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*Integr Cancer Ther* 2009; 8; 37 originally published online Feb 3, 2009;
DOI: 10.1177/1534735409331456

Integrative Cancer Therapies
Volume 8 Number 1
March 2009 37-46
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10.1177/1534735409331456
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# Effects of a Yoga Program on Cortisol Rhythm and Mood States in Early Breast Cancer Patients Undergoing Adjuvant Radiotherapy: A Randomized Controlled Trial

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*Objectives*. This study compares the effects of an integrated yoga program with brief supportive therapy in breast cancer outpatients undergoing adjuvant radiotherapy at a cancer center. *Methods*. Eighty-eight stage II and III breast cancer outpatients are randomly assigned to receive yoga (n = 44) or brief supportive therapy (n = 44) prior to radiotherapy treatment. Assessments include diurnal salivary cortisol levels 3 days before and after radiotherapy and self-ratings of anxiety, depression, and stress collected before and after 6 weeks of radiotherapy. *Results*. Analysis of covariance reveals significant decreases in anxiety ($P < .001$), depression ($P = .002$), perceived stress ($P < .001$), 6 a.m. salivary cortisol ($P = .009$), and pooled mean cortisol ($P = .03$) in the yoga group compared with controls. There is a significant positive correlation between morning salivary cortisol level and anxiety and depression. *Conclusion*. Yoga might have a role in managing self-reported psychological distress and modulating circadian patterns of stress hormones in early breast cancer patients undergoing adjuvant radiotherapy.

**Keywords:** yoga; breast cancer; meditation; cortisol; stress

Psychological distress and morbidity are common sequelae to diagnosis and treatment in early breast cancer patients,[1-3] given that the majority of patients report symptoms of depression, anxiety, social dysfunction, and inability to work.[4-6] These symptoms, coupled with cancer-related intrusive thoughts such as fear of radiation and surgery and image problems, can heighten women's risk for psychological distress.[7-9] This distress been shown to affect cancer-related outcomes in terms of quality of life, mood states (anxiety and depression), toxicity, treatment response, and prognosis.[10]

Although anxiety and depression are some of the most common psychiatric problems seen in cancer patients, many of these problems are not detected, diagnosed, or treated.[1] Patients with breast cancer undergoing radiation treatment also report anxiety and depression before, during, and after treatment.[11,12] One study found the prevalence of anxiety and depression in Indian cancer patients undergoing radiation treatment to be 64% and 50%, respectively,[11] more than that seen in Western populations. Both anxiety and depression can affect treatment-related distress by leading patients to perceive cancer as a threat, increasing attentiveness to somatic symptoms, and causing aversive symptoms.

These affective states and distress have been found to contribute to hypothalamic-pituitary-adrenal (HPA) axis dysregulation in cancer patients.[13,14] Cortisol, a stress hormone and an end-product of the HPA axis, has been reported to be elevated in breast cancer patients both prior to and following treatment.[15-17] Both elevated levels of cortisol and flattened high levels or erratic diurnal fluctuations of cortisol have been shown to cause down-regulation

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of the immune response as a result of stress.[18-20] Such aberrations of cortisol rhythms are attributable to both the physical stress of having cancer[21] and psychological stress.[22,23] Flattened diurnal salivary cortisol rhythms predict early recurrence[14] and mortality from metastatic breast cancer.[24]

Various psychotherapeutic interventions such as cognitive behavioral therapy, social support, and stress management have shown beneficial effects in reducing psychological distress[25-27] and HPA axis dysregulation associated with cancer.[28,29] Studies have shown these interventions to reduce distress, anxiety, and depressed mood and enhance quality of life among women with breast cancer in adjuvant settings.[30,31] Studies have also shown improvement in HPA axis dysregulation,[28] immune responses,[32] and survival[33] following such interventions.

Yoga is among the stress reduction mind–body approaches that have been practiced widely in both Indian and Western populations. Various components and types of yoga practices have shown beneficial effects in reducing distressful symptoms and improving sleep, mood, and quality of life in cancer patients.[34] Results from randomized controlled studies have shown decreases in cortisol levels in noncancer populations following yoga intervention.[35-37] Our earlier studies with yoga intervention have shown decreases in anxiety states,[38] reduction in chemotherapy-induced nausea and vomiting,[39] and improvement in immune response[40] in early breast cancer patients. These findings offer further support for the stress reduction effects of yoga. It may be speculated that these effects are facilitated by reductions in stress hormones that constitute the HPA axis. It is becoming increasingly clear from the accumulating evidence that a mere "elevated," in vivo cortisol level may insufficiently define "stress" and that changes in its circadian patterns are also important.[41,42] However, results from a mindfulness-based stress reduction intervention show inconclusive evidence for changes in salivary cortisol rhythms.[28] This may be because a heterogeneous cancer population was studied and the duration of the intervention was insufficient to affect salivary cortisol rhythms.

We hypothesized that a yoga intervention would help calm the mind and reduce stress, thereby attenuating HPA axis dysregulation and resulting in normal salivary cortisol levels and circadian rhythms in stage II and III breast cancer patients undergoing adjuvant radiotherapy.

In this study, we compared the effects of a 6-week integrated yoga program with the effects of a brief supportive therapy as a control intervention in early operable breast cancer patients undergoing adjuvant radiotherapy.

## Methods

### Subjects

This is a randomized controlled trial wherein 88 women diagnosed with stage II and III breast cancer were recruited over a 2½-year period at 2 comprehensive cancer care centers. The institutional ethics committees of the recruiting cancer centers approved the study. Patients were eligible to participate in this study if they met the following selection criteria at the study start: (a) were recently diagnosed with operable breast cancer; (b) had been prescribed adjuvant radiotherapy; (c) were between 30 and 70 years of age; (d) were assessed as Zubrod's performance status 0-2 (ambulatory >50% of time); (e) had a high school education; and (f) consented to participate in the study. Subjects were excluded if they (a) had any concurrent medical condition that was likely to interfere with treatment; (b) had a major psychiatric illness, neurological illness, or autoimmune disorder; (c) had any known metastases; or (d) were prescribed concurrent chemotherapy cycles during radiotherapy.

Each study participant was prescribed adjuvant radiotherapy with a cumulative dose of 50.4 Gy with fractionations spread over 6 weeks. The details of the study were explained to the participants, and their informed consent was obtained in writing before they started adjuvant radiotherapy and intervention.

### Randomization

Of 103 eligible participants, 88 (85.4%) consented to participate and were randomized, via computer-generated random numbers, to receive yoga (n = 44) or supportive therapy (n = 44) before intervention (prior to radiotherapy). Randomization was performed using opaque envelopes with group assignments. Personnel who had no part in the trial performed randomization. The envelopes were opened sequentially in the order of assignment during recruitment, with the names and registration numbers of the participants written on the covers. The order of randomization was verified with the hospital date of admission records for radiotherapy at study intervals to make sure that field personnel had not altered the sequence of randomization to suit the allocation of consenting participants into 2 study arms.

Among the 88 participants, 75 (yoga n = 42, control n = 33) completed their prescribed radiation therapy of 6 weeks and follow-up assessment. However, only 63 participants provided saliva samples at the study start and only 56 provided saliva samples during postintervention assessment. There were 13 dropouts in the study (see trial profile, Figure 1). The reasons for dropping out were transfer to other hospitals (n = 4), use of other complementary therapies (eg, homeopathy or ayurveda, n = 2),

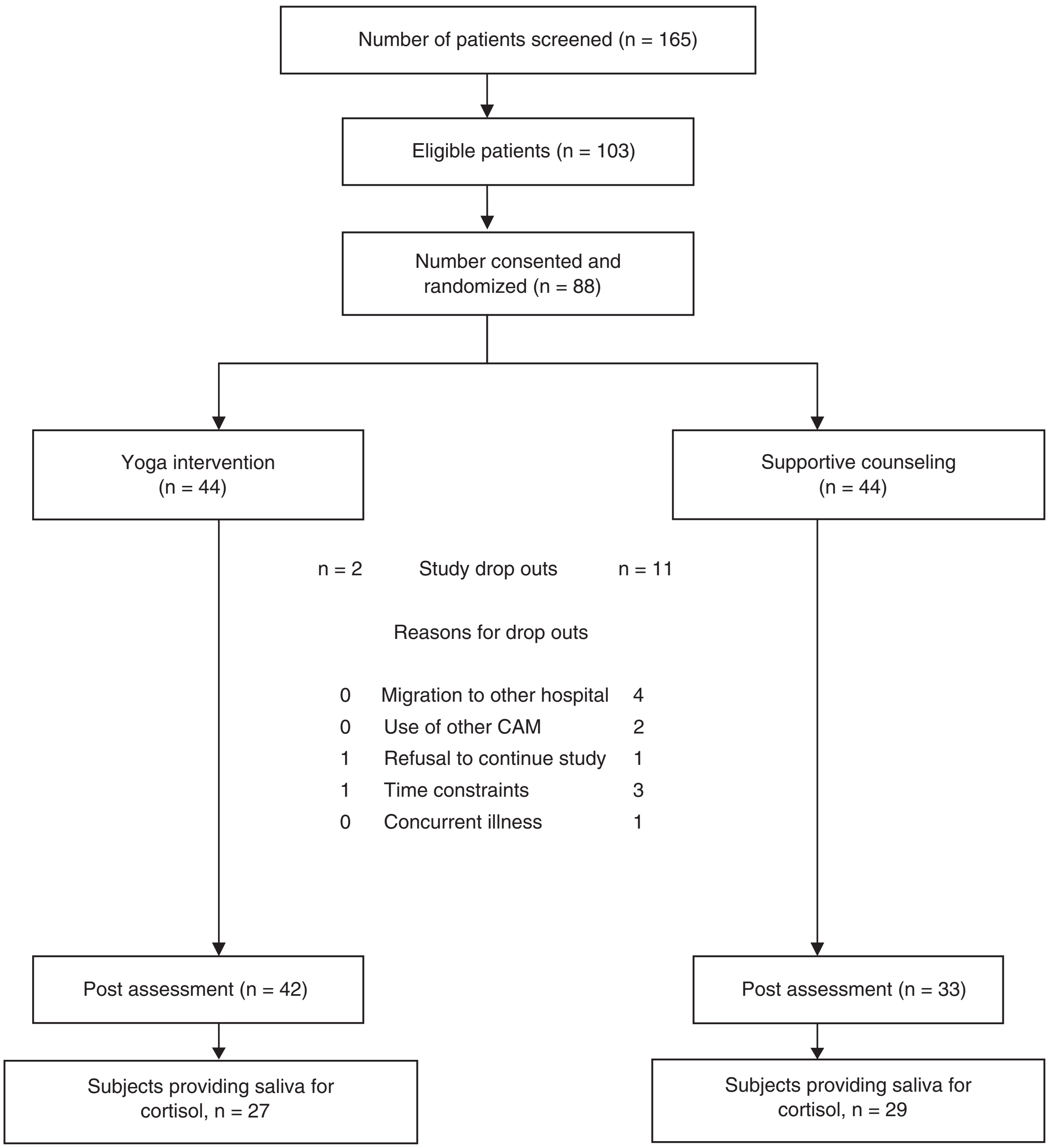


**Figure 1.** Trial profile. CAM, complementary and alternative medicine.

refusal to continue the study (n = 2), time constraints (n = 4), and concurrent illnesses such as infections that delayed radiotherapy and intervention (n = 1).

### Measures

During the initial visit, demographic information was obtained, including age, marital status, education, occupation, obstetric and gynecological history, medical history, and intake of medications; clinical data on the history of breast cancer were abstracted. The following self-report questionnaires were imparted to the subjects during the study:

*Hospital Anxiety and Depression Scale.* Participants were assessed for anxiety and depression using the Hospital Anxiety and Depression Scale (HADS).[43] It is a widely used self-report instrument designed to assess the dimensions of anxiety and depression in nonpsychiatric populations.[44,45] This 14-item questionnaire consists of

2 subscales of 7 items designed to measure levels of anxiety and depression. Each item is rated on a scale from 0 ("not at all") to 3 ("very much"). The reliability of HADS (all 14 items) and the HADS-A and HADS-D subscales is 0.85, 0.79, and 0.87, respectively.[46]

*Perceived Stress Scale.* Perceived stress levels were assessed using the Perceived Stress Scale (PSS).[47] This self-rated scale includes 14 items scored on a 5-point scale. This scale assesses the degree to which participants appraise their daily life as unpredictable, uncontrollable, and overwhelming (eg, "In the last week, how often have you felt that you were unable to control the important things in your life?"). This scale has a reliability of 0.85.

### Diurnal Salivary Cortisol

Participants were asked to give saliva samples 3 times a day for 3 consecutive days before and after adjuvant radiotherapy.

*Saliva collection and storage*. Participants were trained to collect their saliva by chewing on a cotton swab and drooling the saliva into a plastic holder resting inside a sterile centrifuge tube. Samples were collected at 6 a.m., 9 a.m., and 9 p.m. for 3 consecutive days. The samples were stored in a refrigerator and delivered to study personnel after 3 days. Samples were then centrifuged to remove mucous, frozen, and stored at −70° in Eppendorf tubes for analysis.

*Assay procedure*. The samples were thawed and centrifuged at 2500 rpm for 15 minutes, and the supernatant was used for cortisol assessment. Salivary cortisol levels were assessed using an enzyme immunoassay (EIA) method with kits manufactured by Salimetrics Inc (State College, Pa). The tests were run for all the 9 samples collected on 3 consecutive days for each study participant. The tests were standardized under controlled laboratory conditions using standards and positive and negative controls provided by the manufacturer. The detection range with these kits was 0.012 to 3.0 μg/dL. The intra-assay coefficient ranged from 3.35% to 3.65% and interassay coefficient from 3.75% to 6.41% with these samples.

Mean cortisol levels for specific time points over a 3-day period were extrapolated. The diurnal cortisol response was evaluated by calculating the area under the curve (AUC) for 6 a.m., 9 a.m., and 9 p.m. using zero as a reference point. We used AUC, a frequently used method in endocrinology research, to collect information that is contained in repeated measurements over time. This helps to limit the amount of statistical comparisons between groups to minimize correction of the α-error probability. With the AUC variables, the number of repeated measurements is irrelevant and thus the number of statistical comparisons only depends on the number of groups to be compared. With the 2 AUC formulas, AUCb for baseline diurnal cortisol measurements and AUCi for the increase in the AUC with respect to AUCb for the postintervention measure using the trapezoidal method,[48] we could assess different aspects of the time course of the repeated measurements.

### Interventions

Interventions were conducted over a 6-week period for both the groups during the course of their adjuvant radiotherapy with one group receiving an integrated yoga program and the other brief supportive therapy as individual sessions. The yoga intervention consisted of a set of asanas (postures done with awareness), breathing exercises, pranayama (voluntarily regulated nostril breathing), meditation, and yogic relaxation techniques with imagery (mind sound resonance technique and cyclic meditation). Goals of the program were to develop a sense of calmness and relaxation with a perceptible change in coping with day-to-day stressful life experiences. Participants were required to attend a minimum of 3 in-person sessions per week for 6 weeks during their adjuvant radiotherapy treatment in the hospital and to practice at home on the remaining days. Each in-person session lasted 1 hour and was administered by a trained yoga therapist either before or after radiotherapy. The control intervention consisted of brief supportive therapy with education that is routinely offered to patients as a part of their care in this center. We chose to have this as a control intervention mainly to control for the nonspecific effects of the yoga program that may be associated with factors such as attention, support, and a sense of control as described in our earlier study.[39] Subjects and their caretakers underwent counseling by a trained social worker (15-minute sessions once every 10 days) during their hospital visits for adjuvant radiotherapy. The control group received 3 or 4 such counseling sessions during a 6-week period, whereas the intervention group received between 18 and 24 yoga sessions. Although the goals of the yoga intervention were stress reduction and appraisal of changes, the goals of supportive therapy were education, reinforcing social support, and coping preparation.

### Data Analysis

Data were analyzed using SPSS version 16.0 (SPSS Inc, Chicago, Ill). Descriptive statistics were used to assess normality and homogeneity. The data were found to be normally distributed. Paired-sample *t* test was used to assess the within-group changes, and analysis of covariance (ANCOVA) using baseline value as a covariate was used to determine the between-group changes. Data were analyzed for mean saliva collection at 6 a.m., 9 a.m., and 9 p.m. and mean for all 3 together (pooled mean diurnal salivary cortisol) as well as for AUCb and AUCi between groups. Relationships between changes in psychological

**Table 1.** Demographic and Medical Characteristics of the Initially Randomized Sample

| | All Subjects (N = 88) | | Yoga Group (N = 44) | | Control Group (N = 44) | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Stage of breast cancer | | | | | | |
| I | 5 | 5.7 | 2 | 4.5 | 3 | 6.8 |
| II | 18 | 20.4 | 11 | 25.0 | 7 | 15.9 |
| III | 65 | 73.9 | 31 | 70.5 | 34 | 77.3 |
| Grade of breast cancer | | | | | | |
| I | 1 | 1.1 | 1 | 2.3 | 0 | 0 |
| II | 33 | 37.5 | 21 | 51.1 | 10 | 22.7 |
| III | 54 | 61.4 | 22 | 47.7 | 34 | 77.3 |
| Menopausal status | | | | | | |
| Pre | 48 | 54.5 | 26 | 59.1 | 23 | 52.3 |
| Post | 40 | 45.5 | 18 | 40.9 | 21 | 47.7 |
| Histopathology type | | | | | | |
| IDC | 72 | 81.8 | 37 | 84.1 | 35 | 39.7 |
| ILC | 7 | 7.9 | 2 | 4.5 | 5 | 11.4 |
| IPC | 3 | 3.4 | 2 | 4.5 | 1 | 2.2 |
| DCI | 2 | 2.2 | 2 | 4.5 | 0 | 0 |
| CC | 2 | 2.2 | 1 | 2.3 | 1 | 2.2 |
| PC | 2 | 2.2 | 0 | 0 | 2 | 4.5 |
| Regimen | | | | | | |
| S+CT3+RT | 68 | 77.3 | 32 | 72.7 | 37 | 84 |
| S+RT | 20 | 22.7 | 12 | 27.3 | 7 | 15.9 |
| Marital status | | | | | | |
| Single | 2 | 2.2 | 1 | 2.3 | 1 | 2.2 |
| Married | 86 | 97.8 | 43 | 97.7 | 43 | 97.8 |

NOTES: IDC = infiltrating ductal carcinoma; ILC, = infiltrating lobular carcinoma; IPC = infiltrating papillary carcinoma; DCI = ductal carcinoma in situ; CC = comedo carcinoma; PC = papillary carcinoma, S+CT3+RT = adjuvant radiotherapy after mastectomy followed by 3 cycles of chemotherapy; S+RT = adjuvant radiotherapy after mastectomy.

variables to changes in cortisol were assessed using Pearson correlation analysis.

## Results

The mean age of participants was 46 ± 9.13 years in yoga and 48.45 ± 10.21 years in control groups. All patients had mastectomy as primary treatment, 20 subjects received radiotherapy following mastectomy, and 68 subjects received radiotherapy following mastectomy and 3 cycles of chemotherapy. Participants in both groups were comparable with respect to sociodemographic and medical characteristics (Table 1).

### Diurnal Salivary Cortisol Levels

Paired-samples *t* test to assess within-group change following intervention showed a significant decrease in mean salivary cortisol levels at 6 a.m. ($t = 4.21$, $P < .001$) and pooled diurnal mean cortisol in the yoga group ($t = 2.79$, $P = .01$) but not in the control group ($t = 0.34$, $P < .74$, and $t = –0.04$, $P = .96$). We used ANCOVA to assess between-group differences using baseline cortisol value (for the corresponding time) as a covariate. There was a significant decrease in mean salivary cortisol level at 6 a.m. in the yoga group compared with the control group ($F_{1, 56} = 7.45$, $P = .009$). There was also a significant decrease in pooled mean diurnal salivary cortisol level in the yoga group compared with controls ($F_{1, 53} = 5.14$, $P = .03$). There was no significant change between and within groups in salivary cortisol for 9 a.m., 9 p.m., and AUC with respect to baseline (AUCb) and increase (AUCi) (Table 2). Furthermore, we classified patients as having high or low distress by taking the baseline pooled mean diurnal cortisol (0.254 μg/dL) as a cutoff. Subjects in both groups (intervention and control) with pooled diurnal mean cortisol 0.25 μg/dL or less were classified as a low-distress subgroup and those with cortisol greater than 0.25 μg/dL were classified as a high-distress subgroup at baseline. Analysis for effects of intervention (yoga vs supportive therapy) was carried out separately for both subgroups (high-distress and low-distress subgroups). Analysis of covariance using baseline cortisol value for the corresponding time as a covariate in the low-distress subgroup showed a significant decrease in 6 a.m. mean salivary cortisol in the yoga group compared with controls ($F_{1, 28} = 4.48$, $P = .04$). Similarly, there was a significant decease in pooled diurnal mean cortisol levels in the yoga group compared with controls ($F_{1, 28} = 4.93$, $P = .03$). However,

**Table 2.** Comparison of Mean Values of Diurnal Salivary Cortisol Levels Using Paired *t* Test and Analysis of Covariance (ANCOVA)

| Outcome Variables | Yoga (n = 27), Mean (SD) Pre | Yoga (n = 27), Mean (SD) Post | Control (n = 29), Mean (SD) Pre | Control (n = 29), Mean (SD) Post | Effect Size (Cohen's f) |
|---|---|---|---|---|---|
| 6 a.m. | 0.33 (0.17) | 0.22 (0.15)[ab] | 0.38 (0.31) | 0.36 (0.24) | 0.24 |
| 9 a.m. | 0.26 (0.16) | 0.19 (0.14) | 0.24 (0.23) | 0.24 (0.23) | 0.21 |
| 9 p.m. | 0.19 (0.14) | 0.16 (0.16) | 0.16 (0.15) | 0.16 (0.14) | 0.14 |
| Mean pooled diurnal cortisol | 0.25 (0.13) | 0.19 (0.13)[ab] | 0.25 (0.21) | 0.25 (0.18) | 0.27 |
| 6 a.m. AUCb | 1.14 (0.76) | 0.98 (0.63) | 0.69 (0.38) | 0.56 (0.38) | 0.27 |
| 9 a.m. AUCb | 3.25 (2.17) | 2.97 (2.22) | 1.85 (1.15) | 1.58 (0.88) | 0.19 |
| 9 p.m. AUCb | 4.39 (2.84) | 3.96 (2.77) | 2.54 (1.44) | 2.15 (1.18) | 0.19 |
| 6 a.m. AUCi | –0.19 (0.24) | –0.13 (0.33) | –0.12 (0.26) | –0.11 (0.16) | 0.05 |
| 9 a.m. AUCi | –2.11 (2.07) | –1.49 (2.41) | –1.37 (1.94) | –1.12 (1.52) | 0.11 |
| 9 p.m. AUCi | –2.31 (2.28) | –1.62 (2.72) | –1.49 (2.17) | –1.23 (1.65) | 0.11 |

NOTES: AUCb = area under the curve for baseline; AUCi = area under the curve for increase in cortisol with respect to baseline.
[a] $P < .05$ for within group change using paired *t* test.
[b] $P < .05$ for between group change using analysis of covariance.

**Table 3.** Comparison of Diurnal Cortisol Levels Between Yoga and Controls in the Initially Low-Distress (Mean Cortisol ≤0.25 μg/dL) and High-Distress (Mean Cortisol >0.25 μg/dL) Subgroups Using Analysis of Covariance With Baseline Measure as a Covariate

| | Low-distress Subgroup | | | | High-distress Subgroup | | | |
|---|---|---|---|---|---|---|---|---|
| | Yoga (n = 13) | | Control (n = 18) | | Yoga (n = 14) | | Control (n = 11) | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| 6 a.m. | 0.23 ± 0.11 | 0.17 ± 0.12 | 0.21 ± 0.13 | 0.27 ± 0.16 | 0.42 ± 0.16 | 0.27 ± 0.16 | 0.65 ± 0.34 | 0.51 ± 0.28 |
| 9 a.m. | 0.18 ± 0.08 | 0.13 ± 0.07 | 0.12 ± 0.07 | 0.16 ± 0.11 | 0.36 ± 0.16 | 0.25 ± 0.17 | 0.44 ± 0.25 | 0.38 ± 0.31 |
| 9 p.m. | 0.11 ± 0.08 | 0.09 ± 0.06 | 0.08 ± 0.08 | 0.10 ± 0.09 | 0.26 ± 0.14 | 0.22 ± 0.20 | 0.27 ± 0.18 | 0.26 ± 0.18 |
| Mean pooled cortisol | 0.16 ± 0.06 | 0.13 ± 0.05 | 0.13 ± 0.07 | 0.17 ± 0.09 | 0.35 ± 0.10 | 0.24 ± 0.16 | 0.46 ± 0.22 | 0.39 ± 0.20 |

[a] $P < .05$ for analysis of covariance between groups (yoga vs controls).

although there was a trend for a decrease in cortisol levels in the high-distress subgroup, the effects of the intervention were not significant (Table 3).

### Anxiety Scores (HADS-A)

Paired-samples *t* test done to assess within-group change showed a significant decrease in self-report anxiety scores in the yoga group ($t = 7.24$, $P < .001$) and control group ($t = 2.15$, $P = .04$) following intervention. Analysis of covariance on postintervention measures using baseline anxiety as a covariate showed a significant decrease in self-report anxiety in the yoga group compared with controls ($F_{1, 73} = 15.4$, $P < .001$) (Table 4).

### Depression Scores (HADS-D)

Paired-samples *t* test done to assess within-group change showed a significant decrease in self- report depression within the yoga ($t = 6.26$, $P < .001$) and control groups ($t = 3.23$, $P = .01$). Analysis of covariance on postintervention measures using baseline depression scores as a covariate showed a significant decrease in self-report depression in the yoga group compared with controls ($F_{1, 73} = 10.7$, $P = .002$) (Table 4).

### Perceived Stress Score

Paired-samples *t* test done to assess within-group change showed a significant decrease in perceived stress in the yoga group ($t = 5.5$, $P < .001$) but not in the control group ($t = 1.42$, $P = .17$). Analysis of covariance on postintervention measures using baseline perceived stress score as a covariate showed a significant decrease in perceived stress in the yoga group compared with controls ($F_{1, 72} = 18.05$, $P < .001$) (Table 4). Bivariate relationships between salivary cortisol rhythms and psychological variables were determined using pearson correlation analysis. There was a significant negative correlation between 0600 hrs salivary cortisol with anxiety, and depression states (Table 5).

**Table 4.** Comparison of Scores for Anxiety, Depression, and Perceived Stress Between Yoga and Control Groups Following Intervention Using Analysis of Covariance With Baseline Measure as a Covariate

| Outcome Variables | Yoga (n=42), Mean (SD) Pre | Yoga (n=42), Mean (SD) Post | Control (n=33), Mean (SD) Pre | Control (n=33), Mean (SD) Post | Effect Size (Cohen's f) |
|---|---|---|---|---|---|
| HADS-Anxiety | 8.05 (3.87) | 4.88(3.34)[ab] | 9.35 (3.98) | 8.12[c] (3.80) | 0.31 |
| HADS-Depression | 7.57 (4.02) | 4.14(3.45)[ad] | 8.00 (3.47) | 6.53[e] (3.78) | 0.31 |
| Perceived stress | 20.78 (6.10) | 15.17 (4.83)[ab] | 21.41 (6.22) | 20.12 (5.87) | 0.36 |

[a] *P* values < .001 for within-group change using paired *t* test.
[b] *P* values < .001 for between-group change using analysis of covariance.
[c] *P* values < .05 for within-group change using paired *t* test.
[d] *P* values < .01 for between-group change using analysis of covariance.
[e] *P* values < .01 for within-group change using paired *t* test.

**Table 5.** Pearson Correlation (*r* Values) Between Anxiety, Depression, Perceived Stress Scores, and Cortisol Values

| Variables | Anxiety | Depression | Perceived Stress |
|---|---|---|---|
| Cortisol | | | |
| 6 a.m. | 0.24[a] | 0.40[b] | –0.04 |
| 9 a.m. | 0.16 | 0.08 | 0.09 |
| 9 p.m. | 0.02 | 0.03 | –0.15 |
| Pooled mean | 0.22 | 0.24 | –0.06 |
| Cortisol AUCb | | | |
| 6 a.m. | 0.19 | 0.18 | 0.06 |
| 9 a.m. | 0.004 | 0.10 | 0.01 |
| 9 p.m. | 0.05 | 0.12 | 0.03 |
| Cortisol AUCi | | | |
| 6 a.m. | –0.14 | –0.11 | 0.13 |
| 9 a.m. | –0.22 | –0.13 | 0.04 |
| 9 p.m. | –0.21 | –0.13 | 0.05 |

NOTES: AUCb = area under the curve for baseline; AUCi = area under the curve for increase in cortisol with respect to baseline.
[a] *P* values < .05 for Pearson correlation.
[b] *P* values < .01 for Pearson correlation.

## Discussion

This study evaluated the effects of a 6-week integrated yoga program with supportive therapy in stage II and III breast cancer outpatients undergoing adjuvant radiotherapy. The results suggest significant decreases in self-reported anxiety, depression, and perceived stress and in 6 a.m. and pooled mean cortisol levels in the yoga group compared with controls. There was a tendency for a decrease in the above measures in both yoga and control groups following radiotherapy, consonant with the usual symptom trajectory of cancer patients during and after treatment.[49] However, decrements were profound in the yoga group compared with controls, supporting the stress reduction benefits of yoga program.

The effect sizes were more for decreases in anxiety and perceived stress and less for salivary cortisol. This reduction in anxiety is consistent with our earlier study using the same support intervention as a control.[38] However, the decrements in our study are less compared with earlier studies that lacked control interventions and showed large effect sizes (Cohen's d > 0.8) for anxiety reduction on a number of self-report scales.[50-55] Our results for reduction in self-reported symptoms of depression are similar to earlier observations using yoga in cancer and noncancer populations.[26,56-58] The large effect size observed in our study could be attributed to the fact that the period of diagnosis and active treatment is often associated with greater distress[49]; given that we had a homogenous study population and better contact duration and exposure to intervention compared with the above studies, it is reasonable to see these differences.

The decrease in morning salivary cortisol levels suggests possible stress reduction benefits with our yoga intervention. This is similar to earlier observations with yoga interventions in both noncancer[35-37] and cancer[16,29,59] populations. Although these earlier studies measured 1-time plasma cortisol, we chose to assess the diurnal levels of free salivary cortisol because change in the rate of cortisol secretion over a day is considered a robust measure compared with 1-time cortisol assessment.[24,60] Earlier studies with similar stress reduction interventions such as mindfulness-based stress reduction (MBSR) also showed decrements in cortisol in breast cancer patients who had initially high cortisol levels, suggesting that more distressed patients tend to benefit from stress reduction interventions.[28] We similarly divided our sample by initial mean daily cortisol levels and compared the degree of change in subsequent cortisol levels. We found that those people with initially low cortisol levels (below initial mean cutoff) showed significant decreases in 6 a.m. cortisol and mean diurnal cortisol following intervention compared with those with higher initial levels, who in fact displayed a tendency for a decrease in cortisol levels, contrary to earlier findings. Although our intervention showed reductions in anxiety, depression, and perceived stress in both subgroups, these decrements in psychological distress did not translate into significant reductions in cortisol in the high-cutoff group.

It may be hypothesized from these results that distress decreases with time in cancer patients, that the use of stress reduction interventions only augments this process, and that patients with initially high distress and high cortisol levels would probably take longer for attenuation of such high cortisol levels than those with lesser distress or cortisol profiles. Our observations differ from earlier study by Carlson et al,[28] probably attributable to the differences in cancer populations being studied, differences in type of interventions (MBSR vs yoga), lack of a control arm in the former, and the fact that patients in our study were undergoing active treatment throughout the study period.

These observations are important because HPA axis dysregulation in terms of diurnal salivary cortisol rhythm is an important predictor of survival in advanced breast cancer patients.[24] Modulating cortisol levels at an earlier stage would help reduce distress in the future[61] and possibly improve survival in these patients. The changes in stress response patterns and appraisal could have contributed to reductions in cortisol and distress seen with our intervention. The reduction in perceived stress seen with our intervention further supports for this mechanism. An elevated level of cortisol is known to have immunosuppressive effects and is largely responsible for the downregulation of immune function because of stress. Reductions seen in cortisol levels in our study further support for improvements in immune functioning (natural killer cell counts) seen with our earlier study in early breast cancer patients undergoing conventional treatment (surgery, radiotherapy, and chemotherapy).[40] The combination of physical postures, breathing exercises, relaxation, and meditation could have helped attenuate cortisol levels through stress reduction and exercise effects, given that earlier studies documented quality of life and biological benefits for cancer patients with moderate exercise.[62,63] Being physically active (walking and household tasks) has also been shown to reduce the risk for development of breast cancer.[64] Various components of yoga intervention are known to have a calming effect and to correct autonomic imbalances[65-68] and HPA axis disturbances[28] that precede stress responses. This can help reduce perceived stress and maladaptive stress arousal patterns, which are known to cause heightened distress or depressive symptoms[69] in these patients.

The reduced psychological stress and cortisol levels that we found following the yoga program could be attributed to stress reduction rather than mere social support and education, as found in earlier studies.[33] The first major limitation in our study is the inequality in contact duration of interventions. Supportive therapy interventions were used only with the intention of negating the confounding variables such as instructor–patient interaction, education, and attention.[70] Inequality in contact duration of this intervention could have affected its effectiveness because successes of such interventions depend mainly on contact duration and content. Similar supportive sessions have been used successfully as a control comparison to evaluate psychotherapeutic interventions[70,71] and have been effective in controlling chemotherapy-related side effects. Second, the duration of the intervention was only 6 weeks, and we were not able to assess the chronic long-term effects of these interventions on cortisol rhythms. Third, it was not possible to conduct dexamethasone challenge in these participants or measure awakening-related cortisol peaks, which are among the standard tests for assessing HPA axis dysregulation.

## Conclusion

Our study confirmed previous findings of reductions in anxiety and depression following a yoga program. The reduction in perceived stress and cortisol levels further offers support for the stress reduction benefits of our program. However, larger randomized controlled trials with standard behavioral approaches as controls are needed to validate our findings. Future studies should unravel the putative neuroendocrine mechanisms of these interventions and assess stress appraisal following these interventions using laboratory stressors.

## Acknowledgments

This study was supported through a grant from Central Council for Research in Yoga and Naturopathy, Ministry of Health and Family Welfare, Government of India. We are thankful to Gopal Krishna for assisting with laboratory tests, K. N. Jayalakshmi for leading the yoga intervention, and Dr Ravi Kulkarni for assisting with statistical methods. We thank all staff of Bangalore Institute of Oncology and Bharath Hospital Institute of Oncology for their support throughout the project. We thank all patients and their spouses who participated in this study.

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