Original Article

The efficacy of mindfulness-based stress reduction *vs.* standard or usual care in patients with breast cancer: a systematic review and meta-analysis of randomized controlled trials

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Background: Mindfulness-based stress reduction (MBSR) has become an alternative intervention for cancer patients, but its impact on depression and quality of life (QOL) of breast cancer patients remains controversial. The aim of this study was to evaluate the effects of MBSR *vs.* standard or usual care to relieve psychological stress in patients with breast cancer.

Methods: According to the PICOS principles, databases [PubMed, Cochrane Database, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), China Scientific Journal Database (VIP), and Wanfang Database] were searched for randomized controlled trials (RCTs) on the evaluation of MBSR *vs.* standard or usual care for patients with breast cancer, the outcome variables included depression, stress, anxiety, fatigue, sleep and QOL. Review Manager 5.4 was used to evaluate the effects of the results among selected articles. Forest plots and funnel plots were also performed. The risk of bias was assessed using the Cochrane Risk of Bias Tool.

Results: The final analysis included 14 studies with a total of 2,224 patients (1,138 in the MBSR group and 1,086 in the control group). The overall results of risk of bias assessment showed that the reporting bias among articles was high, and other bias was relatively moderate. Funnel plots and Egger's tests showed that there was no significant publication bias. Compared with standard or usual care, MBSR effectively relieved the psychological stress [mean difference (MD), −1.72; 95% confidence interval (CI): (−2.53, −0.92); P<0.0001] and anxiety [standardized mean difference (SMD), −1.36; 95% CI: (−2.13, −0.60); P=0.0005] of breast cancer patients, and improved depression [SMD, −0.62; 95% CI: (−1.20, −0.03); P=0.04] and sleep status [MD, −0.42; 95% CI: (−0.73, −0.10), P=0.009]. However, it had no significant effect on fatigue [SMD, −0.97; 95% CI: (−2.24, 0.31); P=0.14] or QOL [MD, 1.95; 95% CI: (−3.15, 7.05); P=0.45].

Conclusions: MBSR was better than standard or usual care for relieving psychological stress, anxiety, depression, and sleep in patients with breast cancer. Considering the limitations of this article, such as high risk of bias and high heterogeneity of included studies, the interpretation of this conclusion should be cautious.

Keywords: Breast cancer; mindfulness-based stress reduction (MBSR); meta-analysis; quality of life (QOL)

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Introduction

Breast cancer is the most common malignant tumor with the highest incidence in women (1,2), and both the incidence and mortality of breast cancer have shown a gradual upward trend. Due to the disease itself or the adverse effects of cancer treatment, breast cancer patients are prone to negative emotions such as anxiety, depression, and stress, which seriously affect their quality of life (QOL), even lead to further deterioration and recurrence of the disease, increase the mortality of breast cancer, and seriously affect the prognosis (3,4). Therefore, improving the mental health of breast cancer patients is essential for improving the survival rate and QOL of patients (5).

Mindfulness-based stress reduction (MBSR) therapy includes mindful eating, meditation, body scanning, yoga, non-judgmental attitudes, stressors, and emotional management to enhance the ability of patients to co-exist with difficult situations, and improve their QOL (6-8). The MBSR program was developed by John Kabat Zinn of the University of Massachusetts School of Medicine (USA), and is increasingly being used as an alternative intervention for cancer patients (9,10).

Recent studies on the use of MBSR in the treatment of breast cancer patients have discussed the physical and psychological effects (11-14). MBSR has good results for anxiety and stress of breast cancer patients, but the effect on depression and QOL differed, and a unified conclusion has not yet been formed. Huang's research (15) suggested that MBSR could also improve QOL and depression, while Zhang's research (16) suggested that there was insufficient evidence for MBSR to improve the overall QOL. Schell's research (17) suggested that MBSR may have little difference in anxiety or depression compared with standard or usual care in the long run. The reason for controversy may be that the number of cases included in different studies was small, and the assessment tools for mental health were different. We adopt the method of meta-analysis to expand the sample size, and conducted subgroup analysis for different evaluation tools, which can well solve the limitations of the single research.

We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) on the effect of MBSR on the mental health and QOL of breast cancer patients to objectively evaluate the intervention effect of MBSR as the basis for the application of MBSR in the treatment of breast cancer patients. We present the following article in accordance with the PRISMA reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2530/rc).

Highlight box

Key findings

- MBSR was better than standard or usual care for relieving psychological stress, anxiety, depression, and sleep in patients with breast cancer.

What is known and what is new?

- MBSR has good results for anxiety and stress of breast cancer patients.
- MBSR also has good results for depression and sleep in patients with breast cancer.

What is the implication, and what should change now?

- Future research needs to verify the role of MBSR in breast cancer patients by using standardized intervention programs and unified evaluation methods of outcome indicators.

Methods

Literature search strategy

MEDLINE (PubMed), Cochrane Database, Web of Science, Embase, China National Knowledge Infrastructure (CNKI), China Scientific Journal Database (VIP) and Wanfang Database were searched for eligible papers published up until September 2022. We used the following keywords: (I) mindfulness-based stress reduction; (II) mindfulness meditation; (III) breast cancer; (IV) breast neoplasm. The search strategy was adapted to each database using variations of the keywords, using wildcard symbols and Boolean operators to combine the terms. There were no restrictions on the language of publication. We also reviewed the reference lists of potentially relevant articles to find studies that our search strategy may have missed.

Study selection

Studies meeting the following criteria were considered for inclusion: (I) inclusion only of patients diagnosed with breast cancer; (II) RCT; (III) using MBSR as an intervention, MBSR was a systematic group decompression method that last for 6–8 weeks, which included mindfulness meditation, body awareness, mindfulness walking, mindfulness yoga and mindfulness relaxation techniques; (IV) comparison of MBSR with standard or usual care (no specific treatment or wait-list control); (V) reporting the indicators evaluating efficacy, such as depression, stress, anxiety, fatigue, sleep and

QOL. The major exclusion criteria were: (I) not meeting the inclusion criteria; (II) letters, abstracts, reviews, or meta-analysis; (III) the outcomes of interest were not reported or impossible to use; (IV) duplicate article.

Data extraction

Two independent reviewers (HYW and FFL) performed the study selection, data extraction and quality assessment; and disagreements were resolved by consensus or consulting a third reviewer. The following data were extracted: name of primary author, country of study, design, number of participants in each arm, patients' ages [mean or median and standard deviation (SD) or range if available], characteristics of intervention, and study duration.

Quality assessment

The methodological quality of the included RCTs was assessed by the Cochrane Collaboration Risk of Bias Tool (Review Manager 5.4), which included selection, performance, detection, attrition, reporting, and other biases. According to the probability of occurrence of bias risk, it can be divided into three levels: high risk, unclear risk, and low risk. After reading the full text, the author look for relevant content in the full text according to the seven items of quality evaluation. If the description was clear, it was judged as "low risk", if the description was vague, it was judged as "unclear risk", and if there was no relevant description, it was judged as "high risk". For quality evaluation, two researchers (YHW and FHZ) shall independently extract data and cross check them. In case of disagreement, a third party shall be consulted for assistance in judgment.

Statistical analysis

Meta-analysis was performed by Review Manager 5.4 provided by Cochrane (Oxford, UK). The original data of outcome variables for continuous data were extracted from the included literature in the form of mean and SD. Mean difference (MD) was used for pooled continuous variables, risk ratio (RR) was used for pooled classification variables, and 95% confidence interval (CI) was used for both types of indicator. Considering that our outcome variables were tested using different questionnaires, we used the standardized mean difference (SMD) and subgroup analysis. We evaluated the degree of statistical heterogeneity and inconsistency by chi-squared test and I^2 statistics. Heterogeneity was considered significant at $P<0.05$. In detail, I^2 values of <50% indicated moderate heterogeneity, and ≥50% high heterogeneity. If it was high heterogeneity, it was necessary to explore the source of heterogeneity through subgroup analysis or sensitivity analysis. The fixed-effects model was used with the moderate heterogeneity; otherwise the random-effects model was used. We assessed potential publication bias by examining funnel plots and using Egger's test when >10 studies were included in the meta-analysis. P value was used to detect statistical difference, and when $P<0.05$, the difference was statistically significant.

Results

Search process

The database search identified 974 articles, which were reduced to 925 records after removing duplicates. After screening the tittles and abstracts, an additional 831 records were excluded and a further 80 articles were excluded based on study design, insufficient relevant data, or review. Finally, 14 studies met our inclusion criteria for the present meta-analysis (18-31). The results of the search process are shown as a flowchart in *Figure 1*.

Characteristics of included studies

The baseline characteristics of the patients included in the meta-analysis are reported in *Table 1*. The total study sample size was 2,224 (range, 18–336; 1,138 in intervention group, 1,086 in control group). The follow-up time ranged from 6 weeks to 12 months. All studies were published in the English language: seven studies from the USA, and the other seven from China, UK, Demark, Sweden, Iran, and South Korea.

Results of quality assessment

The results of methodological quality assessment of each risk of bias item for each included trial are shown in *Figure 2*. The quality of studies included in the review was evaluated by two independent reviewers, with differences resolved by consensus or through a third reviewer if required. A summary of all types of bias in each study is shown in *Figure 3*. Five studies showed the reporting bias among articles was high, and one study showed the high risk of performance bias, none of the included studies contained

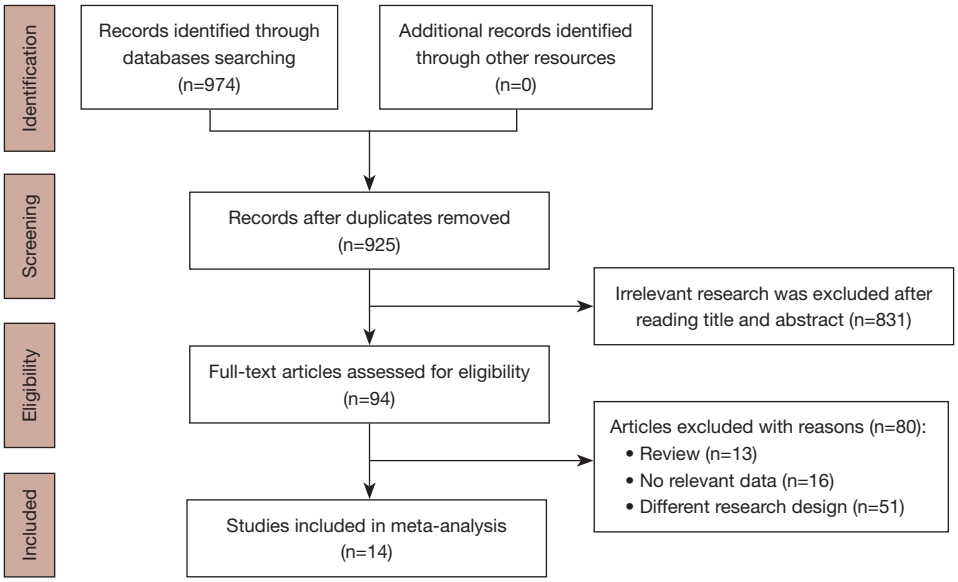

Figure 1 Flow chart of literature search and study selection for systematic review and meta-analysis.

Table 1 Characteristics of patients included in this study

Study	Country	Study design	Treatment		No. of patients		Age (years)*		Study duration	Follow-up
			Intervention	Control	Intervention	Control	Intervention	Control		
Bränström, 2012	Sweden	RCT	MBSR	Wait-list	32	39	NR	NR	Apr 2007 and Mar 2008	6 months
Hoffman, 2012	UK	RCT	MBSR	Wait-list	114	115	49.0±9.26	50.1±9.14	2005 to 2006	14 weeks
Lee, 2017	South Korea	RCT	MBSR	Usual care	9	9	52 [35–64]	57 [37–67]	May 2013 to Aug 2013	8 weeks
Lengacher, 2016	USA	RCT	MBSR	Usual care	167	155	56.5 ± 10.2	57.6±9.2	Apr 2009 to Mar 2013	12 weeks
Boyle, 2017	USA	RCT	MBSR	Wait-list	39	32	46 [28–60]	48 [31–60]	2014 to 2015	3 months
Sarenmalm, 2017	Sweden	RCT	MBSR	Blank	62	52	57.2±10.2		NR	3 months
Lengacher, 2014	USA	RCT	MBSR	Usual care	40	42	57.2±9.2		Mar 2006 to Jul 2007	6 weeks
Witek Janusek, 2019	USA	RCT	MBSR	Active control	84	80	55.0±10.1	55.2±10.1	Oct 2008 to Jan 2014	6 months
Bower, 2015	USA	RCT	MBSR	Wait-list	39	32	46.1 [28.4–60]	47.7 [31.1–59.6]	NR	3 months
Würtzen, 2013	Denmark	RCT	MBSR	Usual care	168	168	53.9±10.1	54.4±10.5	Jun 2007 to Jul 2009	12 months
Lengacher, 2021	USA	RCT	MBSR	Usual care	165	155	NR	NR	Apr 2009 to Mar 2013	12 weeks
Reich, 2017	USA	RCT	MBSR	Usual care	167	155	56.5±10.2	57.6±9.2	Apr 2009 to Mar 2013	12 weeks
Zhang, 2017	China	RCT	MBSR	Usual care	30	30	48.67±8.49	46.00±5.12	2014 to 2015	3 months
Mirmahmoodi, 2020	Iran	RCT	MBSR	Usual care	22	22	44.14±11.19	45.62±10.11	Aug 2017 to Nov 2019	8 weeks

*, data are presented as median ± SD or as median [range]. RCT, randomized controlled trial; MBSR, mindfulness-based stress reduction; NR, not reported; SD, standard deviation.

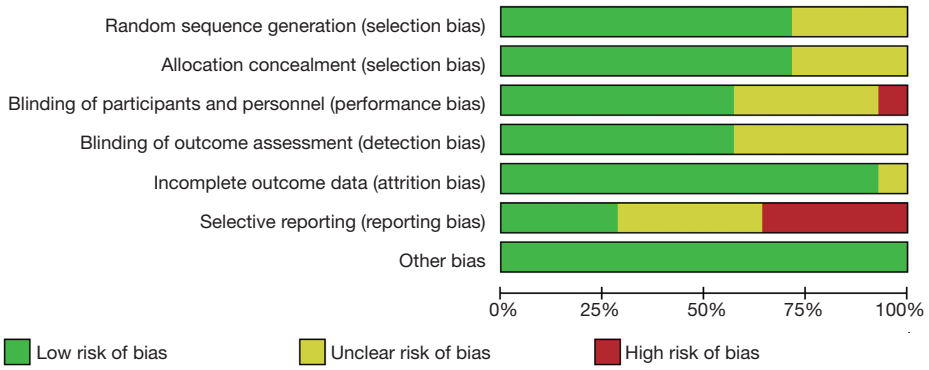

Figure 2 Methodological quality assessment of the included studies.

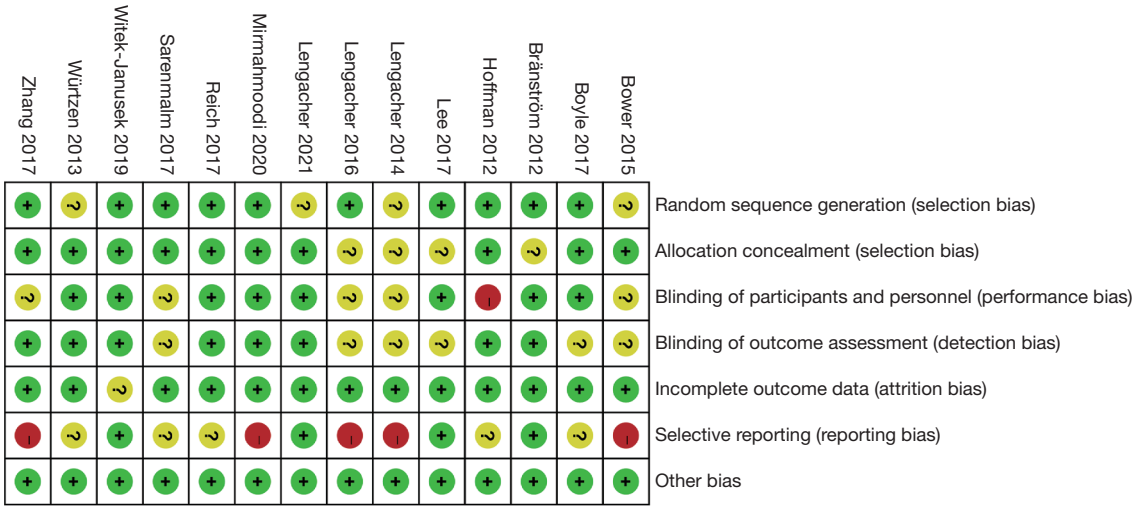

Figure 3 Risk of bias summary of the included studies.

two high risk bias, indicating that the quality of the included articles were acceptable.

Meta-analysis for outcomes

Depression

For depression, three instruments were used to assess the outcomes: the Center for Epidemiologic Studies Depression Scale (CES-D) (32), the Hospital Anxiety and Depression Scale (HADS) (33), and the Profile of Mood States score (POMS) (34). We did subgroup analyses for the different instruments, and the meta-analysis showed that although the MD in the subgroup of the CES-D had no statistical significance (P=0.25), the total SMD showed statistical significance between the intervention and control groups [SMD, −0.62; 95% CI: (−1.20, −0.03); P=0.04; random-effects model] (*Figure 4*).

Stress

For stress, the Perceived Stress Scale (35) was used in 10 studies, with a total sample size of 1,221 patients. The intervention group showed a significantly stress reduction compared with the control group [MD, −1.72; 95% CI: (−2.53, −0.92); P<0.0001; random-effects model], and there was significant heterogeneity among the included studies (I^2=97%; P<0.0001) (*Figure 5*).

Anxiety

To assess anxiety, the State Trait Anxiety Inventory-State (STAI-S) (36), HADS, POMS, and the Revised Symptom-Checklist-90 (SCL-90-r) (37) were used in 9 studies involving 1,532 patients. The results of subgroup analyses of the four groups showed statistical significance, and the total results also showed that intervention group had a better improvement in anxiety control than the control

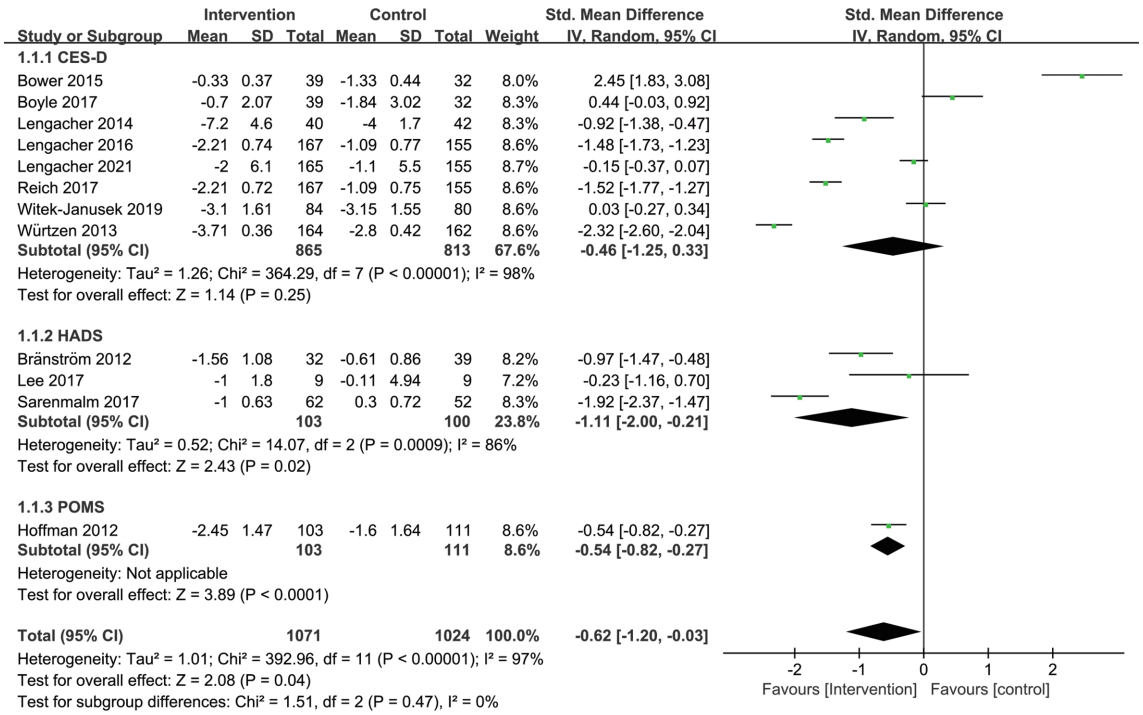

Figure 4 Forest plot: comparison of depression between intervention group and control group. SD, standard deviation; CI, confidence interval; CES-D, Center for Epidemiologic Studies Depression Scale; HADS, Hospital Anxiety and Depression Scale; POMS, Profile of Mood States score.

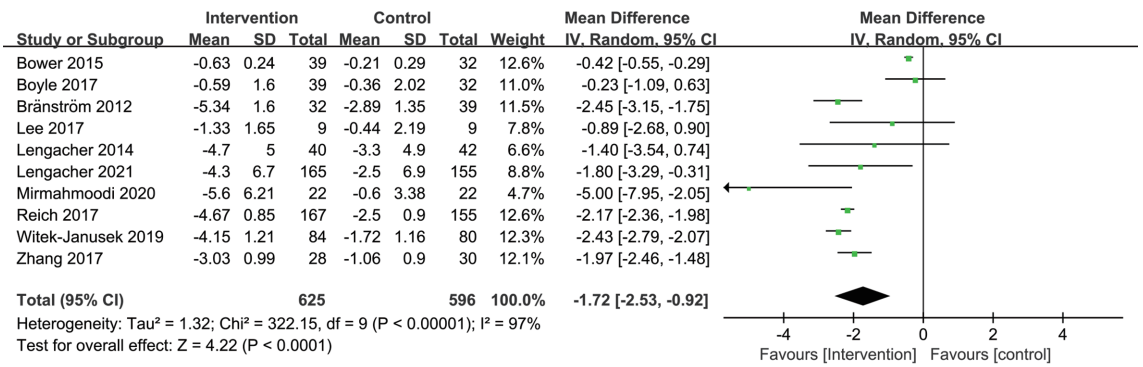

Figure 5 Forest plot: comparison of stress between intervention group and control group. SD, standard deviation; CI, confidence interval.

group [SMD, −1.36; 95% CI: (−2.13, −0.60); P=0.0005; random-effects model], with significant heterogeneity between subgroups (I^2=98%, P<0.00001) (*Figure 6*).

Fatigue

For fatigue, the 6 studies containing 1,413 patients were evaluated by the Fatigue Symptom Inventory and POMS. There was no significant difference between groups regarding fatigue reduction [SMD, −0.97; 95% CI: (−2.24, 0.31); P=0.14; random-effects model]. The pooled study was heterogeneous (I^2=99%; P<0.00001) (*Figure 7*).

Sleep

Sleep disturbances were assessed using the instrument of the Pittsburg Sleep Quality Index in 14 included studies. The pooled results showed that the intervention group had

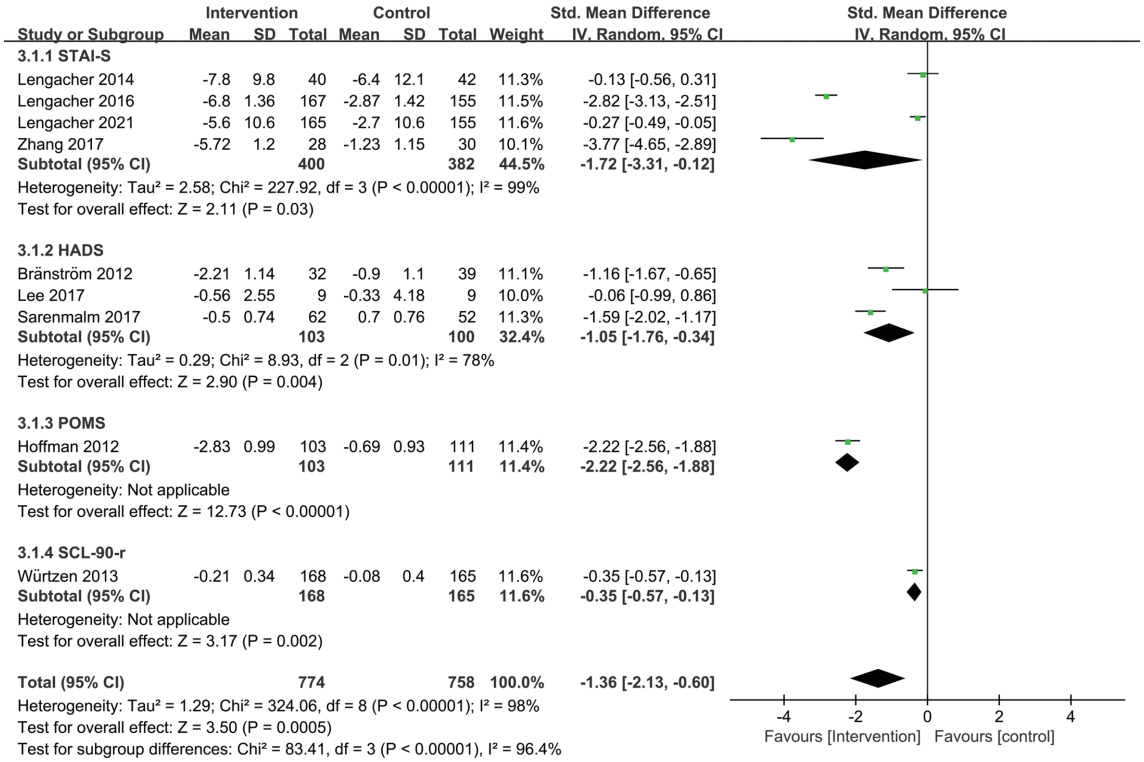

Figure 6 Forest plot: comparison of anxiety between intervention group and control group. SD, standard deviation; CI, confidence interval; STAI-S, State Trait Anxiety Inventory-State; HADS, Hospital Anxiety and Depression Scale; POMS, Profile of Mood States score; SCL-90-r, Revised Symptom-Checklist-90.

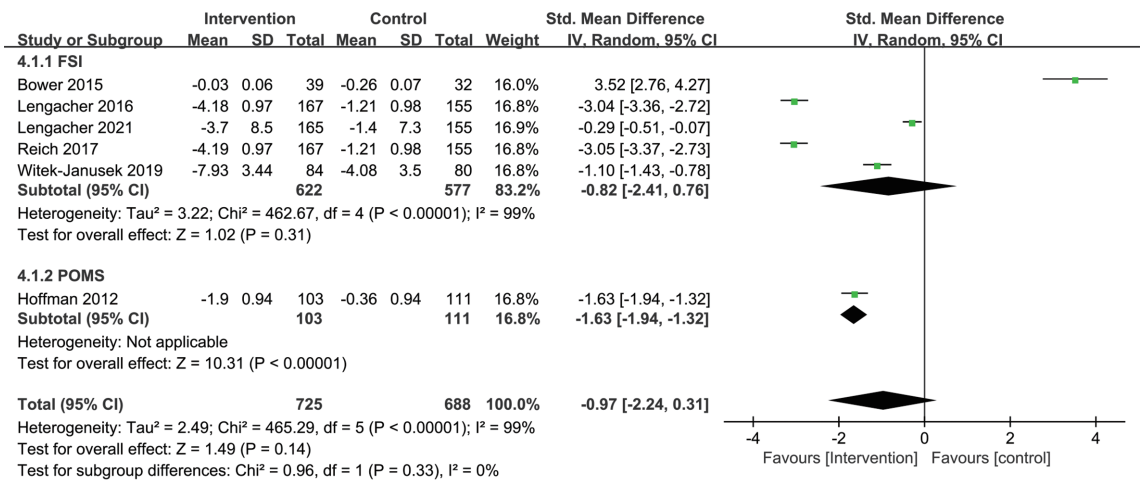

Figure 7 Forest plot: comparison of fatigue between intervention group and control group. SD, standard deviation; CI, confidence interval FSI, Fatigue Symptom Inventory; POMS, Profile of Mood States score.

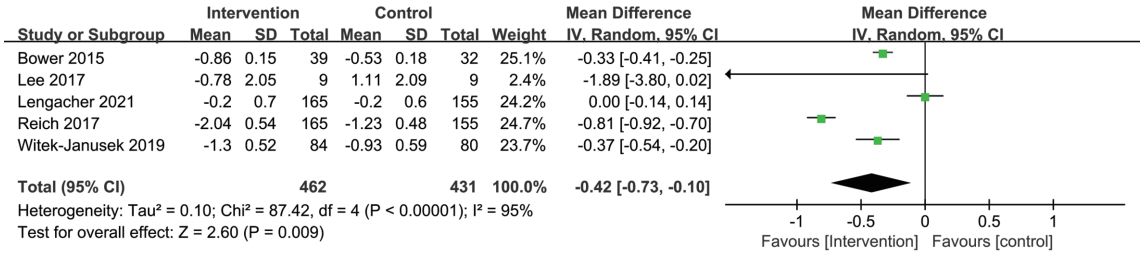

Figure 8 Forest plot: comparison of sleep between intervention group and control group. SD, standard deviation; CI, confidence interval.

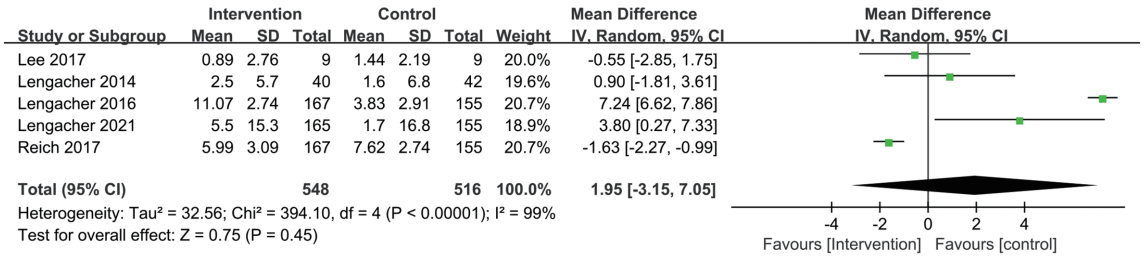

Figure 9 Forest plot: comparison of QOL between intervention group and control group. SD, standard deviation; CI, confidence interval; QOL, quality of life.

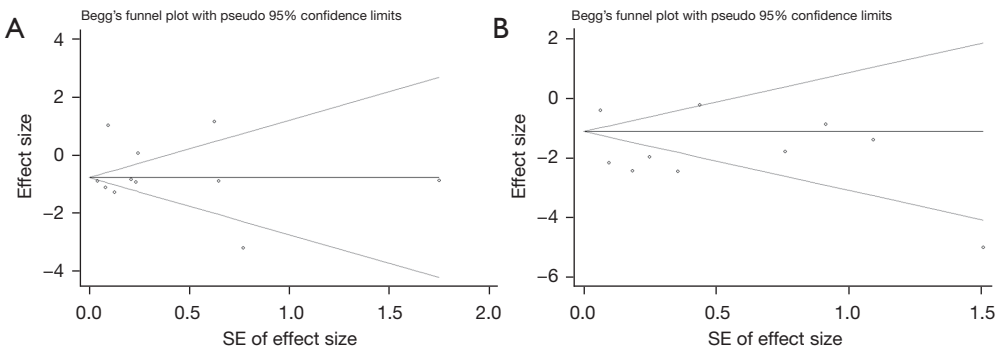

Figure 10 Funnel plot of publication bias risk: (A) depression; (B) stress. SE, standard error.

a better improvement in sleep disturbance than the control group [MD, −0.42; 95% CI: (−0.73, −0.10); P=0.009; random-effects model], with significant heterogeneity (I^2=95%; P<0.00001) (*Figure 8*).

QOL

For QOL, the 5 studies involving 1,064 patients were evaluated by the Medical Outcomes Study Short Form Health Survey. Meta-analysis showed no significant difference between groups regarding QOL improvement [MD, 1.95; 95% CI: (−3.15, 7.05); P=0.45; random-effects model] (*Figure 9*).

Publication bias

Publication bias was evaluated by visually inspecting funnel plots when at least 10 studies were included in the meta-analysis; two funnel plots were produced for the outcomes of depression and stress. Although they showed irregularity (*Figure 10*), the Egger's test for quantitative detection of publication bias showed that bias was not statistically significant (depression, P=0.734; stress, P=0.282).

Discussion

Our study results showed that compared with standard or

usual care, MBSR can effectively relieve psychological stress [MD, –1.72; 95% CI: (–2.53, –0.92); P<0.0001] and anxiety [SMD, –1.36; 95% CI: (–2.13, –0.60); P=0.0005] of breast cancer patients. MBSR can help patients to consciously perceive the present, guide them to establish positive physical reactions and emotions, cultivate acceptance, patience, trust, and other attitudes, and thereby improving patients' cognitive level (38,39).

Breast cancer patients have different levels of depression, and for the loss of female characteristics after breast cancer surgery especially, the psychological response can be even higher than for the cancer (40,41). Studies have shown that providing relevant knowledge about breast cancer on websites and online consultations can effectively reduce the depression level of patients in the long term (42,43). Therefore, future research needs to include the use of digital technology. Compared with standard or usual care, we found that MBSR can improve the depression [SMD, –0.62; 95% CI: (–1.20, –0.03); P=0.04] of breast cancer patients, which is consistent with the results of other meta-analysis such as Haller *et al.* (44) and Hoffman *et al.* (19).

In addition, we found that MBSR improved the sleep status [MD, –0.42; 95% CI: (–0.73, –0.10); P=0.009] of breast cancer patients, but had no significant effect on fatigue [SMD, –0.97; 95% CI: (–2.24, 0.31); P=0.14] or QOL [MD, 1.95; 95% CI: (–3.15, 7.05); P=0.45]. In the meta-analysis of Haller *et al.* (44), MBSR did improve the long-term QOL. The reason for these discrepant findings may be that the process is gradual, so the short-term effect of MBSR on QOL may not be significant (43,45). Future research needs to extend the time of both intervention and follow-up, and use the internet for comprehensive nursing interventions in multiple directions to improve the long-term QOL of breast cancer patients (46,47).

Our study has some limitations. Firstly, although the MBSR included in the study was essentially based on the theoretical framework of John Kabat Zinn's mindfulness therapy, the specific implementation schemes are not completely consistent, which may have a certain effect on heterogeneity. Secondly, the included studies were heterogeneous. The subjects were from different countries (i.e., China, the USA, South Korea, Sweden, Denmark, and Iran) where the acceptance of MBSR will differ according to cultural backgrounds. In addition, the intervention time and follow-up time in this study were relatively short. Future research should include short, medium, and long-term follow-up to observe the effect of MBSR at different stages in the lives of breast cancer patients.

Conclusions

MBSR achieved preliminary affirmation in alleviating the stress, anxiety, depression, and sleep quality of breast cancer patients. However, its effect on fatigue and QOL were not significant, and further research and verification are needed. Therefore, future research needs to analyze standardized intervention programs, and unified evaluation methods of outcome indicators to verify the effect of MBSR in breast cancer patients.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2530/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-2530/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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