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Mindfulness-based stress reduction with acupressure for sleep quality in breast cancer patients with insomnia undergoing chemotherapy: A randomized controlled trial

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ABSTRACT

Purpose: The objective of this randomized controlled trial was to evaluate and compare the effectiveness of mindfulness-based stress reduction (MBSR), acupressure, and MBSR combined with acupressure in improving sleep quality in breast cancer patients with sleep disorders, as well as the potential effects of these interventions on relieving fatigue, anxiety, and depression.

Methods: A four-arm parallel-group randomized controlled trial was conducted in a tertiary hospital in Fujian between July 2019 and January 2021. A total of 147 breast cancer patients were randomly assigned to a usual care group (n = 34), a MBSR group (n = 38), an acupressure group (n = 36), or a combined group (n = 39). We assessed patients' sleep quality (Pittsburgh Sleep Quality Index-PSQI and 6 actigraphy indices), fatigue, anxiety, and depression at baseline and at the mid-intervention (fourth week) and the end of intervention (eighth week).

Results: The ANOVA showed a significant difference ($p < 0.05$) in PSQI, and all sleep parameters measured by wrist actigraphy, and anxiety between groups. The three active treatments led to better PSQI outcomes ($p < 0.001$), reduced fatigue ($p < 0.001$), decreased anxiety ($p < 0.05$), and improved sleep measured by all actigraphy indices with two exceptions (MBSR did not differ from control on Sleep Latency ($p = 0.235$) and mean waking by time (MWBT) ($p = 0.058$)). Both acupressure and the combined intervention outperformed MBSR on four actigraphy indices: Sleep Efficiency (SE), Sleep Latency (SL), Totatl Sleep Time (TST), and Wake after sleep onset (WASO) ($p < 0.05$), and the combined intervention further outperformed MBSR on PSQI ($p = 0.03$) and Number of awakings (NOA) ($p = 0.003$). Moreover, there was no significant difference across all outcomes between acupressure and combined intervention ($p \geq 0.05$).

Conclusions: MBSR, acupressure, and combined therapy all show a remarkable advantages in allemiating sleep quality, fatigue, and anxiety. Acupressure and combined therapy outperformed MBSR in improving sleep quality.

1. Introduction

Global Cancer Statistics 2020 showed that female breast cancer has surpassed lung cancer as the most commonly diagnosed cancer with an estimated 2.3 million new cases (11.7%) (Sung et al., 2021). While advancements in early detection and treatment have increased breast cancer survival rates, the outlook for the physical and psychosocial health of breast cancer patients is still not optimistic (Guimond et al., 2020; Maass et al., 2020). Approximately 14%–93% of breast cancer patients experience sleep problems (Leysen et al., 2019). Long-term sleep disturbances may potentiate the vulnerability of immune alterations caused by chemotherapy and increase susceptibility to infections during cancer care (Ruel et al., 2020). In addition, chemotherapy may cause a series of side effects and further impair patients' sleep quality (Ratcliff et al., 2021). Cancer-related fatigue is another burdensome and long-lasting symptom among breast cancer patients, affecting up to 72% during treatment, and it may remain a continuous burden even after treatment completion (Puigpinos-Riera et al., 2020). Meanwhile, the

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majority of breast cancer patients are reported to experience varying degrees of depression and anxiety during chemotherapy treatment (Hajj et al., 2021; Liu et al., 2021; Pilevarzadeh et al., 2019).

Several interventions have been conducted to alleviate the physical or psychological symptoms experienced by breast cancer patients undergoing chemotherapy (Abrahams et al., 2020; Vallance et al., 2020; VanderWalde et al., 2021). Mindfulness-based stress reduction (MBSR) is an eight-week program originally developed by Professor Jon Kabat-Zinn and characterized by learning to concentrate on the present moment with openness, curiosity, and acceptance (Gu et al., 2015). There are three main formal practical exercises: body scan (mindful body perception), gentle yoga, and traditional sitting meditation (Witek Janusek, Tell and Mathews, 2019). MBSR is widely practiced across varied populations, including in the field of breast and lung cancer to help relieve patients' subjective stress, pain, fatigue, and psychological symptoms including anxiety, depression, and fear of recurrence (Tian et al., 2021; Zhang et al, 2019). In 2019, a review of MBSR for women diagnosed with breast cancer systematically analyzed published randomized clinical trials and found that MBSR can slightly alleviate fatigue (SMD -0.50, 95% CI -0.86 to −0.14), anxiety (SMD -0.29, 95% CI -0.50 to −0.08), moderately reduce depression (SMD -0.54, 95% CI -0.86 to −0.22), and slightly improve sleep quality (SMD -0.38, 95% CI -0.79 to 0.04) in the short term (Schell et al., 2019). Relevant studies conducted in Chinese breast cancer patients have demonstrated that MBSR can improve female sexual function and mental health (Chang et al., 2022) and posttraumatic growth (Zhang et al., 2017), and reduce psychological symptoms (Kang et al., 2021).

Acupressure, a method derived from traditional Chinese medicine, is a treatment in which pressure is applied with fingers, thumbs, or a device on the body's acupoints. Although the mechanism of acupoint stimulation is unclear, there is sufficient evidence that acupoint stimulation can play a significant role in medical treatment. Acupressure is well-received because it is noninvasive, safe, and convenient compared with acupuncture (Ge et al., 2022), and it has shown promise as a treatment for chemotherapy-induced nausea, vomiting, and anxiety in patients with breast cancer (Tan et al., 2020). Several studies have demonstrated the positive effects of acupressure on improving sleep quality in breast cancer patients (Nourizadeh et al., 2022; Yoon and Park, 2019). Moreover, a pilot randomized sham-controlled trial indicated that self-acupressure is feasible for managing the symptom cluster of insomnia, depression, and anxiety in cancer patients undergoing chemotherapy and suggested the potential effectiveness of self-acupressure in improving the targeted symptom cluster (Hoang et al., 2022). In addition, acupressure is also used to improve sleep quality in other various populations such as menopausal women (Abedian et al., 2015), psychogeriatric inpatients (Lu et al., 2013), and hemodialysis patients (Arab et al., 2016). Moreover, acupressure has been demonstrated to decrease cancer-related fatigue in different cancer patients (Khanghah et al., 2019; L. Lin et al., 2021). A community-based randomized controlled trial showed that self-acupressure was also beneficial for reducing cancer-related fatigue in ovarian cancer survivors (Zick et al., 2021). Furthermore, a recent systematic review and meta-analysis including 14 RCTs demonstrated that acupressure is effective in reducing depression and anxiety in various populations (J. Lin et al., 2022). Another systematic review also indicated that acupressure significantly reduced patients' anxiety (Chen et al, 2022a, 2022b).

Although there is relatively abundant evidence indicating that MBSR and acupressure both show a positive effect on ameliorating sleep quality, fatigue, anxiety, and depression in cancer patients, we hypothesize that MBSR combined with acupressure may have stronger positive effects on improving sleep quality, and potentially relieving fatigue, anxiety, and depression compared to MBSR, acupressure, and routine care. Therefore, the primary objective of this randomized controlled trial was to evaluate and compare the effectiveness of MBSR, acupressure, and MBSR combined with acupressure, and routine care in improving sleep quality in breast cancer patients with sleep disorders. The secondary purpose is to evaluate and compare the potential effects of these interventions on relieving fatigue, anxiety, and depression.

2. Methods

2.1. Study design

This study was designed as a four-arm parallel group randomized controlled trial and has been registered in the Chinese Clinical Trial Registry with the number "ChiCTR190002561." We followed the Consolidated Standards of Reporting Trials (CONSORT 2010).

2.2. Setting and participants

The participants were recruited from Mindong Hospital Affiliated to Fujian Medical University between July 2019 and January 2021. The inclusion criteria for patients were as follows: (1) inpatients diagnosed with breast cancer; (2) undergoing chemotherapy; (3) aged 18 years or older; (4) informed of disease diagnosis and treatment; (5) the total score of Pittsburgh Sleep Quality Index (PSQI) $>$ 7 and sleep efficiency according to the wrist actigraphy index of $<$85% simultaneously; and (6) understanding and speaking Chinese. The exclusion criteria for patients were as follows: (1) breast cancer combined with serious organ dysfunction diseases, nervous system diseases, and others; (2) receiving endocrine therapy; (3) taking sleeping pills, antidepressants, and other drugs that might affect observation outcomes; (4) cognitive impairment (comprehension or expression problems); and (5) received psychotherapy or exercise therapy within the last three months.

2.3. Sample size calculation

The sample size was calculated using PASS 15.0 statistical software under the repeat measurement analysis module (Muller and Barton, 1989). In this study, sleep quality (PSQI) was recognized as the primary outcome. The sample size was determined according to the results of our preliminary study with 35 subjects divided into four groups (control, MBSR, acupressure and combined group). Assuming a power of 0.8 with an alpha of 0.05, 24 participants were needed in each group. With an expected attrition rate of 30% (Hoang et al., 2022; Witek Janusek et al., 2019), each study arm required at least 34 participants. Finally, this study recruited 147 participants, which met the requirements of the sample size.

2.4. Randomized allocation

A random sequence set was generated from the Research Randomizer Website (https://www.randomizer.org/). The sequence contained 136 nonrepeating numbers ranging from 1 to 136. The random numbers were packaged in sequentially numbered, sealed, opaque envelopes by a third party to ensure allocation concealment. After the participants were included, we randomly divided them into groups according to the numbers in the envelopes with 1–34 as the MBSR, 35–68 as the acupressure, and 69–102 as the MBSR with acupressure, and 103–136 as the control groups. Afterwards, these steps were repeated for grouping. In addition, as the interventionists were not blind to group allocation, data collection and analysis were performed by a research assistant and a statistician who did not know the group allocation.

2.5. Intervention

2.5.1. Training program for interventionists

One group of six licensed clinical nurses in the breast oncology department undertook the responsibilities of performing interventions. They were required to attend seven MBSR training sessions (90 min/time) and one examination performed by one senior nurse (the first

author) who was trained and qualified in MBSR. The MBSR training program contains an interpretation of the theoretical basis, skill practice, MBSR procedure, and practice exercises. The acupressure training program, containing two training sessions, was performed by one licensed nurse with rich experience in acupressure in the traditional Chinese medicine department. The first training session (lasting 4 h) was conducted to introduce and explain the location, manipulation, and time of acupressure. The second is a practice session (lasting 4 h) for interventionists to feel the manipulation and strength of the acupressure. Then, the operation exam was performed to check the mastery of all interventionists. The main researcher (the first author) monitored all training sessions and checked the MBSR and acupressure mastery of interventionists after the training sessions in the MBSR, acupressure, and MBSR with acupressure groups. To ensure content equivalency, a Chinese standardized session-by-session video of MBSR and an instruction manual of acupressure were used as education and guidance materials, and the interventionists were requested to follow these instruction materials. Notably, each nurse is responsible for the whole-course intervention of the patients she recruited.

2.5.2. Routine care

Control patients received routine care in the breast oncology department including symptom assessment and management, diet guidance, rest and exercise guidance, and usual psychological support.

2.5.3. MBSR

Patients randomized to the MBSR group received weekly group sessions delivered by the primary interventionist in a large recreational area of the breast oncology department. Patients were required to perform MBSR practice once daily (lasting 45 min) for eight weeks (each session for one week). The weekly group session was led by the main researcher (the first author) and one nurse. The participants were required to conduct the individual practice on their own (using the recording) when they were both inpatient and outpatient, which was monitored and guided by one nurse. After discharge, the interventionist informed that participants must attempt to practice this daily on time and delivered weekly group sessions using WeChat (a popular social media application) to address any issues patients encountered during the practice. The MBSR program followed in this study contained eight sessions including breath awareness, seated mindfulness meditation, focusing on one thing, body scanning, compassionate meditation, sounds and thoughts, choiceless awareness, and coming full circle. The session content of the MBSR program is provided in Appendix 1. During hospitalization, the MBSR practice was suggested to be fixed around 10 a.m. daily to avoid interfering with patients' mealtimes and breaks. Patients were allowed to practice on the ward bed or recreational area if they preferred. Each patient was provided a mini speaker box to listen to the instructions of each session for daily practice. Meanwhile, daily face-to-face discussions were held between interventionists and patients to ensure adherence to program content/objectives and to address any issues, and participants were asked to log their daily mindfulness practice. Interventionists were asked to check the log daily mindfulness practice of the participants.

2.5.4. Acupressure

Patients in the acupressure group received a self-administered acupressure program. Five acupoints were selected in this study according to the recommendations of previous studies and included *Yintang*, *Shenmen*, *Neiguan*, *Baihui*, and *Anmian,* which were demonstrated to improve patients' sleep quality (Ge et al., 2022; Yeung et al., 2022). The specific locations of acupoints appear in Appendix 2. Participants were required to perform acupressure twice daily (each acupoint lasting for 6 min at a time) for eight weeks. Since the instructors of interventions were registered clinical nurses in the study setting, the intervention time was fixed in the daytime to avoid disrupting nurses' off-duty hours. In addition, to ensure the consistency of program implementation, the acupressure was suggested to be performed around 10 a.m. and 3 p.m. daily to avoid patients' mealtimes and breaks. Before the formal intervention, the responsible licensed clinical nurses would teach and instruct the manipulation and strength of acupressure for patients or/and their family caregivers. Patients' family members could help patients perform acupressure if necessary. Daily discussions were held between the interventionists and patients or family caregivers to ensure the accurate location and appropriate manipulation and strength. The correctness of acupressure was confirmed if the participants felt sore, numb, distended, and/or warm. After discharge, the interventionists sent daily reminders via WeChat to inform the patients to perform acupressure, and delivered a weekly group meeting to address any issues patients encountered during the practice. Likewise, the interventionist needs to check the completion daily via WeChat.

2.5.5. MBSR combined with acupressure

Patients allocated to the combined group synchronously received MBSR and acupressure for eight weeks. The specific content of the interventions was the same as that set out in the *MBSR* and *Acupressure* sections above. Participants in the combined group were suggested to start the MBSR practice around 10 a.m., followed by half an hour of acupressure. Similarly, patients in the combined group still need to complete one acupressure session around 3 p.m. Daily discussions and weekly group meetings were held between participants and interventionists.

2.6. Data collection

Two research assistants (RA) were included in the study and trained by the principal investigator (the first author) of the research. After obtaining informed consent, the RA collected the baseline data including sociodemographic information (a self-designed questionnaire) and information about sleep, fatigue, anxiety, and depression through a face-to-face questionnaire survey on the day of enrollment (T0). PSQI, Brief Fatigue Inventory (BFI–C), Hospital Anxiety and Depression (HADS), and the sleep parameters of wrist actigraphy data were collected repeatedly at the end of the fourth (T1) and eighth weeks (T2) of intervention. Notably, patients wore the wrist actigraphy for 12 h from 8:00 p.m. to 8:00 a.m. the next day at the data collection point including baseline, the mid-intervention (fourth week), and the end of intervention (eighth week). The data of wrist actigraphy were calculated and generated by ActiLife6.11.4 software. Participants completed questionnaires when they were undergoing chemotherapy in the hospital or waiting for a chemotherapy appointment at the outpatient clinic. If the participant was not scheduled to return to the hospital at the data collection time, a research assistant performed a telephone interview.

2.7. Measurements

2.7.1. Pittsburgh Sleep Quality Index (PSQI)

The PSQI was used to measure patients' sleep disturbance (Buysse et al., 1989). It is a self-reported questionnaire including nine items (the fifth item contains ten subitems.) The score for each domain ranges from 0 to 3, and the total score ranges from 0 to 21 with a higher score indicating poorer sleep quality. The Chinese-version PSQI was found to have satisfactory reliability and validity in patients with lung cancer (Chen et al., 2008). Only the total score was calculated in this study, and a total score greater than 7 indicates that the patient has sleep disorders (Wang et al., 2022). The Cronbach alpha value was 0.70 in this study.

2.7.2. Wrist actigraphy

Wrist actigraphy is an instrument developed to monitor activity intensity and is used in medicine to assess patients' sleep quality. In this study, the Xiaomi Mi Band 2.0 was uniformly selected to monitor patients' sleep quality (Pino-Ortega et al., 2021), and parameters related to wrist actigraphy were set according to the product manual. The data

from the wrist activity meter were analyzed using ActiLife6.11.4 software. The main sleep parameters were (1) sleep efficiency (SE): total sleep time/bedtime; (2) sleep latency (SL): time from going to bed to falling asleep; (3) total sleep time (TST): actual sleep time; (4) wake after sleep onset (WASO): time of waking during sleep; (5) number of awaking (NOA): the number of awakenings during total sleep time; and (6) mean waking by time (MWBT): wake after sleep onset/number of awaking.

2.7.3. Brief Fatigue Inventory (BFI–C)

The nine-item BFI was used to assess participants' fatigue (Mendoza et al., 1999). The first three items assessed fatigue severity at its worst, usual, and right now, and the final six assessed impacts of fatigue on daily activity, mood, walking, work, enjoyment of life, and relations with others. Higher scores indicate more severe fatigue or more interference in life. The Chinese-version BFI–C had excellent internal consistency with Cronbach's coefficient alphas of 0.92 for three fatigue severity items and 0.90 for six fatigue interference items in cancer patients, and a rating of 0–6 for fatigue severity indicates "non-severe", and 7 or greater indicates "severe" (Wang et al., 2004). The Cronbach alpha value was 0.86 in this study.

2.7.4. Hospital Anxiety and Depression (HADS)

The HADS was widely used to assess nonpsychotic anxiety and depression of inpatients (Zigmond and Snaith, 1983). It contains 14 items—7 for assessing anxiety and 7 for depression. Each item is scored from 0 to 3, and the subscale total scores range from 0 to 21 with higher scores indicating more anxiety or depressive symptoms. In this study, the subscale with a score $\geq$8 would represent significant anxiety or depression (Bjelland et al., 2002). The Chinese version demonstrated good validity and reliability in cancer patients (Li et al., 2016). In this study, the Cronbach alpha values were 0.63 and 0.67 for the subscales of anxiety and depression, respectively.

2.8. Statistical analysis

IBM SPSS Statistics for Windows, version 26.0 (IBM SPSS Data Collection, New York, NY, USA), was used to analyze data. Participants' demographic and clinical characteristics were compared using variance analysis, Mann–Whitney *U* test, chi-square, or Fisher's exact test when appropriate. The intention-to-treat (ITT) principle was adopted for analyzing the data. Missing data were supplemented using a multiple imputation approach. A repeated-measures analysis of variance (ANOVA) was used to explore between-group, within-group, and interaction effects, followed by a Least Significant Difference (LSD) test used to compare the outcomes between groups. The data of non-normal distribution (SL, WASO, MWBT) were transformed by rank order followed by repeated-measures ANOVA. The criterion for statistical significance was set at $p < 0.05$ in a two-tailed test.

2.9. Ethical considerations

This study was approved by the Ethics Committee of Mindong Hospital Affiliated to Fujian Medical University (No.: 2019/0621–2). Participants were given detailed information about the study and written informed consent was obtained from each patient before data collection. Patients' wishes are fully respected, and they had the right to withdraw from the study at any time. The information collected was kept confidential and will not be disclosed to others.

3. Results

3.1. Characteristics of participants

Total 147 patients were included and randomly assigned to the routine care (n = 34), MBSR (n = 38), acupressure (n = 36), or MBSR with acupressure group (n = 39). Thirteen patients withdrew from the study after eight weeks due to condition deterioration (n = 1), refusal to participate (n = 10), and family caregivers' refusal (n = 2)—10 in the MBSR group and three from the MBSR with acupressure group. Fig. 1 presents a flowchart of recruitment and specific reasons for participants' dropout. Notably, the 13 dropout patients show a significant ($p < 0.05$) lower fatigue, anxiety, depression, WASO, MWBT, and higher SE and TST in the baseline compared to the completer (Appendix 3). Table 1 demonstrates that there were no significant differences ($p \geq 0.05$) in sociodemographic and clinical characteristics across the four groups. The vast majority of participants were female (98.64%) and married (98.64%). Their mean age was 51.41 $\pm$ 8.85 years, and the majority had a primary-school education level or below (68.03%), were unemployed (81.63%), and had undergone surgery (90.48%) without recurrence (99.32%). In addition, most patients were at neoplasm stage II or below (76.87%). Most (70.75%) had already received between one and five rounds of chemotherapy.

3.2. Study outcomes

The results of interventions on PSQI, sleep parameters measured by wrist actigraphy, fatigue, anxiety, and depression are presented in Table 2. The changes over time in the mean (and standard deviation) of all outcomes are shown in Appendix 4. The results of ANOVA showed a significant difference ($p < 0.05$) in PSQI, and all sleep parameters measured by wrist actigraphy, and anxiety between groups. Simultaneously, ANOVA showed a significant difference ($p < 0.05$) over time in PSQI, and all sleep parameters measured by wrist actigraphy, fatigue, and anxiety. The interaction effects were significant for PSQI, anxiety, and all sleep parameters measured by wrist actigraphy with an exception for SL ($p = 0.243$). Notably, there was no significant difference ($p \geq 0.05$) in the depression between groups, within the group, and interaction effects. The results of further pairwise comparisons between the four groups by LSD are presented in Table 3. The three active treatments led to better PSQI outcomes ($p < 0.001$), reduced fatigue ($p < 0.001$), decreased anxiety ($p < 0.05$), and improved sleep measured by all actigraphy indices with two exceptions (MBSR did not differ from control on SL ($p = 0.235$) and MWBT ($p = 0.058$)). Additionally, MBSR, but not acupressure and combined treatment, led to reduced depression, compared to control ($p < 0.05$). Importantly, both acupressure and the combined intervention outperformed MBSR on four actigraphy indices: SE, SL, TST, and WASO ($p < 0.05$), and the combined intervention further outperformed MBSR on PSQI ($p = 0.03$) and NOA ($p = 0.003$). Moreover, there was no significant difference ($p \geq 0.05$) across all outcomes between acupressure and combined intervention.

4. Discussion

This study is the first to compare the effects of MBSR, acupressure, and MBSR combined with acupressure on sleep quality and fatigue in patients with breast cancer. The main findings are that MBSR, acupressure, and MBSR with acupressure all have varying degrees of positive effect on breast cancer patients' sleep quality, fatigue, and anxiety. Notably, MBSR combined with acupressure shows a remarkable advantage in improving sleep quality in breast cancer patients.

Unexpectedly, the rate of participants refusing to participate (37.76%) was high. This may be partly explained by how most cancer patients and family members are more concerned with disease treatment and prognosis than psychological well-being. In addition, all participants in this study experienced sleep disorders, possibly resulting in their disinterest in participation. Surprisingly, the dropout rate was relatively higher (26.32%) in the MBSR group. This may be because more than half of the patients (64.29%) in the MBSR group had a primary-school education level or below, which may have caused some difficulty in understanding and maintaining the essence of MBSR. This result is consistent with a previous study with a drop-out rate of 28.89%

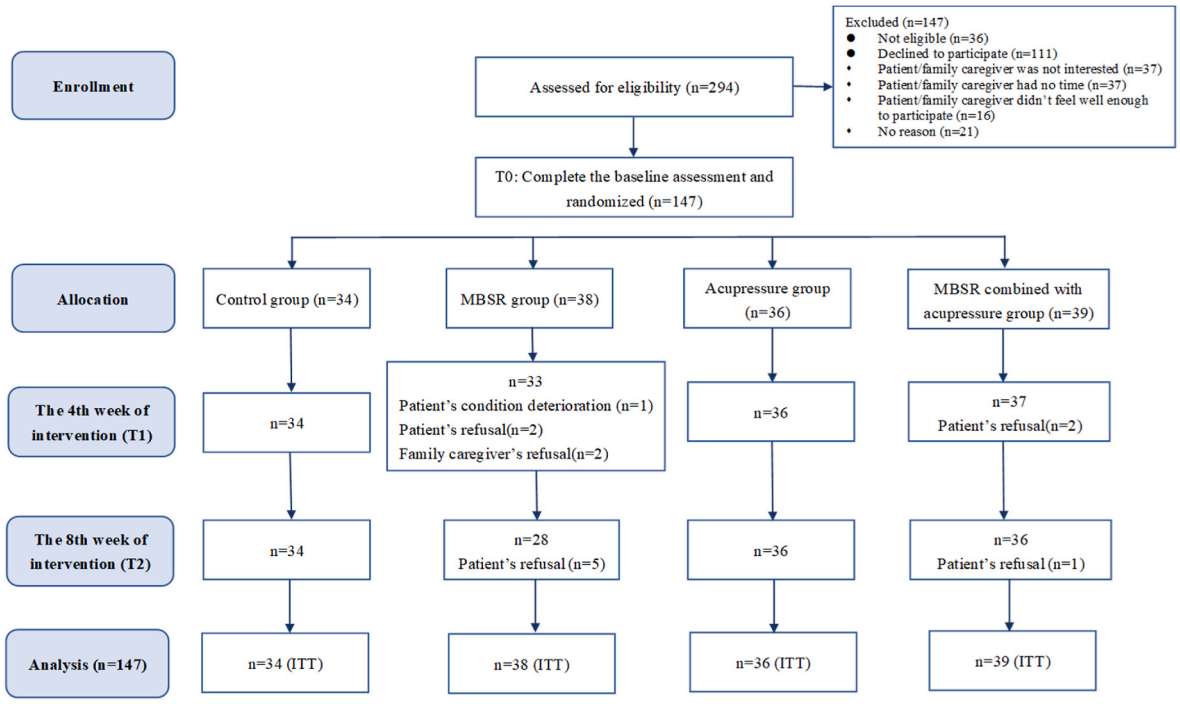

Fig. 1. Participants CONSORT flow chart.

after completion of an eight-week MBSR intervention (Witek Janusek et al., 2019). Another surprising result is that the mean age was significantly lower for dropout patients than for included patients. This might be partly due to the fact that the majority of older patients are more accustomed to a static lifestyle and are more likely to accept and adhere to MBSR practices. The dropout participants also showed lower fatigue, anxiety, depression, WASO, and MWBT as well as higher SE and TST than the included participants. This may explain one reason for dropping out; patients were less motivated to participate after their sleep and psychological problems improved.

In this study, the participants were patients diagnosed with sleep disorders through both self-reporting and actigraphy monitoring; thus, the simple subjective sleep disorder can be partly avoided. This study showed that MBSR, acupressure, and MBSR with acupressure all significantly improved patients' sleep quality compared to the control group. Meanwhile, further pairwise comparison results indicated that acupressure and combined therapy were more effective for improving objective sleep quality than MBSR, and the combined treatment further outperformed MBSR on subjective sleep quality. However, compared to acupressure, combined treatment had no significant advantage in improving sleep quality. This suggests that acupressure alone can improve the objective sleep quality of patients in the short term, while combined treatment was recommended to improve patients' subjective and objective sleep. A recent study indicated that self-administered acupressure taught as a short training course is effective in improving sleep quality in individuals with insomnia disorder (Yeung et al., 2022). Since acupressure can stimulate body nerves, and muscles through finger massage and pressure to promote nerve and muscle regulation and inhibit cerebral cortex response, the human body enters a relaxed and comfortable natural state, and sleep quality is improved (Min et al., 2021).

Although MBSR is not better than acupressure or combined therapy at improving patients' subjective or objective sleep quality, MBSR was effective at improving patients' subjective or objective sleep quality compared with the control group. As MBSR intends to cultivate nonjudgmental awareness of the present moment to develop greater emotional balance, it may reduce stress and facilitate sleep quality in those confronted with cancer (Zhang et al., 2019). Related research indicated that mindfulness meditation can affect cognitive behavior patterns and improve sleep quality by changing brain structures and networks, decreasing automatic responses, and increasing relaxation responses (Black et al, 2015). However, there is limited evidence that MBSR can improve actigraphy sleep parameters, and most studies only focus on patients' self-reported sleep quality rather than objective outcomes (Chen et al., 2020). In addition, the actual effect of MBSR may be affected by the higher rate of loss to follow-up in the MBSR group. Gaining patients' trust and making MBSR more well-received are important for improving compliance with MBSR interventions in future studies.

Our study indicated that MBSR, acupressure, and MBSR with acupressure were all beneficial for relieving breast cancer patients' fatigue. Further, pairwise comparison results showed that there was no significant difference in effect on fatigue among the three intervention groups. This shows that acupressure, MBSR, or combined therapy can be used as an effective strategy for relieving fatigue in breast cancer patients. Research has demonstrated that acupressure is effective at alleviating the fatigue of cancer patients undergoing chemotherapy and has suggested that nursing personnel could incorporate acupressure into clinical practice as part of a multimodal approach to alleviating fatigue in cancer survivors (Khanghah et al., 2019). Although compliance was lower in the MBSR group, patients who remained enrolled in the study still benefited from MBSR practice. In this study, MBSR with acupressure did not demonstrate better effects in alleviating patients' fatigue. The combination of the two interventions could cause patients to be distracted or choose only one intervention in practice based on their preferences.

MBSR, acupressure, and combined therapy all showed a positive effect on patients' anxiety; there was no difference between their outcomes. This result is consistent with those of previous studies indicating that acupressure can promote sleep and calm emotions by stimulating nerve responses and releasing serotonin (Chen et al., 2022a, 2022b). In addition, research has demonstrated that sleep quality is associated with anxiety, which can indirectly explain why MBSR, acupressure, and combined therapy can alleviate patients' anxiety (Maass et al., 2020). Since anxiety is characterized as a kind of agitated emotion produced by excessive worry about the safety of relatives or their own lives, future,

Table 1
Social-demographic and clinical characteristics of participants.

Variables	Total(N = 147) n (%)	Control (N = 34) n (%)	MBSR (N = 38) n (%)	Acupressure (N = 36) n (%)	Combined (N = 39) n (%)	F/χ^2	*p*
Gender						5.949	0.114[a]
Male	2(1.36)	2(5.88)	0(0)	0(0)	0(0)		
Female	145(98.64)	32(94.12)	38(100)	36(100)	39(100)		
Age(Mean ± SD)	51.41 ± 8.85	51.41 ± 10.10	48.58 ± 8.48	53.06 ± 8.29	52.67 ± 8.19	2.013	0.115[b]
Age cohorts						14.002	0.122[a]
≤44	27(18.37)	7(20.59)	11(28.95)	3(8.34)	6(15.38)		
45–59	89(60.54)	20(58.82)	24(63.16)	21(58.33)	24(61.54)		
60–74	29(19.73)	6(17.65)	3(7.89)	12(33.33)	8(20.52)		
75–89	2(1.36)	1(2.94)	0(0)	0(0)	1(2.56)		
Marital status						2.774	0.428[a]
Married	145(98.64)	34(100)	37(97.37)	35(97.22)	39(100)		
Unmarried or Divorced	2(1.36)	0(0)	1(2.63)	1(2.78)	0(0)		
Education level						3.619	0.728[a]
Primary school or below	100(68.03)	26(76.47)	25(65.79)	24(66.67)	25(64.11)		
Middle or high school	27(18.36)	5(14.71)	9(23.68)	7(19.44)	6(15.38)		
University degree	20(13.61)	3(8.82)	4(10.53)	5(13.89)	8(20.51)		
Employment						2.678	0.444[a]
Employed	27(18.37)	6(17.65)	4(10.53)	8(22.22)	9(23.08)		
Unemployed	120(81.63)	28(82.35)	34(89.47)	28(77.78)	30(76.92)		
Relapse						2.951	0.399[a]
Yes	1(0.68)	1(2.94)	0(0)	0(0)	0(0)		
No	146(99.32)	33(97.06)	38(100)	36(100)	39(100)		
Surgery						7.294	0.063[a]
Yes	133(90.48)	33(97.06)	37(97.37)	30(83.33)	34(87.18)		
No	14(9.52)	1(2.94)	1(2.63)	6(16.67)	5(12.82)		
Neoplasm staging						5.064	0.956[a]
0	5(3.40)	2(5.88)	0(0)	1(2.78)	2(5.13)		
I	33(22.45)	8(23.53)	8(21.05)	9(25.00)	8(20.51)		
II	75(51.02)	17(50.00)	20(52.64)	17(47.22)	21(53.85)		
III	25(17.01)	5(14.71)	8(21.05)	7(19.44)	5(12.82)		
IV	9(6.12)	2(5.88)	2(5.26)	2(5.56)	3(7.69)		
Frequency of chemotherapy						2.013	0.339[a]
1-5	104(70.75)	26(76.47)	27(71.06)	24(66.67)	27(69.23)		
6-10	31(21.09)	4(11.76)	9(23.68)	10(27.77)	8(20.51)		
11-15	5(3.40)	1(2.95)	2(5.26)	0(0)	2(5.13)		
16-20	3(2.04)	2(5.88)	0(0)	1(2.78)	0(0)		
20 or above	4(2.72)	1(2.94)	0(0)	1(2.78)	2(5.13)		

Note：.
MBSR: Mindfulness-based stress reduction.
SD: Standard deviation.
[a] χ^2 test.
[b] Analysis of variance.

and fate (Zigmond and Snaith, 1983), the practice of MBSR and acupressure allows patients to focus on the present, relax their mind and body, get rid of worries about irrelevant things, and further ameliorate anxiety. Interestingly, MBSR is beneficial for decreasing depression, compared with the control group. This result is consistent with a previous systematic review indicating that MBSR interventions are highly beneficial for reducing depression in the short term (Chang et al., 2021). However, acupressure and combined therapy were ineffective at alleviating patients' depression. This result is inconsistent with an existing systematic review (Lin et al., 2022). This may be partly explained by the fact that the baseline depression score of participants in this study was >10. The significant difference in anxiety and depression between interventions was not likely to be found due to a ceiling effect because the average baseline HADS scores of participants in this study were over the threshold for clinically significant anxiety and depression.

Notably, in this study, the MBSR and acupressure were delivered by trained clinical nurses. Integrating acupressure and MBSR into clinical nursing care might achieve positive effects. This reflects the dissemination and application potential of MBSR, and acupressure in hospitalized patients. In this study, the adherence of participants in the acupressure group was higher than that of the MBSR and combined groups. This may be partly explained by that acupressure, as a common treatment of traditional Chinese medicine, is more easily accepted and trusted by the Chinese population. MBSR practice requires participants to fully understand instructions and focus their attention, which may be difficult for some older patients with low education levels. Notably, although there was no COVID-19 outbreak in the study setting, many public health measures such as quarantine requirements for admission to the hospital were still being implemented to prevent the spread of COVID-19, which makes recruitment and follow-up of this study more difficult.

4.1. Limitations

Despite the positive effects of MBSR, acupressure, and MBSR with acupressure on patients' sleep quality, fatigue, and anxiety, this study has several limitations. First, the participants were recruited from only one hospital in the south of China, which limits the generalizability of the findings. Second, although the number of participants met the requirements of sample size, the sample size is relatively small, which may reduce the possibility of finding positive results. Third, part of the interventions was performed in an inpatient setting, which may increase the risk of some contamination and confounding factors. Notably, the 10 repeated measure ANOVAs conducted increase the likelihood of a type I error. In addition, although the intervention lasted for eight weeks, the long-term effects cannot be observed due to a lack of further follow-up. A future study with a longer follow-up period should be conducted to confirm the effects. Moreover, since the control group received routine

Table 2
Comparisons of outcomes between three intervention groups and control group at different time points.

Outcomes	Group	T0 (Mean ± SD)	T1 (Mean ± SD)	T2 (Mean ± SD)	Between groups (F, *p*)	Within group (F, *p*)	Interaction effect (F, *p*)
PSQI	Control	11.15 ± 1.73	11.21 ± 2.98	11.26 ± 2.84	13.223, < 0.001	101.560, <0.001	15.529, <0.001
	MBSR	10.82 ± 2.51	10.26 ± 2.89	7.18 ± 2.84			
	Acupressure	11.42 ± 2.38	8.33 ± 2.48	7.03 ± 2.15			
	Combined	11.28 ± 2.73	8.10 ± 2.86	5.92 ± 1.91			
SE	Control	81.32 ± 4.32	82.11 ± 4.98	80.61 ± 9.57	21.856, <0.001	69.126, <0.001	11.986, <0.001
	MBSR	81.86 ± 5.69	84.52 ± 8.37	92.42 ± 6.63			
	Acupressure	82.29 ± 3.33	91.27 ± 6.13	91.86 ± 7.60			
	Combined	80.77 ± 5.81	90.47 ± 6.99	93.74 ± 5.72			
SL*	Control	271.97 ± 89.36	265.99 ± 106.96	221.16 ± 163.04	5.245, 0.002	10.704, <0.001	1.330, 0.243
	MBSR	268.87 ± 117.87	240.79 ± 106.78	191.53 ± 116.83			
	Acupressure	239.18 ± 114.79	162.88 ± 119.22	199.83 ± 117.64			
	Combined	255.81 ± 134.11	181.15 ± 134.80	161.45 ± 133.62			
TST	Control	439.13 ± 23.35	443.41 ± 26.92	435.31 ± 51.70	20.307, <0.001	57.674, <0.001	9.621, <0.001
	MBSR	442.07 ± 30.73	458.01 ± 50.12	491.58 ± 45.32			
	Acupressure	444.34 ± 18.00	492.85 ± 33.11	496.06 ± 41.05			
	Combined	436.17 ± 31.40	490.72 ± 40.00	505.35 ± 32.75			
WASO*	Control	309.41 ± 72.69	289.93 ± 102.45	268.21 ± 126.18	17.301, <0.001	84.082, <0.001	7.011, <0.001
	MBSR	290.70 ± 95.73	238.36 ± 134.11	138.63 ± 101.72			
	Acupressure	309.65 ± 75.28	146.06 ± 92.39	113.81 ± 108.17			
	Combined	292.89 ± 104.75	156.49 ± 99.86	117.04 ± 97.86			
NOA	Control	20.74 ± 5.78	19.03 ± 6.80	19.09 ± 7.75	11.968, <0.001	36.118, <0.001	2.815, 0.011
	MBSR	20.32 ± 5.75	17.55 ± 7.45	13.66 ± 5.23			
	Acupressure	20.39 ± 6.35	14.00 ± 7.06	12.67 ± 4.07			
	Combined	19.82 ± 7.94	12.95 ± 7.67	10.72 ± 5.37			
MWBT*	Control	249.94 ± 92.49	264.21 ± 124.05	256.51 ± 138.05	4.51, 0.005	11.202, <0.001	2.505, 0.024
	MBSR	234.50 ± 101.45	238.38 ± 136.05	195.13 ± 136.77			
	Acupressure	258.03 ± 93.55	187.08 ± 129.10	127.15 ± 119.26			
	Combined	262.95 ± 98.17	215.27 ± 123.32	169.80 ± 151.85			
Fatigue	Control	7.00 ± 2.01	6.90 ± 1.39	7.01 ± 1.54	15.856, <0.001	50.568, <0.001	6.349, <0.001
	MBSR	6.40 ± 1.43	5.61 ± 1.43	4.65 ± 1.26			
	Acupressure	6.79 ± 1.10	5.39 ± 1.30	5.25 ± 1.36			
	Combined	6.69 ± 1.15	5.17 ± 1.28	4.80 ± 1.06			
Anxiety	Control	11.18 ± 2.12	11.24 ± 2.27	11.47 ± 2.29	3.439, 0.019	10.893, <0.001	2.289, 0.039
	MBSR	10.47 ± 3.40	9.74 ± 3.47	9.29 ± 2.95			
	Acupressure	11.25 ± 3.07	10.39 ± 2.76	9.06 ± 3.07			
	Combined	11.15 ± 3.45	10.56 ± 2.54	8.85 ± 2.33			
Depression	Control	10.29 ± 2.26	10.74 ± 2.09	11.44 ± 3.14	2.226, 0.088	0.145, 0.853	0.808, 0.558
	MBSR	9.74 ± 4.68	9.74 ± 3.52	9.34 ± 3.29			
	Acupressure	10.69 ± 3.38	10.42 ± 3.10	10.17 ± 3.46			
	Combined	10.21 ± 3.48	9.92 ± 4.16	9.26 ± 3.06			

These results were obtained from a repeated-measures analysis of variance (ANOVA).
MD: Mean difference.
SD: Standard deviation.
MBSR: Mindfulness-based stress reduction.
PSQI: Pittsburgh Sleep Quality Index.
SE: sleep efficiency.
SL: sleep latency.
TST: total sleep time.
WASO: wake after sleep onset.
NOA: number of awakings.
MWBT: mean waking by time.

care and was not given a placebo, we could not find and explain the contribution of the placebo effect in this study. Lastly, a consistency analysis between subjective and objective sleep quality was not conducted in this study.

5. Conclusion

These findings provide supplementary evidence for ameliorating sleep quality, fatigue, anxiety, and depression in breast cancer patients with sleep disorders by comparing the effects of MBSR, acupressure, and MBSR with acupressure. Compared to MBSR, acupressure and combined therapy demonstrate a remarkable advantage in improving actigraphy-assessed sleep quality. Importantly, MBSR combined with acupressure outperformed MBSR in improving subjective sleep quality. In future clinical practice, we should select appropriate intervention methods according to the symptoms and characteristics of cancer patients with sleep disorders. This study suggested that it would be a valuable attempt to incorporate MBSR and acupressure as complementary therapies for ameliorating patients' sleep quality into daily nursing care.

Credit author statement

Qixi Liu: Conceptualization, project implementation. Chunfeng Wang: Methodology, drafting the article, and revising. Ying Wang: Data curation, Writing – review & editing. Wenkui Xu: Data curation and interpretation of data. Jinqing Wu: Resources, project administration. Chenju Zhan: Resources, project administration. Rong Hu: Methodology, Validation, project design, and supervision.

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Table 3
Pairwise comparisons of sleep quality, fatigue, anxiety and depression between three intervention groups and control group.

Outcomes	MBSR vs. Control		Acupressure vs. Control		Combined vs. Control		MBSR vs. Acupressure		MBSR vs. Combined		Acupressure vs. Combined	
	MD	*p*	MD	*p*	MD	*p*	MD	*p*	MD	*p*	MD	*p*
PSQI	−1.785	<0.001	−2.280	<0.001	−2.770	<0.001	0.495	0.283	0.985	0.030	0.490	0.285
SE	4.920	<0.001	7.124	<0.001	6.976	<0.001	−2.204	0.026	−2.056	0.034	0.148	0.879
SL	−19.311	0.235	−52.410	0.002	−53.569	0.001	33.098	0.040	34.258	0.030	1.160	0.942
TST	24.603	<0.001	38.469	<0.001	38.132	<0.001	−13.866	0.013	−13.529	0.014	0.337	0.951
WASO	−66.620	<0.001	−99.343	<0.001	−100.378	<0.001	32.723	0.038	33.758	0.029	1.035	0.947
NOA	−2.442	0.008	−3.933	<0.001	−5.122	<0.001	1.490	0.096	2.680	0.003	1.190	0.180
MWBT	−34.216	0.058	−66.133	<0.001	−40.883	0.023	31.916	0.072	6.667	0.700	−25.250	0.152
Fatigue	−1.418	<0.001	−1.157	<0.001	−1.418	<0.001	−0.261	0.268	−0.000	1.000	0.261	0.265
Anxiety	−1.461	0.003	−1.063	0.029	−1.106	0.021	0.398	0.397	−0.355	0.442	0.043	0.926
Depression	−1.218	0.024	−0.398	0.465	−1.029	0.055	−0.821	0.122	−0.190	0.714	0.631	0.231

These results were obtained from a Least Significant Difference (LSD) test.
MD: Mean difference.
SD: Standard deviation.
MBSR: Mindfulness-based stress reduction.
PSQI: Pittsburgh Sleep Quality Index.
SE: sleep efficiency.
SL: sleep latency.
TST: total sleep time.
WASO: wake after sleep onset.
NOA: number of awaking.
MWBT: mean waking by time.

Data availability

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

Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejon.2022.102219.

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