Mindfulness-based cancer recovery in survivors recovering from chemotherapy and radiation

Anne H Blaes, MD, MS,^a Danyelle Fenner, BS,^b Veronika Bachanova, MD, PhD,^a Carolyn Torkelson, MD,^c Melissa Geller, MD, MS,^d Tufia Haddad, MD,^e Ryan Shanley, MS, and ^fMary Jo Kreitzer, PhD^g

^aUniversity of Minnesota, Department of Medicine, Division of Hematology/Oncology/Transplantation, Minneapolis; ^bUniversity of Minnesota Medical School; ^cUniversity of Minnesota, Department of Family Medicine, Minneapolis; ^dUniversity of Minnesota Department of Obstetrics and Gynecology, Minneapolis; ^eMayo Clinic, Rochester, Minnesota; ^fUniversity of Minnesota Masonic Cancer Center Biostatistical Core, Minneapolis; and ^gUniversity of Minnesota Center for Spirituality and Healing and School of Nursing, Minneapolis

Background Sleep impairment, fatigue, and anxiety are common conditions in cancer survivors. Small studies suggest mindfulness-based interventions may be helpful for cancer-related fatigue.

Objective To evaluate mindfulness-based cancer recovery (MBCR) for cancer survivors who are recovering from chemotherapy or radiation therapy.

Methods 42 cancer survivors who were within 6 months of completion of chemotherapy or radiation were randomized 2:1 to 8 weekly MBCR classes (n = 28) or wait-list control (n = 14). The Pittsburgh Sleep Quality Index (PSQI), Functional Assessment in Cancer Therapy – Fatigue (FACT-F), and 20-item State-Trait Anxiety Inventory (STAI) were used to assess sleep, fatigue, and anxiety at baseline (time of enrolment), at 2 months (on completion of the MBCR course), and 4 months (2 months after completion of the course). 32 of 42 participants participated in an optional blood draw to assess immune function.

Results 79% of the MBCR group attended at least 7 of the 9 MBCR sessions. At the 2-month assessment, sleep quality (PSQI, range 0-21, >5 = poorer sleep quality) in the MBCR group improved from the baseline 8.9 to 6.4, compared with the wait-list group (baseline 7.2 to 7.6); and at 4 months after course completion, it was 6.1 compared with 7.8, respectively (P = .03). There was a non-statistically significant improvement in fatigue (FACIT-F, P = .19). There was a trend toward improvement in the anxiety scores (STAI, range 20-80, higher score = greater anxiety) in the MBCR group compared with the wait-list group at 2 months (31.8 vs 39.4, respectively; P = .07) and 4 months (32.8 vs 40.7; P = .10). Immune function measures were not statistically significant. Limitations It is possible the psychological support of being in contact with a facilitator and/or other cancer survivors had a beneficial effect in the outcomes of those in the MBCR group.

Conclusion MBCR has a high compliance rate and results in sustained improvements in sleep quality, fatigue, and anxiety. MBCR may be useful for cancer survivors struggling with sleep, fatigue, and anxiety.

Funding Hourglass Fund, Masonic Cancer Center, University of Minnesota; University of Minnesota Foundation (immune function protocol); National Institutes of Health Office of Women's Health Building Interdisciplinary Research Careers in Women's Health (BIRCWH) NIH # K12-HD055887.

In 2016, there were an estimated 15.5 million cancer survivors in the United States. Sixty-four percent of cancer survivors have survived 5 or more years since diagnosis, 40% have survived 10 or more years, and 15% have survived 20 or more years.¹ Many cancer survivors suffer from a myriad of symptoms, ranging from physical symptoms such as hot flashes, insomnia, and fatigue to psychosocial symptoms including depression and anxiety after they have completed aggressive chemotherapy and radiation for curative-intent cancers.² Up to 51% of patients with breast cancer report sleep difficulties. Of those, 19% meet criteria for insomnia syndrome and 95% will have chronic problems (ie, a duration of more than 6 months).^{3,4} In a an open-invitation, internet-based survey by the Lance Armstrong Foundation of 1,024 self-identified cancer patients, 72% reported they had to deal with depression as a result of their cancer and 82% reported a reduction or loss of sexual function. Fear of recurrence of cancer remained active in 66% of survivors. Taken together, these studies suggest that anxiety, fatigue,

Accepted for publication February 29, 2016. Correspondence: Anne Blaes, MD, MS; Blaes004@umn.edu. Disclosures: The authors report no disclosures or conflicts of interest. JCSO 2016;14(8):351-358. ©2016 Frontline Medical Communications. doi: 10.12788/jcso.0244.

and sleep impairment are common among cancer survivors who are recovering from chemotherapy and radiation. Such symptoms may lower overall health-related quality of life among survivors.⁵ Given the cost and side effects of pharmaceutical agents and some patients' preference for more holistic approaches to care, non-pharmacologic interventions may be beneficial and a reasonable alternative to improve symptom management.

Mindfulness-based cancer recovery (MBCR) is a modification of mindfulness-based stress reduction (MBSR), a type of mind-body intervention. Mind-body non-pharmacologic interventions are defined as practices that focus on the connection and integration of the mind and body and the ability for those connections to effect changes on physical, emotional, and spiritual levels for the purpose of promoting health and well-being. MBCR is a step-by-step program designed to help cancer patients cope with their cancer diagnosis and treatment. MBSR was developed by Dr Jon Kabat-Zinn⁶ and then modified by Dr Linda Carlson⁷ for application in caring for cancer patients. The practice of mindfulness helps individuals pay attention in the present moment with an open and accepting attitude, while minimizing worry and rumination. MBSR has been shown to improve an array of physical and mental health outcomes in a variety of settings.^{6,8-11}

Little is known about the impact of MBCR on individuals with cancer. In the last 2 years, several randomized controlled trials have reported beneficial effects of mindfulness-based interventions on stress, mood, depression, quality of life, sleep, and fatigue in cancer populations.12-14 Johns and colleagues15 examined the effect of mindfulness on cancer-related fatigue and demonstrated that participants in a 7-week MBSR program showed improved fatigue, fatigue severity, vitality, and depression outcomes compared with those in a wait-list control group. The effects persisted at 1-month post-MBSR classes. Other investigators have compared the effects of cognitive behavioral therapy and mindfulness-based therapy on insomnia and have found both interventions to be helpful in cancer survivors.¹⁶ In other non-randomized studies, 6- and 8-week mindfulness-based programs improved quality of life among women with breast or gynecologic cancers.¹⁷ Most of these studies used self-report measures and were performed in women, with the majority of participants having breast cancer. Although these data suggest that MBCR programs can have a positive impact on overall health-related quality of life, few data exist on how these programs affect recovery from chemotherapy and radiation.

Although the physiological effects of MBCR are poorly understood, the symptoms experienced by cancer survivors may be linked to stress-induced immunosuppression. Study findings have suggested that breast cancer survivors have reduced levels of mononuclear natural killer (NK) cell activity and interferon-gamma production and elevations in cortisol levels.¹⁸ Participants in an 8-week MBSR program showed improvements in NK cell activity and reductions in cortisol levels compared with non-MBSR controls.¹⁹ Findings in another study that evaluated the effect of MBSR in breast and prostate cancer survivors demonstrated a reduction in cortisol and pro-inflammatory cytokine levels.²⁰ However, in other studies, 8-week MBSR programs did not result in changes in overall lymphocyte number. There were, however, changes in the expression of lymphocytes with reductions in interleukin 10 production and interferon-gamma.²¹

The primary objective of the present 2:1 randomized controlled study was to determine whether an 8-week MBCR program improved the quality of life and/or immune function of patients with a variety of cancers recovering from chemotherapy or radiation.

Methods

Study design and eligibility criteria

Consented participants were randomized in a 2:1 ratio to 8 weekly MBCR classes or a wait-list control group. Those who were randomized to the wait-list group were given a voucher to participate in mindfulness classes at another time after the completion of the study. Cancer survivors aged 18 years or older who had been diagnosed and treated for cancer during 2012-2013 at the University of Minnesota Cancer Center or in the surrounding Minneapolis, MN, area were eligible for the study. Men and women of all cancer types were eligible to participate. All survivors had localized disease and had completed chemotherapy or radiation within 6-month period before enrollment. Individuals who required ongoing chemotherapy or radiation were not eligible for the study. Those with underlying psychiatric disorders who were deemed not able to participate in the classes or from whom consent could not be obtained were excluded. Those with mild to moderate depression and anxiety were eligible for participation. All study procedures were approved through the University of Minnesota institutional review board. The trial was registered at clinicaltrials.gov (NCT01601548).

Study questionnaires

Participants were assessed with questionnaires at baseline, at 2 months (on completion of the course) and 4 months (2 months after completion of the course). Baseline was defined as at study enrollment; baseline had to be within 6 months of completing cancer treatments such as chemotherapy, surgery or radiation. The questionnaires used to assess overall wellness were: 36-item Medical Outcomes Study-Short Form (SF-36), Functional Assessment in Cancer Therapy-Fatigue (FACT-F), Pittsburgh Sleep Quality Index (PSQI), 20-item State-Trait Anxiety Inventory (STAI), Medical Outcomes Study Sexual Functioning Scale, and the Self-Compassion Scale-Short Form (SCS). We report data here from the PSQI, FACT-F, and the STAI.

The PSQI is a well-validated tool to assess quality of sleep.^{22,23} Its total score is comprised of 7 components, each with a score of 0-3, so that the total score range is 0-21, with higher scores associated with poorer sleep quality. Any score greater than 5 is considered poor sleep quality. The FACT- F^{24} assesses levels of fatigue and how fatigue affects daily functioning. The survey is comprised of 13 questions. The total score is the sum of all 13 questions (possible range, 0-52), with a higher number indicating less fatigue. The STAI²⁵ is composed of 20 questions (eg, *I feel calm* or *I feel upset*) that have 4 possible responses (1, Not At All; 2, Somewhat; 3, Moderately So; 4, Very Much So). Questions such as *I feel calm* were reverse scored so that a higher score represented more anxiety. The responses are scored with a range 20-80, with a higher score indicating more anxiety.

MBCR intervention

Participants who were randomized to the MBCR intervention arm participated in 8 weekly, 2.5-hour classes and a retreat day during the second half of the 8-week program. The classes were offered through the Center for Spirituality and Healing at the University of Minnesota by the center's faculty who have completed extensive training and certification in MBSR and received training on the MBCR program from Dr Linda Carlson. Two classes of fewer than 15 participants were offered so that classes could be kept small. Participants remained with their same class throughout the course of the 8-week session. During class sessions, participants were presented with mindfulness meditation techniques and also shared their experiences relating to the meditation practices. Patients were expected to practice home meditation for 45 minutes a day. In addition to home meditation, there were reading assignments and reflective exercises that relate to mindfulness. The full-day silent retreat provided an opportunity for class participants to gain extended experience with mindfulness techniques. During the course, several meditation techniques were taught: body scan, seated meditation, walking meditation, mindful eating, and mindful yoga practice. Participants were encouraged to incorporate meditation practices and mindfulness into their daily routines. They were asked to complete a log of daily home practice sessions, both formal and informal.

Immunological studies

Participants were eligible to participate in an optional blood draw to evaluate immune function and NK-cell function. Peripheral blood was collected at enrollment, at 2 months, and 4 months, and analyzed by flow cytometry to determine number of NK cells, T cells, regulatory T cells, B cells (using antibodies against CD45, CD3, CD56, CD19, CD25, Foxp3), NK-cell subsets (using antibodies against CD16, KIR, NKG2A), and activation status of NK cells (using antibodies against CD69, HLA-DR, CD31, CD2, CD11a). We also tested NK-cell proliferation and cytotoxicity in 4-hour Cr-release assay against K562 cell line.²⁶ Serum was also collected at the same intervals and analyzed for IL-4, IL-6, IL-10, IFN gamma by enzyme-linked immunoadsorbent assay (ELISA; R&D Systems, Minneapolis, MN).

Statistical analysis

Baseline differences between treatment groups were compared using an unequal variance 2-sample t test for continuous variables, and Fisher exact test was used for categorical variables. For comparisons at 2 months and 4 months, each participant's change from baseline was computed and group differences were tested with a 2-sample ttest. All P values are 2-sided and were calculated using R 3.0. Randomization was done by a SAS random number generator. The study was initially planned for 45 participants, with 90% power to conclude significance at the 0.05 level for a true effect size of 1.1. Fewer than 1% of questions were not answered; if the questionnaire was otherwise complete, the missing response was scored as the mean of the participant's other responses on that questionnaire.

Results

Cancer survivor characteristics

A total of 42 cancer survivors were enrolled in the study and were randomized 2:1 (28 MBCR group, 14 controls; Table 1). The most common cancer diagnosis was breast cancer for the study group (64%) and the controls (79%). Two participants had more than one form of cancer. Most of the participants were women (90%). Mean age was 55

TABLE 1 Baseline characteristics of participants						
	Gre	oup				
Characteristic	MBCR (n = 28)	Control (n = 14)	P value			
Mean age, y (SD)	55 (10)	57 (10)	0.55			
Female, n (%)	26 (93)	12 (86)	0.59			
Type of cancer, n (%)						
Breast	18 (64)	11 (79)	0.49			
Non-Hodgkin lymphoma	3 (11)	2 (14)				
Kidney	O (O)	1 (7)				
Other ^a	7 (25)	0 (0)				
Treatment, n (%)						
Chemotherapy	19 (68)	9 (64)				
Radiation	3 (11)	3 (21)				

 $^{\rm o}3$ bladder, 1 cholangiocarcinoma, 1 endometrial, 1 ovarian, and 1 melanoma

	Baseline		2 mo.		4 mo.	
Component	MBCR (n = 27)	Control (n = 13)	MBCR (n = 25)	Control (n = 7)	MBCR (n = 24)	Control (n = 11)
Sleep duration	0.6	0.7	0.4	0.9	0.3	0.7
Sleep disturbance	2.0	1.9	1.8	1.9	1.7	1.8
Sleep latency	1.4	0.8	0.9	1.3	1.0	1.2
Day dysfunction	1.3	1.2	1.0	1.0	0.9	1.3
Sleep efficiency	1.0	0.8	0.6	1.0	0.5	1.0
Sleep quality	1.2	1.2	0.8	1.3	0.9	1.2
Need meds to sleep	1.3	0.4	1.0	0.3	0.8	0.6
Total score	8.9	7.2	6.4	7.6	6.1	7.8

MBCR, mindfulness-based cancer recovery

°Each of the 7 components range from 0 (best sleep quality) to 3 (worst sleep quality) with a total possible range 0-21

TABLE 3 Mean response to fatigue questions from the Functional Assessment in Cancer Therapy-Fatigue^a

0	Baseline 2 mo.		4 mo.			
Question	MBCR (n = 28)	Control (n = 13)	MBCR (n = 26)	Control (n = 8)	MBCR (n = 24)	Control (n = 11)
*I feel fatigued	1.7	1.9	2.2	2.5	2.3	2.1
*I feel weak all over	2.6	2.8	3.0	3.1	3.1	3.0
*I feel listless	2.4	2.7	3.1	2.5	3.0	2.7
*I feel tired	1.6	1.9	2.3	2.4	2.4	2.3
*I have trouble start- ing things because I am tired	2.1	2.5	2.8	2.8	2.9	2.5
*I have trouble finish- ing things because I am tired	2.1	2.5	2.7	2.6	2.8	2.6
I have energy	2.1	1.9	2.4	2.4	2.4	2.1
l am able to do my usual activities	2.5	2.5	3.0	3.0	2.9	2.7
*I need to sleep during the day	2.6	2.8	2.9	3.3	3.3	3.0
*I am too tired to eat	3.6	3.7	3.8	3.6	3.8	3.5
*I need help doing my usual activities	3.5	3.2	3.6	3.6	3.5	2.8
*I am frustrated by being too tired to do the things I want to do	2.0	2.5	2.9	2.9	2.8	2.4
*I have to limit my social activity because I am tired	2.4	2.6	3.0	2.8	3.0	2.6
Total score	31.4	33.3	37.8	37.4	38.2	34.6

^oPossible responses are 0 (most fatigued) to 4 (least fatigued), with a total score range of 0-52 with higher scores indicating less fatigue.

*Indicates question was reverse scored.

years (range, 36-79 years). One participant withdrew from the study because of progressive disease. Most participants (66%) had received chemotherapy, and 6 participants (14%) received radiation only. All of the participants had completed chemotherapy and radiation within 6 months of study enrollment. In all, 79% of the MBCR group attended at least 7 of the 9 MBCR sessions. The number of completed questionnaires at baseline, 2 months, and 4 months was 28, 26, and 24 in the MBCR group.

Sleep

The PSQI was used to assess the quality of sleep, with higher scores associated with poorer sleep quality. At baseline, MBCR participants reported a median of 6.9 hours of sleep a night, with a total sleep quality score of 8.9, compared with controls who had a mean 7.0 hours of sleep a night with a total sleep quality score of 7.2 (Table 2). Any score >5 was considered poor sleep quality, which accounted for 63% of responses. Most components - including sleep latency, daytime dysfunction due to sleepiness, sleep efficiency, overall sleep quality, and needing medication to sleep contributed an average of 1 point each to the total score. Sleep duration contributed less (0.5) and sleep disturbances more (1.8)to the total score. The most common disturbances were waking up during the night, having to use the bathroom, and feeling too hot. Some participants volunteered explanations for sleep disturbances, including bodily pain, worry and anxiety, or a restless partner or cat. Total sleep quality (range, 0-21) improved in those who received MBCR (8.9, to 6.3, to 6.1) and persisted at 4 months, compared with controls (7.2, to 7.6, to 7.8; *P* = .03; Figure 1A).

Fatigue

Fatigue was measured using the FACT-F (range, 0-52) in which higher scores indicate less fatigue. At baseline, the MBCR participants had a mean score of 33.3, and the controls, 31.4 (Table 3). There was an improvement in fatigue in both groups with time (Figure 1B). Mean improvement from baseline to 4 months was 6.8 for the MBCR group and 1.3 for controls (P = .19). The increase of 6.8 in the MBCR group equates to about a half point per question.

Anxiety

The STAI was used to assess anxiety (range, 20-80), with a higher score indicating more anxiety. Baseline anxiety was similar between the 2 groups (Figure 1C). Total anxiety increased with time in the control group and decreased in the MBCR group (Figure 1C). Scores improved from 38.4, to 31.8, to 32.8 in the MBCR group, but increased slightly from 37.7, to 39.4, to 40.7 in the controls (P = .07 at 2 months and P =.10 at 4 months; Figure 1C). This improvement in the intervention group persisted for 2 months after completing the classes. While there was a trend toward improvement in anxiety with MBCR, this did not meet statistical significance.

Compliance and home practice

Sixteen of the 28 MBCR participants logged home practice time throughout the 8-week intervention. Of those 16 participants, the mean practice frequency was 5 days a week for 40 minutes a day. We used that information to determine whether home practice time correlated with improvement in sleep, anxiety, and fatigue. There seemed to be a low to moderate correlation between home practice and changes in outcome at both 2 and 4 months (correlation coefficients, 0.24-0.31 at 4 months).

Immune function

A total of 32 of 42 participants elected the optional blood draw to evaluate immune function (MBCR group: 23 participants [22 women, 1 man]; controls: 9 [8 women, 1 man]). There was no statistically significant difference between the 2 groups in the percentage of NK cells (P = .52), T cells (P = .54), or lymphocytes (P = .46) between baseline and at 4 months. There was also no difference at 4 months between the ratio of NK cells to T cells (P = .32), NK cells to T-regulatory cell ratio (P = .45).

Discussion

We aimed to determine whether MBCR would be beneficial in improving multiple emotional, psychological, and physical

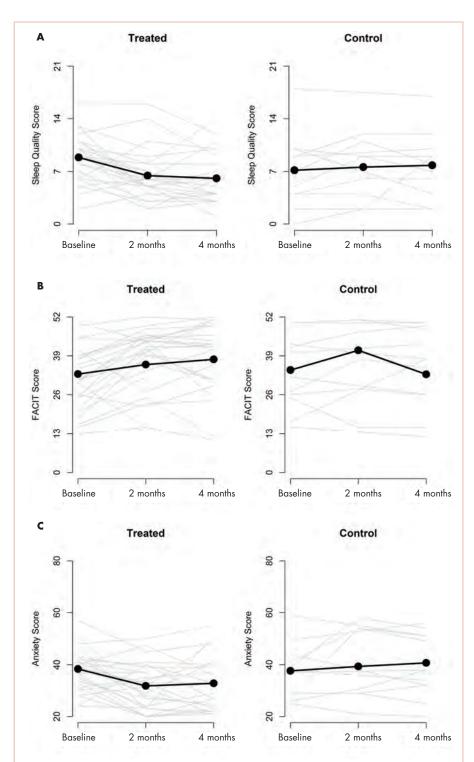


FIGURE 1 Quality of life assessments before mindfulness-based cancer recovery intervention, immediately after intervention (2 months), and at 4 months. **A**, Sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI). **B**, Fatigue as measured by the Functional Assessment in Cancer Therapy-Fatigue (FACT-F). **C**, Anxiety as measured by the State Trait Anxiety Index (STAI).

Gray lines show individual scores over time. Black lines show the group mean at each time. The possible range of each instrument is shown on the y-axis.

Item Question		Baseline		2 mo.		4 mo.	
	Question	MBCR (n = 28)	Control (n = 13)	MBCR (n = 26)	Control (n = 7)	MBCR (n = 24)	Control (n = 11)
1	*I feel calm	1.9	1.9	1.5	2.0	1.6	2.1
2	*I feel secure	1.6	1.6	1.4	1.7	1.4	2.1
3	I feel tense	2.0	2.0	1.8	2.3	1.8	2.2
4	I feel strained	1.8	2.0	1.7	1.9	1.6	2.5
5	*I feel at ease	2.2	2.3	1.8	2.0	1.8	2.4
6	l feel upset	1.5	1.5	1.3	1.6	1.4	1.5
7	l am presently worrying over possible misfortunes	2.2	2.0	1.7	2.1	1.5	2.1
8	*I feel satisfied	2.0	2.3	1.7	2.0	1.8	2.2
9	I feel frightened	1.6	1.9	1.3	1.7	1.3	1.5
10	I feel uncomfortable	1.9	1.6	1.5	1.7	1.6	1.9
11	*I feel self-confident	2.1	1.8	1.7	2.4	2.1	2.3
12	l feel nervous	2.0	1.8	1.7	1.6	1.7	1.6
13	l feel jittery	1.5	1.5	1.2	1.6	1.3	1.5
14	I feel indecisive	2.3	1.8	1.5	1.9	1.7	2.0
15	*I am relaxed	2.2	2.0	1.8	2.3	1.8	2.3
16	*I feel content	2.1	2.1	1.8	2.3	1.9	2.2
17	l am worried	2.1	2.2	1.8	2.4	1.8	2.4
18	I feel confused	1.5	1.3	1.3	1.7	1.5	1.5
19	*I feel steady	2.1	2.2	1.6	2.1	1.7	2.3
20	*I feel pleasant	1.9	1.8	2.0	2.1	1.6	2.2
	Total score	31.4	33.3	37.8	37.4	38.2	34.6

TABLE 4 Mean response to anxiety questions from the State-Trait Anxiety Inventory^a

°Possible responses are 1, Not At All; 2, Somewhat; 3, Moderately So; 4, Very Much So, with a total score range of 20-80 with higher scores indicating greater anxiety.

*Indicates question was reverse scored.

facets of well-being in cancer survivors who were recovering from chemotherapy and radiation. Our data demonstrate that MBCR is beneficial in improving the quality of life of cancer survivors in the areas of sleep quality, fatigue, and anxiety. Moreover, our findings show that these improvements occur during the 8-week intervention and continue for 2 months after completion of the MBCR course. Finally, the high compliance rate of 79% and participant completion of more than two-thirds of the sessions also demonstrates that the 8-week MBCR intervention is acceptable to cancer survivors.

About half of all patients with cancer suffer from insomnia and some form of fatigue. In our study, 63% of all participants had poor sleep as indicated by a PSQI score of >5. This is consistent with other literature.²⁷ Indeed, 25%-50% of all prescriptions for cancer patients have been written for insomnia.¹⁶ Different forms of non-pharmacological therapies have been evaluated to help determine which interventions may be beneficial. Findings from a study in which cancer patients received a total of about 5 hours of cognitive behavioral therapy demonstrated an improvement in sleep in 80% of the participants.28 Other investigators have looked at mindfulness compared with usual care in breast cancer survivors and have found improvements in objective sleep parameters in 78% of the mindfulness group, compared with 74.6% of the usual care group (P = .04). There were fewer waking bouts and more sleep time in the mindfulness group compared with the usual care group.¹⁴ Recently, a non-inferiority randomized control trial compared mindfulness-based therapy with cognitive behavioral therapy as a treatment for insomnia in a study sample of predominantly women with breast or gynecologic cancers.²⁹ Sleep time increased by 45 minutes with

the mindfulness-based intervention and 36 minutes in the CBT group, with associated decreases in time to fall asleep as well (14 minutes and 22 minutes, respectively). Time awake at night did not differ between the 2 groups. At 3-month follow-up, mindfulness seemed to be non-inferior to the cognitive behavioral therapy (P = .02).^{16,29} The mindfulness intervention resulted in an improvement in insomnia severity with time, where this effect decreased in the CBT group. Although we did not compare interventions in our study, our findings demonstrate that MBCR can be helpful in treating sleep disturbances after the completion of chemotherapy and radiation. It also confirms that improvements in sleep persist after the use of MBCR.

It is not known whether insomnia contributes to fatigue, however, cancer-related fatigue is a significant problem impairing the quality of life of up to 56% of cancer survivors.15 The National Comprehensive Cancer Network now has treatment-related guidelines for the management of cancer-related fatigue, with non-pharmacologic therapies as the primary recommendation.²⁷ In a meta-analysis of 57 non-pharmacologic interventions, Kangas and colleagues³⁰ conclude that exercise and psychosocial therapies can be beneficial for those with cancer-related fatigue. Johns and colleagues enrolled only cancer participants with cancerrelated fatigue into a trial that compared participants in a mindfulness-based intervention with a wait-list control group. Both fatigue severity and vitality improved with the mindfulness-based intervention compared with the control group, and these effects persisted at 1 month after the completion of the study. Although not all studies support our findings,³¹ many other studies, which, like ours had participant good compliance and high attendance, support the conclusion that mindfulness-based therapy improves fatigue in cancer patients.

Although impairment in sleep and extreme fatigue can be experienced by cancer survivors, many survivors completing chemotherapy and radiation are also impaired by anxiety. Although our results did not meet statistical significance, there was a significant trend in improvement in anxiety in the MBCR group that was not seen in the control group. This finding suggests that MBCR improves anxiety levels in cancer patients recovering from treatment. A recent study of an 8-week mindfulness-based course for the self-management of anxiety, depression, and quality of life resulted in improvements in participants with metastatic breast cancer.³² It is possible this can be achieved with a 6-week instead of an 8-week course.17 In those with recurrent breast and gynecologic cancers, mindfulness-based therapy in conjunction with biobehavioral components can result in reductions in distress, anxiety, and improvements in overall mental health.¹³

Although findings from our study and others' support the benefits of mindfulness-based therapy in improving the quality of life of cancer patients, we were not able to demonstrate any impact of MBCR on immune function. Previous findings from Witek-Janusek and colleagues have suggested that that an 8-week mindfulness-based intervention in breast cancer survivors improved NK-cell activity and reduced cortisol levels.¹⁹ Although the overall lymphocyte numbers were not altered in other studies, the expression and activity of the lymphocytes were altered with reductions in interleukin 10 and interferon-gamma in those undergoing a mindfulness-based intervention.^{20,21} In our study, we were not able to identify any differences in white blood cell count number, NK-cell number, or T-cell number with the use of mindfulness-based cancer recovery. It is possible that with the small number of participants, we were not able to detect these differences. Another factor contributing to the lack of immune response could be that most patients had recently completed chemotherapy before they enrolled in the study and their immune functions may not have fully recovered from the cytotoxic chemotherapy they received before the intervention.

Our study has several limitations. First, given the small number of men who participated, we were unable to identify any gender-specific differences. Second, it is possible that the social and psychological support of being in contact with a facilitator and/or other cancer survivors had a beneficial effect in the outcomes measured by participants in the MBCR group. Participants randomized to the control group did not have any facilitator contact them weekly during the 8 weeks of the intervention. It is possible the lack of human contact and psychological support for the control arm may have led to some unmeasured bias in our study.

Despite these limitations, our randomized control trial demonstrates that MBCR can be completed in individuals recovering from chemotherapy and radiation with excellent compliance rates. It may be difficult, however, to recruit men for such an intervention. In addition to establishing the feasibility of MBCR, our study provides data supporting a novel way of improving measures of quality of life without the use of pharmacologic therapy. Our trial provides additional data that MBCR may be beneficial in the treatment of cancer-related insomnia, fatigue, and anxiety in those who have recently completed chemotherapy and radiation. Larger, randomized studies are necessary to determine if immune function is affected by MBCR and to evaluate the effect of MBCR in heterogeneous cancer populations, most notably men. Further studies will determine whether individuals benefiting from MBCR use fewer health care services and whether these types of interventions are cost effective.

Acknowledgment

The authors acknowledge all of their MBCR facilitators who helped make this study possible and from whom the participants specifically benefited.

References

- 1. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin. 2016; 66(4): 271-289.
- Hewitt M, Greenfield S, Stovall E. From cancer patient to cancer survivor: lost in transition. Washington, D.C.: Institute of Medicine and National Research Council of the National Academies; 2005.
- Savard J, Simard S, Blanchet J, Ivers H, Morin CM. Prevalence, clinical characteristics, and risk factors for insomnia in the context of breast cancer. Sleep. 2001;24(5):583-590.
- Savard J, Morin CM. Insomnia in the context of cancer: a review of a neglected problem. J Clin Oncol. 2001;19(3):895-908.
- Feuerstein M, ed. Handbook of cancer survivorship. Bethesda, Maryland: Springer; 2007.
- Kabat-Zinn J, Massion AO, Kristeller J, et al. Effectiveness of a meditation-based stress reduction program in the treatment of anxiety disorders. Am J Psychiatry. 1992;149(7):936-943.
- 7. Kreitzer MJ, Gross CR, Ye X, Russas V, Treesak C. Longitudinal impact of mindfulness meditation on illness burden in solid-organ transplant recipients. Prog Transplant. 2005;15(2):166-172.
- Gross CR, Kreitzer MJ, Reilly-Spong M, et al. Mindfulnessbased stress reduction versus pharmacotherapy for chronic primary insomnia: a randomized controlled clinical trial. Explore (NY). 2011;7(2):76-87.
- Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int J Behav Med. 2005;12(4):278-285.
- Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology. 2004;29(4):448-474.
- Labelle LE, Campbell TS, Faris P, Carlson LE. Mediators of mindfulness-based stress reduction (MBSR): assessing the timing and sequence of change in cancer patients. J Clin Psychol. 2015;71(1):21-40.
- Thornton LM, Cheavens JS, Heitzmann CA, Dorfman CS, Wu SM, Andersen BL. Test of mindfulness and hope components in a psychological intervention for women with cancer recurrence. J Consult Clin Psychol. 2014;82(6):1087-1100.
- 13. Lengacher CA, Reich RR, Paterson CL, et al. The effects of mindfulness-based stress reduction on objective and participantive sleep parameters in women with breast cancer: a randomized controlled trial. Psychooncology. 2015;24(4):424-432.
- 14. Johns SA, Brown LF, Beck-Coon K, Monahan PO, Tong Y, Kroenke K. Randomized controlled pilot study of mindfulness-based stress reduction for persistently fatigued cancer survivors. Psychooncology. 2014.
- Burki TK. Waking up to the merits of mindfulness. Lancet Oncol. 2014;15(2):e57.
- Stafford L, Thomas N, Foley E, et al. Comparison of the acceptability and benefits of two mindfulness-based interventions in women with breast or gynecologic cancer: a pilot study. Support Care Cancer. 2015;23(4):1063-1071.
- 17. Witek-Janusek L, Albuquerque K, Chroniak KR, Chroniak C, Durazo-Arvizu R, Mathews HL. Effect of mindfulness-based stress reduction on immune function, quality of life and coping in women

newly diagnosed with early stage breast cancer. Brain Behav Immun. 2008;22(6):969-981.

- Witek-Janusek L, Albuquerque K, Chroniak KR, Chroniak C, Durazo-Arvizu R, Mathews HL. Effect of mindfulness-based stress reduction on immune function, quality of life and coping in women newly diagnosed with early stage breast cancer. Brain Behav Immun. 2008;22(6):969-981.
- Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. Brain Behav Immun. 2007;21(8):1038-1049.
- Carlson LE, Speca M, Patel KD, Goodey E. Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress, and immune parameters in breast and prostate cancer outpatients. Psychosom Med. 2003;65(4):571-581.
- 21. de la Vega R, Tome-Pires C, Sole E, et al. The pittsburgh sleep quality index: validity and factor structure in young people. Psychol Assess. 2015;27(4):e22-7.
- 22. Simoes-Wust AP, Hassani TA, Muller-Hubenthal B, et al. Sleep quality improves during treatment with bryophyllum pinnatum: an observational study on cancer patients. Integr Cancer Ther. 2015;14(5):452-459.
- Cella D, Tulsky T, Gray G. The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol. 1993;11:570-579.
- 24. Julian LJ. Measures of anxiety: State-trait anxiety inventory (STAI), beck anxiety inventory (BAI), and hospital anxiety and depression scale-anxiety (HADS-A). Arthritis Care Res (Hoboken). 2011;63(suppl 11):S467-472.
- Miller JS, Oelkers S, Verfaillie C, McGlave P. Role of monocytes in the expansion of human activated natural killer cells. Blood. 1992;80(9):2221-2229.
- National Comprehensive Cancer Network. NCCN clinical practice guidelines for oncology: cancer-related fatigue V. Updated 2010.
- 27. Garland SN, Carlson LE, Stephens AJ, Antle MC, Samuels C, Campbell TS. Mindfulness-based stress reduction compared with cognitive behavioral therapy for the treatment of insomnia comorbid with cancer: A randomized, partially blinded, noninferiority trial. J Clin Oncol. 2014;32(5):449-457.
- 28. Garland SN, Rouleau CR, Campbell T, Samuels C, Carlson LE. The comparative impact of mindfulness-based cancer recovery (MBCR) and cognitive behavior therapy for insomnia (CBT-I) on sleep and mindfulness in cancer patients. Explore (NY). 2015;11(6):445-454.
- 29. Kangas M, Bovbjerg DH, Montgomery GH. Cancer-related fatigue: A systematic and meta-analytic review of non-pharmacological therapies for cancer patients. Psychol Bull. 2008;134(5):700-741.
- 30. Speca M, Carlson LE, Goodey E, Angen M. A randomized, wait-list controlled clinical trial: The effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. Psychosom Med. 2000;62(5):613-622.
- 31. Eyles C, Leydon GM, Hoffman CJ, et al. Mindfulness for the selfmanagement of fatigue, anxiety, and depression in women with metastatic breast cancer: A mixed methods feasibility study. Integr Cancer Ther. 2015;14(1):42-56.