

Mindfulness based stress reduction (MBSR(BC)) in breast cancer: evaluating fear of recurrence (FOR) as a mediator of psychological and physical symptoms in a randomized control trial (RCT)

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Abstract To investigate the mechanism(s) of action of mindfulness based stress reduction (MBSR(BC)) including reductions in fear of recurrence and other potential mediators. Eighty-two post-treatment breast cancer survivors (stages 0–III) were randomly assigned to a 6-week MBSR(BC) program ($n = 40$) or to usual care group (UC) ($n = 42$). Psychological and physical variables were assessed as potential mediators at baseline and at 6 weeks. MBSR(BC) compared to UC experienced favorable changes for five potential mediators: (1) change in fear of recurrence problems mediated the effect of MBSR(BC) on 6-week change in perceived stress ($z = 2.12$, $p = 0.03$) and state anxiety ($z = 2.03$, $p = 0.04$); and (2) change in physical functioning mediated the effect of MBSR(BC) on 6-week change in perceived stress ($z = 2.27$, $p = 0.02$) and trait anxiety ($z = 1.98$, $p = 0.05$). MBSR(BC) reduces fear of recurrence and improves physical functioning which reduces perceived stress and anxiety. Findings sup-

port the beneficial effects of MBSR(BC) and provide insight into the possible cognitive mechanism of action.

Keywords Fear of recurrence · Cancer · Mindfulness-based stress reduction (MBSR) · Oncology

Introduction

Breast cancer is a major health problem and comprises the largest population of cancer survivors estimated at 2.6 million women in the United States (National Cancer Institute, 2010). Although some survivors of breast cancer adjust reasonably well over time to their disease-related emotional distress, fear of recurrence has been shown to chronically plague 24–89 % of women with breast cancer (Girgis et al., 2000; Hartl et al., 2003; Mehnert et al., 2009; Polinsky, 1994; Stanton et al., 2005; Stephens et al., 2008; van den Beuken-van Everdingen et al., 2008). The high prevalence of fear of recurrence as a distressing psychological and physical problem occurs regardless of risk, cancer site and can persist years after treatment (Armes et al., 2009; Baker et al., 2005; Deimling et al., 2006; Hodges & Humphris, 2009; Humphris et al., 2003; Llewellyn et al., 2008; Matthews, 2003; Mehta et al., 2003; Simard et al., 2010). Fear of recurrence induces particularly high morbidity among breast cancer survivors and is a complex phenomenon. Fear of recurrence is often viewed as a multidimensional phenomenon, including emotional components of anxiety and fear, and a cognitive dimension, including worry, preoccupation and intrusive thoughts (Lee-Jones et al., 1997; Simard et al., 2010).

Fear of recurrence is often triggered by antecedents such as physical symptoms, or perceived risk resulting in

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psychological distress, decreased quality of life, and functional impairment (Simard et al., 2010; van den Beuken-van Everdingen et al., 2008) while contributing indirectly to fatigue (Minton & Stone, 2008; Young & White, 2006). For some patients this leads to behavioral consequences including increased health care visits, and double checking for recurrence (Cannon et al., 2011; Hawkins et al., 2010).

Since fear of recurrence is an established source of significant emotional distress among breast cancer survivors, it represents a logical, clinically-relevant target for intervention (Connell et al., 2006; Costanzo et al., 2007; Fredette, 1995; Johnson Vickberg, 2001; Oxlad et al., 2008; Schmid-Buchi et al., 2008). The need for post-treatment intervention is not time dependent, per se, (Mehnert et al., 2009) in that fear of cancer recurrence has been found to persist up to 32 years after surgery (Polinsky, 1994). Additionally, in terms of appropriate intervention targeting, fear of recurrence may vary by age, with younger women having higher levels (Costanzo et al., 2007; Curran et al., 1998; Kornblith et al., 2007; Mast, 1998; Mehnert et al., 2009; van den Beuken-van Everdingen et al., 2008). Few interventions have been tested to reduce fear of recurrence, however, fear of progression was reduced among cancer survivors by short psychotherapeutic interventions of a cognitive-behavioral group therapy and supportive-experiential group therapy (Herschbach et al., 2010).

Over the past 25 years, research on mindfulness delivered through MBSR meditative practices has demonstrated effectiveness in reducing psychological and physical symptoms in a wide variety of clinical and non-clinical populations (Bohlmeijer et al., 2010; Brown et al., 2007; Chiesa & Serretti, 2009; Grossman et al., 2004; Matchim & Armer, 2007; Musial et al., 2011). The effects of MBSR on fear of recurrence in a randomized trial by our team, was found to significantly reduce fear of recurrence among 84 breast cancer survivors (Lengacher et al., 2009) however in another pre-post study, only a trend towards reduction of fear of recurrence was found among 19 prostate cancer survivors (Chambers et al., 2012).

The foundations of the MBSR program are built on the healing power of “mindfulness” that is operationalized through two cognitive processes, awareness and attention (Brown & Cordon, 2009). Through the MBSR program patients learn to self-regulate awareness and attention (Bishop, 2002) and cultivate non-judging acceptance to implement change (Bishop et al., 2004; Brown et al., 2007; Kabat-Zinn, 1990, 2003). Through the “awareness” mode of cognitive processing, subjective experiences are processed such as images or feelings; these are held very briefly and are followed by appraisal or evaluation, such as being pleasant or unpleasant. These reactions are conditioned by past experiences, and can be associated with a memory; however, they are easily assimilated into other schemas. The “attention”

mode of processing involves a “stepping back” process (Brown & Cordon, 2009) in which feelings and images are perceived objectively as they appear. Through attention, registration of bare facts is observed. Collectively, through cultivation of attention and awareness, persons are taught to be present in reality rather than only reacting to it and ruminating over past emotional experiences. Recent efforts have identified 3 specific components of mindfulness: (1) intention, which involves motivation and knowing why one is paying attention; (2) attention, which is knowing what is happening directly; and (3) attitude, which is paying attention through acceptance, caring qualities of mindfulness, or “affectionate attention” (Cullen, 2006; Shapiro et al., 2008).

For cancer survivors, the meditative approach and training in the cognitive process of mindfulness facilitates self-regulation of emotions during distress and suffering. This training emphasizes a moment-to-moment, non-judgmental and non-reactive awareness to internal and external experiences, thus reducing rumination and elaboration of distressful experiences (Baer, 2003; Bishop et al., 2004). Through the process of non-judging acceptance and focusing attention to the breath and body sensations, beneficial changes through self-regulation become evident (Perlman et al., 2010). Through the cognitive process of self-regulation the patient may regulate reaction to the triggers for fear of recurrence such as worry or rumination.

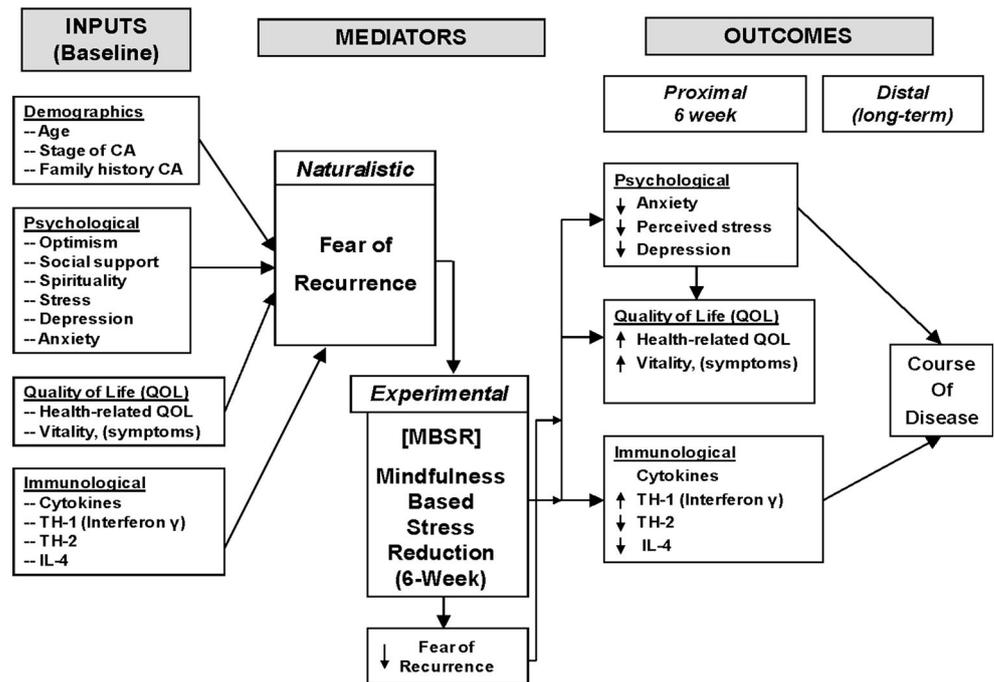
Because of the empirically-established benefits of MBSR among cancer survivors in reducing psychological distress, depression, anxiety and fear of recurrence, and improving quality of life (Lengacher et al., 2009), this current research proposed to examine and establish the mechanism(s) by which elements of MBSR (i.e. breath awareness, body scan, walking meditation, sitting meditation and yoga) lead to specific clinical improvements. In this realm, and given the significant morbidity induced by fear of cancer recurrence, it is surprising that this pervasive fear has not been examined systematically, in particular, in relation to stress reducing interventions. Therefore, in this study, we adopted the theoretical logic model by Evans (Evans, 1992), a heuristic device for psychosocial research, to postulate and examine how change in fear of recurrence as a result of participation in the MBSR program may mediate a range of positive changes in psychological and physical symptoms and quality of life (Fig. 1).

Methods

Sample and setting

Eighty-four breast cancer survivors were recruited from the H. Lee Moffitt Cancer Center and Research Institute, in Tampa, Florida beginning March 1, 2006 through July 23,

Fig. 1 Hypothesized Biobehavioral Logic Model postulates how change in fear of recurrence as a result of participation in the MBSR program may mediate a range of positive changes in psychological and physical symptoms and quality of life



2007. All study subjects had been diagnosed with primary stage 0, I, II, or III breast cancer, had completed treatment within the prior 18 months and were able to read and speak English at the 8th grade level. Exclusion criteria included stage IV breast cancer, mastectomy, severe psychiatric diagnosis (e.g. bipolar disorder), and breast cancer recurrence. Eighty-two of the 84 subjects (97.6 %) had complete 6-week follow-up data and form the basis of this analysis.

Study design and random assignment

Subjects were randomly assigned in a 1:1 ratio to either MBSR(BC) or a usual care (UC) group. Randomization was stratified in an unblocked manner using a random number generator by stage of cancer and type of treatment received (radiation alone vs. radiation + chemotherapy). Study personnel (excluding the statistician) remained blinded to treatment assignment until a sufficient subgroup of patients (e.g. 10 or more) had been assembled with random assignment subsequently carried out.

Procedures

At orientation, subjects were consented, randomized, and completed baseline assessments. Subjects completed the assessments again within 2 weeks following the 6-week MBSR(BC) program or control period.

Intervention procedures

Subjects randomized to MBSR(BC) (n = 40) attended weekly 2-h sessions conducted by an MBSR trained psychologist. Participant materials included a training manual and 4 audio tapes for home practice. Home practice consisted of sitting meditation, body scan, walking meditation, and gentle yoga. Subjects were also required to complete a diary on a daily basis documenting home practice which was collected weekly prior to class. The MBSR(BC) intervention is a 6-week program adapted specifically for breast cancer survivors and based upon Kabat-Zinn’s 8-week program (Kabat-Zinn, 1990). Participants learn the use of four meditative practices including sitting meditation, walking meditation, body scan, and yoga while integrating mindful attention to self-regulate and manage stressful symptoms (Kabat-Zinn et al., 1985; Teasdale et al., 1995).

Fidelity

A training manual was developed to maintain the consistency of the intervention. Sessions were standardized and delivered by a single trained psychologist. The program was monitored each week for consistency by an independent observer who recorded the timing of activities and assessed the quality of each session through a qualitative post-observation report.

Compliance

All participants were asked to formally meditate (sitting, walking, body scan) and perform yoga exercises for 15–45 min per day 6 days per week for the duration of the 6-week MBSR(BC) program. They were also asked to engage in informal practice for 15–45 min per day. Participants recorded their practice in a diary for each day during the 6-week period.

Usual care (UC) group

Subjects randomized to the UC group (waitlisted control group) were offered the MBSR(BC) program after the initial 6-week study period.

Measures

In prior published data (Lengacher et al., 2009), we reported that enrollment in the 6-week MBSR(BC) program (compared to UC regimen) was associated with significantly better adjusted post-intervention scores on measures of psychological status and quality of life. Therefore, to assess fear of recurrence as a potential mediator of the effect of the MBSR program, as well as other selected variables (i.e. “how” MBSR(BC) works), we conducted the analysis using 6 outcome measures in which MBSR(BC) demonstrated evidence of efficacy: *perceived stress*, *depressive symptoms*, *state anxiety*, *trait anxiety*, and *aggregate mental and physical health*. *Fear of recurrence* (cancer) was assessed at orientation and within 2 weeks following the 6-week intervention period by the 30-item Concerns about Recurrence Scale. This assessment measures the extent and nature of women’s fears about the possibility of breast cancer recurrence in two sections. The first section has four items that assess “worry” related to recurrence, scored as (1) “I don’t think about it at all” to (6) “I think about it all the time.” The second section has 26 items that assess the nature of the fear regarding recurrence and extent to which they worry about each item. These items are scored on a five-point Likert scale ranging from (0) not at all, to (4) extremely. Overall, internal consistency reliability is 0.87 for breast cancer subjects (Vickberg, 2003a, b). *State and trait anxiety* was measured by the State-Trait Anxiety Inventory a two 20-item instrument which measures both state anxiety (present anxiety) and trait anxiety (long term characteristic anxiety); higher scores are indicative of more anxiety—scored from (1) not at all to (4) almost always with possible scores for each scale range from 20 to 80. Internal consistency reliability is 0.95 (Spielberger et al., 1983). *Depression* was measured by the Center for Epidemiological Studies Depression Scale (CES-D), a 20-item measure that assesses

depressive symptoms during the previous week on a four-point scale ranging from (1) Rarely or none of the time to (4) most or all of the time. Scores range from 0 to 60 (Radloff, 1977) Alpha coefficient reliability is 0.92 for breast cancer survivors. *Optimism* was measured by the Life Orientation Test-Revised (LOT-R). This instrument contains 6 target items and 4 filler items that assess expectancy for positive and negative life outcomes on a 5-point Likert scale from (0) strongly disagree to (4) strongly agree. Higher scores indicate better optimism. Coefficient alpha reliability is 0.74–0.78 (Scheier et al., 1994). *Perceived stress* was measured by the 14-item Perceived Stress Scale that assesses how often in the past month one appraises life situations as “stressful.” Higher scores indicate more stress. Items are scored as (0) never to (4) very often, with scores ranging from 0 to 56. Internal consistency reliability is 0.84–0.86 (Cohen et al., 1983). *Quality of life* was measured by the Medical Outcomes Studies Short-Form General Health Survey (MOS SF-36), with 36 items that assess Physical Functioning, Physical Role Functioning, Bodily Pain, General Health, Vitality, Social Functioning, Emotional Role Functioning, and Mental Health. Higher scores indicate better quality of life and subscale scores range from 0 to 100 with higher scores indicating a more favorable health status. Estimated internal consistency scores range from 0.62 to 0.94 with the majority of scores having exceeded 0.80 (Ware et al., 1993). *Social support* was measured by the Medical Outcomes Social Support Survey, which has 20 items and individual subscales of social support including tangible, affectionate, positive social interactions, and emotional or informational. Higher scores are indicative of more social support. Scores range from (0) none of the time to (5) all of the time with a total range from 0 to 100. Internal consistency reliability is 0.97 for the full instrument and 0.91–0.96 for the subscales (Sherbourne & Stewart, 1991). Additional measures completed by study subjects have been reported elsewhere (Lengacher et al., 2009). *Standard socio-economic demographic data* were collected on study subjects to allow for description of the sample on age, gender, ethnicity, highest level of education completed, marital status, income status, and employment status. *Clinical history* data were collected at baseline and 6 weeks to assess whether there were any new problems, whether treatment related or not. Data were collected on site of cancer diagnosis, date of cancer diagnosis, date treatment ended, number of weeks on radiation, and number of weeks on chemotherapy.

Statistical methods

To assess mediation effects, we followed the 3-variable framework described by MacKinnon et al. (2007), and as

depicted in Fig. 2. In this model, MBSR (X1) is assumed to have both a direct and indirect path to the outcome perceived stress (Y). “c” is the direct path, and “a → b” is the indirect path passing through the mediating variable fear of recurrence (X2). Thus, by definition, for fear of recurrence to be a significant mediating variable, the following 2 conditions must be present: (1) the independent variable (X1) is associated with the outcome variable (Y) (i.e. path “c”, as previously reported); and (2) the independent variable (X1) is associated with the mediating variable (X2) (path “a”). For both mediators and outcomes, we used change (difference) scores between the baseline and 6-week assessments. With respect to mediators, this was done to minimize potential confounding due to small yet possibly influential between-group differences (MBSR(BC) vs. control) in baseline values. Because this analysis aimed to examine the relative change in potential mediators following MBSR(BC), both usual care and intervention subjects were required in the analysis (i.e. the full sample as opposed to MBSR(BC) subjects only).

Initially, student *t*-tests were used to compare baseline values of potential mediators by random assignment, followed by use of the Wilcoxon Rank Sum test to compare change in mediating variables reported at 6-week follow-up (i.e. path “a”). Spearman correlation coefficients were calculated to estimate the strength of relationships between 6-week change in potential mediators and 6-week change in outcomes of interest (i.e. path “b”) for the full cohort, irrespective of random assignment. These analyses were followed by use of the Sobel test (Baron & Kenny, 1986) to examine the indirect effect of potential mediating variables (X2) taking into account the direct effect of MBSR(BC) on the outcomes of interest (i.e. “a → b” path). Wilcoxon Rank Sum tests were also used to compare 6-week change in outcome measures by change in mediators dichotomized as above or below the median (i.e. to maximize subgroup statistical power), and then stratified by random assignment.

Finally, since the Concerns about Recurrence Scale does not provide guidelines for estimating “clinically significant” changes in fear of recurrence, we calculated the reliable change index (RCI) using the method proposed by Jacobson et al., (1984). Specifically, we calculated the difference in change scores for the MBSR(BC) versus usual care group

(i.e. pre-post-test scores for each group) and common standard deviation of the difference in change scores. The RCI also takes into account test–retest reliability. Since the time period between pre- and post-testing was lengthy (6-weeks), and the study involved an intervention (i.e. change is expected), we used Cronbach’s internal consistency reliability coefficient as an estimate of test–retest reliability.

Results

A previous article details the CONSORT diagram regarding the number of participants recruited, enrolled and lost to follow-up for this study (Lengacher et al., 2011). Although 84 participants were assessed at baseline, 82 completed the follow-up for the study, with a total of *n* = 40 in the MBSR(BC) group and *n* = 42 in the control group. The mean age of the 82 study subjects (with non-missing data) was 57.2 ± 9.2 years with 47 women (57.3 %) age 55 or older. Fifty-nine subjects (71.9 %) were non-Hispanic White, 9 (11.0 %) were Hispanic-White, 10 (12.2 %) were non-Hispanic Black, and the remaining 4 (4.9 %) were of other race/ethnicity classification. Thirty-six women (43.9 %) had a college or professional degree and 57.3 % were employed. Clinically, stage of breast cancer was as follows: stage 0 (17.1 %); stage I (52.4 %); stage II (23.2 %); stage III (7.3 %). Thirty-three women (40.2 %) were treated with radiation and chemotherapy and the remaining 49 women (59.8 %) were treated with radiation only. The median time since treatment completion to study entry was 12.5 weeks and 50 % of all women had completed treatment within the past 12 weeks. Prior to MBSR(BC) (or control condition), age was inversely associated with fear of recurrence concerns (*r* = −0.35, *p* = 0.001) and fear of recurrence problems (*r* = −0.26, *p* = 0.02). Full baseline and clinical demographics have been previously described elsewhere (Lengacher et al., 2009).

Potential mediators by random assignment (i.e. path “a”)

At baseline, nearly all potential mediators examined had similar mean values by random assignment with the excep-

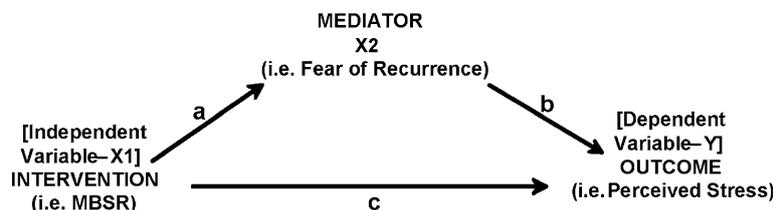


Fig. 2 Three-variable framework used to assess mediation effects. In this model, MBSR (X1) is assumed to have both a direct and indirect path to the outcome perceived stress (Y). “c” is the direct path, and

“a → b” is the indirect path passing through the mediating variable fear of recurrence (X2)

tions of mean perceived stress being higher in the control group compared to MBSR(BC) (19.1 vs. 16.0, $p = 0.04$), and mean state anxiety being higher in the control group (40.4 vs. 35.3, $p = 0.05$) (Table 1). From baseline to 6-weeks, the MBSR(BC) group experienced more favorable changes (differences) than the UC group for several potential mediators including fear of recurrence concerns (2.8 vs. 0.2, $p = 0.007$), fear of recurrence problems (11.4 vs. 0.2, $p = 0.02$), depression (7.2 vs. 4.0, $p = 0.04$), physical functioning (3.8 vs. 0.5, $p = 0.01$), and energy (8.8 vs. 5.0, $p = 0.07$). Thus, these 5 potential mediators were considered in subsequent analyses. Regarding the relative (between-group) magnitude of change in fear of recurrence, the RCI was 2.13 and 3.02 for fear of recurrence concerns and fear of recurrence problems, respectively. For interpretation, an RCI of ≥ 1.96 indicates reliable or clinically significant change (Jacobson et al., 1984).

Potential mediators and outcomes of interest (i.e. path “b”)

Small to modest statistically significant correlations were observed between several mediators and outcomes of interest (Table 2). This included: (1) change in depression (mediator) being associated with change in perceived stress ($r = 0.47$), state anxiety ($r = 0.50$), trait anxiety ($r = 0.51$), and aggregate mental health ($r = 0.49$); (2) change in physical functioning (mediator) being associated with change in perceived stress ($r = 0.43$), trait anxiety ($r = 0.38$), and aggregate physical health ($r = 0.54$); and (3) change in energy (mediator) being associated with change in perceived stress ($r = 0.45$) and aggregate mental health ($r = 0.59$) ($p < 0.001$ for all correlations). Change in fear of recurrence problems

(mediator) was associated with change in perceived stress ($r = 0.34$), state anxiety ($r = 0.34$), and trait anxiety ($r = 0.34$) ($p < 0.01$ for all correlations).

Indirect effects of potential mediating variables

After removing direct effects of MBSR(BC) on outcomes of interest (path “c”), the strongest and most consistent evidence for mediating effects (i.e. “how” MBSR(BC) works) was for change in fear of recurrence problems and change in physical functioning. As seen in Table 3, change in fear of recurrence problems mediated the effect of the MBSR(BC) program on 6-week change in perceived stress ($z = 2.12$, $p = 0.03$) and state anxiety ($z = 2.03$, $p = 0.04$). Similarly, change in physical functioning mediated the effect of the MBSR(BC) program on 6-week change in perceived stress ($z = 2.27$, $p = 0.02$) and trait anxiety ($z = 1.98$, $p = 0.05$). Results were similar when stratified by “dose” of MBSR(BC) categorized as below or above the median in total number of minutes practiced (data not shown).

Figures 3 and 4 graphically depict mediating effects of change in fear of recurrence problems and change in physical functioning. Women who experienced a greater reduction in fear of recurrence (i.e. at or above the median value of 2.5 units) experienced greater reduction in change in perceived stress ($p = 0.005$, Fig. 3: left side). Of note, even though more women in the MBSR(BC) group experienced a greater mean reduction in fear of recurrence than in the UC group (25 vs. 16 women), the concomitant mean change (reduction) in perceived stress was similar (6.0 vs. 5.3 units, $p = 0.57$). Similar results were observed for change (improvement) in physical functioning being associated with change

Table 1 Mean values of potential mediators by random assignment (i.e. path “a”)

Potential mediator	Pre-intervention			Change at 6-week assessment ^a		
	Control (n = 42)	MBSR (n = 40)	<i>p</i> value	Control (n = 42)	MBSR (n = 40)	<i>p</i> value
Perceived stress	19.1 (7.2)	16.0 (6.7)	0.04	3.3 (4.9)	4.7 (5.0)	0.16
Fear of recurrence concerns	11.5 (4.9)	12.3 (5.0)	0.49	0.2 (4.0)	2.8 (3.9)	0.007
Fear of recurrence problems	36.1 (21.2)	38.3 (24.6)	0.67	0.2 (18.0)	11.4 (19.3)	0.02
Optimism	42.6 (9.0)	44.9 (10.0)	0.28	1.6 (7.9)	2.5 (7.5)	0.20
Spirituality	7.1 (2.5)	7.6 (1.9)	0.33	0.3 (1.8)	0.1 (1.2)	0.82
Emotional/information support	33.0 (6.4)	33.1 (7.1)	0.95	1.6 (5.0)	−0.1 (4.7)	0.09
Depression	14.2 (8.5)	13.3 (12.0)	0.71	4.0 (1.7)	7.2 (4.6)	0.04
State anxiety	40.4 (11.9)	35.3 (12.0)	0.05	6.4 (12.1)	7.8 (9.8)	0.17
Pain (SF-36)	48.9 (10.5)	49.1 (9.7)	0.92	1.3 (6.0)	3.3 (6.5)	0.30
Physical functioning (SF-36)	46.6 (9.6)	46.3 (9.4)	0.90	0.5 (5.9)	3.8 (5.5)	0.01
Energy (SF-36)	43.5 (11.4)	45.8 (11.8)	0.44	5.0 (9.4)	8.8 (10.5)	0.07
General health (SF-36)	48.9 (9.7)	50.3 (9.6)	0.51	1.6 (6.8)	2.5 (5.7)	0.38

^a Positive values for baseline to 6-week change represent improvement in psychological, emotional, and physical status. *p* values are based on the Wilcoxon Rank Sum test. Values presented are means and standard deviations (parentheses)

Table 2 Correlation coefficients between potential mediators and outcomes of interest (i.e. path “b”)

Potential mediator	Outcome measure (change from baseline to 6 weeks) (n = 82)					
	Perceived stress	Depression	State anxiety	Trait anxiety	SF-36 mental health	SF-36 physical health
Δ in fear of recurrence concerns	0.23*	0.22*	0.27*	0.28*	0.12	0.13
Δ in fear of recurrence problems	0.34**	0.17	0.34**	0.34**	0.18	0.11
Δ in depression	0.47***	–	0.50***	0.51***	0.49***	–0.07
Δ in physical functioning (SF-36)	0.43***	0.25*	0.26*	0.38***	0.01	0.54***
Δ in energy (SF-36)	0.45***	0.25*	0.16	0.23*	0.59***	0.27*

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Table 3 Estimates of indirect effects of potential mediating variables

Potential mediating path	Outcome measure (change from baseline to 6 weeks) ^a (n = 82)						
	Perceived stress	Depression	State anxiety	Trait anxiety	SF-36 mental health	SF-36 physical health	
MBSR → Δ in fear of recurrence concerns → outcome	1.73 (0.08)	0.78 (0.40)	1.67 (0.10)	0.68 (0.49)	1.00 (0.32)	0.03 (0.98)	
MBSR → Δ in fear of recurrence problems → outcome	2.12 (0.03)	1.00 (0.32)	2.03 (0.04)	1.59 (0.11)	1.59 (0.11)	0.40 (0.69)	
MBSR → Δ in depression → outcome	1.70 (0.09)	–	1.75 (0.08)	1.76 (0.08)	1.80 (0.07)	–1.43 (0.15)	
MBSR → Δ in physical functioning (SF-36) → outcome	2.27 (0.02)	1.08 (0.28)	1.26 (0.21)	1.98 (0.05)	0.49 (0.62)	–	
MBSR → Δ in energy (SF-36) → outcome	1.58 (0.11)	1.38 (0.17)	0.96 (0.34)	1.25 (0.21)	1.63 (0.10)	1.31 (0.19)	

^a Values presented are z-scores and p values (parentheses) based on the Sobel test

(reduction) in perceived stress (Fig. 3: right side: $p = 0.001$) irrespective of random assignment.

As seen in Fig. 4 (left side), women who experienced a greater reduction in fear of recurrence (i.e. at or above the median value of 2.5 units) experienced greater reduction in change in state anxiety ($p = 0.0009$). Similarly, women who experienced a greater improvement in physical functioning (i.e. at or above the median value of 2.1 units) experienced greater reduction in change in trait anxiety ($p = 0.002$). Again, even though women in the MBSR(BC) group were more likely to experience large (i.e. above the median) improvements in change in fear of recurrence and change in physical functioning, when women in the UC group experienced such changes, they also experienced improvements in state and trait anxiety.

In total, these results indicate that MBSR(BC) is associated with reduced fear of recurrence and improved physical functioning which, in turn, are associated with reduced perceived stress and state and trait anxiety. However, women in the UC group who experienced reduced fear of recurrence and improved physical functioning (e.g. by mechanisms other than MBSR(BC)) also experienced significantly reduced perceived stress and anxiety.

Discussion

Results from this study provide new insight into the mechanism of action of the MBSR(BC) intervention

among breast cancer survivors who are in transition off treatment. This is the first randomized clinical trial to examine fear of recurrence as a potential mediator (i.e. mechanism of action). The majority of research on fear of recurrence among breast cancer survivors has investigated the psychological consequences of fear of recurrence, rather than examining fear of recurrence as a mechanism of action for an intervention by which psychological and physical symptoms may be reduced. Importantly, fear of recurrence is highly prevalent in breast cancer survivors and is associated with considerable psychological distress influenced by both family-related and individual (e.g. treatment experience) concerns (Johnson Vickberg, 2001).

While we examined fear of recurrence as a principal mediator of the MBSR(BC) program, we considered other possible mechanisms (pathways). In aggregate, our results show that among breast cancer survivors who have recently completed treatment, MBSR(BC) leads to both reduced fear of recurrence and improved physical functioning which, in turn, favorably leads to lower levels of perceived stress and anxiety. These results may indicate that one of the mechanisms of how MBSR(BC) works is through the cognitive process of self-regulation of fear of recurrence to improve stress and anxiety and improve physical functioning.

In this realm, it also provides the rationale to examine other outcome measures potentially associated with MBSR(BC), such as measures of immune function (e.g. inflammatory markers) and chronic stress (e.g. telomeres).

Fig. 3 Baseline to 6-week changes in perceived stress by random assignment (MBSR (M) versus Usual Care (C)). The data are further stratified by baseline to 6-week change in fear of recurrence (potential mediator) using the median split of <2.5 units versus ≥ 2.5 units (left side of figure) and change in physical functioning (potential mediator) using the median split of <2.1 units versus ≥ 2.1 units (right side of figure). The shaded rectangles depict the interquartile range; the lower and upper ends of the vertical lines depict the 5th and 95th percentiles, respectively

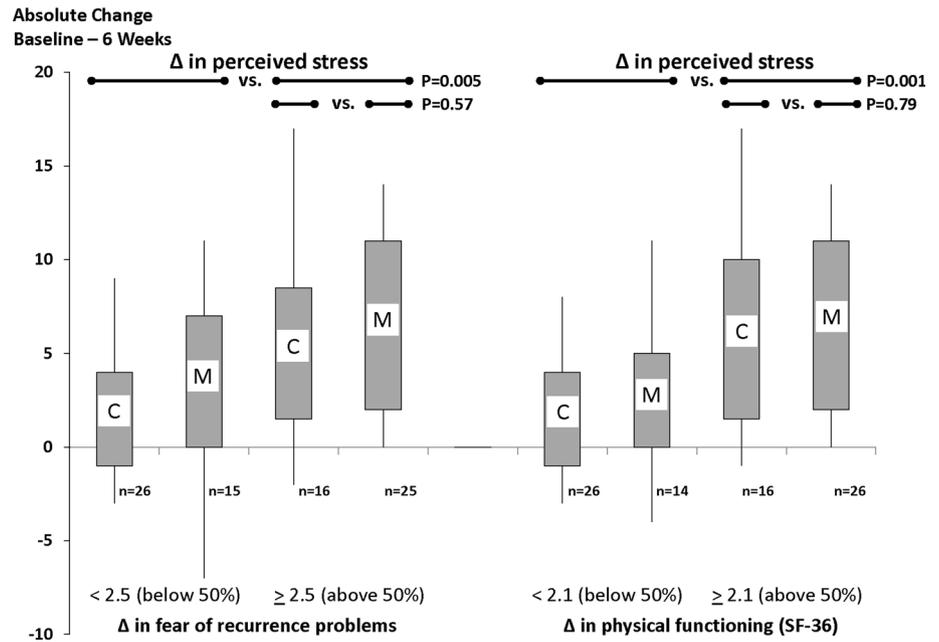
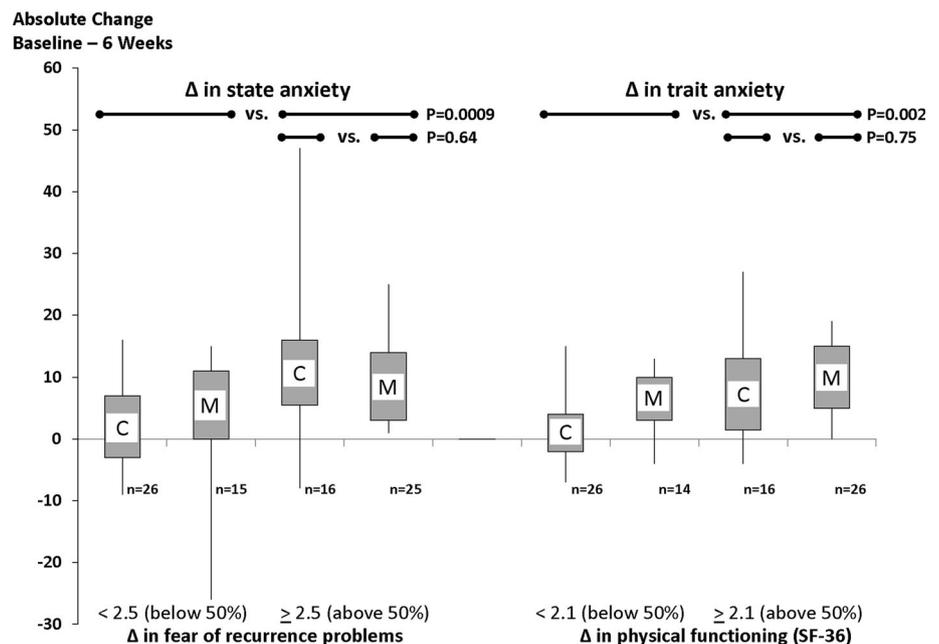


Fig. 4 Baseline to 6-week changes in state anxiety (left side) and trait anxiety (right side) by random assignment (MBSR (M) vs. Usual Care (C)). The data are further stratified by baseline to 6-week change in fear of recurrence (potential mediator) using the median split of <2.5 units versus ≥ 2.5 units (left side of figure) and change in physical functioning (potential mediator) using the median split of <2.1 units vs. ≥ 2.1 units (right side of figure). The shaded rectangles depict the interquartile range; the lower and upper ends of the vertical lines depict the 5th and 95th percentiles, respectively



Participants in the MBSR(BC) group experienced greater reduction in fear of recurrence concerns, fear of recurrence problems, and depression, as well as improved physical functioning and energy. Such findings of improved physical and psychological status are consistent with other studies among breast cancer patients (Lengacher et al., 2009). Since our study included a usual care group and a MBSR(BC) group, we were able to directly compare changes in measures of fear of recurrence and in turn, changes in measures of psychological symptoms (i.e. potential mechanisms of MBSR). To our knowledge, only

one other study has investigated the potential mechanism of MBSR (Nyklíček & Kuijpers, 2008). Participants were sixty males and females from a community in the Netherlands who were experiencing distress. Results showed that mindfulness mediated the positive effects on perceived stress and quality of life in the MBSR group, supporting a partial mediation effect of mindfulness (Nyklíček & Kuijpers, 2008). Our study did not include a direct measure of mindfulness—this precluded us from being able to directly examine mindfulness as a principal mediator of the MBSR(BC) program.

As anticipated, participants in the MBSR(BC) group were more likely than those in the usual care group to experience favorable reductions in fear of recurrence and improved physical functioning. Thus MBSR(BC) may be having a direct effect upon the antecedents that often trigger fear of recurrence, such as physical symptoms and reminders of cancer. Irrespective of random assignment, when participants experienced reductions in fear of recurrence and improved physical functioning, the net influence of these effects on reducing perceived stress and anxiety were similar. Thus, it appears that changes in fear of recurrence and physical functioning mediate changes in stress and anxiety regardless of whether one undergoes an MBSR program, and over time, breast cancer survivors may be expected to experience a general improvement in these mediators. Moreover, since the delivery of this MBSR(BC) program involved considerable time commitment, alternate delivery forms of the MBSR(BC) intervention should be a consideration along with other brief psychotherapy interventions tailored to reduce fear of recurrence for breast cancer survivors.

While fear of recurrence and physical functioning were the strongest mediating variables identified in our analysis, we also observed trends whereby MBSR(BC)-induced reductions in symptoms of depression and improvements in energy level appeared to mediate favorable improvements in both overall mental and physical health. The consistency of these findings provides evidence of clustering of multiple symptoms among breast cancer survivors. Future studies may wish to examine interventions designed to simultaneously reduce multiple (clusters) of symptoms, as opposed to conventional approaches aimed at single symptoms.

Limitations

A limitation of this study is that the sample included only early stage breast cancer survivors who had completed treatment; thus, findings may not generalize to advanced stage cancer patients or survivors of other types of cancer. In addition, as noted above, our study did not include a direct measure of mindfulness which, in concept, may be the principal mediator as to “how” the MBSR program works. Importantly, our study was limited to short-term effects of the MBSR(BC) program (i.e. 6 weeks). The extent to which the MBSR(BC) program at large, as well as initial MBSR-induced reductions in fear of recurrence and improvements in physical functioning impact long-term symptomatology and quality of life among breast cancer survivors is unknown. Finally, the symptoms reported at baseline were generally low for both groups, indicating a potential floor effect with little room for improvement. Therefore, the possibility exists that the effects of MBSR(BC) may be underestimated in the study and it is also possible that this

sample did not have sufficiently severe symptoms to test the full extent of the effects of MBSR(BC).

Conclusions

We found that among breast cancer survivors and compared to a usual care control regimen, MBSR(BC) resulted in significant reductions in fear of recurrence and improved physical functioning which, in term, mediated significant reductions in perceived stress and anxiety. Based on an established metric (RCI), the change in fear of recurrence influenced by MBSR(BC) appeared to be reliable and clinically relevant. However, despite the positive effects attributed to the MBSR(BC) program, when control participants experienced reductions in fear of recurrence and improved physical functioning (i.e. less often and through mechanisms other than MBSR(BC)), they too tended to experience reductions in perceived stress and anxiety. These findings reinforce the beneficial health effects of the MBSR(BC) program, and provide a rationale for development of other interventions that aim specifically to reduce fear of recurrence and improve physical functioning after completion of treatment for breast cancer.

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Conflict of interest The authors have no conflicts to report.

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