Original Article

Mindfulness-Based Cognitive Therapy for Psychological Distress, Fear of Cancer Recurrence, Fatigue, Spiritual Well-Being, and Quality of Life in Patients With Breast Cancer—A Randomized Controlled Trial

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Abstract

Context. Mindfulness-based interventions have been receiving growing attention in cancer care.

Objectives. The purpose of this randomized controlled trial is to examine the effectiveness of mindfulness-based cognitive therapy (MBCT) for psychological distress (anxiety and depression), fear of cancer recurrence (FCR), fatigue, spiritual well-being, and quality of life (QOL) in Japanese ambulatory patients with Stage I–III breast cancer.

Methods. A total of 74 patients were randomly assigned to either an eight-week MBCT intervention group ($n = 38$) or a wait-list control group ($n = 36$). The primary outcome was psychological distress, measured on Hospital Anxiety and Depression Scale. The secondary outcomes were FCR (Concerns About Recurrence Scale—overall anxiety subscale), fatigue (Brief Fatigue Inventory), spiritual well-being (Functional Assessment of Chronic Illness Therapy—Spiritual), QOL (Functional Assessment of Cancer Therapy—General), and mindfulness skills (Five Facet Mindfulness Questionnaire). The participants were assessed at baseline (T0), Week 8 (T1), and Week 12 (T2). The results were analyzed using a intention-to-treat linear mixed model.

Results. The participants in the MBCT group experienced significantly better outcomes in their psychological distress (Cohen's $d = 1.17$; $P < 0.001$), FCR ($d = 0.43$; $P < 0.05$), fatigue ($d = 0.66$; $P < 0.01$), spiritual well-being ($d = 0.98$; $P < 0.001$), and QOL ($d = 0.79$; $P < 0.001$) compared with the control group. The difference remained significant at T2 (four weeks after completion of the intervention).

Conclusion. MBCT was demonstrated to improve well-being that encompasses psychological, physical, and spiritual domains in Japanese patients with nonmetastatic breast cancer. The favorable effect was maintained up to four weeks after the completion of the intervention. J Pain Symptom Manage 2020;60:381–389.

Key Words

Breast cancer, fatigue, fear of cancer recurrence, mindfulness, psychological distress, quality of life

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Key Message

This article describes a randomized controlled trial that demonstrated the effectiveness of mindfulness-based cognitive therapy for psychological distress (anxiety and depression), fear of cancer recurrence, fatigue, spiritual well-being, and quality of life in Japanese ambulatory patients with Stage I–III breast cancer.

Introduction

Breast cancer is the most common kind of cancer among women.[1] Patients experience a variety of physical, psychosocial, and spiritual problems related to the illness and its treatment. Clinically significant psychological distress is experienced by up to 50% of patients with breast cancer.[2,3] Even for patients with a good prognosis or for patients who have completed cancer treatment, potential risk of cancer progression and relapse continues to cause long-term distress to patients and survivors, known as the fear of cancer recurrence (FCR).[4,5] Furthermore, physical symptoms such as fatigue and pain impair their social functioning and quality of life (QOL).[6,7] In fact, FCR and fatigue are the two most common symptoms that cancer survivors experience after completion of cancer treatment.[4–6,8]

Mindfulness-based approaches have been recently establishing strong evidence in cancer care.[9] Mindfulness-based interventions (MBIs) guide patients to focus on the present moment, foster their awareness, and cultivate compassionate attitudes through meditation, yoga, group discussion, and daily contemplative practices. These processes lead to better control in their emotion, cognition, and behavior, and ultimately to the stability of the mind.[9,10] The most commonly used MBIs are mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT). Although there is no substantial difference in the structure of these two programs; MBCT incorporates a cognitive therapy approach and provides more explicit psychoeducation on the relationship among mood, cognition, and functioning compared with MBSR.[11]

A series of systematic reviews demonstrate that MBIs are effective to alleviate psychological distress of patients with cancer.[12–16] However, the effectiveness of MBIs for physical symptoms has been controversial. Although a few studies have shown beneficial effects of MBIs for fatigue and pain,[17–20] the results have been inconsistent.[21,22] Furthermore, research for patients with breast cancer so far has been largely focused on MBSR, and there have been only a few randomized controlled trials of MBCT in this context.[12,14,15] Of those MBCT trials, there has been only one study that specifically targeted patients with breast cancer.[19] This study demonstrated the efficacy of MBCT on pain and QOL but failed to demonstrate a significant effect on anxiety, depression, or well-being. Thus, to date, the effectiveness of MBCT for patients with breast cancer has not been confirmed.

In contrast, in our previous observational study, we demonstrated that MBCT yielded significant improvement in psychological distress, spiritual well-being, and QOL in a sample of Japanese patients with breast cancer.[23]

For these reasons, the present study aimed to examine the effectiveness of MBCT for psychological distress (anxiety and depression) of patients with breast cancer in randomized controlled design. Also, we aimed to examine whether MBCT alleviates other important clinical issues, such as FCR, fatigue, spiritual well-being, and QOL. The authors hypothesized that MBCT is effective for these outcomes.

Methods

Design

This was a randomized controlled trial comparing an MBCT intervention and the wait-list control (WLC) in ambulatory nonmetastatic breast cancer patients.

Participants

The eligibility criteria were the following: 1) clinical diagnosis of Stage 0–III breast cancer, 2) aged between 20 and 74 years, 3) the Hospital Anxiety and Depression Scale (HADS) total score of five or higher, 4) Eastern Cooperative Oncology Group performance status of 0–2, 5) expected clinical prognosis of one year or longer, 6) ability to communicate in Japanese, and 7) submission of written informed consent. Patients were excluded if they had the experience of MBCT or MBSR, or if they had any serious physical or psychiatric symptoms to impede with study participation.

Recruitment

The participants were recruited at Keio University Hospital, a tertiary medical facility in central Tokyo, Japan. The participants were recruited by self-referral through flyers or by referral from oncologists and other medical staff during the period between January 2015 and August 2016. Potential participants were invited to an introductory session, where they were explained about the details of the study and submitted written informed consent.

Assessments

Assessments were conducted at three time points—at baseline (before random allocation) (T0), at eight

weeks (postintervention for the intervention group) (T1), and at 12 weeks (i.e., four weeks after the completion of the intervention for the intervention group) (T2).

Intervention

The intervention group received an eight-week MBCT program (two hours per week) in a group format (Table 1). The details of the program are illustrated elsewhere.[23] The program was based on the original MBCT program,[11] with minimal modification to fit with the needs of patients with breast cancer.[23] Although the original MBCT program has a daylong retreat session between the sixth and seventh weeks, we deleted this session because it was considered too burdensome for Japanese patients with cancer to join a daylong program. We added brief psychoeducation to the first session regarding the distress of patients with cancer and on how MBIs can be helpful for it. Lectures and exercises on compassion were provided. Other components of the original MBCT program were kept unchanged. The program consisted of formal meditational exercises, psychoeducation based on cognitive therapy, and discussion and interaction among the participants to facilitate their learning. Homework was assigned to the participants at every session, which was supposed to take 20–45 minutes every day. Participants were provided with a meditation-guide compact disc. Each group consisted of four to nine participants.

The therapists were clinical psychologists, psychiatrists, and nurses who had five to seven years of mindfulness experience and had undergone MBCT training provided by the Oxford Mindfulness Center. The therapists followed the intervention protocol schedule at each session to ensure treatment integrity. A research assistant directly observed the session and checked for treatment adherence.

For the participants who were allocated to the intervention group, there was no restriction on any cointerventions during the study period.

Control

The participants who were allocated to the control group received assessments only during the study period. They were asked to refrain from participating in any type of MBIs or from engaging in meditational exercise (including yoga) during the study period. They were invited to an MBCT program conducted by the research team after the study period.

Measurements

Primary Outcome. The primary outcome was psychological distress (anxiety and depression), measured by the HADS.[24] The HADS is a 14-item self-administered questionnaire that measures the severity of anxiety and depression by seven items each. Scores for each subscale range from zero (no distress) to 21 (maximum distress). Higher scores indicate a greater level of psychological distress.

Table 1
Contents of the Program

Session	Theme	Contents
1	Overview of mindfulness	Psychoeducation: psychological reactions of patients with cancer/what is mindfulness Exercise: Mindfulness eating (raisin exercise)/body scan Homework: mindfulness eating/body scan
2	Facing difficulties	Psychoeducation: association of mood and thoughts Exercise: body scan/mindful breathing meditation Homework: body scan/mindful breathing meditation/pleasant activity and event record
3	Mindful breathing	Psychoeducation: pleasant activities and events Exercise: mindfulness meditation/gentle yoga/mindful walking Homework: mindfulness meditation/gentle yoga/mindful walking
4	Staying present	Psychoeducation: reactions to pleasant and unpleasant events Exercise: mindfulness meditations Homework: mindfulness meditations/three-minute breathing space exercise
5	Allowing (letting it be)	Psychoeducation: compassion (appreciation and gratitude in life) Exercise: mindfulness meditation/compassion meditation (loving & kindness) Homework: building pleasant habits/record of appreciation and gratitude/mindfulness meditations
6	Thoughts are not facts	Psychoeducation: cognitive biases Exercise: mindfulness meditations/compassion meditation Homework: record of appreciation and gratitude/mindfulness meditations
7	Taking care of yourself	Psychoeducation: choosing functional behaviors/behavioral activation/identifying triggers Exercise: mindfulness meditations/compassion meditation Homework: responses to triggers/record of appreciation and gratitude/mindfulness meditations
8	Dealing with future struggles	Review of and course/personal reflections of course/plans for future practice/farewell Exercise: body scan/mindfulness meditations

Secondary Outcomes

Fear of cancer recurrence. We used the Concerns About Recurrence Scale (CARS) to evaluate the participants' FCR.[25] The CARS has been validated in measuring FCR in patients with breast cancer. In the present study, only the subscale of overall FCR (four items) was used to lessen the burden of the participants to administer. Higher scores indicate a greater level of FCR.

Fatigue. We used the Brief Fatigue Inventory (BFI) to evaluate the participants' fatigue.[26] The BFI is a validated measure that consists of 10 items. The higher scores indicate more intense fatigue.

Spiritual Well-Being. We used the Functional Assessment of Chronic Illness Therapy—Spiritual (FACIT-Sp) to measure the participants' spiritual well-being.[27] The FACIT-Sp is a 12-item self-administered instrument, which comprises two subscales—the sense of meaning and faith.

Quality of Life. We evaluated the participants' QOL using the Functional Assessment of Cancer Therapy—General.[28] This widely used questionnaire consists of 27 items, with a higher score indicating better QOL. The questionnaire comprises four domains—physical, social, emotional, and functional well-being.

Mindfulness Skills. We used the Five Facet Mindfulness Questionnaire to assess the participants' mindfulness skills.[29] This 39-item self-administered questionnaire measures five domains of mindfulness skills—observing, describing, acting with awareness, nonjudging of inner experience, and nonreacting with inner experience. This scale was used as a process measure of the intervention—to measure whether the participants have taken up mindfulness skills.

Adherence to the Intervention. The participants' adherence to the intervention was evaluated using the attendance of the program and homework. The patients who attended less than four (of eight) sessions were considered to be dropouts.

Sample Size and Randomization

The sample size of the study was calculated based on the results of our pilot study.[23] We assumed that the HADS total score would decrease from 17.0 to 11.8, with SD of 8.0 in the MBCT group, whereas the score would remain unchanged in the control group. These estimates were considered to satisfy the minimal clinically important difference of the HADS.[24] With 80% power and alpha of 0.05, the required sample size was calculated as 37 participants in each arm. We estimated the dropout rate as 15%, resulting in 88 participants in total.

The participants were randomly assigned to MBCT or WLC at a ratio of 1:1. The randomization was managed by an organization independent of the research team (Keio University Clinical and Translational Research Center). Block randomization was conducted by a computer-generated random number list using an electronic software (http://www.randomization.com), stratified by the participants' anxiety levels at baseline (10 ≥ vs. <10 on the HADS-anxiety subscale [HADS-A]).

Statistical Analysis

Demographic and clinical characteristics of the participants were analyzed by t-test or Chi-squared test to examine differences between the groups at baseline. For minor missing values (<20% of a scale), we imputed them with mean scores of the scale. Primary and secondary outcomes were analyzed by a repeated-measures approach using a linear intention-to-treat mixed-effects model. The model included interactions of intercept, time, and time × group as fixed effects. The effect size was calculated using Cohen's *d* statistics. The effect sizes were considered large when d = 0.8 or higher, $d = 0.5–0.8$ as medium, and $d = 0.2–0.5$ as low. Statistical analyses were performed with SPSS, Version 25 (IBM SPSS, Chicago, IL).

Results

Participants

Of the 108 potential participants, 34 patients were excluded (six ineligible, four declined, and 24 not shown up for the introductory session), resulting in 74 participants who submitted written informed consent. Because the dropout rate was lower than expected (7.9%), we aborted recruitment before reaching the target sample size. These 74 participants were randomized to either the MBCT group ($n = 38$) or the control group ($n = 36$) (Consolidated Standards of Reporting Trials diagram: Fig. 1).

The participants' mean age was 53.7 years, ranging from 38 to 70. Patients with Stage I and II breast cancer comprise the majority. The mean length of time since cancer diagnosis was approximately three years. There was no significant difference in the demographic and clinical characteristics of the participants between the intervention group and the control group (Table 2).

Intervention Adherence

Three of 38 patients in the MBCT group attended less than four sessions and considered as dropouts

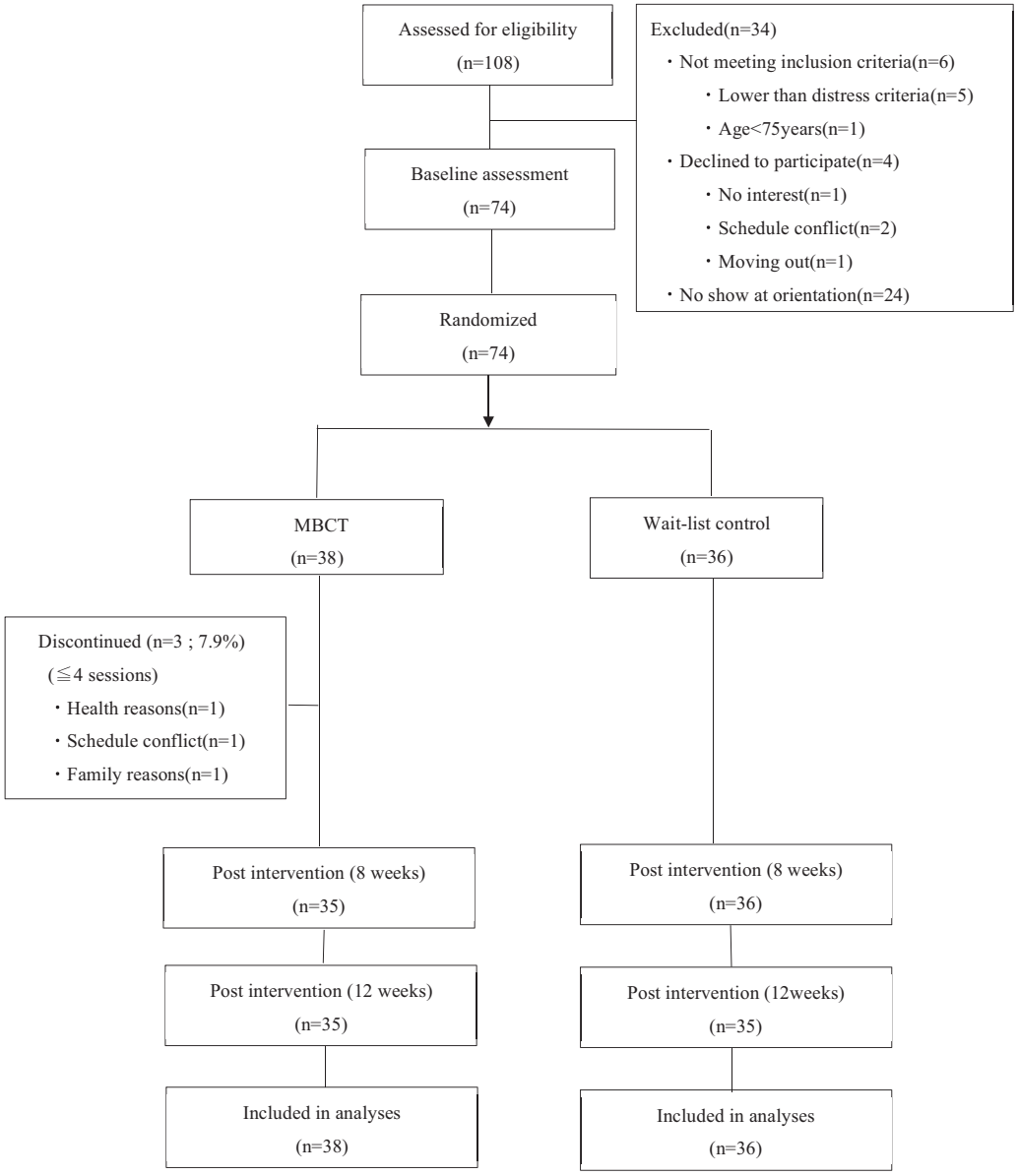

Fig. 1. Consolidated Standards of Reporting Trials study flow diagram. MBCT = mindfulness-based cognitive therapy.

(dropout rate 7.9%). The reasons for not attending were health problems, work circumstances, and family issues. The mean number of attended sessions was 6.76. The mean time spent on homework was 24.2 minutes per day (SD 14.6).

Primary Outcome

The MBCT group experienced significantly greater improvement at the eighth week in their psychological distress (both in anxiety and depression), compared with the control group (the mean difference in the HADS total score of 7.82, with 95% CI of 11.28−6.35; $P < 0.001$), with an effect size of Cohen's $d = 1.17$. The difference remained significant at 12 weeks (Table 3).

Secondary Outcomes

The MBCT group experienced significantly greater improvement compared with the control group in all the secondary outcomes. The effect sizes were large for spiritual well-being (FACIT-Sp: Cohen's $d = 0.91$; $P < 0.001$), moderate for fatigue (BFI: $d = 0.66$; $P < 0.01$) and QOL (Functional Assessment of Cancer Therapy—General total score: $d = 0.79$; $P < 0.001$), and small for FCR (CARS: $d = 0.43$; $P < 0.05$). The total score of the Five Facet Mindfulness Questionnaire showed a significant increase, suggesting that the participants successfully acquired mindfulness skills through the program (Table 3). No adverse events were observed during the study.

Table 2
Sociodemographic and Clinical Characteristics of the Participants

Characteristic	MBCT $n = 38$ (%)	WLC $n = 36$ (%)	*P*
Sociodemographic			
Age (yrs); mean	53.21; SD = 8.4	54.19; SD = 9.27	0.63
Married	23 (60.5)	30 (83.3)	0.08
Not married	15 (39.5)	6 (16.7)	
Employed	17 (44.7)	18 (50.0)	0.65
Unemployed	21 (55.3)	18 (50.0)	
Clinical			
Time since diagnosis (month); mean	39.25; SD = 37.24	41.12; SD = 64.92	0.88
Cancer stage			
0 (carcinoma in situ)	9 (23.7)	6 (16.7)	0.81
I	13 (34.2)	14 (38.9)	
II	14 (36.8)	15 (41.7)	
III	2 (5.3)	1 (2.7)	
Treatment			
Breast surgery	37 (97.4)	35 (97.2)	0.97
Chemotherapy	20 (52.6)	18 (50.0)	0.82
Radiotherapy	26 (68.4)	21 (58.3)	0.37
Hormonal therapy	30 (78.9)	25 (69.4)	0.35
Performance status			
0	34 (89.5)	31 (86.1)	0.66
1	4 (10.5)	5 (13.9)	

MBCT = mindfulness-based cognitive therapy; WLC = wait-list control.

Discussion

The present study demonstrated that our MBCT intervention significantly reduced psychological distress (both anxiety and depression) in patients with nonmetastatic breast cancer. Also, MBCT was proven effective for increasing spiritual well-being and QOL and reducing the FCR and fatigue. The effect was maintained at four weeks after the completion of the treatment. To the best of authors' knowledge, this is the first study in Japan that demonstrated the effectiveness of MBCT in patients with cancer.

The HADS total score decreased from 16.13 to 6.18 after the MBCT intervention. Although there has been a variation in proposed cutoff scores for the HADS, patients with cancer with a HADS total score of 13 or more are considered to require psycho-oncologic support.[30] In a sample of Japanese patients with cancer, a cutoff score of 11 or higher corresponds to adjustment disorder.[31] In the present study, MBCT contributed to alleviating the participants' psychological distress from a clinical level to a subclinical level. This drastic improvement in psychological distress agrees with the findings of the past MBCT study that had been conducted in a mixed cancer population.[32]

Alleviation of FCR by MBCT is noteworthy. FCR is one of the commonest problems of cancer survivors. It has been known that FCR will not resolve spontaneously even long after cancer remission, thus specific intervention is needed for cancer survivors who suffer from clinically significant FCR.[4] It is reasonable that MBCT is effective for alleviating FCR because MBCT considers rumination as a key focus of intervention, and rumination is one of the key psychological mechanisms of FCR.[33] So far, a few psychological approaches have been developed to address FCR.[34–36] They are all relatively new and were specifically developed for FCR. MBCT may have an advantage over such interventions in that it is not only effective for FCR but also covers a broad spectrum of symptom burden.

Also, it is noteworthy that MBCT relieved patients' fatigue. Fatigue is one of the two commonest symptoms of cancer survivors, which significantly impairs the QOL of patients with cancer. Effective pharmacotherapy has not been established. Although physical exercise and sleep management have been proven effective, their effect sizes are not intense.[8] Furthermore, it is often not easy for clinicians to lead fatigued cancer survivors to physical exercise.

Furthermore, our MBCT intervention substantially improved patients' QOL and spiritual well-being. It is of note that MBCT not only alleviated negative psychological aspects of patients with cancer but also increased positive aspects of their daily lives. Spiritual well-being serves to buffer clinically important issues, such as pain, fatigue, depression, and wish of hastened death.[37] Mindfulness, which cultivates a sense of wholeness and internal unity, may have the potential to elucidate self-insight of patients with cancer regarding the meaning of life despite the presence of a life-threatening illness.

A recent meta-analysis on the effectiveness of MBIs for patients with cancer and survivors demonstrated that larger effects were observed in studies adhering to the original MBI manuals, with younger patients, with passive control conditions, and with shorter time to follow-up.[16] Our study fits with these characteristics.

The strength of the present study includes a robust randomized controlled trial design and the low attrition rate. This attrition rate is substantially low compared with the past MBIs. A recent meta-analysis showed that the median attrition rate of MBIs in anxiety disorder and depressive disorders was 15.5%.[38] Our MBCT program, which was tailored to fit the needs of patients with breast cancer, seems to have been well accepted by Japanese patients with breast cancer.

Study Limitations

The present study has some limitations. First, the study sample was relatively small and was limited to ambulatory nonmetastatic breast cancer patients in a single facility. Second, using of a WLC instead of an active control weakens the robustness of the study. The effectiveness of our intervention may partly derive from nonspecific effect of group therapy.

Table 3
Primary and Secondary Outcomes of MBCT and WLC Groups With Effect Sizes

	MBCT	WLC	Difference in Mean Change		
	Mean (SD)	Mean (SD)	Score[a,b] (95% CI)	*P*	Cohen's *d*
Primary outcome					
HADS-overall					
T0	16.13 (7.47)	14.81 (6.99)			
T1	6.18 (4.83)	14.00 (8)	−7.82 (−11.28 to −6.35)	<0.001	1.17
T2	6.77 (5.64)	13.33 (6.97)	−6.56 (−10.09 to −5.22)	<0.001	1.03
HADS-anxiety					
T0	8.29 (3.52)	7.61 (3.36)			
T1	3.49 (2.62)	6.89 (3.98)	−3.40 (−5.39 to −2.63)	<0.001	1.01
T2	3.83 (3.04)	6.64 (3.64)	−2.81 (−4.80 to −2.04)	<0.001	1.06
HADS-depression					
T0	7.84 (4.38)	7.19 (4.21)			
T1	2.48 (2.82)	7.11 (4.53)	−4.63 (−6.49 to −3.73)	<0.001	1.22
T2	2.94 (2.98)	6.69 (4.17)	−3.75 (−5.62 to −2.88)	<0.001	1.28
Secondary outcome					
FCR					
T0	13.58 (5.31)	13.78 (4.93)			
T1	10.53 (4.93)	12.69 (5.16)	−2.16 (−3.66 to −0.15)	0.033	0.43
T2	10.29 (4.62)	13.03 (4.71)	−2.74 (−4.30 to −0.81)	0.004	0.59
BFI					
T0	3.54 (2.28)	3.22 (2.42)			
T1	1.80 (1.8)	3.37 (2.81)	−1.57 (−2.67 to −0.75)	0.001	0.66
T2	1.81 (1.84)	3.04 (2.37)	−1.23 (−2.35 to −0.45)	0.004	0.58
FACIT-Sp					
T0	21.58 (8.86)	24.28 (7.36)			
T1	32.70 (9.63)	24.61 (8.25)	8.09 (7.66–13.95)	<0.001	0.91
T2	32.51 (10.09)	24.83 (8.72)	7.68 (7.34–13.56)	<0.001	0.82
FACT-G					
T0	65.20 (16.77)	68.91 (16.63)			
T1	84.94 (14.59)	71.59 (18.73)	13.35 (10.38–21.33)	<0.001	0.79
T2	85.41 (16.08)	71.90 (18.5)	13.51 (11.27–22.1)	<0.001	0.78
FFMQ					
T0	117.32 (18.4)	118.89 (13.03)			
T1	133.67 (17.87)	120.47 (14.37)	13.2 (8.22–21.38)	<0.001	0.82
T2	137.03 (18.85)	119.19 (13.44)	17.84 (12.84–25.86)	<0.001	1.09

MBCT = mindfulness-based cognitive therapy; WLC = wait-list control; HADS = Hospital Anxiety and Depression Scale; FCR = fear of cancer recurrence; BFI = Brief Fatigue Inventory; FACIT-Sp = Functional Assessment of Chronic Illness Therapy—Spiritual; FACT-G = Functional Assessment of Cancer Therapy—General; FFMQ = Five Facet Mindfulness Questionnaire.
Note: Data presented as mean (SD) unless otherwise noted.
[a]The difference in mean change scores is the between-group difference in the least squares mean treatment change score from baseline to the data point; mixed-effect model for repeated-measures analysis.
[b]The between-group difference is the intervention group value minus the control group value.

Despite these limitations, our study is noteworthy because this is the first study that demonstrated that our MBCT program, which was specifically targeted for patients with breast cancer, significantly improved a wide spectrum of symptoms encompassing psychological, physical, and spiritual domains. Also, this is the first study in Japan that demonstrated the effectiveness of MBCT in patients with cancer. Given that MBCT can improve wide range of symptoms (anxiety, depression, FCR, fatigue, spiritual well-being, and QOL), and given that the program can be delivered to many patients at a time in a group format, it would be a fascinating option for patients with breast cancer who suffer from such symptoms.

Future research implications include examining the long-term effects of the program because the present study evaluated the participants only up to four weeks after completion of the intervention. Another research implication is dismantling the mechanism of the intervention. The program may be shortened if essential components of the program become clearer. Because we observed that MBCT was effective for multiple symptoms, disentangling the interrelations between each variable and elucidating the focus of MBCT can contribute to a more efficient way to address symptoms of patients with cancer. Exploring the biological effects of MBIs is another orientation of research.[39,40]

Conclusions

To the best of authors' knowledge, this is the first study that demonstrated that an MBCT program that was specifically targeted for patients with breast cancer significantly improved a wide spectrum of symptoms encompassing psychological, physical, and

spiritual domains. Also, this is the first study in Japan that demonstrated the effectiveness of MBCT for patients with cancer. Given that MBCT can be delivered to many patients at a time in a group-therapy format, it would be a fascinating option in clinical practice.

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Data availability: The data of this study are available from the corresponding author on reasonable request.

Ethical approval: This study was approved by the Institutional Review Board of Keio University School of Medicine and was registered in the Japanese Clinical Trial Registry (registry ID: UMIN000016142).

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