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Mindfulness-Based Interventions on Psychological Comorbidities in Patients with Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis

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Abstract

Background: Inflammatory bowel disease (IBD) is a chronic, lifelong disease, so IBD patients are highly susceptible to negative emotions, such as anxiety and depression, resulting in a reduced quality of life. Mindfulness-based intervention (MBI) is widely used to reduce stress, anxiety and depression in people. Therefore, this study conducted a systematic review of mindfulness-based intervention training on anxiety, depression, and quality of life in patients with IBD through meta-analysis.

Methods: Search papers in PubMed, Web of Science, Cochrane Library, Google Scholar, CNKI, Wanfang, and Embase databases. The search time limit was from the establishment of the database to May 2023. Randomized controlled trial studies of the effect of mindfulness intervention training on patients with IBD were screened, the included results were integrated and analyzed, and ReviewManager 5.4 was used for meta-analysis.

Results: A total of 14 studies with a total of 1030 IBD patients were included. A total of 10 studies showed that the anxiety of patients in the mindfulness intervention group was significantly reduced by (standard mean difference (SMD) = -0.73, 95% confidence interval (CI): -1.01 to -0.45) compared to the control group. 8 studies showed that the intervention group significantly reduced patients' depression (SMD = -0.60, 95% CI: -0.78 to -0.42). 7 stud-

ies showed that the patient's quality of life improved after mindfulness intervention (SMD = 0.66, 95% CI: 0.45–0.87).

Conclusion: Mindfulness-based intervention training can improve anxiety, depression, and quality of life in patients with inflammatory bowel disease in the short term, but the long-term effects need to be confirmed by more randomized controlled trials.

Keywords

mindfulness; inflammatory bowel disease; anxiety; depression; quality of life; meta-analysis

Introduction

Inflammatory bowel disease (IBD) mainly includes ulcerative colitis (UC) and Crohn's disease (CD), and the cause is currently unknown [1]. It is a group of chronic, non-specific intestinal inflammatory lifelong diseases characterized by diarrhea, abdominal pain, weight loss, malnutrition, and weakness. Currently, the number of patients worldwide is about 28 million, and there is a gradually increasing trend [2,3].

The number of IBD cases in our country has increased significantly in the past two decades, and the incidence rate has been increasing year by year [4,5]. At this stage, there is no radical cure for clinical treatment. The lifelong recurrence due to the course of the disease, uncomfortable symptoms such as abdominal pain and diarrhea, and the difficulty in controlling clinical symptoms make patients with inflammatory bowel disease extremely prone to psychosocial mal-

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adaptation, and their quality of life is seriously affected [6]. Additionally, patients are also prone to negative emotions such as anxiety and depression [6].

The 2018 consensus opinion on the treatment and diagnosis of inflammatory bowel disease states that the main treatment goals for patients with current IBD are to induce and maintain clinical remission and mucosal healing, prevent and treat complications, and improve the patient's quality of life [7]. In the past, clinical treatments for inflammatory bowel disease and improvement of patients' clinical symptoms were usually used as the evaluation indicator. In contrast, the overall evaluation of the patient's psychological, social, and role status was ignored. Patients facing a sudden disease often experience discomfort, especially psychosocial adaptation. Therefore, conducting a comprehensive and effective assessment of the psychosocial adaptation of patients with inflammatory bowel disease is particularly important. Patients' psychological and social adaptability can significantly affect their quality of life [8]. The study shows that psychosocial variables also have varying degrees of impact on the active disease status of inflammatory bowel disease [9].

Anxiety and depression are the most common psychological problems among patients with inflammatory bowel disease and are important factors affecting their quality of life [10]. A study [11] show that depression among IBD patients is higher than the healthy control [11]. When IBD is active, the incidence of depression rises. Navabi *et al.* [12] have shown that when IBD patients are in the active stage of the disease, they are more likely to suffer from anxiety and depression. The antidepressant drug duloxetine was applied to IBD patients, and the patients' anxiety, depression were ameliorated, and quality of life was significantly improved after 12 weeks [13]. A large number of surveys and studies have also confirmed that domestic IBD patients are prone to negative emotions, which impacts the patient's quality of life [6,14,15].

Mindfulness is often considered as paying attention on purpose and without judgment. Its core is to face various psychosomatic events with an objective and accepting attitude, which helps to reduce negative emotions such as anxiety and depression [16]. Mindfulness-based intervention (MBI) refers to training techniques such as meditation, breathing awareness, and mindfulness yoga enable individuals to accept current events with non-judgmental thinking [17]. Mindfulness intervention is also gradually being used in the treatment of IBD patients. MBIs are increasingly used to reduce stress, anxiety, and depression in this population [18]. A study showed that mindfulness training substantially improved the severity of intestinal symptoms and

reduced intestinal pain in patients [19]. Research shows that mindfulness intervention can ameliorate depression, anxiety, stress, and improve quality of life, etc., without obvious side effects in patients with IBD [18]. At present, there are very few meta-analyses on the impact of mindfulness intervention at home and abroad on depression, anxiety, and quality of life in IBD patients. This study collected randomized controlled studies on mindfulness therapy intervention in IBD patients and conducted a meta-analysis to evaluate the impact of mindfulness intervention on depression, anxiety, and quality of life in IBD patients and to provide evidence-based reference for the clinical application of mindfulness intervention in IBD patients.

Data and Methods

Literature Search Strategy

Specific and systematic searches were carried out on the databases PubMed, Embase, Web of Science, Google Scholar, CNKI, and Wanfang databases; the search terms were: "inflammatory bowel disease, IBD Ulcerative colitis, Crohn's disease, CD, UC", "acceptance and commitment therapy", "mindfulness meditation, mindfulness intervention, mindfulness-based intervention, mindfulness, mindfulness decompression therapy, mindfulness-based stress reduction therapy (or MBSR), mindfulness-based cognitive therapy (or MBCT)". The search formula was "inflammatory bowel disease, mindfulness-based, stress reduction therapy", the search time limit was from the establishment of the database to May 2023, the search results were limited to clinical research and not restricted by language or race, and manual searches performed by reading relevant works and summarizing references. Search strategies were adjusted to comply with the pertinent regulations of every database. The protocol for this systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Supplementary File 1).

Literature Inclusion Criteria

- (1) Randomized clinical trial (RCT), no matter whether it is single-blind, double-blind, or non-blind.
- (2) The trial includes a parallel control group and an observation group.
- (3) Research object. Confirmed IBD patients, including CD and UC, are not limited to their race, nationality, or disease course.
- (4) Outcome measures involve anxiety, depression, and quality of life.

Literature Exclusion Criteria

(1) Non-randomized trials. (2) Duplicate publications or data duplication. (3) Studies without a control group. (4) Animal experiments. (5) Research methods, results, and conclusions that cannot be explained or do not correspond to each other. (6) Statistical methods and data analysis that have obvious errors. (7) Literature with imperfect experimental design. (8) Literature for which data could not be extracted, or data were incomplete. (9) Review, animal experiments, special adverse reaction reports and pharmacology, pharmacokinetics, and other non-clinical research. (10) The test results and conclusions are inconsistent with the reality. (11) Less than 2 outcome measures. (12) Accompanied by other digestive tract diseases or serious complications such as gastric ulcer, moderate to severe dysplasia, and gastric cancer. (13) Non-Chinese and English literature.

Literature Screening and Data Extraction

Literature screening: Two researchers, based on the inclusion and exclusion criteria, independently screened the literature, targeting titles and abstracts, including primary screening, secondary screening, and cross-checking to determine possible relevant studies. Firstly, preliminary screening: read and analyzed the articles' titles and abstracts, and eliminated the literature not included in the inclusion criteria or duplicate studies. Second, re-screening: the full text of the papers obtained from the primary screening was analyzed, and then the literature was further screened according to the inclusion criteria. Finally, cross-checked the obtained literature. For documents with incomplete or questionable information, contacting the corresponding authors for detailed information was necessary. Finally, it was judged whether the literature was included in the study based on researcher consensus. A third researcher participated in the judgment if no consensus could be reached. The selected documents were included in the Table 1 (Ref. [20–33]) for extraction and summary.

Data extraction: The content of data extraction includes title, first author, basic information of the literature, year of publication, intervention method, research type, evaluation tools, and observation indicators.

Intervention

The observation group adopted intervention methods based on mindfulness training techniques (meditation, mindful breathing, mindfulness yoga, mindful walking,

body scanning, etc.), which are conventional treatments. In contrast, the control group adopted conventional treatment or psychological care. Mindfulness therapy requires long-term persistence, and its application time needs to be at least three weeks. However, the frequency is determined by each investigator on a case-by-case basis.

Quality Evaluation

Eligible literature was assessed for methodological quality using the Jadad scoring scale. The scale scores random sequence generation, blinding, allocation concealment, and patient withdrawal or withdrawal on a scale of 1 to 7. A Jadad score of 4–7 is considered high-quality literature, and 1–3 is considered low-quality literature.

Statistical Method

All analyses were pooled using RevMan 5.4 statistical software (RevMan, The Cochrane Collaboration, Oxford, UK), with weighted mean differences (WMD) and 95% confidence interval (CI) for continuous data and relative risk (RR) and 95% CI for dichotomous data. The heterogeneity index (I^2) was used to evaluate the heterogeneity of the treatment effect. When there is no significant heterogeneity among the studies ($I^2 < 50\%$), the fixed effect model is used; when there is significant heterogeneity among the studies ($I^2 \geq 50\%$), a random effects model is used. Sensitivity analysis was performed on factors that may cause heterogeneity, and literature with high sensitivity was excluded. A descriptive analysis was performed for those who could not perform using meta-analysis. This study also used a PRISMA extension for scoping reviews [34].

Results

Literature Search Results

Systematically retrieved the original literature on inflammatory bowel disease, Ulcerative colitis, mindfulness meditation, mindfulness-based intervention, etc., published in databases such as CNKI, Wanfang, EMBASE, Web of Science, and PubMed, using subject headings combined with free words for systematic retrieval, and manually retrieved 871 literature. 293 articles were only comments or abstracts, or animal experiments, and 163 were obtained. After reading the complete text, 74 articles that could not obtain the full text and incomplete experimental design were eliminated, and finally, 14 articles were obtained [20–33]. The literature screening process is shown in Fig. 1.

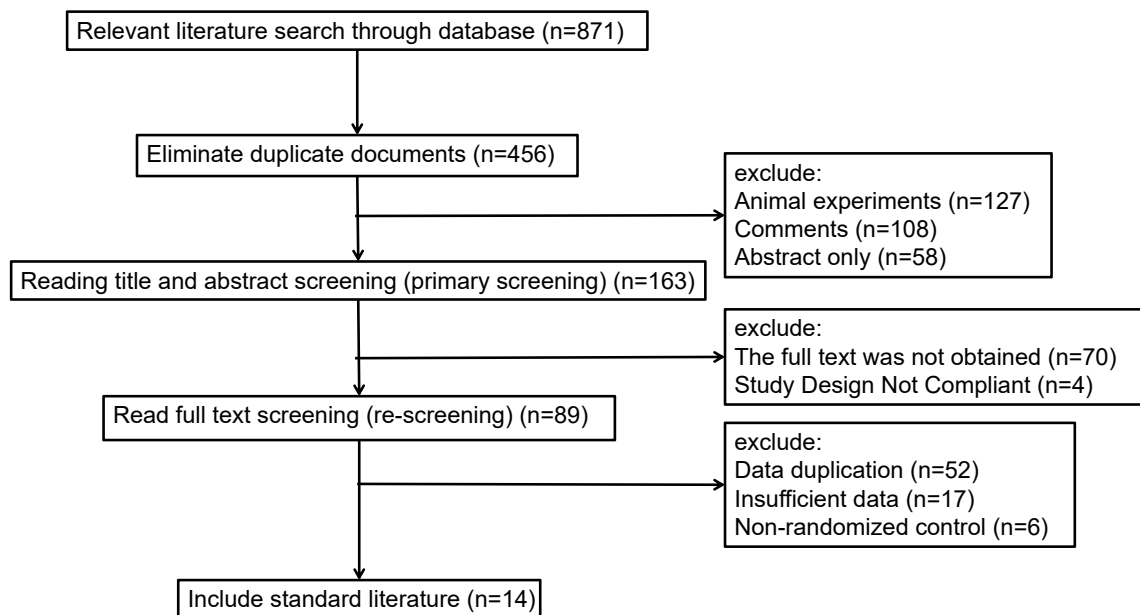


Fig. 1. Flow chart of literature search.

Basic Characteristics and Quality Evaluation of Included Literature

The demographic and baseline characteristics of the patients are shown in Table 1 (Ref. [20–33]). In the literature included, the control group used treatment/educational lectures treatment, while the treatment group used mindfulness therapy.

The Jadad score of the included literature was 4 to 5, which was high quality, and none of the 14 included studies had withdrawal.

The Effect of the Anxiety of IBD Patients with Mindfulness Therapy

Ten studies reported the effect of the anxiety of IBD patients with mindfulness therapy according to the change of Depression-Anxiety-Stress Scale (DASS), Beck Anxiety Inventory (BAI), State-Trait Anxiety Inventory (STAI), Hospital Anxiety and Depression Scale (HADS), and Self-rating Anxiety Scale (SAS) scores, as displayed in Table 1 [21,24,25,27–33]. However, due to the different meters used by each research, some studies explain the specific situation, and some studies only use the scores of the volume table as the result. Therefore, we used continuous variables and binary meta-analysis. As can be seen from Figs. 2,3, in the included studies, the anxiety of patients in the mind-

fulness intervention group was significantly reduced (risk ratio (RR) = 1.94, 95% CI: 1.52–2.46), (standard mean difference (SMD) = –0.73, 95% CI: –1.01 to –0.45). The results revealed that heterogeneity was very low in the results. Therefore, meta-analysis results are reliable.

The Effect of the Depression of IBD Patients with Mindfulness Therapy

Eight studies specifically described the depression of IBD patients in the two groups after different treatment methods [21,24,25,27–31]. The results showed that the intervention group significantly reduced patients' depression (SMD = –0.60, 95% CI: –0.78 to –0.42). In other words, mindfulness can reduce depression in IBS patients. As shown in Fig. 4. The heterogeneity test results showed $I^2 = 62\%$, and we performed a relevant subgroup analysis (Fig. 5). Sensitivity analysis was performed by excluding documents one by one. The results showed that after excluding the study [28], the heterogeneity was 0%, indicating that this article is the source of high heterogeneity.

Table 1. Basic characteristics and Jadad score of included studies.

Researcher	Nation	Number of cases	Research object	Interventions		Efficacy index	Jadad score
		observation group/control group		Treatment group	Control group		
Goren G <i>et al.</i> , 2022 [20]	Israel	55/61	CD patients	Cognitive Behavioral and Mindfulness-based stress reduction with Daily Exercise (COBMINDEX) program	Conventional treatment/Educational lectures	②	5
Ewais T <i>et al.</i> , 2021 [21]	Canada	33/31	IBD patients	Mental health professionals intervene to teach mindfulness courses	Conventional treatment/Educational lectures	①②⑨	4
González-Moret R <i>et al.</i> , 2020 [22]	Spain	37/20	IBD patients	Mindfulness therapy: Four internet-based treatment modules and four face-to-face support sessions.	Conventional treatment	⑨	5
Lu R <i>et al.</i> , 2020 [23]	China	33/34	IBD patients in remission and mild to moderate activity	Nurses conduct group intervention, accepting emotions + mindful breathing, cognitive detachment + focusing on the present, clarifying values + modeling, setting goals + committing to action	Conventional treatment/Educational lectures	②	4
Wynne B <i>et al.</i> , 2019 [24]	Ireland	37/42	UC/CD patients	An intervention plan is established based on acceptance and commitment therapy, and the psychologist conducts the intervention.	Routine care	①⑨	4
Du Z <i>et al.</i> , 2019 [25]	China	48/48	UC patients	Mindfulness-based stress reduction therapy: group intervention by nurse, mindful breathing, mindful walking, mindful yoga, body scan, homework	Routine care	⑧⑨	4
Cramer H <i>et al.</i> , 2017 [26]	Germany	39/38	UC patients in the remission stage	Mindfulness yoga: group intervention by yoga trainer, Hatha yoga, breathing + meditation techniques, family practice	Provides evidence-based self-care books	②	4
Neilson K <i>et al.</i> , 2016 [27]	Australia	33/27	UC/CD patients	Mindfulness-based stress reduction therapy: Group intervention by psychologists and psychiatrists, guided meditation, family exercises, group discussions, and various mindfulness-enhancing activities.	Routine care	⑥⑦⑨	4
Schoultz M <i>et al.</i> , 2015 [28]	UK	22/22	IBD patients	Mindfulness-based cognitive therapy includes group intervention with a therapist, formal practice/meditation combination, cognitive behavioral exercises, informal exercises and discussions, and family exercises.	Routine care	②③④⑨	4

Table 1. Continued.

Researcher	Nation	Number of cases observation group/control group	Research object	Interventions		Efficacy index	Jadad score
				Treatment group	Control group		
Gerbarg PL <i>et al.</i> , 2015 [29]	USA	16/13	UC/CD patients	Breathing-Body and Mind Workshop Therapy: Group intervention by trainer, Qigong movements combined with breathing, meditation, and family exercises	Conventional treatment/Educational lectures	②③④⑨	4
Jedel S <i>et al.</i> , 2014 [30]	USA	27/28	UC patients in the solution period	Mindfulness-based stress reduction therapy: group intervention with a psychologist, formal practice or meditation, informal practice, and homework	Courses and videos on the impact of stress on physical and mental health	②③⑤⑨	5
Berrill JW <i>et al.</i> , 2014 [31]	UK	33/33	UC/CD patients	Multi-session therapy: group intervention with therapist, 6 face-to-face sessions (stressor/behavior/symptom diary and mindfulness meditation)	Conventional treatment	③⑤⑨	4
Sharma P <i>et al.</i> , 2015 [32]	India	50/50	UC/CD patients in remission	Mindfulness yoga: group intervention by yoga trainer, relaxation training, breathing training, yoga asanas, yoga meditation, family practice	Routine care		4
Yang X <i>et al.</i> , 2011 [33]	China	15/15	CD patients	Mindful Yoga: Yoga Nidra, Yoga Meditation	Routine care	⑧	4

Note: ① Depression-Anxiety-Stress Scale (DASS-21). ② Inflammatory Bowel Disease Life Quality Questionnaire (IBDQ). ③ Beck Depression Inventory (BDI). ④ Beck Anxiety Inventory (BAI). ⑤ State-Trait Anxiety Inventory (STAI). ⑥ Hospital Anxiety and Depression Scale (HADS). ⑦ World Health Organization Quality of Life Scale Short Form (WHOQOL-BREF). ⑧ Self-rating Anxiety Scale (SAS). ⑨ Self-rating Depression Scale (SDS). CD, Crohn's disease; IBD, Inflammatory bowel disease; UC, ulcerative colitis.

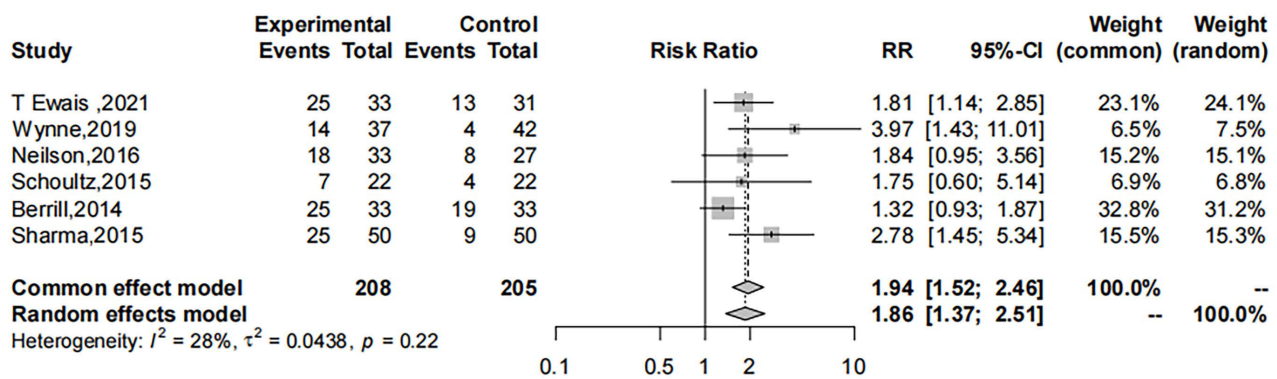


Fig. 2. Binary meta-analysis forest plot of the effect of the anxiety of IBD patients with mindfulness therapy with 6 articles. RR, relative risk; CI, confidence interval.

The Impact of Mindfulness Intervention on the Quality of Life of Patients with IBD

Six studies specifically described the impact of mindfulness intervention on the quality of life [19,21,26–29]. The results showed that the patient's quality of life improved after mindfulness intervention (SMD = 0.66, 95% CI: 0.45–0.87) (Fig. 6). According to some interviews included in the literature, it can be learned that the help of mindfulness in patients' daily lives is mainly reflected in the improvement of mentality and physical condition, thereby achieving the purpose of improving the quality of life. The results showed that the heterogeneity after subgroup allocation was 93.8% (Fig. 7). Then, sensitivity analysis was performed by excluding the literature one by one. The results show that after excluding the studies [23,27], the heterogeneity is 0%, indicating that the 2 articles are the source of high heterogeneity.

Discussion

Mindfulness therapy is a general term for psychological training methods based on [32,33] mindfulness, which emphasizes "living in the present moment" and increasing confidence in "living with the disease" [32,33]. Many previous studies have shown that mindfulness intervention is effective in various chronic diseases. It can relieve stress, depression, anxiety, tension, and pain, improve sleep, and assist in the treatment of physical and mental diseases [35–37].

Mindfulness-Based Intervention Training can Improve Anxiety and Depression Levels in IBD Patients

This study shows that, in total, 10 studies reported the effect of the anxiety of IBD patients with mindfulness therapy according to the change of DASS, BAI, STAI, HADS, and SAS scores. The anxiety of patients in the mindfulness intervention group was significantly reduced (RR = 1.94, 95% CI: 1.52–2.46), (SMD = –0.73, 95% CI: –1.01 to –0.45). It suggested that mindfulness-based intervention training can improve anxiety in patients with IBD. A previous study has shown that mindfulness can activate brain areas related to positive emotions, such as the anterior insula, hippocampus, inferior temporal gyrus, prefrontal lobe, and cingulate gyrus. Gray matter density increases significantly. These brain areas are related to emotional regulation and cognitive control functions, which can promote patients' positive emotions and maintain emotional stability [38].

In this study, we showed that the intervention group significantly reduced patients' depression (SMD = –0.60, 95% CI: –0.78 to –0.42). Previous research has discussed the mechanism of mindfulness's role in depression [39]. Mindfulness intervention enhances the patient's immune system function, reduces cortisol levels, and reduces the recurrence of the disease, thereby reducing depression levels [39]. It also can reduce the negative emotions experienced by individuals and reduce the level of depression.

We compared another study and found that [40] meta-analysis results by Ye Y *et al.* [40] showed that MBI can only improve depression after intervention. This may be related to the fact that the study included fewer types of mindfulness studies, and the results have a certain bias. Some studies have shown that mindfulness intervention can reg-

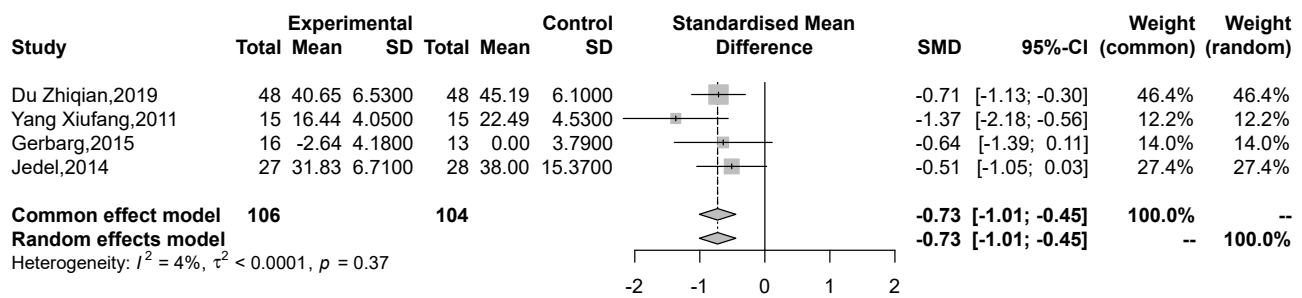


Fig. 3. Continuous variables meta-analysis forest plot of the anxiety of IBD patients with mindfulness therapy with 4 articles. SMD, standard mean difference.

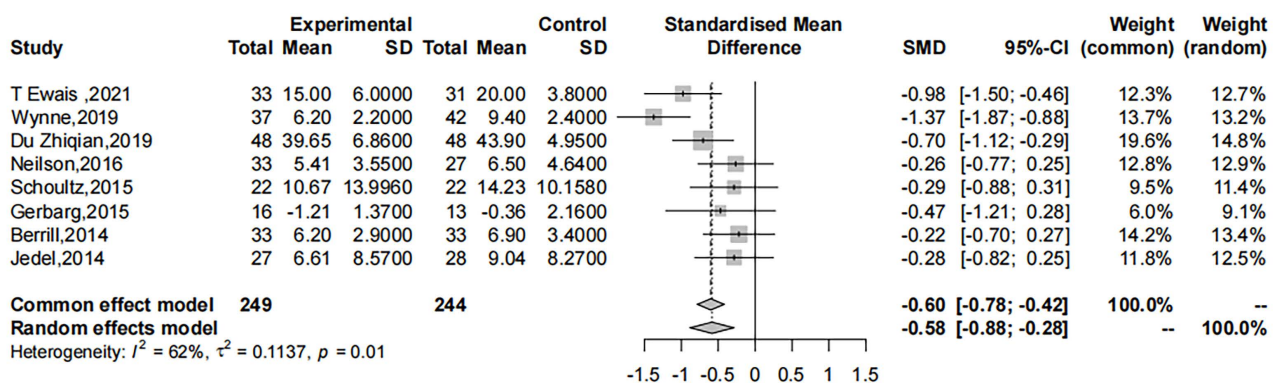


Fig. 4. Meta-analysis forest plot of the effect of the depression of IBD patients with mindfulness therapy with 8 articles (Mean and SD).

ulate areas of the brain related to emotional control by increasing the activity of the prefrontal cortex and reducing the volume of the right amygdala, helping individuals reduce their levels of anxiety and depression [39,40]. These results once again prove the reliability of this study. Same as the result of the study of Ewais *et al.* [41]. This may be related to the difference between the definition of long-term effects in that study and this study. This study is not yet clear on the long-term effect of mindfulness intervention on reducing depression levels in IBD patients. This may be due to the following reasons: (1) The effect of improving depression is difficult to maintain after the intervention ends. (2) Studies on the impact of anxiety in IBD patients are all group interventions, and the literature shows that its efficacy is weaker than individual intervention [42]. (3) The intervention measures last 1 to 2 hours each time. After the intervention, it is difficult for patients to practice independently for a long time, making the long-term intervention ineffective. (4) Moreover, there are few descriptions of quality control during the follow-up period, and it is difficult to count patient compliance, resulting in unclear long-term effects.

Mindfulness-Based Intervention Training can Improve the Quality of Life of IBD Patients

This study shows that mindfulness in the intervention group improved the quality of life of patients after the intervention (SMD = 0.66, 95% CI: 0.45–0.87) compared to the control group. This is consistent with the research results of Ewais *et al.* [41]. Some studies have also shown that mindfulness intervention can improve the quality of life in the short term after disease recurrence and the quality of life of patients with irritable bowel syndrome [43,44]. Dober *et al.* [45] showed significantly better post-intervention effects than other studies. A study has shown that the quality of life of IBD patients is most closely related to the severity of disease activity, followed by the patient's psychosocial adaptation [46]. These results are consistent with the results of this study. The improvement of the quality of life of patients with inflammatory bowel disease by mindfulness-related therapy may be related to its ability to regulate the level of inflammation in the patient's body. As shown in the study by Gerbarg PL *et al.* [29], patients' C-reactive protein levels decreased after breathing, exercise, and meditation. Previous study by Tait JL *et al.* [47] also showed that lower perceptions of health-related quality of life (HR-

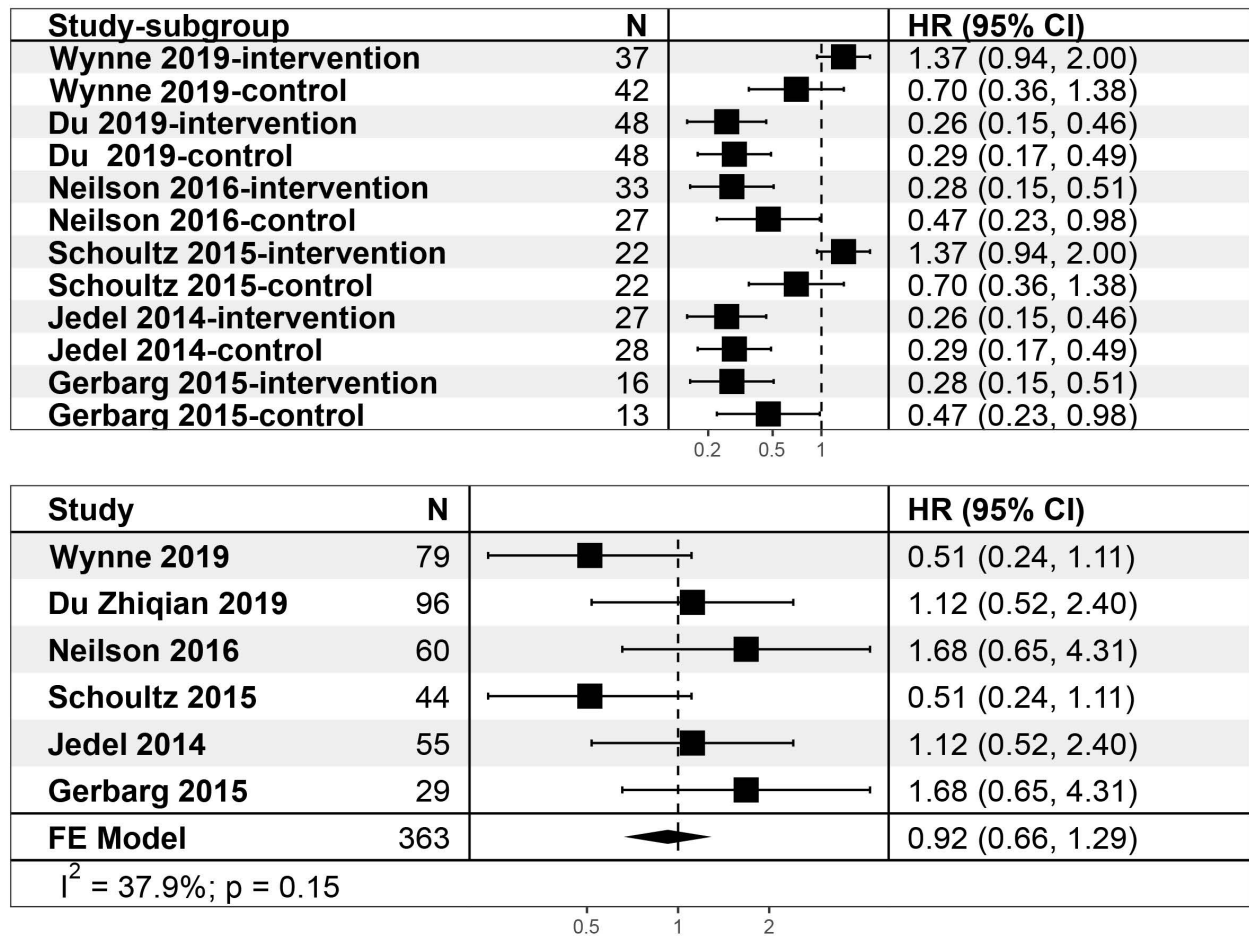


Fig. 5. Subgroup analysis results of the effect of depression on a total of 363 IBD patients. HR, Hazard Ratio.

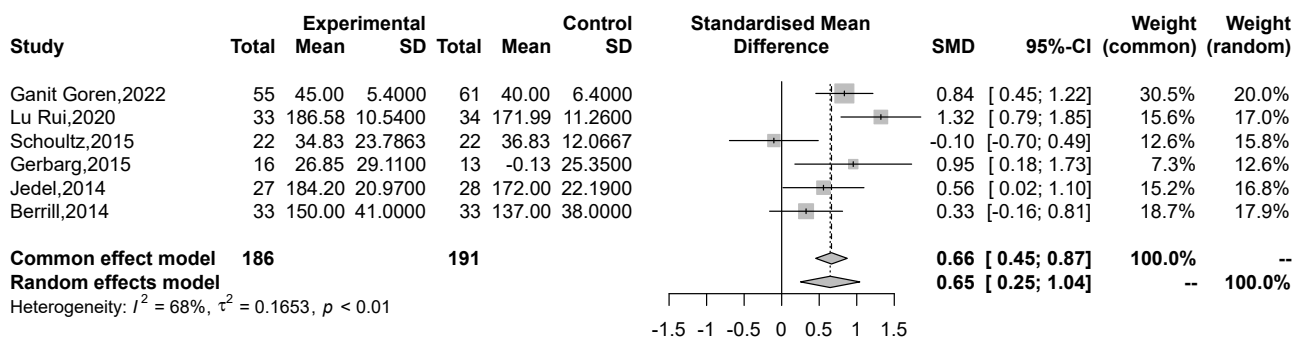


Fig. 6. Meta-analysis forest plot of the impact of mindfulness intervention on the quality of life between 2 groups with 6 articles.

QoL) are related to higher hs-CRP levels. There may be more complex biological mechanisms behind it. For example, long-term inflammation may cause an imbalance in the body's redox reaction balance, mediating cell aging [48].

Limitations of This Study

This study only searched published Chinese and English literature, which may have publication bias. Although the interventions included in the articles all use mindfulness as the theoretical framework, the specific interventions differ. The intervention time, number of interventions, follow-

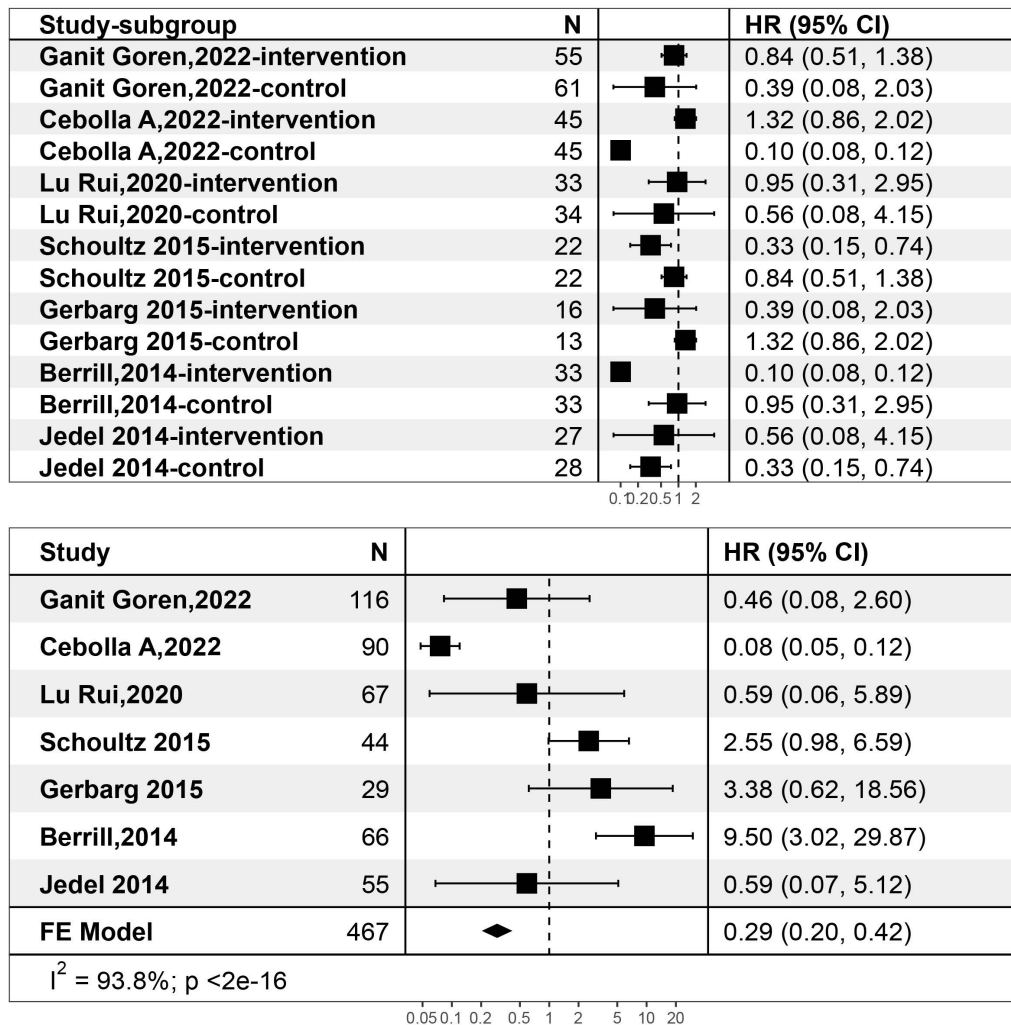


Fig. 7. Subgroup analysis results of the impact of mindfulness intervention on the quality of life between 2 groups with a total of 467 patients. HR, Hazard Ratio.

up time, and the assessment tools used for the same outcome indicators differ. Due to the limited amount of literature included, it is difficult to conduct more subgroup analyses, and the sample size of some studies is small. This may lead to some heterogeneity between studies. In addition, the number of included domestic studies is small. We look forward to more high-quality randomized controlled studies in this field in the future.

Conclusion

In summary, mindfulness-based intervention training can effectively improve the anxiety and depression levels of IBD patients, and the quality of life of patients has been significantly improved. It is suggested that the application of mindfulness-based intervention training in IBD patients

can be consciously promoted in clinical nursing to reduce the psychological stress of patients. After the intervention, researchers are recommended to take corresponding follow-up measures to improve patient compliance to improve long-term intervention effects.

Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Author Contributions

XQ: Conception, Design, Materials, Data Collection, Analysis, Literature Review, Writing. JZ: Supervision,

Materials, Data Collection, Analysis, Literature Review, Writing. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.62641/aep.v52i4.1559>.

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