Yoga Practice Predicts Improvements in Day-to-Day Pain in Women With Metastatic Breast Cancer

Abstract

Context. Women with metastatic breast cancer (MBC) experience a significant symptom burden, including cancer pain. Yoga is a mind-body discipline that has shown promise for alleviating cancer pain, but few studies have included patients with metastatic disease or examined the acute effects of yoga practice.

Objectives. To determine whether daily pain changed significantly during a randomized controlled trial of the Mindful Yoga program among women with MBC and whether time spent in yoga practice was related to daily pain.

Methods. On alternate weeks during the intervention period, we collected daily measures of pain from a subset of 48 women randomized to either yoga (n = 30) or a support group condition (n = 18). We also assessed daily duration of yoga practice among patients randomized to yoga.

Results. Pain levels were low for women in both conditions, and no differential treatment effects were found on daily pain. However, among women randomized to yoga, a dose/response relationship was found between yoga practice duration and daily pain. When patients had spent relatively more time practicing yoga across two consecutive days, they were more likely to experience lower pain on the next day. This finding is consistent with an earlier MBC study. Meditation practice showed the strongest association with lower daily pain.

Conclusion. Findings suggest that yoga practice (meditation practice in particular) is associated with acute improvements in cancer pain, and that yoga interventions may be more impactful if tested in a sample of patients with advanced cancer in which pain is relatively elevated. J Pain Symptom Manage 2021;61:1227–1233. © 2020 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words
Yoga, meditation, cancer pain, metastatic breast cancer, randomized trial, daily diary

Key Message
This article describes analyses of daily measures of pain and yoga practice rates collected during a pilot randomized controlled trial of the Mindful Yoga program among women with metastatic breast cancer. The results suggest that yoga practice, and especially meditation practice, is associated with acute improvements in cancer pain.
In many women with MBC, the symptom burden remains significant with quality of life often impacted by cancer-related pain. Medications to treat cancer pain often are minimally effective and eschewed because of side effects (e.g., sedation, constipation).1

Thus, there is a clear need to test novel nonpharmacological treatments that may improve pain and other cancer-related symptoms in women with MBC. We recently completed the first-known randomized controlled trial (RCT) of a yoga intervention tailored for patients who are relatively more fragile because of advanced cancer.3 This single-blinded attention-controlled trial examined the acceptability of the Mindful Yoga program for MBC and the feasibility of conducting a future efficacy test of this intervention. In brief, our study found that Mindful Yoga program was highly acceptable to patients, but that the yoga intervention’s mode of delivery, involving eight in-person group sessions, may need to be modified to improve feasibility for this population. Although this pilot RCT was not powered to analyze symptomatic changes, we did report on modest improvements in the yoga group in six-month follow-up measures of some cancer-related symptoms (e.g., pain interference, fatigue, anxiety, depression), despite floor effects because of low symptom levels in both treatment conditions. The research demands, including a total of 12 in-person study visits (four for assessments + eight during interventions), may have precluded patients experiencing a higher symptom burden from participating in the study.

The aim of the present article is to address additional planned analyses from this RCT to answer two questions: Did daily pain change differentially across the yoga and control groups during the intervention period? And regarding the yoga group, were day-to-day variations in time spent in yoga practice related to daily pain?

Method
Participants
Of the 63 randomized patients reported on in our earlier article, 48 provided the diary assessments that are the focus of this report. Factors associated with completion rates are described in the Results section later. All 48 patients were recruited from the Duke breast oncology clinic and were receiving treatment for Stage IV MBC; aged 18 years and older; had a life expectancy of nine months and/or greater as estimated by their treating oncologist; and could speak and read English. Exclusion criteria were cognitive impairment as assessed by the six-item Mini-Mental Status Examination; Eastern Cooperative Oncology Group rating of $\geq 3$ or Karnofsky Performance Status $< 60$ as rated by the oncology provider; treatment for serious psychiatric illness (e.g., schizophrenia, severe depression) in the past six months; current engagement in yoga practice one day or more per week; and resting systolic blood pressure $> 180$ mm and/or diastolic blood pressure $> 100$ mm, or resting heart rate $> 100$ beats per minute at the baseline assessment. This trial is registered at ClinicalTrials.gov (NCT01927081), where study materials are publicly available.

Procedures
All procedures were approved by the Duke Medical Center Institutional Review Board. Informed consent was obtained from all study participants. During the study, participants continued to receive their usual medical care. Medications and treatments received during the study were documented but not restricted. Each participant was paid $40 for completing diaries as an honorarium for their time.

After completing consent and baseline assessment, participants were randomized in a series of cohorts with 2:1 allocation (as recommended by the funding agency) to Mindful Yoga program or social support. The study statisticians (M. O. and L. S.) generated the randomization scheme before the start of recruitment; it was kept in a study database inaccessible to blinded study personnel. The study coordinator who executed the randomization schedule did not have access to the data and was not involved in the outcome assessments. The principal investigator, study statisticians, and study staff involved in collecting outcome assessments were blinded to treatment condition.

Measures
Demographic information was collected at baseline, and medical information was collected via medical record. During the eight-week intervention period, participants completed brief daily diaries on alternate weeks (four rather than eight weeks, so as to reduce assessment burden). Similar diaries have been used in cancer studies to evaluate symptom outcomes.4 Advantages of daily diary data include their demonstrated reliability and validity, their ability to capture reports of internal events (e.g., pain, emotions) in individuals’ natural settings and closer to their real-time occurrence, and enhanced statistical power for the analysis of small clinical samples.5

Diary data were collected via an interactive telephone voice system. Participants were provided a toll-free number to call each day during collection weeks. Patients were trained at baseline to use the
system, and patients were called periodically to inquire about any difficulties. Prerecorded voice prompts asked patients to enter their responses by pressing numbers on their telephone. Data were automatically transferred into a computerized database. This method minimizes data errors and marks each data bit with a precise date and time of collection.

Pain on the same day the diary was completed was assessed using a 0-9 scale anchored at 0 = no pain at all and 9 = worst possible pain. We have used this same pain scale in a previous study of yoga for patients with cancer. The 10-point scale differs from the standard 11-point numerical rating scale, several studies comparing a variety of pain scales suggest that they yield similar results in terms of predictive validity. For example, Jensen et al. reported that 6-point and 11-point numerical rating scales were both strongly associated (r = 0.97 vs. r = 0.99) with a 101-point visual analogue scale.

Patients in the yoga condition also recorded how many minutes they spent that day engaged in each of the three types of practices: meditation, breathing, and yoga postures.

Interventions

General Factors. Each intervention consisted of eight 120-minute group sessions, with 5-10 patients per group. Sessions were generally held weekly, but to accommodate holidays and inclement weather, the sessions occurred during the course of nine rather than eight weeks. Intervention instructors received prior training in the respective protocols and followed detailed treatment manuals. All sessions were video recorded and reviewed by investigators who provided verbal and written feedback to the instructors on a weekly basis. The interventions are more thoroughly described in our previous publications.

Mindful Yoga. This intervention was originally developed to address cancer-related pain, fatigue, and emotional distress. The intervention was led by registered yoga teachers (i.e., registered yoga teacher [RYT] certification from Yoga Alliance) with prior experience in teaching yoga techniques to medical patients. Mindful Yoga program emphasizes developing mindfulness via substantial meditation (25 minutes per class), gentle postures (40 minutes), breathing techniques (10 minutes), presentations on yogic principles for optimal coping (20 minutes), and group discussions with opportunities for sharing and asking questions (25 minutes). During posture exercises, the inner dimensions of practice were emphasized (e.g., nonreactive monitoring of sensory, mental, and emotional fluctuations) along with proper alignment and breathing techniques.

Several aspects of this intervention were geared toward relief of pain, fatigue, and emotional distress. First, Mindful Yoga program cultivates a healthy acceptance of and willingness to learn from pain and other stressful experiences. The important role of acceptance in decreasing the emotional distress and sympathetic activation associated with pain and other unpleasant symptomatology has received increased research focus and clinical attention. Second, research has shown that yoga produces the relaxation response (an integrated set of changes that includes increased breath volume, decreased heart rate, etc.). Because autonomic dysregulation has been implicated in the generation of pain and fatigue, psychophysically soothing techniques are likely to promote the alleviation of these symptoms. Third, the yoga postures in this intervention served not only simply as healthy physical movements but also as a forum for developing nonreactive awareness of bodily sensations, including pain and fatigue. Mindfulness strategies and the application of other yogic principles (e.g., acceptance) were directly integrated into the practice of the poses so that participants could become aware of and modulate subtle patterns of unskillful reactivity (e.g., fear, guarding).

Participants were encouraged to practice a combination of meditation, breathing, and posture strategies at home, 15-30 minutes per day, five to six days per week, guided by professionally produced video recordings. Participants also received brief session summary handouts each week that included instructions for the informal application of yoga practice to daily life (e.g., in-the-moment acceptance of pain).

Social Support Group. This condition controls for attention, time, and nonspecific treatment effects such as general social support. The control intervention was led by a licensed clinical social worker experienced in working with patients with advanced cancer. The scheduling of the sessions was identical to that for the yoga intervention. Modeled after the control group protocol used by Breitbart et al., the instructor focused on discussion of issues and themes that emerge for patients coping with MBC, including the following: coping with medical tests; communicating with health care providers; coping with family and friends; vocational issues; body image and physical functioning concerns; fears about future physical or psychological changes, recurrence, and mortality; and plans for the future. Using a supportive approach, the therapist encouraged patients to share concerns related to the cancer diagnosis and treatment,
describe their experiences and emotions related to these experiences, voice problems that they have in coping with cancer, and offer support and advice to other group members.14

Statistical Analysis

Planned analyses addressed these questions: Were there differences between the yoga and control groups in daily pain, including slope trajectories during the intervention period? Regarding the yoga group, were day-to-day variations in time spent in yoga practice related to daily pain?

To examine these questions, we fit a series of mixed-effects models via SAS Proc Mixed (Version 9.4; SAS Institute, Inc., Cary, NC). Before model estimation, spline plots were generated to confirm that the distribution of the daily data was consistent with a linear model of time. Time was coded as zero on the day of the eight-week intervention period, one on the second day, and so on.

For the first research question, examining treatment group differences of overall daily pain, fixed-effect coefficients included time, treatment, and the time × treatment interaction. Random effects included the intercept, linear slope, and correlation. The default assumption of compound symmetry was applied to within-person residuals.

For the second research question, testing whether doing more yoga, or less yoga, on a given day was related to a typical patient’s pain that day, we generated a series of models for meditation, breathing, posture, and total practice rates. The predictors for same-day models were duration of practice and time across the intervention period (in weeks). Practice rates were person centered (i.e., adjusted by subtracting the person’s mean practice rate from the corresponding day’s minutes of practice) so that rates represented whether a person practiced more or less than their average amount of practice. Importantly, person centering also controls for potentially spurious within-person associations.11,15 To facilitate interpretation of results, practice times were divided by 10 to convert to 10-minute units. In addition to same-day models, we examined whether there were associations between the running average of practice rates across two consecutive days and pain on the next day. This query was based on a finding from our previous small MBC trial showing that variations in daily pain were related to the duration of yoga practice across two consecutive days.11 The predictors in these lagged models were duration of practice, time (days), and—to control for pain on the corresponding days—the running average of pain during the two preceding days. As before, practice rates were person centered, and duration was converted to 10-minute units. Separate models were executed for meditation, breathing, posture, and total practice rates.

Because of the exploratory nature of these analyses, adjustments were not made to account for multiple testing.

Results

Daily Diary Adherence and Preparation for Analyses

Of the 63 randomized patients, 48 (76.2%) completed at least one daily diary (yoga = 30 of 43; control = 18 of 20). Preparatory analyses showed that participants were less likely to complete diaries if they were employed (part time or full time; \( P = 0.001 \)); had dependent children (\( P = 0.011 \)); or were in the yoga condition (\( P = 0.041 \)). None of the baseline medical variables (e.g., cancer treatment history) were related to completion rates. Among the 15 participants without diaries, 13 were in the yoga group. The yoga group also included 15 of the 18 employed participants (83.3%) and 17 of the 22 participants with dependent children (77.3%). Step-wise regression showed that after accounting for employment (\( P = 0.014 \)) and dependent children (\( P = 0.084 \)), treatment condition was no longer significantly associated with completion rates (\( P = 0.163 \)).

The mean diary completion rate across the 48 participants who completed at least one diary was 71%, consisting of a total of 948 daily assessments (mean = 19.8; SD = 7.6; range 2–32). The mean completion rate when including 15 participants who provided no diaries was 54%. This completion rate is comparable with rates varying 47%–89% from the few cancer trials that have reported on daily diaries recorded in patients’ homes.4,11

Most data (67.2%) were collected as originally planned, that is, daily on alternate weeks during the intervention period via the phone system, with participants with odd-numbered identification numbers completing the diaries on the odd weeks1,3,4,6 and those with even-numbered identification numbers completing the diaries on the even weeks.2,5,7,11 However, factors such as weather-related changes in the sequence of intervention weeks led to some variations in the diary collection process. To retain as much valid data as possible, before beginning analyses, we implemented several minor modification procedures as follows: 1) We included diaries that were completed in paper form and mailed to us on a daily basis before the interactive telephone voice system becoming fully functional (211 diaries across 11 participants); 2) we retained diaries that, because of weather-related changes in the sequence of intervention weeks, were completed on days that did not correspond with the initial plan (61 diaries across seven participants, including four who submitted either 31 or 32 diaries.
rather than the expected maximum of 28 diaries); and 3) when participants sometimes completed two diaries within the same 24-hour period, we retained these whenever the two entries were at least 12 hours apart and could be recoded to fit into missing diary gaps corresponding to either the previous day or the next day (21 diaries across 11 participants). In the final phase of analyses, we also decided it was prudent to eliminate four extreme outlier observations from across three patients, who had reported spending >100 minutes practicing meditation on those days (results that included the outliers differed only in that the findings were statistically more significant).

Descriptive Findings

Baseline demographic and medical data for the 48 participants included in this analysis are presented in Table 1. There were no significant differences across the conditions. Please see our prior published report on this pilot RCT for full study enrollment and participation information, including the Consolidated Standards of Reporting Trials (CONSORT) diagram.3,16

Treatment Effects on Daily Pain

As shown in Table 2, the mixed-effects analysis produced a significant main effect for treatment condition, indicating differentially higher baseline pain in the yoga group vs. the control group. However, treatment was not predictive of significant changes in pain during the intervention period; the slope estimates for each condition are also shown in Table 2. To more closely examine baseline differences in pain, a data set was abstracted from the full data set using only observations submitted during the first week of each patient’s diary recordings (yoga: mean = 2.36; SD = 1.70; range 0–6.34, with four patients reporting no pain; control: mean = 1.42; SD = 1.14; range 0–3.84, with two patients reporting no pain). Analysis of variance of these data confirmed a significant baseline group difference ($F[1, 46] = 4.27; P = 0.045$).

Within-Person Relations Between Yoga Practice and Daily Pain

These and all subsequent analyses were conducted with data from yoga condition participants only ($n = 30$). On average, on the days patients completed diaries (excluding four outlier observations as described previously), they engaged in 13.87 minutes of meditation (SD = 5.99), 12.29 minutes of breathing practice (SD = 7.77), and 14.17 minutes doing yoga postures (SD = 8.19), for a total practice rate of 40.78 minutes (SD = 17.49) per day. Total practice rates were strongly and positively correlated with class attendance rates ($r = 0.75$; Pearson two-tailed test).

Same-Day Practice Results. Analyses of variations in the total time spent in the three yoga practices in relation to same-day levels of pain produced no significant associations.

Lagged Practice Results. Associations with the two preceding days’ running average of yoga practice are shown in Table 3. Relatively more total time during the two preceding days spent in the three yoga practices (meditation, breathing, and postures) was significantly predictive of acutely improved pain. In addition, relatively more time in meditation practice alone, and breathing practice alone during the two proceeding days, was significantly predictive of acutely improved pain, with meditation showing a somewhat stronger association with pain improvements than breathing.

Discussion

This investigation examined the impact of the Mindful Yoga intervention on daily pain in a sample of women with MBC. Our results did not demonstrate differential effects of the yoga program relative to the
control condition on overall levels of pain. However, among women in the yoga group, we did find an acute dose/response relationship between day-to-day variations in patients’ length of yoga practice and pain on subsequent days. When patients had spent relatively more time practicing yoga across two consecutive days, they were more likely to experience lower pain on the next day. This acute effect was most strongly associated with meditation practice, and secondarily with breathing practice, both of which independently demonstrated significant dose/response relationships to daily pain. These results are consistent with our earlier small pilot study, which found that when MBC patients practiced yoga more than usual, they reported improvements in pain across two consecutive days (in that study, we assessed only the total practice time, rather than separately for meditation, breathing, and postures).11

The absence of mean differences in daily pain between the yoga and social support groups conforms with what we observed in analyses of prepost summary questionnaires.3 However, this was inconsistent with previous RCTs, which had reported that Mindful Yoga program led to improvements in pain and other symptoms among survivors of early stage breast cancer and women with fibromyalgia.6,17,18 The lack of similar effects in this study may be due to the low overall pain level in our sample, which may have resulted from excessive study demands preventing patients with a higher symptom burden from participating. It is plausible that if Mindful Yoga program was tested in a sample of patients with advanced cancer in which pain was relatively elevated, then a significant impact of the yoga intervention on daily pain would become evident. In future studies, the yoga intervention’s mode of delivery, involving eight 120 minutes in-

### Table 2

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*aP ≤ .01.

### Table 3

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*p ≤ 0.01.

*p ≤ 0.05.
person group sessions, may need to be modified to improve feasibility for this population. Alternatives may include shorter sessions, open rather than closed groups, substituting home-based modules, or conducting sessions via videoconference.

It is notable that the yoga practice rates were quite good in this study. On average, participants spent 41 minutes doing a combination of meditation, breathing, and posture practices on the days diaries were completed. This compares favorably with our earlier small trial, when the average practice time was 21 minutes. However, because our sample for the present study excluded 13 yoga participants who did not submit diaries, we cannot be certain of the accuracy of this practice estimate.

Nonetheless, we believe the strong emphasis placed on home practice during the yoga intervention sessions likely contributed to the relatively good yoga practice rates described herein. Group discussions during classes included a review of participants’ practice engagement, along with problem-solving obstacles to home practice.

Furthermore, the meditation practice was most strongly associated with acute relief of pain in this study. Given the relatively fragile condition of many of the participants in this trial, it may be that they found meditation particularly accessible and soothing.

Important limitations of this study should be noted. The generalizability of these preliminary findings is restricted by the small sample, which was mostly white, well educated, living in partnered relationships, but largely excluded women who were employed or had dependent children. Despite limitations, this study adds to the literature on the promising benefits of yoga. In particular, our findings point to the potential benefits of meditation, which can be easily practiced by patients with advanced and debilitating illnesses.

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The authors declare no conflicts of interest.

References


