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Mindfulness meditation for younger breast cancer survivors: A randomized controlled trial

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Abstract

Purpose—Premenopausal women diagnosed with breast cancer are at risk for psychological and behavioral disturbances after cancer treatment. Targeted interventions are needed to address the needs of this vulnerable group.

Methods—This randomized trial provided the first evaluation of a brief mindfulness-based intervention for younger breast cancer survivors designed to reduce stress, depression, and inflammatory activity. Women diagnosed with early-stage breast cancer before age 50 who had completed cancer treatment were randomly assigned to a 6-week Mindful Awareness Practices (MAPS) intervention (n = 39) or wait-list control (n = 32). Participants completed questionnaires at pre- and post-intervention to assess stress and depressive symptoms (primary outcomes) as well as physical symptoms, cancer-related distress, and positive outcomes. Blood samples were collected to examine genomic and circulating markers of inflammation. Participants also completed questionnaires at a three-month follow-up.

Results—In linear mixed models, the MAPS intervention led to significant reductions in perceived stress (P = .004) and marginal reductions in depressive symptoms (P = .094), as well as significant reductions in pro-inflammatory gene expression (P = .009) and inflammatory signaling (P = .001) at post-intervention. Improvements in secondary outcomes included reduced fatigue, sleep disturbance, and vasomotor symptoms and increased peace and meaning and positive affect (Ps < .05). Intervention effects on psychological and behavioral measures were not maintained at

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three-month follow-up, though reductions in cancer-related distress were observed at this assessment.

Conclusions—A brief mindfulness-based intervention showed preliminary short-term efficacy in reducing stress, behavioral symptoms, and pro-inflammatory signaling in younger breast cancer survivors.

BACKGROUND

Breast cancer is the most common cancer in women and the leading cause of death in women under 55 years of age. Approximately 25% of breast cancer cases occur premenopausally.[1] The management of younger women presents many challenges, as the diagnosis often comes at a time when women are in the midst of child-rearing and career development and feel “too young” to be confronting a life-threatening illness. In empirical studies, younger women report increased psychological stress and depression, fatigue, sleep disturbance, and vasomotor symptoms after cancer diagnosis relative to older women.[2–5] Further, younger women perceive cancer as more threatening[6] and report greater fear of recurrence.[7]

Despite their high levels of distress, very few interventions have been developed for younger breast cancer survivors. Indeed, we identified only two nonpharmacologic randomized controlled trials focusing on younger women.[8, 9] Thus, interventions are required that specifically address the emotional and physical needs of this vulnerable group. This is particularly important as younger survivors report feeling more isolated and less satisfied with traditional support groups due to their age.[10] Mindfulness meditation has emerged as a promising intervention for cancer populations[11–13] and may be a particularly good option for younger survivors given their interest in mind-body treatments.[14] Mindfulness involves bring attention to one’s present moment experiences, including thoughts, feelings, and physical sensations, with openness, curiosity, and acceptance.[15] Interventions have been developed to cultivate mindfulness through formal meditation and informal practice, and randomized controlled trials have documented benefits of mindfulness-based interventions among breast cancer survivors, including improvements in depressive symptoms, stress, and fatigue.[16–20] However, the feasibility and efficacy of mindfulness interventions specifically for younger women have not been examined.

In addition, the effects of mindfulness on key biological and psychological processes relevant for breast cancer survivorship are unclear. These include inflammation, which is involved in cancer growth and progression[21] and may also contribute to behavioral problems in breast cancer survivors[22]. Inflammatory processes are regulated in part by signals from the central nervous system, including stress hormones[23], and individuals who report higher levels of stress and depression also show elevations in inflammatory activity.[24, 25] Thus, interventions that reduce stress could potentially lead to reductions in inflammation. There is preliminary evidence from non-randomized trials that mindfulness may have beneficial effects on pro-inflammatory cytokine production in cancer patients.[26] However, these effects have not been evaluated in a randomized trial, nor have effects of mindfulness on the molecular processes that regulate cytokine production been examined. Further, very few trials have examined effects of mindfulness on positive psychological outcomes, such as

positive affect and meaning/purpose in life, although these are increasingly recognized as important dimensions of quality of life in cancer survivorship.[27]

This randomized controlled trial was designed to evaluate the feasibility and efficacy of a mindfulness-based intervention for women who had been diagnosed with breast cancer at or before age 50. The primary outcomes were perceived stress and depressive symptoms, which are elevated in younger breast cancer survivors and are targeted by this treatment. Effects on inflammatory activity were also assessed, focusing on pro-inflammatory gene expression and associated transcription factors. We also explored effects on secondary outcomes that are known to be concerns for younger survivors and are relevant for quality of life, including behavioral symptoms, cancer-related distress, and positive psychological processes.

METHODS

Design

This was a single-center, two-armed RCT which took place at the UCLA Medical Center, Los Angeles, CA between March 2011 and October 2012. The UCLA Institutional Review Board approved study procedures, and written informed consent was obtained from participants. The ClinicalTrials.gov Identifier is NCT01558258.

Participants

Participants were recruited through invitations to women enrolled in an earlier study,[28] physician referrals, and Internet recruitment. Interested women completed a telephone screening to determine eligibility. Inclusion criteria were: 1) diagnosed with Stage 0 – III breast cancer at or before age 50; and 2) completed local and/or adjuvant cancer therapy (except hormonal therapy) at least 3 months previously. We included women up to 10 years after cancer treatment, as the need for and benefits from stress management are not time-limited. Exclusion criteria were: 1) breast cancer recurrence, metastasis, or another cancer diagnosis (excluding non-melanoma skin cancer); 2) active, uncontrolled medical illness that could impact inflammation; and 3) unable to commit to intervention schedule.

Randomization

Given class scheduling considerations, participants were randomized in blocks. Once a sufficient number of participants to comprise the mindfulness and control groups (8–14 women) had been screened as eligible and completed the baseline assessment, they were randomized (4:3) to the intervention and wait-list control group, with slightly more allocated to the intervention to maintain adequate group size. Randomized condition assignments were kept in sealed envelopes in the research office, following CONSORT guidelines.

Assessments

In-person assessments were conducted before and within 1–2 weeks after the intervention. At each assessment, participants completed questionnaires and provided fasting blood samples at morning appointments. The post-treatment assessment was the primary endpoint

of the trial. A follow-up questionnaire packet was mailed to participants at three months post-intervention to assess persistence of treatment effects.

Intervention

The intervention was based on the Mindful Awareness Practices (MAPs) program at UCLA (http://marc.ucla.edu) and tailored for younger survivors by including information about maintaining health and preventing breast cancer recurrence. Participants met for 6 weekly, 2 hour group sessions that included presentation of theoretical materials on mindfulness, relaxation, and the mind-body connection; experiential practice of meditation and gentle movement exercises (e.g., mindful walking); and a psycho-educational component for cancer survivors. Lecture, discussion, and group process focused on solving problems concerning impediments to effective practice, working with difficult thoughts and emotions, managing pain, and cultivation of loving kindness. Home practice is a key component of MAPs and participants were instructed to practice mindfulness techniques on a daily basis, beginning with 5 minutes per day and increasing to 20 minutes per day. In the final class, participants were encouraged to continue practicing, both formally and informally, and given instructions for doing so.

The wait-list condition controlled for naturally occurring changes in stress and other outcomes over the assessment period. After the 3-month follow-ups were completed, those assigned to the control group were offered participation in the MAPs classes.

Psychological and behavioral outcomes

The primary psychological outcomes were perceived stress[29] and depressive symptoms.[30] Secondary outcomes included fatigue,[31] sleep quality,[32] musculoskeletal pain,[33] and menopausal symptoms.[33] Cancer-specific distress was assessed using measures of fear of cancer recurrence[34] and cancer-related intrusive thoughts.[35] Positive psychological outcomes included positive affect[36] and meaning and purpose in life[37]. All were assessed at baseline, post-intervention, and 3-month follow-up.

Self-reported demographic and disease-related variables were assessed at baseline. To assess home practice, participants in the mindfulness condition completed daily reports of the number of minutes they engaged in formal mindfulness practice each day over the 6-week intervention period. At the 3-month follow-up, they were asked to indicate how many days they had meditated for at least 5 minutes in the past week.

Inflammatory outcomes

The primary biological outcomes were functional genomic markers of inflammation, which may be more sensitive to intervention effects than “noisier” circulating markers.[38] Genomic outcomes were: 1) expression of a set of 19 pro-inflammatory gene transcripts previously found to be up-regulated in the context of chronic stress,[23] and 2) promoter-based bioinformatics measures of the activity of the pro-inflammatory transcription factor NF-κB, a key regulator of pro-inflammatory cytokine production. Secondary bioinformatics analyses also assessed activity of three other a priori-selected inflammation-related transcription factors: the anti-inflammatory glucocorticoid receptor (GR), CREB family factors, and Type

I interferon response factors. RNA was extracted (Qiagen RNEasy) from peripheral blood mononuclear cells isolated from 10 ml venipuncture samples collected into sodium heparin Vacutainers, tested for suitable mass (Nanodrop ND1000) and integrity (Agilent Bioanalyzer), and subject to genome-wide transcriptional profiling using Illumina HT-12 v4 BeadArrays in the UCLA Neuroscience Genomics Core following the manufacturer's standard protocol (Illumina Inc). Quantile-normalized gene expression values were log2-tranformed before analysis.

Circulating markers of inflammation were also assessed, including IL-6, C reactive protein (CRP), and the soluble TNF receptor type II (a marker of TNF activity), which have been linked to the psychological and behavioral outcomes of interest[39] and to breast cancer progression[40] and may be influenced by mind-body interventions.[38, 41] Blood samples for circulating markers were collected by venipuncture into EDTA tubes, placed on ice, centrifuged for acquisition of plasma, and stored at −80°C for subsequent batch testing. Plasma levels of IL-6 and CRP were determined by high sensitivity ELISA (R&D Systems for IL-6; Immundiagnostik, ALPCO Immunoassays for CRP) and levels of sTNF-RII by regular ELISA (R&D systems), as previously described.[42] All samples were run in duplicate, and samples for an individual participant were run in parallel to avoid inter-assay variability. Inflammatory markers were log transformed before analysis to normalize distributions, and one outlier for CRP was removed from analysis (CRP = 50 μg/L).

Statistical analyses

Specifying alpha of 0.05 and assuming 85% retention, we estimated that sample sizes of 40 and 30 in the intervention and control arms, respectively, would provide 80% power to detect a standardized effect size of 0.6, the expected effect size based on results of other mindfulness-based trials in cancer populations.[11]

Primary analyses were intent-to-treat, conducted using linear mixed effects models to allow inclusion of all available data. The model included group assignment (mindfulness, wait list), time (baseline, post-intervention, and 3 month follow-up for questionnaire-based outcomes) with control covariates as fixed effects and a random intercept for participant. Genomic analyses also included standard RNA indicators of major leukocyte subset prevalence (*CD3D*, *CD3E*, *CD4*, *CD8A*, *CD19*, *NCAM1*/CD56, *FCGR3A*/CD16, *CD14*) as covariates. The Group x Time interaction at post-intervention was the primary effect of interest. Analyses were conducted using SAS 9.1 and Stata 12.

Group differences in transcription factor activity were assessed using TELiS promoter-based bioinformatics analyses, where the ratio of response element frequencies in the promoters of up- vs. down-regulated genes was taken as a measure of differential activity of transcription control pathways, and (log) ratios were averaged over 9 different parametric combinations of promoter length (−300, −600, and −1000 to +200 bp upstream of RefSeq-designated transcription start site) and motif detection stringency (TRANSFAC mat_sim values of .80, .90, and .95) to ensure robust results.[43] To identify the primary cellular sources of differentially expressed genes, we conducted Transcript Origin Analysis (TOA).[44] Both TELiS and TOA were based on genes showing > 1.2-fold differential change in expression over time in mindfulness vs. control.

Exploratory analyses evaluated the dose-response relationship between mindfulness practice and changes in the primary psychological outcomes and circulating inflammatory markers among intervention group participants. Linear regression models tested whether number of minutes practiced (including class time and home practice) was associated with post-intervention values on the outcome of interest, controlling for baseline levels of that outcome.

RESULTS

We screened 151 women for eligibility and randomized 71 to either the intervention (n = 39) or wait-list control group (n = 32); see Figure 1. All completed baseline questionnaires, though blood samples were not obtained from six women at baseline due to difficulties with venipuncture. Sixty-five participants completed the post-treatment questionnaire, yielding a follow-up rate of 92% at the primary endpoint. Fifty-nine participants (83%) completed the 3-month follow-up. Groups were comparable at baseline on most demographic and disease-related variables (Table 1). Women in the intervention group were less likely to be married and more likely to have received radiation and/or have a history of smoking than women in the control group (*P*s ≤ .10). The control group also reported higher depressive symptoms (see Table 2). These variables were included as covariates in all analyses, with the exception of analyses with CES-D as the outcome variable, which already included all CES-D measurements as dependent variables. Across groups, the percentage of women who endorsed clinically significant depressive symptoms (as indicated by scores ≥ on the CES-D) was 48%.

Among the 38 women who received the mindfulness intervention (defined as attending 2 or more classes), the mean number of classes attended was 5.24 (range = 2–6) and the total number of minutes of mindfulness practice during the 6-week intervention period (including time spent in the mindfulness classes and home practice) was 897 minutes (range = 305–1527). At the 3 month follow-up, 8 of the 31 respondents (25%) indicated that they had not meditated, 7 (23%) indicated that they had meditated on 1–2 days, 9 (29%) indicated that they had meditated on 3–4 days, and 7 (23%) indicated that they had meditated on 5–7 days in the past week.

Intervention effects at post-intervention

Adjusted means for psychological and behavioral outcomes are shown in Table 2. The mindfulness intervention led to significant reductions in perceived stress from pre- to post-intervention relative to wait-list control (*P* = .004 for Group x Time interaction; see Figure 2). A similar trend was observed for depressive symptoms (*P* = .095). The effect sizes for change in perceived stress and depression were 0.67 and 0.54, respectively. Similar *p* values emerged from analyses that adjusted for multiplicity using the Hommel procedure (*P* = .008 for perceived stress; *P* = .095). In terms of secondary outcomes, mindfulness led to significant improvements in fatigue (*P* = .007), subjective sleep disturbance (*P* = .015), and hot flashes/night sweats (*P* = .015) from pre- to post-intervention. Mindfulness also led to significant increases in positive affect (*P* = .03) and peace and meaning (*P* = .001). Effects on other self-report outcomes were not significant. Analyses controlling for additional

covariates, including time since diagnosis, chemotherapy, and endocrine therapy, yielded comparable results.

In genome-wide transcriptional profiling of PBMC samples, primary analyses of a 19-transcript composite of pro-inflammatory genes showed a significantly greater decline from baseline to post-intervention in the mindfulness group vs. controls (P = .009 for Group x Time interaction; see Figure 3A). Across all transcripts assayed, 24 genes showed >1.2-fold greater up-regulation over time in the mindfulness group vs. controls and 42 genes showed >1.2-fold greater down-regulation (individual genes listed in Supplementary Data File 1). TELiS promoter-based bioinformatics analyses implicated reduced activity of the pro-inflammatory transcription factor NF-κB (P = .0016) and increased activity of the anti-inflammatory GR (P = .018) in structuring these empirical differences in gene expression (Figure 3B). Results also indicated increased activity of transcription factors involved in Type I interferon signaling (P = .007) and a non-significant reduction in activity of CREB family transcription factors (P = .143). Parallel Transcript Origin Analyses identified monocytes and plasmacytoid dendritic cells as the primary cellular context for down-regulated genes and B lymphocytes as the primary cellular context for up-regulated genes (all P < .01; Figure 3C). Similar results emerged in analyses that additionally controlled for age, body mass index, chemotherapy, endocrine therapy, white/non race, and years post-diagnosis. The sole exception was the indicated reduction in GR signaling activity, which failed to reach statistical significance in the additionally-adjusted analyses (p = .766).

There were no significant intervention effects for CRP, IL-6, or sTNF-RII (all P > .20). Adjusted means for circulating inflammatory markers are shown in Table 3.

Intervention effects at 3-month follow-up

Secondary analyses examined intervention effects at the 3-month follow-up (Table 2). There were no group differences in change from baseline to 3-month follow-up for perceived stress or depressive symptoms (see Figure 2). Similarly, there was no group difference in change from baseline to 3-month follow-up for physical symptoms or positive affect. However, there was a significant group difference for fear of recurrence (P = .048 for Group x Time interaction) and cancer-related intrusive thoughts (P = .002), with the mindfulness group showing significantly greater decreases in these outcomes at 3 month follow-up than controls. The mindfulness group also showed marginally greater increases in peace and meaning at the 3-month follow-up (P = .069).

Mindfulness practice as a predictor of primary outcomes

Exploratory analyses showed that intervention group participants who practiced mindfulness more frequently (including attending classes and home practice) had lower levels of IL-6 at post-intervention, controlling for baseline IL-6 (P = .025). Minutes of practice were not associated with stress, depressive symptoms, or other inflammatory markers (Ps > .05).

DISCUSSION

This trial sought to determine the feasibility and efficacy of a brief mindfulness intervention on psychological, behavioral, and biological outcomes among breast cancer survivors

diagnosed at or before age 50. There was excellent adherence to the intervention, with a class attendance rate of 87%. Relative to wait-list control, the 6-week intervention led to significant improvements in perceived stress and a trend towards improvement in depressive symptoms, both of which were high in this group. In addition, the intervention led to improvements in fatigue, sleep disturbance, menopausal symptoms, and positive psychological processes. Mindfulness also led to significant reductions in pro-inflammatory gene expression and bioinformatic indications of pro-inflammatory signaling. Although the intervention did not result in changes in plasma markers of inflammation, women in the mindfulness group who practiced more frequently did evidence lower levels of IL-6 at post-treatment.

Previous RCTs of mindfulness for breast cancer survivors have shown improvements in stress,[18] depression,[16–18, 20] and physical symptoms.[45] Our results add to this growing literature and demonstrate that mindfulness also has beneficial effects on psychological and behavioral outcomes in younger breast cancer survivors. Further, our trial indicates that the benefits of mindfulness may extend to genomic markers of inflammation, including reductions in pro-inflammatory gene expression and activity of the pro-inflammatory transcription factor NF-κB. To our knowledge, this is the first trial to demonstrate effects of mindfulness on inflammatory gene expression in cancer patients. Effects of mindfulness on circulating markers of inflammation may be more difficult to detect, as previous trials in non-cancer populations have found only marginally significant decreases in these markers[38, 46] or have observed effects only among individuals who practiced more frequently,[47] similar to our findings.

Although acute effects of mindfulness on stress, depressive symptoms, and other outcomes have been demonstrated in cancer populations, the persistence of these effects in the weeks and months post-intervention is less clear. Several trials of mindfulness-based stress reduction (MBSR) for cancer survivors reported significant effects on depressive symptoms at post-intervention but *not* at follow-up assessments conducted between one and 24 months after the intervention,[19, 20, 48] consistent with our results. One recent trial conducted with a relatively large sample of 336 breast cancer survivors did find beneficial effects of MBSR on depressive symptoms that persisted over a 12 month follow-up period.[16] Sustained effects have also been observed on other outcomes, including spirituality.[19] It is unclear why participants in our study did not sustain the improvements in stress, depression, and other symptoms seen at post-treatment, though they did show improvements in cancer-specific distress at the follow-up assessment. It is possible that these women may require more support to continue their mindfulness practice and maintain its benefits, particularly given their high baseline levels of stress and depression. In general, the impact of mindfulness on different dimensions of well-being and the persistence of those effects is an important topic for future research. The maintenance of intervention effects is particularly relevant for younger women with early-stage breast cancer, as they can expect to survive for several decades after diagnosis and cancer treatment.

Limitations of this study include the relatively small sample, which limits statistical power to discover statistically significant associations between the intervention and the expression of any given gene transcript. The sets of differentially expressed genes reported here serve

only as inputs into higher-order gene set-based bioinformatics analyses testing a limited number of a priori hypotheses regarding shared transcription factor promoter motifs (i.e., inflammation-related NF-κB, GR, and CREB) and shared cellular origin (i.e., pro-inflammatory monocytes) as documented in previous gene expression reference studies. It will be important to replicate these findings in a larger trial, and to determine whether effects are generalizable to diverse groups of younger breast cancer survivors. In addition, the use of a wait-list control group does not control for non-specific effects of the intervention, and it is possible that intervention effects may simply have been due to attention. Future studies should compare mindfulness to an active control condition and include a longer-term follow-up to determine persistence of effects on psychological and biological outcomes.

Women diagnosed with premenopausal breast cancer are in need of strategies to help them manage elevated levels of stress, distress, and physical symptoms over a potentially long survivorship period. Results from this trial suggest that a brief mindfulness intervention may offer short-term benefit for these women and lead to improvements in psychological, behavioral, and biological outcomes. If these effects can be maintained over time, there is potential benefit for improving cancer survivorship.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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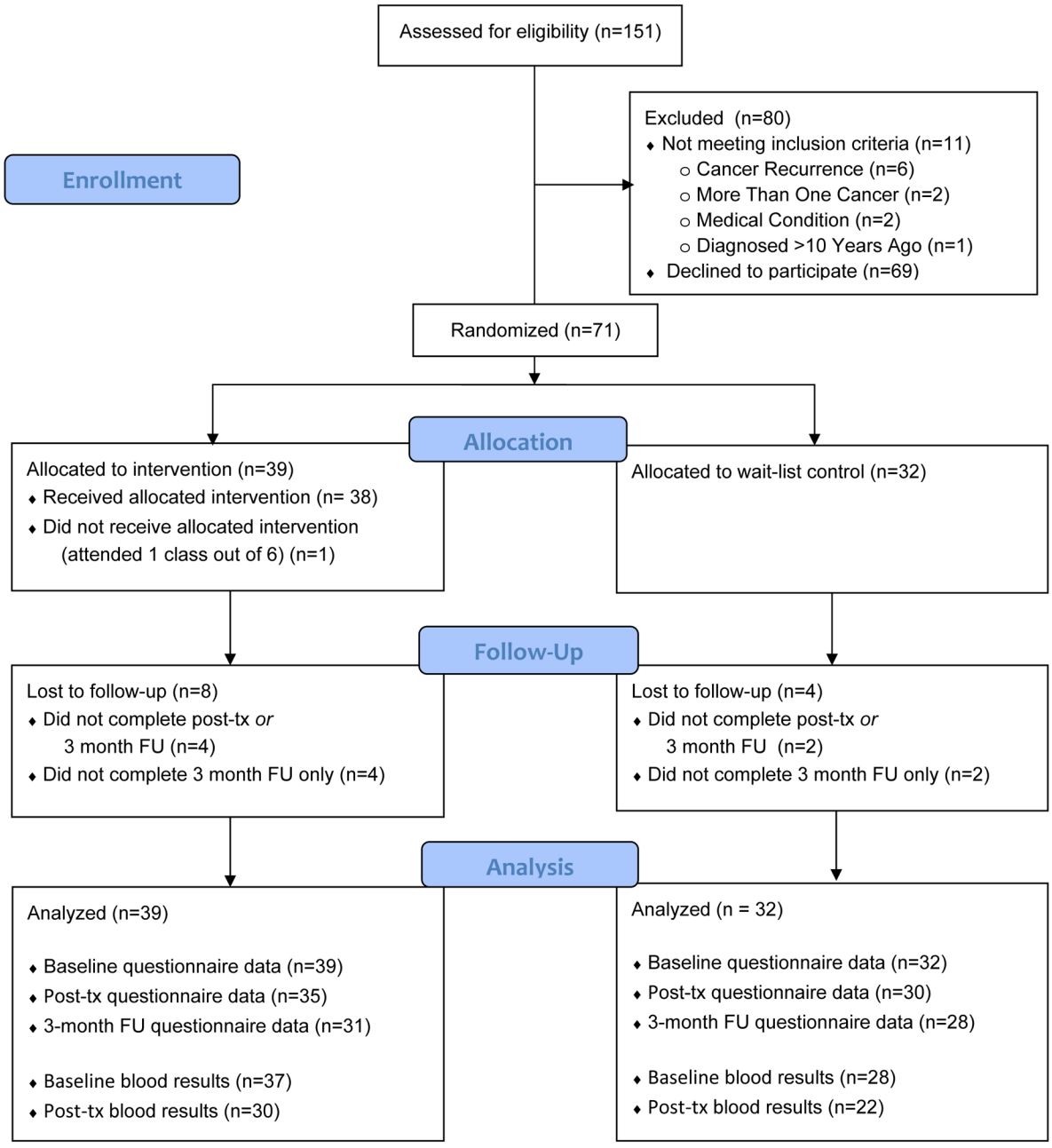

Figure 1.
CONSORT diagram

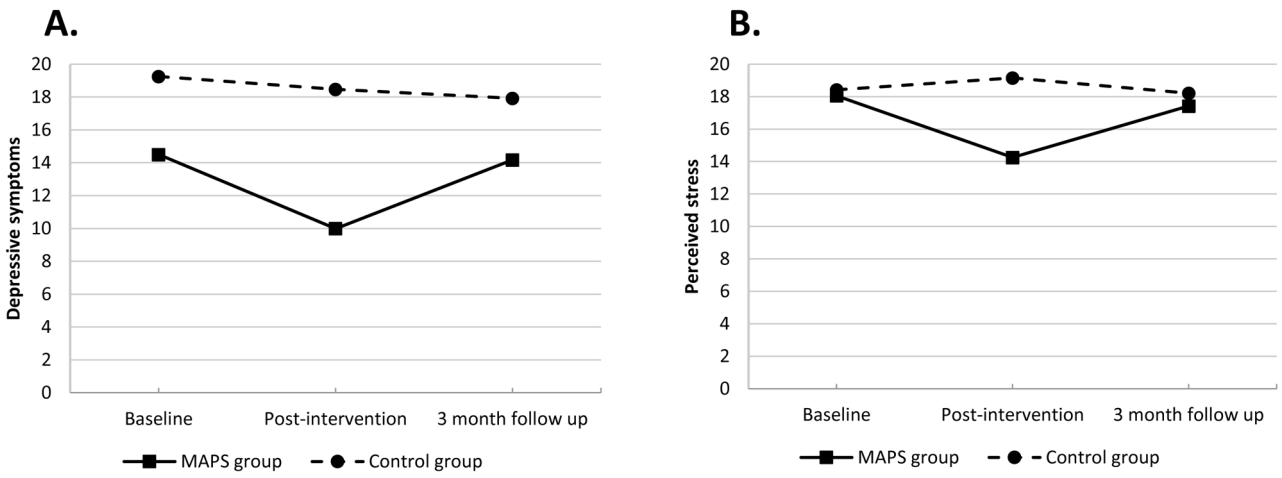

Figure 2.

Adjusted means for perceived stress (A) and depressive symptoms (B) in the intervention group and controls. Linear mixed regression analyses revealed significant reductions in stress and marginally significant reductions in depressive symptoms in the MAPS group vs. controls from baseline to post-intervention. These effects were not maintained at the three-month follow-up.

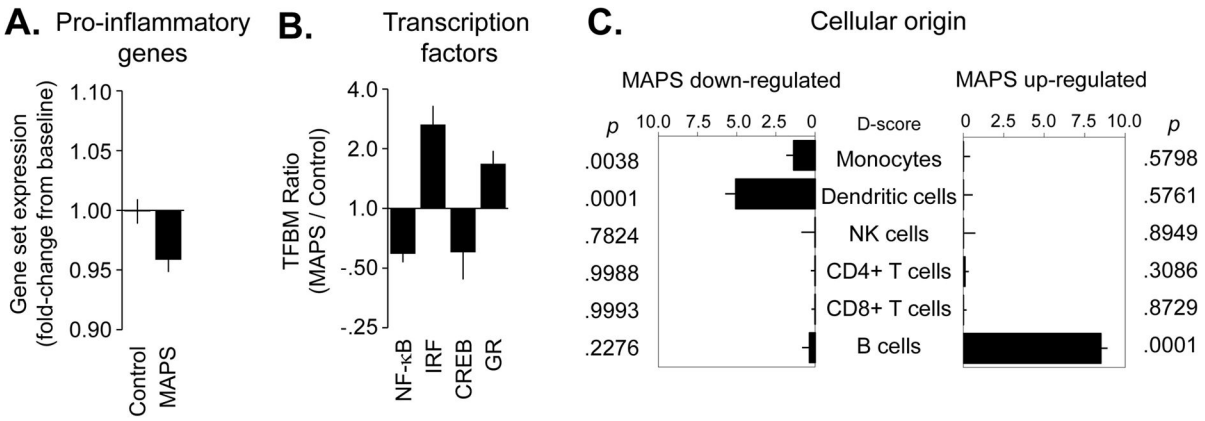

Figure 3.

(A) Transcriptional profiling of PBMC samples showed a significantly greater decline in a 19-transcript composite of pro-inflammatory genes in the MAPS group vs. controls. (B) Bioinformatics analysis of transcription factor activity indicated reduced activity of the pro-inflammatory transcription factor NF-κB and increased activity of the anti-inflammatory glucocorticoid receptor (GR) in the MAPS group vs. controls. Analyses also indicated increased activity of interferon-related transcription factors (IRF) but no significant difference in CREB activity. (C) Transcript origin analyses identified genes down-regulated in intervention participants as originating primarily from monocytes and dendritic cells, and up-regulated genes as originating predominately from B lymphocytes.

Table 1

Demographic and Clinical Characteristics of Study Participants

Characteristic	MAPS (n=39)	Control (n=32)
Age, mean (range)	46.1 (28.4–60)	47.7 (31.1–59.6)
Years since diagnosis, mean (SD)	4.0 (2.4)	4.1 (2.3)
Ethnicity, #		
White	29	25
African-American	1	1
Asian	3	5
Other	6	1
Married, %*	56	75
Education, %		
Less than college	13	22
College graduate	23	25
Post-college	64	53
Employed full- or part-time, %	80	63
Income >$100K, %	62	58
Received chemotherapy, %	77	69
Received herceptin, %	21	31
Received radiation, %*	77	56
Currently on endocrine therapy, %	62	66
Smoking, %		
Ever smoked*	28	53
Currently smoke	5	13

*Chance imbalance between groups, as indicated by $p < .10$ on chi-square or two-sample t-test.

Table 2

Adjusted means and results for psychological and behavioral outcomes

	Baseline (n=71)		Post-intervention (n=65)			3 month follow-up (n=59)		
Outcome	**MAPS**	**Control**	**MAPS**	**Control**	**p value[a]**	**MAPS**	**Control**	**p value[b]**
Primary outcomes								
Perceived stress (PSS)	18.05 (.99)	18.42 (1.12)	14.25 (1.04)	19.15 (1.14)	**0.004**	17.42 (1.09)	18.21 (1.16)	0.796
Depressive symptoms (CESD)	14.50 (1.58)	19.25 (1.75)	9.99 (1.64)	18.47 (1.80)	0.095	14.17 (1.70)	17.92 (1.82)	0.664
Secondary outcomes								
Fatigue (FSI)	4.18 (.24)	3.56 (.26)	3.61 (.25)	4.08 (.27)	**0.007**	4.15 (.26)	3.30 (.27)	0.572
Sleep quality (PSQI)	8.13 (.62)	8.39 (.70)	6.48 (.65)	8.70 (.71)	**0.015**	7.27 (.67)	7.86 (.72)	0.647
Pain (BCPT)	1.31 (.17)	1.56 (.19)	1.27 (.17)	1.37 (.19)	0.444	1.17 (.18)	1.38 (.19)	0.881
Hot flashes (BCPT)	1.24 (.19)	1.31 (.22)	0.94 (.20)	1.53 (.22)	**0.015**	1.20 (.20)	1.22 (.22)	0.827
Fear of recurrence (QLACS)	11.61 (.86)	10.68 (.94)	9.67 (.88)	10.42 (.96)	0.128	8.94 (.91)	10.26 (.97)	**0.048**
Intrusive thoughts (IES)	1.59 (.17)	1.39 (.19)	1.34 (.18)	1.34 (.20)	0.385	1.12 (.18)	1.67 (.20)	**0.002**
Positive affect (PANAS-PA)	29.60 (1.03)	31.65 (1.15)	31.99 (1.08)	30.50 (1.18)	**0.033**	29.94 (1.13)	31.99 (1.20)	0.996
Meaning & peace (FACIT)	16.86 (.60)	17.95 (.67)	18.43 (.63)	16.53 (.69)	**0.001**	18.26 (.65)	17.65 (.70)	0.069

[a] P value for group x time interaction testing group difference in baseline to post-intervention means.

[b] P value for group x time interaction testing group difference in baseline to 3 month follow-up means.

Adjusted for marital status, radiation therapy (yes/no), history of smoking (yes/no), and baseline CES-D.

Table 3

Adjusted means and results for circulating inflammatory markers

	Baseline (n=65)		Post-intervention (n=52)		
Outcome	**MAPS**	**Control**	**MAPS**	**Control**	**P value[a]**
CRP (μg/L)	1.24 (1.70)	1.45 (1.81)	1.22 (1.66)	1.32 (1.75)	.415
IL-6 (pg/ml)	1.24 (.87)	1.16 (.58)	1.19 (.67)	1.32 (.63)	.158
sTNFRII (pg/ml)	2342.8 (503)	2335.5 (1244)	2209.3 (461)	2211.2 (1042)	.857

[a] P value for group by time interaction testing group difference in baseline to post-intervention means.

Adjusted for marital status, radiation therapy (yes/no) history of smoking (yes/no), baseline CES-D, body mass index, and age.

Note that log-transformed values were used in analyses.