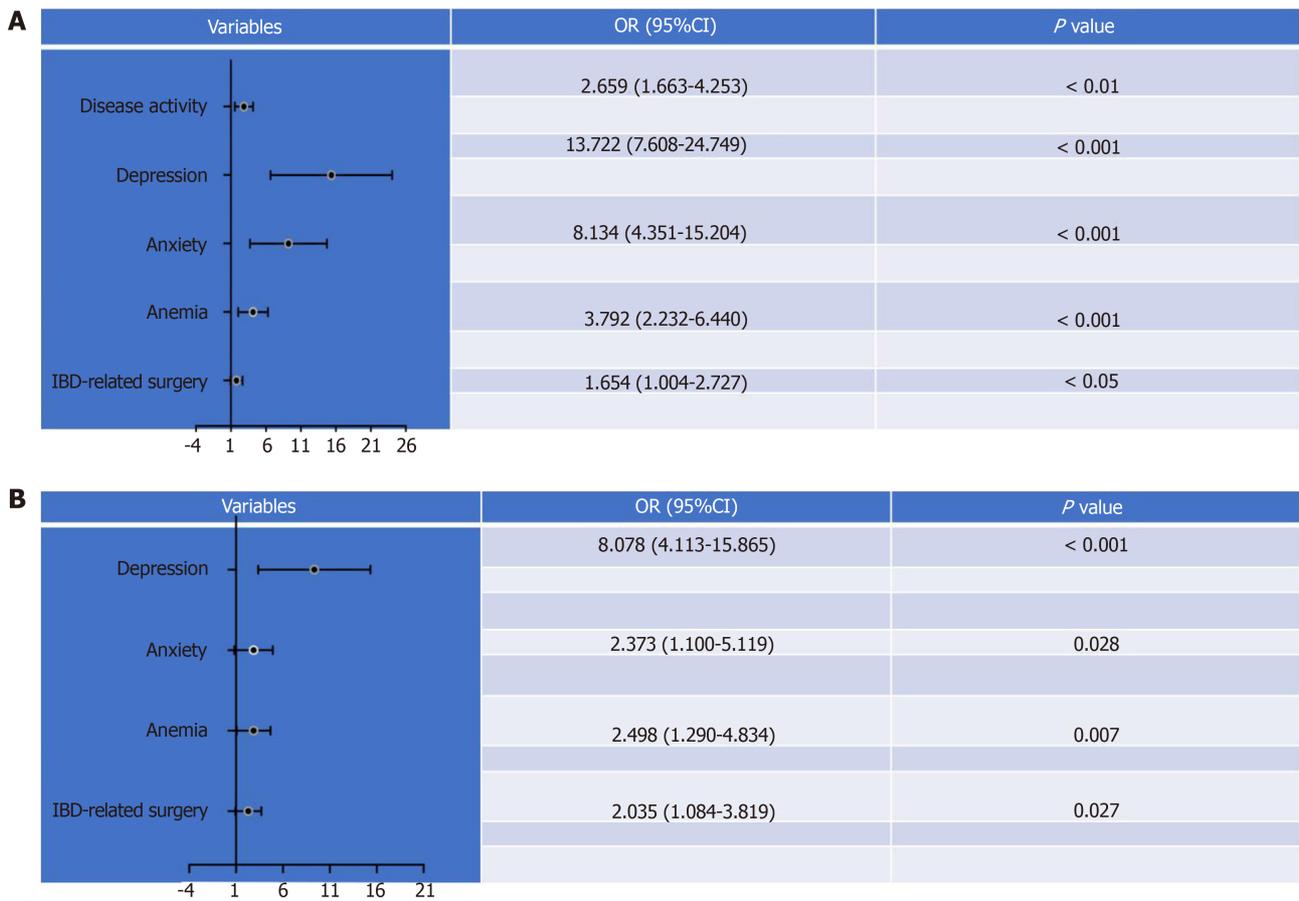


Figure 2 Factors associated with the presence of fatigue. A: Univariate analysis; B: Multivariate analysis. OR: Odds ratio; IBD: Inflammatory bowel disease.

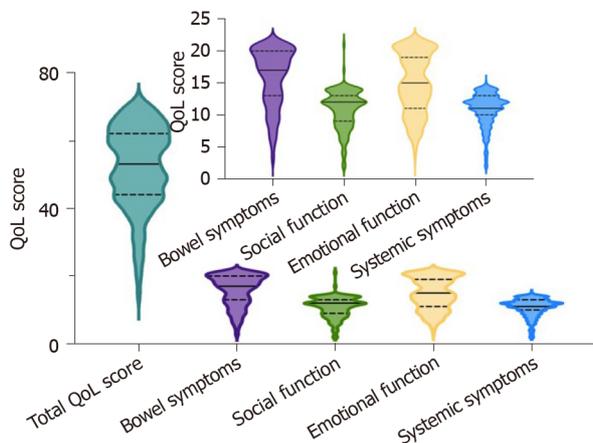


Figure 3 Quality of life score in the inflammatory bowel disease patients. The solid line indicates the median, and the dotted line indicates the interquartile range. The small insert within the graphs in Figure 3 enlarges the scores of the four domains of short inflammatory bowel disease questionnaire (bowel symptoms, systemic symptoms, emotional function, and social function) in the inflammatory bowel disease patients.

(IQR: 4-9), and 6 (IQR: 4-11), respectively (Figure 5). Fatigue had the strongest positive correlation with OWI ($r = 0.605$; $P < 0.0001$), followed by activity impairment ($r = 0.566$; $P < 0.0001$), presenteeism ($r = 0.543$; $P < 0.0001$), and absenteeism ($r = 0.480$; $P < 0.0001$) (Figure 6A). Compared with physical fatigue, mental fatigue, reduced activity, and reduced motivation, general fatigue was the most strongly associated with WP loss (OWI: $r = 0.552$, $P < 0.0001$; activity impairment: $r = 0.549$, $P < 0.0001$; presenteeism: $r = 0.519$, $P < 0.0001$; absenteeism: $r = 0.442$, $P < 0.0001$) (Figure 6B).

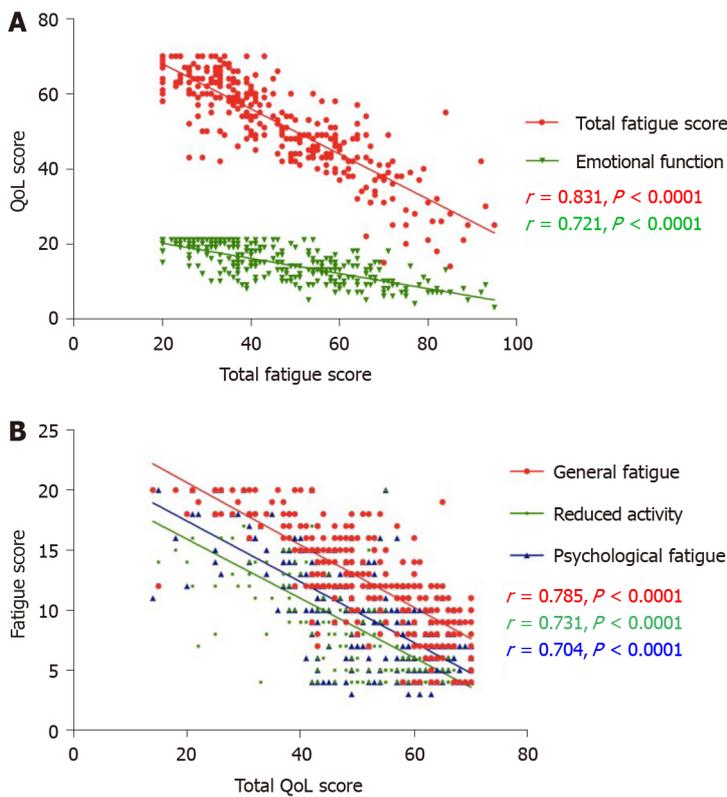


Figure 4 Fatigue and quality of life. A: Correlation between total fatigue scores and quality of life scores (total quality of life scores: Spearman's $r = -0.831, P < 0.0001$; emotional function: Spearman's $r = -0.721, P < 0.0001$) in the inflammatory bowel disease patients; B: Correlation between total quality of life scores and fatigue (general fatigue: Spearman's $r = -0.785, P < 0.0001$; reduced activity: Spearman's $r = -0.731, P < 0.0001$; psychological fatigue: Spearman's $r = -0.704, P < 0.0001$) in the inflammatory bowel disease patients.

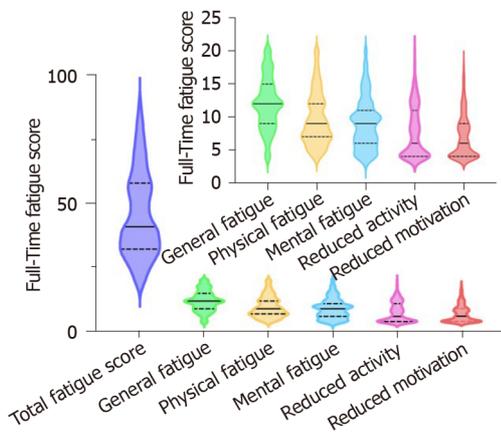


Figure 5 Fatigue score in inflammatory bowel disease patients with full-time jobs. The solid line indicates the median, and the dotted line indicates the interquartile range. The small insert within the graphs in Figure 5 enlarges the scores of the five subscales of multidimensional fatigue inventory (general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue) in the inflammatory bowel disease patients.

DISCUSSION

In the present study, we found that the prevalence of fatigue in patients with IBD in Eastern China was 60.77%, including 71.88% in the active stage and 49.01% in the remission stage. Major factors associated with fatigue were depression, anxiety, anemia, and IBD-related surgery. Female sex, disease activity, and hypoalbuminemia do not increase the risk of fatigue. In addition, fatigue had a negative impact on QoL and was positively correlated with WP loss.

Multifactorial analysis showed that depression and anxiety were risk factors for fatigue, and depression, in particular, is the strongest risk factor for fatigue. Several previous studies are consistent with our findings^[36-38]. In chronic diseases, fatigue and

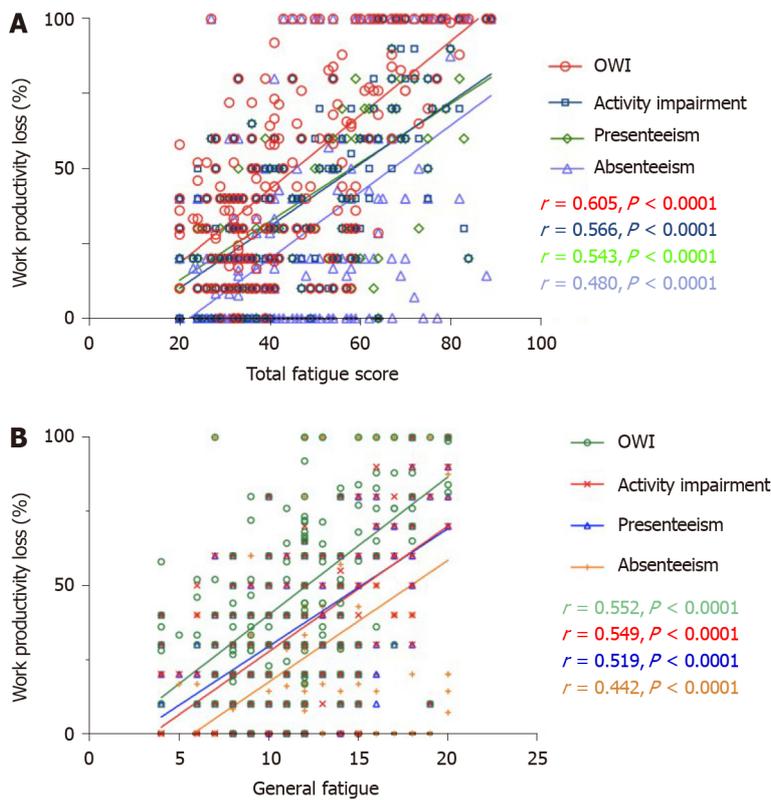


Figure 6 Fatigue and work productivity. A: Correlation between total fatigue scores and work productivity loss [overall work impairment: Spearman's $r = 0.605, P < 0.0001$; activity impairment: Spearman's $r = 0.566, P < 0.0001$; presenteeism: Spearman's $r = 0.543, P < 0.0001$; absenteeism: Spearman's $r = 0.480, P < 0.0001$] in inflammatory bowel disease patients with full-time jobs; B: Correlation between general fatigue and work productivity loss (overall work impairment: Spearman's $r = 0.552, P < 0.0001$; activity impairment: Spearman's $r = 0.549, P < 0.0001$; presenteeism: Spearman's $r = 0.519, P < 0.0001$; absenteeism: Spearman's $r = 0.442, P < 0.0001$) in inflammatory bowel disease patients with full-time jobs. OWI: Overall work impairment.

psychiatric disorders such as depression and anxiety coexist^[39,40], including IBD^[41]. The immune-inflammatory pathway and gut-brain axis may be possible pathways for the coexistence of fatigue and psychological disorders in IBD^[39-42]. One of the reasons for such a high prevalence of fatigue and psychiatric comorbidity in patients with IBD in Eastern China may be due to limited therapeutic drug options. The use of biologics as an effective treatment for IBD in China is very limited. First, the options are limited, with only infliximab entering the Chinese market. When IBD patients fail to respond to infliximab therapy, they are faced with the situation of either having no drugs available or using hormones with more side effects. Second, it is expensive, as only CD is reimbursed by health insurance, which increases the financial burden of patients. The limited availability of medication, the recurrence of disease symptoms, the side effects of hormone therapy, and the heavy financial burden contribute to the development of fatigue and psychiatric disorders in Chinese patients with IBD. Anemia is the most common extraintestinal manifestation of IBD, which occurs in up to 20% of outpatients and up to 68% of inpatients with IBD^[43,44]. The major causes of anemia in IBD are iron^[45], vitamin B12, and folic acid deficiency^[46]. The side effects or complications of some drugs for IBD are anemia. For example, methotrexate can lead to folic acid deficiency and megaloblastic anemia^[47]. One of the side effects of azathioprine and 6-mercaptopurine is myelosuppression^[48]. Sulfadiazine and 5-aminosalicylate have rare hemolytic complications^[49,50]. The relationship between fatigue and IBD-related surgery has rarely been reported. In our study, IBD-related surgery was found to be a risk factor for fatigue in IBD patients, which may be related to postoperative complications, postoperative pain, fear of stoma care, environmental (especially family) reactions, and acceptance of new conditions^[29,51,52]. However, a clinical study in Poland that included 60 IBD patients concluded that surgical treatment reduced fatigue symptoms^[53], which was contrary to the findings of our study. The difference may be due to different sample sizes, and our study has a larger sample size. In addition, the study in Poland compared the fatigue scores at one day before surgery and three months after surgery. The clinical symptoms of patients at 3 mo after operation were improved, but the postoperative complications were not fully

exposed. Our study included not only patients at 3 mo after the operation but also patients many years after operation and repeated surgery. Postoperative complications, disease activity, the annoyance of anastomotic care, and fear of reoperation were fully exposed. All of these factors will lead to fatigue in IBD patients. Surprisingly, female sex, disease activity, and hypoalbuminemia did not significantly increase fatigue among IBD patients in Eastern China. In previous studies^[37,54], female sex was found to be a strong predictor of fatigue, but no good explanation for this association was found. Our study, however, found that female sex was not a risk factor for fatigue. This may have been because of the small sample size in our study. The association between fatigue and disease activity in IBD is controversial. Fatigue scores were higher and more frequent among IBD patients with active disease than in the reference population and among those with quiescent IBD, but contrasts with the findings of others^[9,36,55]. In this study, univariate analysis showed that disease activity was a risk factor for fatigue but not in multivariate analyses. Therefore, more research is needed to clarify the relationships between female sex and disease activity and fatigue in Chinese patients with IBD. The common symptom of hypoalbuminemia is fatigue, but our findings suggest that it is not a risk factor for fatigue in patients with IBD in Eastern China. This may have been because of the small number of patients affected (29.3% of all those studied) or because fatigue was strongly associated with other factors, such as depression, anemia, anxiety, or IBD-related surgery.

Risk factors for fatigue, such as depression, anxiety, anemia, and IBD-related surgery, were found to decrease QoL in IBD patients in previous studies^[56-59], which explained why fatigue also leads to a decrease in QoL in IBD patients. Our further analysis found that psychological factors are particularly important in the relationship between fatigue and QoL. To improve the QoL of patients with IBD, the risk factors for fatigue should be identified and corrected in time to prevent the occurrence of fatigue. In addition to the impact on the QoL of the patient, fatigue can also lead to WP loss or even unemployment, which has significant economic consequences. Our study found that fatigue had an impact on the OWI, activity impairment, presenteeism, and absenteeism, among which general fatigue had the strongest impact. The appeal conclusion showed that the effect of fatigue on WP loss was also the result of a comprehensive effect, in which physical and psychological factors played an important role.

Although fatigue and its negative consequences are common in patients with IBD, the issue is rarely discussed in China. The underlying cause may be fatigue, especially during remission, which is considered a difficult and frustrating symptom, and the risk factors for fatigue are unclear, so there is little opportunity to help patients. Indeed, in China, there are few studies on the relationship between IBD and fatigue, which cannot provide clinical guidance. It is hoped that our findings will draw the attention of clinicians and patients to the role of fatigue in patients with IBD, improve the QoL of patients with IBD, and reduce the loss of WP by intervening in risk factors that contribute to fatigue. For example, in clinical practice, the joint management of patients' fatigue and psychological disorders is very important. Patients with depression and anxiety should pay close attention to their fatigue through targeted psychological counseling and intervention, such as health lectures, psychological counseling, individual counseling, and other ways to reduce patients' depression and anxiety, improve patients' fatigue, promote patients' health, and improve their QoL. IBD patients with anemia should correct their anemia in time. For IBD patients who have undergone surgery, postoperative complications, postoperative pain, and patients' fear of colostomy nursing should be properly addressed.

There are several limitations to our study. First, the size of the study sample was too small. Further large sample size studies are warranted for a more accurate estimation of the prevalence of fatigue and definitive identification of risk factors for fatigue. Second, our study was a single-center clinical study, which cannot represent the overall situation of IBD patients in China.

CONCLUSION

In conclusion, we have shown that the prevalence of fatigue is considerably high in patients with IBD in Eastern China, even in clinical remission, and the risk factors for fatigue are depression, anxiety, anemia, and IBD-related surgery. Female sex, disease activity, and hypoalbuminemia do not increase the risk of fatigue. In addition, fatigue reduces the QoL of IBD patients in Eastern China and damages WP. The results of our study provide a scientific basis for effectively preventing and improving fatigue in IBD

patients.

ARTICLE HIGHLIGHTS

Research background

Fatigue is frequent and disabling in patients with inflammatory bowel disease (IBD), but the prevalence and risk factors for fatigue in Chinese patients with IBD are unknown. In addition, neither the relationship between fatigue and quality of life (QoL) nor the relationship between fatigue and work productivity (WP) has been reported in Chinese IBD patients.

Research motivation

Fatigue is a very common but relatively neglected problem in patients with IBD. The prevalence rate of IBD in China is the highest in Asia, but there is little research on fatigue in patients with IBD. Neither the relationship between fatigue and QoL nor the relationship between fatigue and WP in Chinese IBD patients has been reported.

Research objectives

Our primary aim was to investigate the prevalence of fatigue related to IBD in Eastern China, and to identify the risk factors associated with fatigue. Our second objective was to assess the impact of fatigue on QoL and to evaluate the relationship between fatigue and WP.

Research methods

A cross-sectional study was conducted in a Regional Tertiary IBD Diagnostic and Treatment Center in Eastern China. Clinical data of patients were collected, and disease activity was evaluated. Blood samples were analyzed to assess anemia, albumin, and inflammation. Fatigue was assessed using the multidimensional fatigue inventory. QoL and WP were measured using the short inflammatory bowel disease questionnaire and the work productivity and activity impairment general health questionnaire, respectively. The patients also completed assessments of depression (Patient Health Questionnaire-9) and anxiety (Generalized Anxiety Disorder 7-item Scale).

Research results

A total of 311 IBD patients were enrolled in this study, 168 of whom were Crohn's disease patients, and 143 of whom were ulcerative colitis patients. The prevalence of fatigue in patients with IBD was 60.77%, including 71.88% in the active stage and 49.01% in the remission stage. The median fatigue total score was 43 (IQR: 33-59) in the full study population. In a univariate logistic regression analysis, factors such as disease activity, depression, anxiety, anemia, and IBD-related surgery were individually related to a significantly increased risk of fatigue in IBD patients. Multivariate logistic regression analysis indicated that depression [odds ratio (OR) = 8.078, 95% confidence interval (CI): 4.113-15.865], anxiety (OR = 2.373, 95%CI: 1.100-5.119), anemia (OR = 2.498, 95%CI: 1.290-4.834), and IBD-related surgery (OR = 2.035, 95%CI: 1.084-3.819) were related to fatigue in IBD patients. There was a negative correlation between fatigue and QoL ($r = -0.831$; $P < 0.0001$) but a positive correlation between fatigue and WP loss.

Research conclusions

The prevalence of fatigue in IBD patients in Eastern China is remarkably high even in clinical remission. Factors such as depression, anxiety, anemia, and IBD-related surgery are major risk factors for fatigue in IBD patients. In addition, fatigue has a negative impact on QoL and is positively correlated with WP loss.

Research perspectives

The prevalence of fatigue is considerably high in IBD patients in Eastern China even in clinical remission. In addition, fatigue reduces the QoL of IBD patients in Eastern China and damages WP. Clinicians and patients should be aware of and prevent the incidence of fatigue. The future research direction is to conduct a multicenter study to evaluate the incidence of fatigue in Chinese IBD patients, and more accurately screen out the risk factors leading to the incidence of fatigue in Chinese IBD patients, to effectively prevent the incidence of fatigue.

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