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Randomized, Controlled Trial of Yoga in Women With Breast Cancer Undergoing Radiotherapy

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A B S T R A C T

Purpose
Previous research incorporating yoga (YG) into radiotherapy (XRT) for women with breast cancer finds improved quality of life (QOL). However, shortcomings in this research limit the findings.

Patients and Methods
Patients with stages 0 to III breast cancer were recruited before starting XRT and were randomly assigned to YG (n = 53) or stretching (ST; n = 56) three times a week for 6 weeks during XRT or waitlist (WL; n = 54) control. Self-report measures of QOL (Medical Outcomes Study 36-item short-form survey; primary outcomes), fatigue, depression, and sleep quality, and five saliva samples per day for 3 consecutive days were collected at baseline, end of treatment, and 1, 3, and 6 months later.

Results
The YG group had significantly greater increases in physical component scale scores compared with the WL group at 1 and 3 months after XRT ($P = .01$ and $P = .01$). At 1, 3, and 6 months, the YG group had greater increases in physical functioning compared with both ST and WL groups ($P < .05$), with ST and WL differences at only 3 months ($P < .02$). The group differences were similar for general health reports. By the end of XRT, the YG and ST groups also had a reduction in fatigue ($P < .05$). There were no group differences for mental health and sleep quality. Cortisol slope was steepest for the YG group compared with the ST and WL groups at the end ($P = .023$ and $P = .008$) and 1 month after XRT ($P = .05$ and $P = .04$).

Conclusion
YG improved QOL and physiological changes associated with XRT beyond the benefits of simple ST exercises, and these benefits appear to have long-term durability.

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INTRODUCTION

Radiotherapy (XRT) is often the final step in the multimodal treatment regimen for women with breast cancer. Patients often experience treatment-related adverse effects (fatigue, pain, lymphedema, neuropathy, cardiotoxicity, sleep disturbances, and cognitive problems) that negatively affect physical, psychological, social, and spiritual aspects of quality of life (QOL)[1,2] and may create negative health consequences.[3]

Research on yoga (YG) in patients with cancer has increased considerably in the last decade, and a variety of YG programs studied in cancer have reported improvements in stress and QOL,[4] fatigue and emotional health,[5,6] pain, vitality, and QOL,[7] positive affect,[5] joint pain, fatigue, and sleep distur-

bance,[8,9] and fatigue in women with metastatic breast cancer[10] and obese breast cancer survivors.[11] Studies of a Patanjali-based integrated YG program for patients with breast cancer developed by the Vivekananda Yoga Anusandhana Samsthana (VYASA) have consistently reported improvement in anxiety, symptom severity, and distress,[12-14] nausea and vomiting,[15] and affect and global QOL[14] as well as beneficial effects on natural-killer cell counts[16] and radiation-induced DNA damage.[13]

Previous YG research has a number of limitations, including small sample size (ranging from 18 to 168); absence of objective outcome measures; lack of active control groups; and lack of long-term follow-up after the end of the YG program. One objective measure of interest is cortisol rhythm. Studies have revealed that both elevated levels of

cortisol and a blunted, less steep, diurnal cortisol slope are associated with worse survival in women with breast cancer.[17,18] Vadiraja et al[14] also reported significantly reduced morning and overall mean cortisol levels in patients with breast cancer participating in a YG program.

We previously reported that participation in the VYASA YG program two times a week for patients with breast cancer undergoing XRT resulted in significantly better general health perception (GH) and physical functioning (PF) scores at the end of XRT and greater benefit finding 3 months after XRT than in women in a waitlist (WL) control group.[19] This study tested the hypotheses that participation in YG three times a week during XRT would have long-term effects on physical and mental health (MH) aspects of QOL (primary outcomes), fatigue, depression, and sleep disturbances and result in steeper cortisol slope (secondary outcomes) relative to an active stretching (ST) or WL control groups.

PATIENTS AND METHODS

Patients

Women with stages 0 to III breast cancer were recruited before XRT. Inclusion criteria were ≥ 18 years old; ability to read, write, and speak English; and scheduled to undergo daily adjuvant XRT for 6 weeks at MD Anderson Cancer Center. Patients with lymphedema; metastatic bone disease; deep vein thrombosis; documented diagnosis of a formal thought disorder (eg, schizophrenia); extreme mobility problems; or who had practiced YG in the year before diagnosis were excluded. The protocol was approved by the institutional review board.

Randomization and Schedule

Eligible patients were identified through an institutional database or by referring physicians and were approached at their simulation appointment. After giving written informed consent, participants completed a baseline assessment including self-report measures and provided saliva samples to assess diurnal cortisol rhythm. Blood samples for future assays, an actigraphy watch (worn 24 hours a day for 7 days to assess sleep quality), and questionnaires assessing plausible mediators were also collected and will be reported in a subsequent article. Participants were then randomly assigned to one of three groups: 1) YG; 2) ST; or WL control by using a form of adaptive randomization,[20] according to age, stage of disease, time since diagnosis, type of surgery, and chemotherapy (neoadjuvant or adjuvant). Follow-up assessments were conducted during the last week of treatment and 1, 3, and 6 months later. Participants were given a gift certificate ($20 value) after each assessment completion. Participants in the WL group received usual care, completed all assessments on the same timeline as the active groups, and were offered YG or ST classes at the end of their study participation. All participants were asked to refrain from participating in any other YG classes while on study.

Intervention Programs

Participants in the YG and ST groups attended up to three 60-minute classes per week during their 6 weeks of XRT. Classes were held near the radiation treatment center in large conference-style rooms dedicated to behavioral research. Classes were offered to accommodate participants' schedules, most often being given in a one-on-one just before or after XRT. Each participant received an audio CD and a written manual of the program to encourage at-home practice. Compliance was determined weekly during XRT and at each follow-up with an evaluation and practice log that asked about length and frequency of practice at home.

The integrated YG program, described previously,[19] included the following: (1) preparatory warm-up synchronized with breathing; (2) selected postures, or asana (forward-, backward-, and side-bending asanas in sitting and standing position, cobra posture, crocodile, and half-shoulder-stand with support); (3) deep relaxation (supine posture); (4) alternate-nostril breathing, or pranayama; and (5) meditation. The program was taught by VYASA-trained teachers.

The ST program included exercises recommended specifically for women undergoing or recovering from breast cancer treatment.[21,22] The exercises included standing, lying down, and sitting positions and approximated the gross movements of the YG exercises (eg, horizontal arm stretch, breast stroke, neck stretch, quarterback throwing a football). Participants were introduced the stretches in a stepped approach and learned all of the material over the course of the first four classes. Classes were taught by physiotherapists from Rehabilitative and Physical Therapy at MD Anderson.

Measures

General QOL was assessed by the Medical Outcomes Study 36-item short-form survey (SF-36). The SF-36 assesses PF, physical impediments to role functioning, bodily pain, GH, vitality, social functioning, emotional impediments to role functioning, MH, and includes an overall physical component scale (PCS) and mental component scale (MCS).[23,24] The PCS and MCS were the primary outcomes. If the component scale was significant, then the subscales were analyzed as secondary outcomes. Higher scores reflect better QOL, with increases from baseline indicating improved QOL. Normed-based scoring is presented with a population mean = 50 and standard deviation = 10. A change of five points or more is considered clinically significant.[25,26]

Fatigue was assessed by using the Brief Fatigue Inventory,[27] a questionnaire used in clinical settings to assess fatigue severity and its impact on QOL. Lower scores reflect less fatigue.

Sleep disturbances were assessed by using the Pittsburgh Sleep Quality Index (PSQI),[28] a questionnaire that assesses sleep disturbances over a 1-month period. We report on the total score. Lower scores reflect fewer sleep disturbances.

Depression was assessed by using the Centers for Epidemiological Studies-Depression (CES-D) measures,[29] a well-validated measure focusing on affective components of depression. Lower scores reflect fewer depressive symptoms.

Cortisol

Five saliva samples (waking, 45 minutes later, approximately 8 and 12 hours after waking, and at bedtime) were obtained for 3 consecutive days at each assessment. Participants chewed on a cotton swab (Salivette; Sarstedt, Newton, NC), placed it in a plastic tube (Sarstedt), and then it was frozen at −80°C for later time-resolved immunoassay with fluorescence detection performed at the University of Dresden. Values < 0.0001 and > 70 nmol/L were classified as missing. If patients missed a collection point, they were told to leave the tube empty. Of the data received, 2.8% of the saliva samples were classified as missing (either empty or not within range). Approximately 30% of the patients (21% to 34%, depending on the time point) did not provide saliva samples. There were no differences between patients providing samples and those who did not on the basis of group assignment, medical, demographic, or outcome measures. Slopes were calculated without the waking sample, using the other four samples throughout the day. A steeper, more negative cortisol slope indicates better cortisol regulation. Medical information was obtained from medical records.

Data Analyses

For analysis of the self-report measures, we examined change from baseline to follow-up. To test group differences, PROC MIXED procedures in SAS version 9.2 were used. Changes from baseline were regressed on group, time (treated as categorical), and group × time interaction; the intercept was treated as random effect; the covariance structure was unstructured. There were no significant group × time interactions, and group comparisons at each assessment are presented from the mixed models. Because of non-normality, cortisol levels were log-transformed, and slopes were calculated and regressed on saliva collection time (hours after waking up in the morning); the slopes were then used as the dependent variable in the general linear model analyses as described above, examining slopes covarying for baseline levels. All analyses were controlled for randomization factors. We also controlled for baseline SF-36 GH scores in the SF-36 GH analyses due to imbalances across groups. The primary and secondary outcomes remained the same, and we present the results without covariates.

The primary outcomes were the PCS and MCS subscales of the SF-36 at 1 month post-XRT. Although our pilot work only found group differences in

PCS measures at the end of XRT,[19] we hypothesized that increasing the amount of YG from two to three times a week would result in more lasting effects (ie, at least 1 month post-XRT). The end of XRT time point and the longer term follow-up at 3 and 6 months were designated as secondary time points. We adjusted the α level for significance to $P = .029$ by conducting a Bonferroni correction taking into account the correlation between the two variables.[30] Assuming a two-tailed significance level of $P = .029$, with 50 patients per group and 80% power, we would detect differences between any pair of group means of 0.63 standard deviation units, a similar effect size to that found in our previous study (range, 0.44 to 0.47).[19] The secondary outcomes of the subscales from the component scores of the SF-36, Brief Fatigue Inventory, PSQI, CES-D, and cortisol slope at each time point were regarded as exploratory analyses.

RESULTS

Two hundred ninety-four eligible women were approached and 191 consented to participate. Thirteen dropped out before, and 15 after, they were randomly assigned, for a final sample size of 163 (YG = 53, ST = 56, WL = 54; Fig 1). Retention was high, with no group differences in loss to follow-up or number of classes attended on the basis of whether patients provided follow-up data or not. In addition, there were no differences between patients with and without missing data on the basis of medical, demographic, or baseline outcome measures.

All groups were similar in baseline demographic, medical, self-report measures (except for SF-36 GH), and cortisol slopes (Tables 1 and 2). Eighty-seven percent of YG and 85% of ST participants attended ≥ 12 classes (mean, YG = 13.8; ST = 14.7). Only three patients in each group attended fewer than half the classes. Practice outside of class was high (> twice per week) for the YG group 1 month post-treatment and then declined at 3 and 6 months (71%, 55%, and 45%, respectively). Practice outside of class (> twice per week) for the ST group was lower at 1 month and then increased somewhat at 3 and 6 months (53%, 69%, and 60%, respectively). Baseline and follow-up means of self-report measures are presented in Table 2.

SF-36

Significantly greater increases from baseline were observed in PCS scores for the YG group compared with the WL group at 1 and 3 months ($P = .01$ and $P = .01$, respectively; Fig 2). No other comparisons reached significance. There were no significant effects for the MCS.
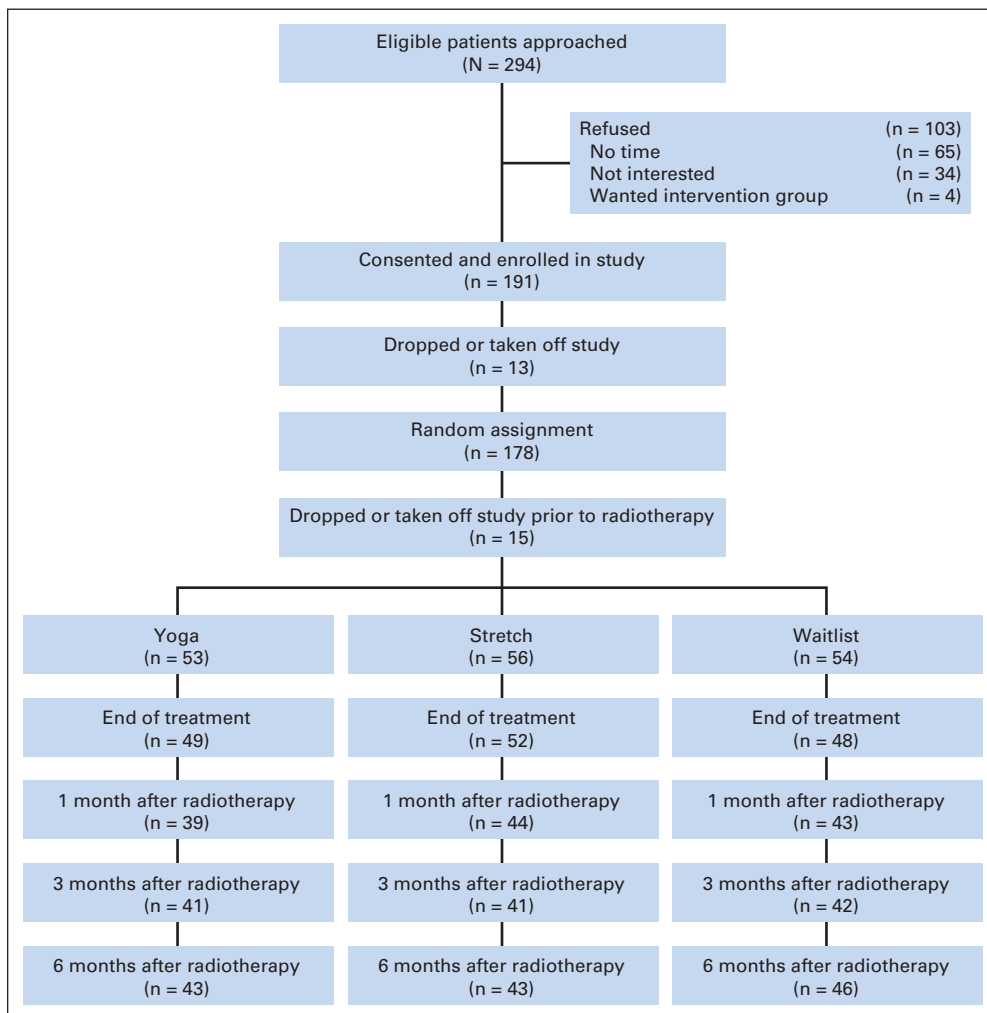

Fig 1. Flow of study participants over study period.

Patient Demographics and Clinical Characteristics	Yoga (n = 53; 33%)		Stretch (n = 56; 34%)		Waitlist (n = 54; 33%)		P
	No.	%	No.	%	No.	%	
Age							.79
Mean ± SE	52.38 ± 1.35		51.14 ± 1.32		52.11 ± 1.34		
Range, years	26-77		25-79		30-69		
Disease stage							.99
0	5	10	6	11	7	13	
I	16	30	18	32	17	31	
II	15	28	14	25	15	28	
III	17	32	18	32	15	28	
Surgery							.71
Mastectomy (without reconstruction)	12	23	17	31	12	22	
Mastectomy (with reconstruction)	6	11	3	5	5	9	
Breast conserving	35	66	36	64	37	69	
Chemotherapy							.73
Yes	36	68	34	61	34	63	
No	17	32	22	39	20	37	
Marital status (n = 151)							
Married and living together	31	67	37	71	34	64	.75
Not cohabitating	15	33	15	29	19	36	
Ethnicity (n = 150)*							.56
Black/African American	9	19	9	17	7	13	
White	32	68	28	55	37	71	
Latino/Hispanic/Mexican	4	9	8	16	5	10	
Asian/Pacific Islander	2	4	4	8	1	2	
Other	0	0	2	4	2	4	
Employment status (n = 140)							.1
Employed full-time	14	31	17	35	10	22	
Employed part-time	1	2	4	8	8	17	
Employed, taken time off	11	25	10	20	5	11	
Not employed	19	42	18	37	23	50	
Education (n = 152)							.59
High school or technical school	10	21	12	23	17	32	
Some college	17	36	14	27	15	28	
Higher education	20	43	26	50	21	40	
Income (n = 149)							.17
> $75,000	31	67	26	51	26	50	
< $75,000	15	33	25	49	26	50	

Table 1. Baseline Characteristics of Study Participants by Group

*Minority representation reflects that of women diagnosed with breast cancer in Harris County.

Analyses of the PCS subscales revealed significant effects for the PF and GH. Group differences in PF scores revealed significantly greater increases for the YG group compared with the WL group at 1, 3, and 6 months ($P < .002$; $P < .0001$; $P = .001$, respectively), with marginal group differences at the end of treatment ($P = .08$); greater increases for the YG group compared with the ST group at 1 and 3 months ($P = .01$; $P = .05$, respectively), with marginal group differences at 6 months ($P = .08$); and greater increases in the ST group compared with the WL group at 3 months ($P = .02$; Fig 2). GH outcomes followed a similar pattern, with significantly greater increases in GH scores for the YG group compared with the WL and ST groups at 1 and 3 months (all $P < .01$; Fig 2). No significant group effects were found for other SF-36 subscales.

Fatigue

Significantly greater decreases in fatigue were observed for the YG and ST groups compared with the WL group by the end of treatment ($P = .04$; $P = .02$, respectively), with marginally significant differences observed for the YG group compared with the WL group at 1 month ($P = .09$) and for the ST group compared with the WL group at 3 months ($P = .07$; Fig 3). There were no significant group differences at any time point for CES-D or PSQI scores.

Salivary Cortisol

GLM analysis of cortisol slopes, covarying for baseline, revealed a group main effect at the end of treatment (adjusted means: YG −0.104, SE 0.011; ST −0.072, SE 0.009; WL −0.064, SE 0.010; $P = .02$), with the YG group having a significantly steeper slope than the ST and WL groups ($P = .023$ and $P = .008$, respectively). There was also a marginally significant group main effect at the 1-month follow-up (adjusted means: YG −0.104, SE 0.011; ST −0.073, SE 0.010; WL −0.073, SE 0.010; $P = .07$), with the YG group having a significantly steeper slope than the ST and WL groups ($P = .05$ and $P = .04$, respectively; Fig 4). There were no differences in slope at the other time

Table 2. Raw Means and Standard Deviations of Self-Report Measures at Baseline and Follow-Up Time Points

	Baseline						Last Week of Treatment							1 Month Post-Treatment							3 Months Post-Treatment							6 Months Post-Treatment						
	YG		ST		WL			YG		ST		WL			YG		ST		WL			YG		ST		WL			YG		ST		WL		
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	P	No.	%	No.	%	No.	%	P	No.	%	No.	%	No.	%	P	No.	%	No.	%	No.	%	P
PCS	41.8	1.3	43.0	1.1	44.9	1.4		42.3	1.3	44.5	1.1	44.1	1.2	.20	47.0*	1.3	46.8	1.4	45.5	1.2	.04	48.2*	1.2	47.4	1.4	46.1	1.2	.05	46.9	1.4	47.5	1.4	46.6	1.1	.18
PF	41.9	1.3	44.7	1.2	45.9	1.2		43.7	1.4	46.0	1.1	45.7	1.3	.06	47.3*†	1.3	46.6	1.3	47.0	1.1	.005	48.7*†	1.1	47.2‡	1.2	46.3	1.4	.0001	47.8*	1.4	47.4	1.4	46.5	1.2	.005
GH	44.8	1.5	50.4	1.2	47.7	1.2		47.1	1.4	50.6	1.1	48.0	1.3	.01	47.9*†	1.5	49.2	1.4	46.9	1.5	.003	49.2*†	1.4	50.5	1.3	46.3	1.5	.005	47.7	1.6	51.7	1.3	49.8	1.1	.35
RF	36.8	1.5	37.1	1.3	38.3	1.6		39.1	1.4	41.1	1.4	40.8	1.5	.70	44.2	1.5	43.8	1.7	43.5	1.5	.50	45.0	1.6	45.5	1.7	44.3	1.4	.66	44.3	1.6	46.4	1.5	44.1	1.3	.28
BP	44.2	1.4	44.8	1.2	44.6	1.5		44.3	1.3	46.4	1.3	45.1	1.4	1.00	47.5	1.5	48.3	1.6	48.4	1.4	.98	49.0	1.4	48.9	1.5	47.5	1.5	.84	46.8	1.5	48.3	1.4	48.3	1.3	.81
MCS	42.2	1.7	45.8	1.4	42.0	1.8		47.2	1.9	49.5	1.2	47.1	1.7	.20	46.2	2.1	47.0	1.7	49.1	1.5	.07	46.5	2.0	50.1	1.6	46.6	1.9	.80	46.8	1.9	50.8	1.5	48.8	1.4	.75
CES-D	15.4	1.5	11.7	0.8	15.1	1.4		17.3	1.4	17.8	1.1	15.8	1.4	.07	13.1	1.7	11.6	1.4	12.3	1.3	.19	13.9	1.7	9.6	1.4	12.9	1.6	.68	13.9	1.8	10.4	1.4	11.5	1.3	.23
PSQI	8.3	0.6	8.5	0.5	8.2	0.5		6.7	0.5	8.3	0.6	7.3	0.5	.90	7.0	0.6	7.7	0.7	5.8	0.6	.40	6.5	0.5	7.3	0.5	6.4	0.6	.5	7.1	0.5	7.2	0.6	6.4	0.6	1.00
BFI	3.2	0.3	3.0	0.3	2.6	0.3		2.9*	0.3	2.5‡	0.3	3.2	0.4	.30	2.7	0.4	2.7	0.3	2.7	0.3	.22	2.6	0.3	2.3	0.4	3.0	0.4	.15	2.8	0.4	2.5	0.3	2.6	0.3	.56

NOTE. The baseline P values are from analysis of variance of raw scores. The follow-up P values represent the group main effects from the MIXED models analyses of change scores and the noted group differences are from the same MIXED models. Significant group differences are labeled below.

Abbreviations: BFI, Brief Fatigue Inventory; BP, Medical Outcomes Study 36-Item Short-Form Survey (SF-36) Bodily Pain; CES-D, Center for Epidemiologic Studies-Depression; GH, SF-36 General Health; MCS, SF-36 Mental Component Score; PCS, SF-36 Physical Component Score; PF, SF-36 Physical Functioning; PSQI, Pittsburg Sleep Quality Index; RP, SF-36 Role-physical; ST, stretching; WL, waitlist; YG, yoga.

*YG versus WL, $P \leq .05$.

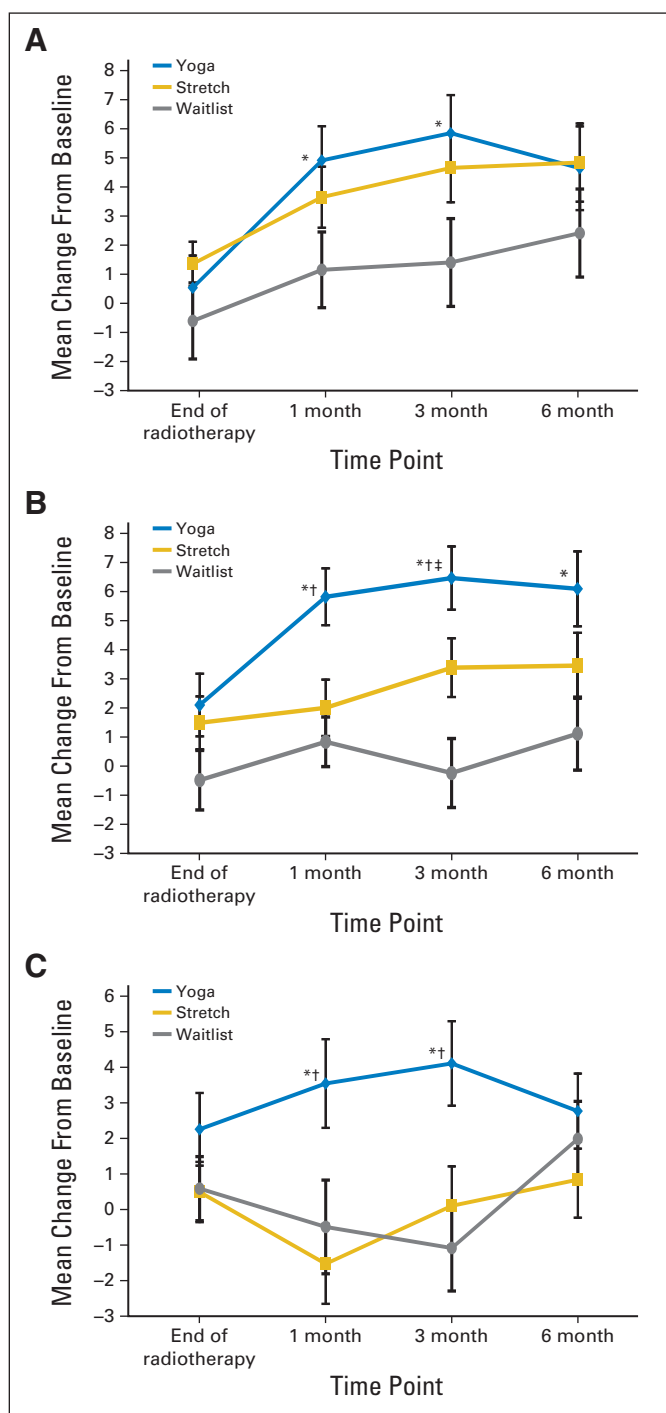†YG versus ST, $P \leq .05$.
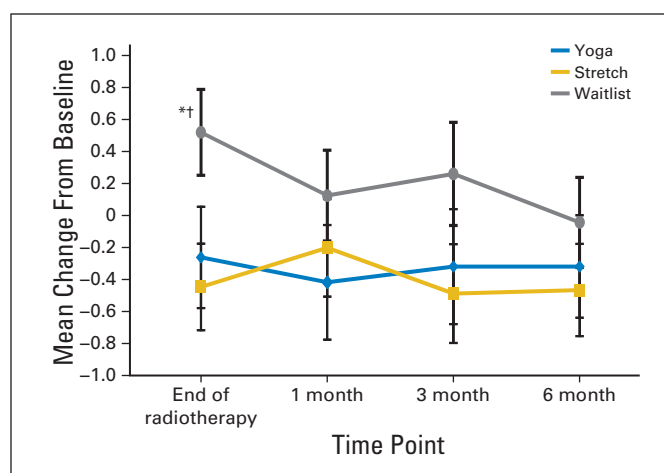
‡ST versus WL, $P \leq .05$.

Fig 3. Change from baseline for fatigue. Significance values are from the MIXED models of change scores at each follow-up time point. (*) Yoga versus waitlist, $P < .05$. (†) Stretch versus waitlist, $P < .05$.

imputations (SAS version 9.2 MI procedure) with Markov Chain Monte Carlo method and then used the MIANALYZE procedure to generate statistical inferences. All the analyses remained the same or resulted in smaller P values except for cortisol slopes, but the pattern remained the same (end of treatment: YG v ST, $P = .083$; YG v WL, $P = .015$; 1-month follow-up: YG v ST, $P = .21$; YG v WL, $P = .14$).

DISCUSSION

To our knowledge, this is the first study to compare the effects of YG against active ST and WL control groups in a cancer population. Compared with the WL group, the YG group had higher PCS scores 1 and 3 months after XRT (primary outcome), better PF at 1, 3, and 6 months, better GH at 1 and 3 months, less fatigue by the end of XRT, and steeper cortisol slopes at the end of XRT and 1 month later. Compared with the ST group, the YG group reported better PF 1 and 3 months after XRT, GH at 1 and 3 months, and had steeper cortisol slopes by the end of treatment. The improvement in PF in the YG group is also considered clinically significant because there was $\geq$ five-point increase, which was not the case for the other two groups.[25,26] Although the ST group reported less fatigue by the end of XRT and improved PF 3 months after treatment relative to the WL group, no other differences emerged between the ST and WL groups. There were no significant group differences for MH outcomes or sleep disturbances.

The present findings of improvements in PF and GH are consistent with the results of the pilot study using the same YG intervention.[19] There was, however, a more lasting effect of delivering YG three times a week in the current study versus two times a week in the pilot study, with group differences in PF lasting through the 6-month follow-up versus just 1 week after the end of XRT. Although the minimum frequency of YG practice to achieve positive benefits has yet to be determined, it is generally believed that daily practice is ideal. Class attendance was extremely high, as was observed in the pilot study,[19] and higher than that reported by other studies.[31,32]

The lack of benefit for measures of MH, fatigue, and sleep disturbances is also consistent with the pilot trial.[19] Even though the YG

Fig 2. Change from baseline in Medical Outcomes Study 36-item short-form survey (SF-36) subscale scores. (A) SF-36 PCS change from baseline; (B) SF-36 physical function change from baseline; (C) SF-36 general health change from baseline. Significance values are from the MIXED models of change scores at each follow-up time point. (*) Yoga versus waitlist, $P < .05$. (†) Yoga versus stretch, $P < .05$. (‡) Stretch versus waitlist, $P < .05$.

points (data not shown) or waking cortisol levels at any time point (data not shown).

Although there were no group differences between patients with and without missing data on demographic, medical, or the outcome variables at baseline, we imputed the missing data by using multiple
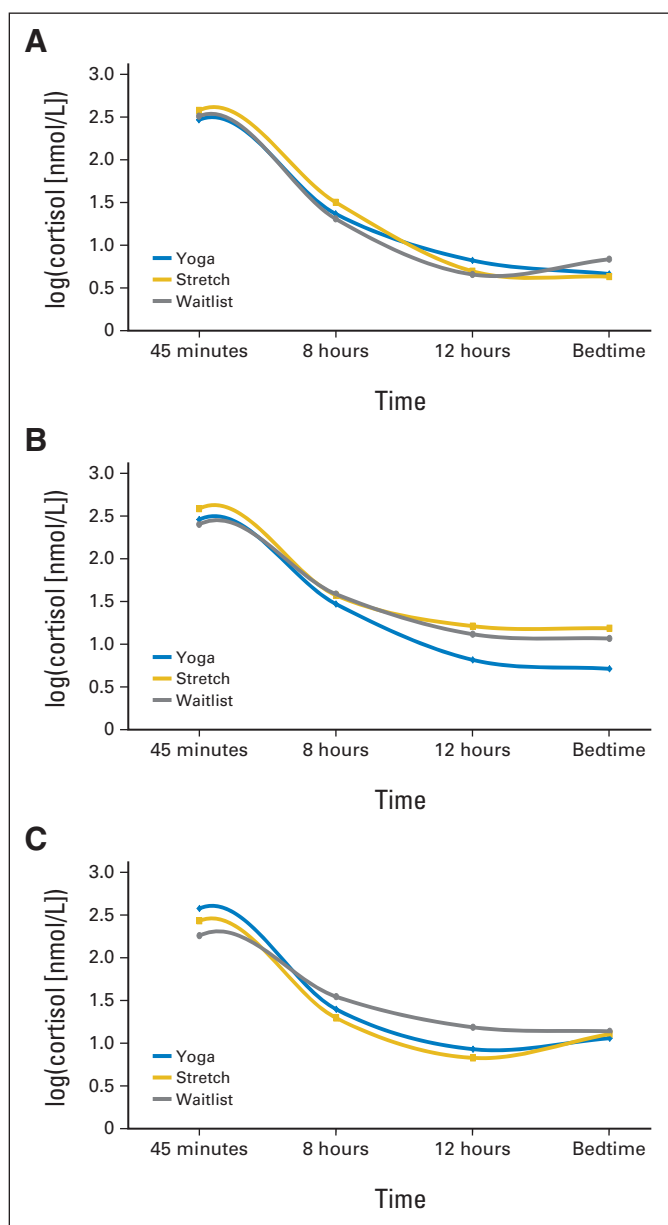
Fig 4. Log-transformed cortisol level daily curves. (A) Daily log-cortisol mean at baseline. No group differences. (B) Daily log-cortisol mean at end of radiotherapy. Yoga has steeper slope than stretch and waitlist groups ($P = .027$ and $P = .008$, respectively). (C) Daily log-cortisol mean at 1 month. Yoga has steeper slope than waitlist ($P = .05$ and $P = .04$, respectively). Significance values are from the GLM analysis of cortisol slopes at each time point, covarying for baseline.

program included components to address aspects of MH through relaxation and meditation, this was a minor component relative to the physical movements the women practiced. In addition, MCS scores of the women by the end of XRT were not clinically significantly different than the general population, and they improved across the course of 6 months, suggesting a possible ceiling effect for MH. The same pattern was seen for fatigue and sleep disturbances. Although some studies show that YG improves these outcomes, most research has been conducted in cancer survivors after treatment has ended, used YG pro-

grams that were perhaps less physical with more of a focus on relaxation,[5,6] or targeted specific symptoms.[9,33,34] In addition, improvements in PF may become more apparent over time with other outcomes being more stable.[35] Yet, it may be beneficial to examine if programs placing a greater emphasis on relaxation and meditation may have resulted in improved MH and sleep quality outcomes.

The current study also examined an objective measure of stress arousal by assessing the diurnal changes in circulating cortisol levels during waking hours. Although there was a blunting of the cortisol slope by the end of XRT, participants in the YG group had a significantly steeper cortisol slope than the other groups. Although the clinical significance of this finding is unclear, it does suggest the positive effects of YG on the stress hormone cortisol. There is evidence that a blunted cortisol slope is associated with tumor progression[18] and decreased survival[17] in patients with breast cancer, so maintaining a sustained steep cortisol slope may therefore have prognostic implications.

Although this study controlled for the ST and attention components associated with the YG program, the ST group did not learn any aspects of relaxation. However, the YG group resulted in greater improvement in PF, likely resulting from the physical aspects of YG. Study groups were not blinded, and treatment expectations were not assessed. In addition, because of the number of secondary outcomes and multiple comparisons, significant group differences for secondary outcomes (fatigue and cortisol slope) should be interpreted cautiously.

The current study found that, for some outcomes, YG yielded better subjective and objective results than either ST or usual care. There were fewer differences between ST and WL groups. Although physical therapy is a reimbursable expense in the United States and will likely help patients recover faster, expanding to include services such as YG should be considered. Future studies should examine methods to increase practice frequency outside of class, examine the benefits of different YG components by using appropriate controls, conduct such trials in a blinded manner, assess expectations, and conduct multilevel cost-benefit analyses.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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