Published in final edited form as:

J Natl Compr Canc Netw. 2023 February ; 21(2): 153–162.e2. doi:10.6004/jnccn.2022.7080.

Effect of Yoga and Mediational Influence of Fatigue on Walking, Physical Activity, and Quality of Life Among Cancer Survivors

Po-Ju Lin, PhD, MPH[1], **Brian J. Altman, PhD**[2], **Nikesha J. Gilmore, PhD**[1], **Kah Poh Loh, MBBCh, BAO, MS**[3], **Richard F. Dunne, MS, MD**[3], **Javier Bautista, MS, MBA**[4], **Chunkit Fung, MD**[3], **Michelle C. Janelsins, PhD, MPH**[1], **Luke J. Peppone, PhD, MPH**[1], **Marianne K. Melnik, MD**[5], **Kim O. Gococo, MD**[6], **Michael J. Messino, MD**[7], **Karen M. Mustian, PhD, MPH**[1]

[1]Department of Surgery, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, New York;

[2]Department of Biomedical Genetics, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, New York;

[3]Department of Medicine, Wilmot Cancer Institute, University of Rochester Medical Center, Rochester, New York;

[4]Department of Mathematics, University of Rochester, Rochester, New York;

[5]Cancer Research Consortium of West Michigan NCORP, Grand Rapids, Michigan;

[6]NCORP of the Carolinas (Greenville Health System), Greenville, South Carolina;

[7]Southeast Clinical Oncology Research Consortium NCORP, Winston Salem, North Carolina.

Abstract

Background: Cancer-related fatigue (CRF) negatively affects survivors' walking, engagement in physical activity (PA), and quality of life (QoL). Yoga is an effective therapy for treating CRF; however, evidence from large clinical trials regarding how reducing CRF through yoga influences CRF's interference with survivors' walking, engagement in PA, and QoL is not available. We examined the effects of yoga and the mediational influence of CRF on CRF's interference with walking, PA, and QoL among cancer survivors in a multicenter phase III randomized controlled trial.

Patients and Methods: Cancer survivors (n=410) with insomnia 2 to 24 months posttreatment were randomized to a 4-week yoga intervention—Yoga for Cancer Survivors (YOCAS)—or standard care. A symptom inventory was used to assess how much CRF interfered with survivors' walking, PA, and QoL. The Multidimensional Fatigue Symptom Inventory-Short Form was used

Correspondence: Po-Ju Lin, PhD, MPH, Division of Supportive Care in Cancer, Department of Surgery, Wilmot Cancer Institute, University of Rochester Medical Center, 265 Crittenden Boulevard, Box 658, Rochester, NY 14642. Po-Ju_Lin@URMC.Rochester.edu.

Author contributions: *Conception and design:* Lin, Mustian. *Data analysis:* Lin, Bautista. *Data interpretation:* Lin, Bautista, Mustian. *Writing—original draft:* Lin. *Writing—review and editing:* All authors.

Disclosures: The authors have disclosed that they have not received any financial considerations from any person or organization to support the preparation, analysis, results, or discussion of this article.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

to assess CRF. Two-tailed *t* tests and analyses of covariance were used to examine within-group and between-group differences. Path analysis was used to evaluate mediational relationships between CRF and changes in CRF's interference with walking, PA, and QoL among survivors.

Results: Compared with standard care controls, YOCAS participants reported significant improvements in CRF's interference with walking, PA, and QoL at postintervention (all effect size = −0.33; all $P \leq .05$). Improvements in CRF resulting from yoga accounted for significant proportions of the improvements in walking (44%), PA (53%), and QoL (45%; all $P \leq .05$).

Conclusions: A significant proportion (44%–53%) of the YOCAS effect on CRF's interference with walking, PA, and QoL was due to improvements in CRF among cancer survivors. Yoga should be introduced and included as a treatment option for survivors experiencing fatigue. By reducing fatigue, survivors further improve their walking, engagement in PA, and QoL.

Background

Cancer is the second leading cause of death in the United States.[1] With advances in cancer screening and treatment, survival rates have increased by 20% over the past 4 decades.[2] Despite increased survival rates, quality of life (QoL) is often dramatically diminished due to cancer-related and treatment-related toxicities.[3–6]

Cancer-related fatigue (CRF) is one of the most pervasive toxicities experienced by survivors.[5,7–11] Although most patients experience CRF during treatment, up to 40% of survivors continue experiencing this debilitating fatigue after completion of treatment.[12–17] These survivors often report a lack of energy, tiredness, and a need to slow down and rest, which interferes with their ability to work, resume daily routines (eg, walking), and engage in physical activity (PA).[6,18]

Evidence suggests that yoga alleviates a variety of cancer-induced and treatment-induced toxicities, and could, therefore, improve QoL among cancer survivors.[19–32] We previously showed that our yoga intervention, Yoga for Cancer Survivors (YOCAS), effectively improves CRF, insomnia, cognitive impairment, arthralgias, and pain among cancer survivors.[33–37] To our knowledge, no nationwide, multicenter, phase III randomized controlled trial (RCT) has studied how reducing CRF through yoga consequently influences CRF's interference with survivors' daily activities such as walking and engaging in PA and QoL. Here we report the effect of YOCAS on CRF's interference with survivors' walking, PA, and QoL as secondary outcomes from our phase III RCT, and examine whether yoga-induced improvements in CRF mediate changes in CRF's interference with walking, PA, and QoL among survivors.

Patients and Methods

Study Design

We used data collected from our nationwide, multicenter, phase III RCT (ClinicalTrials.gov identifier: NCT00397930) conducted via the University of Rochester Cancer Center NCI Community Oncology Research Program Research Base (URCC NCORP RB) to examine the effect of YOCAS on CRF's interference with walking, PA, and QoL (as secondary

outcomes) among cancer survivors. The primary and other secondary outcomes along with detailed study design and methods have been published previously.[33–37] See supplemental eAppendix 1 (available with this article at JNCCN.org) for information on study recruitment and randomization.

Participants

Participant inclusion criteria included (1) any type of cancer diagnosis, excluding a metastatic diagnosis; (2) completion of primary treatment 2 to 24 months prior to enrollment; (3) persistent sleep disturbance (≥3 on symptom inventory scale); (4) age ≥21 years; and (5) ability to read and understand English. Participants were excluded if they (1) regularly practiced yoga within 3 months or planned to start a new yoga program during the study period; (2) were diagnosed with sleep apnea or metastatic cancer; and (3) were currently receiving any form of cancer treatments except hormonal therapy.

Yoga Intervention

YOCAS is a standardized 4-week yoga intervention that is based on gentle hatha and restorative yoga consisting of breathing exercises, physical alignment postures, and mindfulness exercises.[33] Participants in the YOCAS group received 8 yoga sessions (75 minutes per session, twice per week) at low to moderate intensity. Each yoga session was delivered by a Yoga Alliance–registered instructor in a group setting (10–15 participants per group) at community-based sites (eg, community centers, cancer centers, and yoga studios).[33]

To ensure the standardization, quality, and fidelity of the yoga intervention, each instructor completed a 2-hour training session conducted by the URCC NCORP RB and was instructed to follow the provided intervention manual and a DVD to deliver YOCAS sessions. The study coordinator from each participating NCORP community oncology practice also attended a randomly selected yoga session to observe and verify whether proper content was delivered.

Standard Care Control

Participants in the standard care control group continued their usual follow-up clinic visits with their oncologists and primary care providers. They received the same amount of time and attention from the research team regarding study measures but had no yoga exposure.

Measures

Medical records were reviewed to confirm participants' eligibility and collect clinical information (eg, cancer type, previous treatment). Demographic data were collected via the study-specific form. Race data were collected using the NCI Clinical Trials Reporting Program criteria for clinical trials. For data reporting purposes, we condensed racial categories to White, Black, and Other (comprising Native Hawaiian or Other Pacific Islander, Asian, American Indian, Alaska Native, and unknown).

Adherence and compliance were monitored by patient-reported daily diaries and yoga attendance logs completed by yoga instructors. A feedback form was used to collect the

helpfulness of the YOCAS intervention and whether yoga participants would recommend the intervention to other survivors experiencing similar symptoms. Adverse events were monitored using NCI's Common Terminology Criteria for Adverse Events and were reported to the URCC Data Safety Monitoring Committee.

CRF's Interference With Walking, PA, and QoL—The symptom inventory is a commonly used and widely accepted tool for both research and clinical assessments of the severity of symptoms and how symptoms interfere with patients' daily living.[38] We modified the MD Anderson Symptom Inventory and included 12 common symptoms and 8 interference items.[36,37] Participants were asked to rate the severity of each symptom on a scale of 0 to 10 (0 = not present; 10 = as bad as you can imagine) and how much their fatigue interfered with the 8 items of their life (including daily living, mood, work, relations with other people, general physical activity, walking, exercise, and quality of life) with a scale of 0 to 10 (0 = did not interfere; 10 = completely interfered). In this study, we used 3 Symptom Inventory interference items to assess CRF's interference with walking, PA, and QoL. Higher scores indicate worse interference.

CRF—CRF was measured via the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI),[39,40] a validated, 30-item, commonly used fatigue instrument that generates a total score indicating overall CRF level and 5 subdomain scores indicating general, physical, emotional, and cognitive fatigue and vigor levels. Higher scores indicate worse fatigue levels. CRF results were previously published.[34,37] In this study, the total MFSI scores were used for mediation analysis.

Statistical Analyses

Among 410 participants who consented and were randomized, 328 provided complete baseline and postintervention symptom inventory and MFSI data. A sample size of 328 (YOCAS: n=168; standard care: n=160) provided >90% power to detect an effect size of 0.33 in between-group differences in CRF's interference with walking, PA, and QoL scores assuming a correlation coefficient of 0.5 between baseline and postintervention at a significance level of 5% with a 2-tailed F test using analysis of covariance (ANCOVA).

Between-group differences in baseline demographic data and characteristics were examined with 2-tailed *t* tests for continuous variables and chi-square tests for categorical variables. Within-group differences in CRF's interference with walking, PA, and QoL were assessed using 2-tailed *t* tests. Between-group intervention effects on CRF's interference with walking, PA, and QoL at postintervention were assessed using ANCOVA with the intervention arm as the group factor and baseline value as a covariate. Two-tailed *t* tests and ANCOVA were performed using SAS 9.4 (SAS Institute Inc.). The effect size was calculated using the between-group mean change (postintervention minus baseline) in CRF's interference with walking, PA, and QoL divided by the standard deviation of baseline scores.

The mediation analysis was conducted using path modeling on change scores in CRF with change scores in CRF's interference with walking, PA, and QoL as the dependent variables to derive path coefficients. The path modeling included a direct path between the intervention arm (YOCAS vs standard care) and each outcome variable (CRF's interference

with walking, PA, and QoL), a path between the intervention arm and CRF, and a path between CRF and each outcome variable. Statistical significance of mediation was assessed using nonparametric bootstrap 95% confidence intervals for the indirect path coefficient from the intervention arm to each outcome variable on CRF. Statistical significance was determined as $P \leq .05$.

Data analyses followed the intent-to-treat principle and were based on complete cases (see supplemental eAppendix 1 for the description of intent-to-treat, multiple imputation, and mediation analysis).

Results

Figure 1 shows the CONSORT diagram. Among 413 survivors who consented to participate in the study, 3 were excluded due to ineligibility, 410 were randomized to either YOCAS (n=206) or standard care (n=204), 357 provided complete baseline symptom inventory and MFSI data, and 328 provided complete baseline and postintervention symptom inventory and MFSI data. Eighty-one enrolled participants, including 37 YOCAS participants and 44 standard care controls, dropped out of the study due to medical issues (n=12), personal issues (n=47), unknown reasons (n=20), and starting their own yoga program (n=2). One YOCAS participant did not provide complete baseline data. The proportion of dropouts between YOCAS (18%) and standard care (22%) was not significantly different.

Demographics and Baseline Characteristics

Table 1 shows the demographics and baseline characteristics of 357 participants (YOCAS: n=176; standard care: n=181) who provided complete baseline symptom inventory and MFSI data. Mean [SD] age of participants was 54.3 [10.2] years; most were female (96%), White (93%), married or in a committed relationship (73%), educated at a college level or higher (81%), employed (81%), and breast cancer survivors (77%). Participants had completed surgery (90%), chemotherapy (71%), and/or radiation therapy (67%) prior to enrollment. On average, there was a mean [SD] of 15.7 [8.2] months since their first cancer treatment. No significant between-group differences were found in demographics and baseline characteristics.

Adherence, Compliance, and Adverse Events

YOCAS participants attended an average of 6.5 of 8 prescribed yoga sessions and reported practicing 1 additional session per week on their own. The average rating of exertion was 3.4 on a 0 to 10 scale (with 0 = “nothing at all” and 10 = “very, very strong”), indicating that the intensity of the YOCAS session was low to moderate. YOCAS participants, on average, practiced 182 minutes of yoga each week or 728 minutes across the 4-week intervention period, which was 128 minutes more than the prescribed yoga dose (eight 75-minute sessions = 600 minutes). No significant yoga contamination was found in the standard care group; 7 standard care controls reported an average of 20 minutes of yoga practice weekly during the intervention period. No study intervention–related adverse events were reported.

CRF's Interference With Walking, PA, and QoL

YOCAS participants reported significant improvements in CRF's interference with walking (−0.6 ± 0.2; P=.01), PA (−0.9 ± 0.2; P<.01), and QoL (−1.0 ± 0.2; P<.01) from baseline to postintervention, whereas standard care controls reported no change in these outcomes. In addition, ANCOVA revealed significantly greater improvements in CRF's interference with walking (−0.9 ± 0.3; P<.01; effect size = −0.33; 95% CI, −0.54 to −0.11), PA (−0.9 ± 0.3; P<.01; effect size = −0.33; 95% CI, −0.52 to −0.15), and QoL (−0.9 ± 0.3; P<.01; effect size = −0.33; 95% CI, −0.51 to −0.14) in YOCAS participants than in standard care controls at postintervention, controlling for baseline values (Figure 2, Table 2). More than 90% of YOCAS participants found these changes to be clinically meaningful; they explicitly stated that the YOCAS intervention was helpful and they would recommend it to other survivors for managing these side effects.

Mediational Effect of CRF on CRF's Interference With Walking

YOCAS participants, compared with standard care controls, reported significantly greater improvements in CRF from baseline to postintervention.[34] Mediation analysis revealed that improvements in CRF significantly mediated the intervention effect on CRF's interference with walking. The path mediation model of CRF and CRF's interference with walking adjusted with the intervention effect is demonstrated in Figure 3. The total effect of YOCAS compared with standard care on symptom inventory walking interference score was −1.01 points (P<.01), indicating that YOCAS improved CRF's interference with walking by 1.01 points compared with the effect of standard care on walking. Improvements in CRF significantly mediated the YOCAS effect on CRF's interference with walking by 0.45 points in addition to the direct YOCAS effect on CRF's interference with walking of 0.57 points, suggesting that 44% (95% CI, 24%–100%) of the improvements in CRF's interference with walking was mediated through improvements in CRF.

Mediational Effect of CRF on CRF's Interference With PA

Mediation analysis revealed that improvements in CRF significantly mediated the intervention effect on CRF's interference with PA. The path mediation model of CRF and CRF's interference with PA adjusted with the intervention effect is demonstrated in Figure 4. The total effect of YOCAS compared with standard care on symptom inventory PA interference score was −1.02 points (P<.01), indicating that YOCAS improved CRF's interference with PA by 1.02 points compared with the effect of standard care on PA. Improvements in CRF significantly mediated the YOCAS effect on improvements in CRF's interference with PA by 0.54 points in addition to the direct YOCAS effect on CRF's interference with PA of 0.47 points, suggesting that 53% (95% CI, 34%–100%) of the improvements in CRF's interference with PA was mediated through improvements in CRF.

Mediational Effect of CRF on CRF's Interference With QoL

Mediation analysis revealed that improvements in CRF significantly mediated the intervention effect on CRF's interference with QoL. The path mediation model of CRF and CRF's interference with QoL adjusted with the intervention effect is demonstrated in Figure 5. The total effect of YOCAS compared with standard care on symptom inventory

QoL interference score was −0.96 points (P<.01), indicating that YOCAS improved CRF's interference with QoL by 0.96 points compared with the effect of standard care on QoL. Improvements in CRF significantly mediated the YOCAS effect on improvements in CRF's interference with QoL by 0.43 points in addition to the direct YOCAS effect on CRF's interference with QoL of 0.52 points, suggesting that 45% (95% CI, 26%–100%) of the improvements in CRF's interference with QoL was mediated through improvements in CRF.

Discussion

To our knowledge, this is the first nationwide, multicenter, phase III RCT demonstrating how reducing fatigue through a standardized, 4-week, yoga intervention (YOCAS) has broader implications on survivors' daily activities and QoL. Our findings suggest that YOCAS, the gentle hatha and restorative yoga–based, low- to moderate-intensity yoga intervention, practiced 2 to 3 times per week (182 minutes per week; 32–75 minutes per session) for 4 weeks significantly improves CRF's interference with walking, PA, and QoL among cancer survivors. A significant proportion (44%–53%) of the YOCAS effect on CRF's interference with walking, PA, and QoL is due to improvements in CRF. By practicing YOCAS, survivors not only reported less CRF but consequently improved their engagement in daily activities such as walking and PA, and overall QoL, suggesting the broader therapeutic impact of yoga on symptom management in cancer survivors.

Although most oncology guidelines[41–45] mention that it is reasonable to recommend the use of yoga for treating CRF, compelling level 1/category 1 scientific evidence from multiple blinded phase III RCTs is insufficient to make yoga a gold standard treatment. Results of this study add substantial value to the scientific evidence supporting the use of yoga for treating CRF and its interference with essential daily activities such as walking, PA, and QoL.[24–26,28–30,32–37,46–48] In addition, our YOCAS participants demonstrated high adherence and compliance to the yoga intervention, found the yoga intervention helpful, and claimed they would recommend it to other survivors experiencing similar side effects, which underlines the clinically meaningful effect of yoga on symptom management.[33] Because these were secondary exploratory analyses, future phase III RCTs designed a priori with CRF and its interference with walking, PA, and QoL as primary outcomes are needed.

Although the results of this study are compelling regarding the use of yoga for treating CRF and its interference with daily activities and QoL, yoga remains underprescribed as an element of supportive care among cancer survivors.[49,50] Improving awareness and enhancing accessibility of yoga therapy in cancer care and collaborations with yoga therapists and integrative medicine can lead to dissemination and implementation of yoga therapy in the oncology setting and extension of the benefits of yoga to greater numbers of cancer survivors.[50–53] We understand that not all survivors will want to use yoga for treating CRF and other side effects. For those patients, it is reasonable to recommend the use of other behavioral interventions noted in oncology supportive care treatment guidelines (eg, exercise, cognitive behavioral therapy).

Certain limitations should be considered when interpreting our results and developing future studies, including (1) the generalizability of the results: most of our study participants were

White, female, educated at a college level or higher, and breast cancer survivors, who do not represent the diversity of the cancer population; (2) the lack of a comparison with an active behavioral placebo: the study design did not compare YOCAS with an active behavioral placebo controlling for subject contact time and attention of the intervention; therefore, we cannot assess whether the improvements in CRF and in CRF's interference with walking, PA, and QoL are specific to YOCAS; (3) use of only 3 items of the self-reported symptom inventory questionnaire to evaluate CRF's interference with walking, PA, and QoL might not comprehensively evaluate the true interference level; (4) CRF and the 3 main outcomes were assessed only at baseline and postintervention: this assessment arrangement could not capture temporal changes for mediation analysis and evaluate sustainability of the intervention effect; (5) although compliance with YOCAS was good in this study, the effective dose of yoga might be challenging for survivors with more severe medical, physical, financial, or environmental barriers; and (6) 20% of enrolled participants dropped out due to personal, medical, and other reasons.

Future phase II/III RCTs should consider testing yoga intervention among survivors with diverse demographic backgrounds and various cancer types and treatment histories, and develop strategies to improve participant retention. Comparing yoga intervention to known effective treatments such as exercise or psychosocial interventions for alleviating CRF and its interference with daily activities and QoL could further elucidate the magnitude of each yoga component or their combination (breathing, postures, and mindfulness) versus the active component from other interventions, provide more direct clinical evidence, and identify multiple treatment options for symptom management. Collecting and analyzing objective biophysiologic data and assessing mediational relationships might help reveal the etiologic and pathophysiologic mechanisms of CRF and its connection to survivors' walking, PA, and QoL. The study of temporal and dose–response relationships can help oncologists and yoga therapists prescribe yoga doses more precisely. Combining yoga with other behavioral interventions can also be considered to elicit greater improvements in CRF and its interference with walking, PA, and QoL among cancer survivors.

Conclusions

Our findings suggest that the standardized 4-week YOCAS yoga program improved CRF's interference with walking, PA, and QoL among cancer survivors. More importantly, 44% to 53% of the improvements in CRF's interference with walking, PA, and QoL are attributable to improvements in CRF resulting from yoga. Our findings provide strong clinical evidence for oncologists to include yoga as a treatment option when designing a cancer care plan for survivors experiencing CRF and its interference with walking, PA, and QoL.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We acknowledge and thank all the cancer survivors who participated in this study, the participating NCORP community oncology practices, URCC NCORP RB staff, and Wilmot Cancer Institute Human Biopsychology

Shared Resource PEAK Human Performance Clinical Research Laboratory staff for their help with this nationwide, multicenter phase III RCT. We also acknowledge and thank Drs. Susan Rosenthal and Elaine Smolock for editorial assistance.

Funding:

Research reported in this publication was supported by the National Cancer Institute at the National Institutes of Health under awarded number U10CA037420 with supplemental funding from the Office of Cancer Complementary and Alternative Medicine, UG1CA189961 with supplemental funding from the Division of Cancer Prevention, R01CA181064, and T32CA102618.

References

1. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021. CA Cancer J Clin 2021;71:7–33. [PubMed: 33433946]
2. Howlader N, Noone AM, Krapcho M, et al., eds. SEER cancer statistics review, 1975–2017. Accessed August 15, 2022. Available at: https://seer.cancer.gov/csr/1975_2017/
3. Curt GA, Breitbart W, Cella D, et al. Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. Oncologist 2000;5:353–360. [PubMed: 11040270]
4. Andrykowski MA, Donovan KA, Laronga C, et al. Prevalence, predictors, and characteristics of off-treatment fatigue in breast cancer survivors. Cancer 2010;116:5740–5748. [PubMed: 20734399]
5. Hofman M, Ryan JL, Figueroa-Moseley CD, et al. Cancer-related fatigue: the scale of the problem. Oncologist 2007;12(Suppl 1):4–10. [PubMed: 17573451]
6. Barsevick AM, Cleeland CS, Manning DC, et al. ASCPRO recommendations for the assessment of fatigue as an outcome in clinical trials. J Pain Symptom Manage 2010;39:1086–1099. [PubMed: 20538190]
7. Patrick DL, Ferketich SL, Frame PS, et al. National Institutes of Health State-of-the-Science Conference statement: symptom management in cancer: pain, depression, and fatigue, July 15–17, 2002. J Natl Cancer Inst 2003;95:1110–1117. [PubMed: 12902440]
8. Henry DH, Viswanathan HN, Elkin EP, et al. Symptoms and treatment burden associated with cancer treatment: results from a cross-sectional national survey in the U.S. Support Care Cancer 2008;16:791–801. [PubMed: 18204940]
9. Kuhnt S, Ernst J, Singer S, et al. Fatigue in cancer survivors—prevalence and correlates. Onkologie 2009;32:312–317. [PubMed: 19521117]
10. Servaes P, Verhagen C, Bleijenberg G. Fatigue in cancer patients during and after treatment: prevalence, correlates and interventions. Eur J Cancer 2002;38:27–43. [PubMed: 11750837]
11. Lawrence DP, Kupelnick B, Miller K, et al. Evidence report on the occurrence, assessment, and treatment of fatigue in cancer patients. J Natl Cancer Inst Monogr 2004;2004:40–50.
12. Bower JE, Ganz PA, Desmond KA, et al. Fatigue in long-term breast carcinoma survivors: a longitudinal investigation. Cancer 2006;106:751–758. [PubMed: 16400678]
13. Servaes P, Gielissen MF, Verhagen S, et al. The course of severe fatigue in disease-free breast cancer patients: a longitudinal study. Psychooncology 2007;16:787–795. [PubMed: 17086555]
14. Bower JE, Ganz PA, Desmond KA, et al. Fatigue in breast cancer survivors: occurrence, correlates, and impact on quality of life. J Clin Oncol 2000;18:743–753. [PubMed: 10673515]
15. Abrahams HJG, Gielissen MF, Schmits IC, et al. Risk factors, prevalence, and course of severe fatigue after breast cancer treatment: a meta-analysis involving 12 327 breast cancer survivors. Ann Oncol 2016;27: 965–974. [PubMed: 26940687]
16. Garabeli Cavalli Kluthcovsky AC, Urbanetz AA, de Carvalho DS, et al. Fatigue after treatment in breast cancer survivors: prevalence, determinants and impact on health-related quality of life. Support Care Cancer 2012;20:1901–1909. [PubMed: 21994001]
17. Sprauten M, Haugnes HS, Brydøy M, et al. Chronic fatigue in 812 testicular cancer survivors during long-term follow-up: increasing prevalence and risk factors. Ann Oncol 2015;26:2133–2140. [PubMed: 26265167]
18. Curtis EB, Krech R, Walsh TD. Common symptoms in patients with advanced cancer. J Palliat Care 1991;7:25–29.

19. Banasik J, Williams H, Haberman M, et al. Effect of Iyengar yoga practice on fatigue and diurnal salivary cortisol concentration in breast cancer survivors. J Am Acad Nurse Pract 2011;23:135–142. [PubMed: 21355946]
20. Ben-Josef AM, Chen J, Wileyto P, et al. Effect of Eischens yoga during radiation therapy on prostate cancer patient symptoms and quality of life: a randomized phase II trial. Int J Radiat Oncol Biol Phys 2017;98: 1036–1044. [PubMed: 28721886]
21. Bower JE, Garet D, Sternlieb B, et al. Yoga for persistent fatigue in breast cancer survivors: a randomized controlled trial. Cancer 2012;118: 3766–3775. [PubMed: 22180393]
22. Carson JW, Carson KM, Porter LS, et al. Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. Support Care Cancer 2009;17:1301–1309. [PubMed: 19214594]
23. Chandwani KD, Perkins G, Nagendra HR, et al. Randomized, controlled trial of yoga in women with breast cancer undergoing radiotherapy. J Clin Oncol 2014;32:1058–1065. [PubMed: 24590636]
24. Danhauer SC, Mihalko SL, Russell GB, et al. Restorative yoga for women with breast cancer: findings from a randomized pilot study. Psychooncology 2009;18:360–368. [PubMed: 19242916]
25. Kiecolt-Glaser JK, Bennett JM, Andridge R, et al. Yoga's impact on in-flammation, mood, and fatigue in breast cancer survivors: a randomized controlled trial. J Clin Oncol 2014;32:1040–1049. [PubMed: 24470004]
26. Littman AJ, Bertram LC, Ceballos R, et al. Randomized controlled pilot trial of yoga in overweight and obese breast cancer survivors: effects on quality of life and anthropometric measures. Support Care Cancer 2012; 20:267–277. [PubMed: 21207071]
27. Stan DL, Croghan KA, Croghan IT, et al. Randomized pilot trial of yoga versus strengthening exercises in breast cancer survivors with cancer-related fatigue. Support Care Cancer 2016;24:4005–4015. [PubMed: 27129840]
28. Vadiraja SH, Rao MR, Nagendra RH, et al. Effects of yoga on symptom management in breast cancer patients: a randomized controlled trial. Int J Yoga 2009;2:73–79. [PubMed: 20842268]
29. Yagli NV, Ulger O. The effects of yoga on the quality of life and depression in elderly breast cancer patients. Complement Ther Clin Pract 2015; 21:7–10. [PubMed: 25697379]
30. Lin PJ, Peppone LJ, Janelsins MC, et al. Yoga for the management of cancer treatment-related toxicities. Curr Oncol Rep 2018;20:5. [PubMed: 29388071]
31. Kleckner IR, Dunne RF, Asare M, et al. Exercise for toxicity management in cancer-a narrative review. Oncol Hematol Rev 2018;14:28–37. [PubMed: 29713475]
32. Zetzl T, Renner A, Pittig A, et al. Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer. Support Care Cancer 2021;29:2973–2982. [PubMed: 33026490]
33. Mustian KM, Sprod LK, Janelsins M, et al. Multicenter, randomized controlled trial of yoga for sleep quality among cancer survivors. J Clin Oncol 2013;31:3233–3241. [PubMed: 23940231]
34. Lin PJ, Kleckner IR, Loh KP, et al. Influence of yoga on cancer-related fatigue and on mediational relationships between changes in sleep and cancer-related fatigue: a nationwide, multicenter randomized controlled trial of yoga in cancer survivors. Integr Cancer Ther 2019;18:1–11.
35. Janelsins MC, Peppone LJ, Heckler CE, et al. YOCAS yoga reduces self-reported memory difficulty in cancer survivors in a nationwide randomized clinical trial: investigating relationships between memory and sleep. Integr Cancer Ther 2016;15:263–271. [PubMed: 26621521]
36. Peppone LJ, Janelsins MC, Kamen C, et al. The effect of YOCAS yoga for musculoskeletal symptoms among breast cancer survivors on hormonal therapy. Breast Cancer Res Treat 2015;150:597–604. [PubMed: 25814054]
37. Sprod LK, Fernandez ID, Janelsins MC, et al. Effects of yoga on cancer-related fatigue and global side-effect burden in older cancer survivors. J Geriatr Oncol 2015;6:8–14. [PubMed: 25449185]
38. Cleeland CS, Mendoza TR, Wang XS, et al. Assessing symptom distress in cancer patients: the MD Anderson Symptom Inventory. Cancer 2000; 89:1634–1646. [PubMed: 11013380]
39. Stein KD, Jacobsen PB, Blanchard CM, et al. Further validation of the multidimensional fatigue symptom inventory-short form. J Pain Symptom Manage 2004;27:14–23. [PubMed: 14711465]

40. Stein KD, Martin SC, Hann DM, et al. A multidimensional measure of fatigue for use with cancer patients. Cancer Pract 1998;6:143–152. [PubMed: 9652245]
41. Bower JE, Bak K, Berger A, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: an American Society of Clinical Oncology clinical practice guideline adaptation. J Clin Oncol 2014;32:1840–1850. [PubMed: 24733803]
42. Jankowski C, Berger AM, Aranha O, et al. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue. Version 2.2022. Accessed January 15, 2022. To view the most recent version, visit https://www.nccn.org
43. Howell D, Keshavarz H, Broadfield L, et al. A pan Canadian practice guideline for screening, assessment, and management of cancer-related fatigue in adults. Accessed January 15, 2022. Available at: https://www.capo.ca/guidelines
44. Lyman GH, Greenlee H, Bohlke K, et al. Integrative therapies during and after breast cancer treatment: ASCO endorsement of the SIO Clinical Practice Guideline. J Clin Oncol 2018;36:2647–2655. [PubMed: 29889605]
45. Mitchell SA, Hoffman AJ, Clark JC, et al. Putting evidence into practice: an update of evidence-based interventions for cancer-related fatigue during and following treatment. Clin J Oncol Nurs 2014;18(Suppl):38–58. [PubMed: 25427608]
46. McCall M, McDonald M, Thorne S, et al. Yoga for health-related quality of life in adult cancer: a randomized controlled feasibility study. Evid Based Complement Alternat Med 2015;2015: 816820. [PubMed: 26170884]
47. Cramer H, Lauche R, Klose P, et al. Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database Syst Rev 2017;1: CD010802. [PubMed: 28045199]
48. Zhi WI, Baser RE, Zhi LM, et al. Yoga for cancer survivors with chemotherapy-induced peripheral neuropathy: health-related quality of life outcomes. Cancer Med 2021;10:5456–5465. [PubMed: 34213086]
49. Rosen JE, Gardiner P, Saper RB, et al. Complementary and alternative medicine use among patients with thyroid cancer. Thyroid 2013;23: 1238–1246. [PubMed: 23350883]
50. Larbi OM, Jiang C, McLane B, et al. Interest and willingness to pay for integrative therapies of patients with cancer and caregivers. JCO Oncol Pract 2021;17:e1622–1630. [PubMed: 33492981]
51. Kacel EL, Pereira DB, Estores IM. Advancing supportive oncology care via collaboration between psycho-oncology and integrative medicine. Support Care Cancer 2019;27:3175–3178. [PubMed: 31062108]
52. McCall M, Thorne S, Ward A, et al. Yoga in adult cancer: an exploratory, qualitative analysis of the patient experience. BMC Complement Altern Med 2015;15:245. [PubMed: 26198820]
53. Womack DM, Kennedy R, Chamberlin SR, et al. Patients' lived experiences and recommendations for enhanced awareness and use of integrative oncology services in cancer care. Patient Educ Couns 2022;105:2557–2561. [PubMed: 34865887]

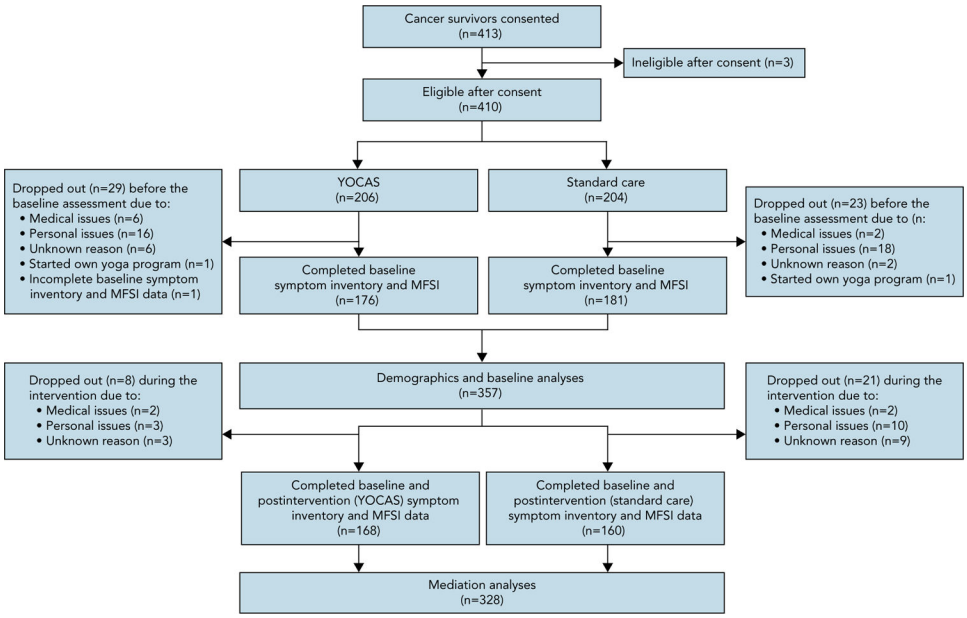

Figure 1.

CONSORT diagram.

Abbreviations: MFSI, Multidimensional Fatigue Symptom Inventory; YOCAS, Yoga for Cancer Survivors.

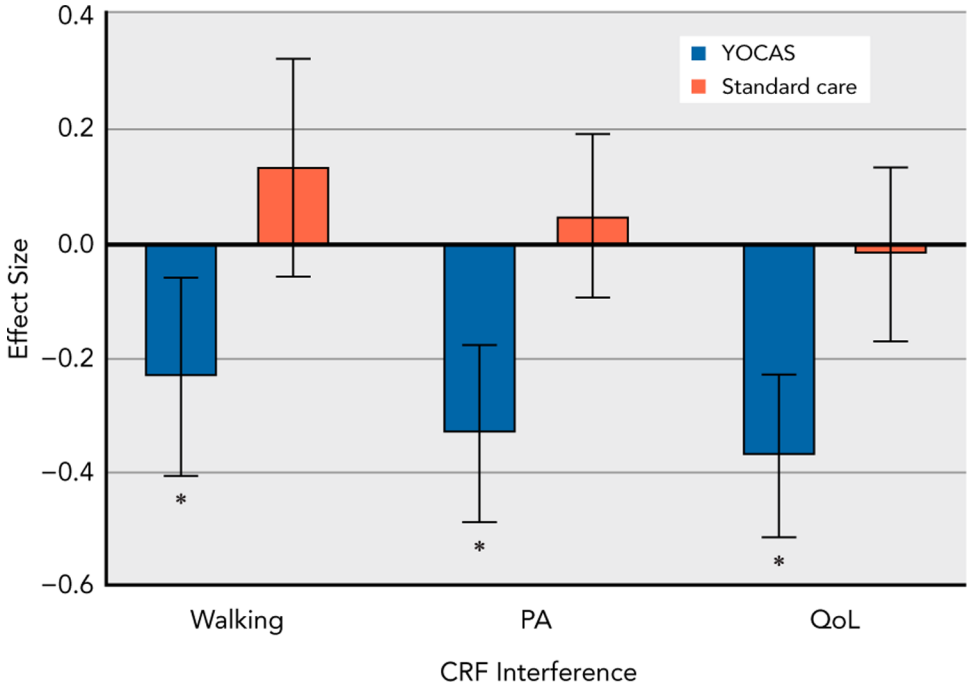

Figure 2.

Changes in CRF's interference with walking, PA, and QoL. Data are presented as effect size and its 95% confidence limits.

Abbreviations: CRF, cancer-related fatigue; PA, physical activity; QoL, quality of life; YOCAS, Yoga for Cancer Survivors.

*$P \leq .05$.

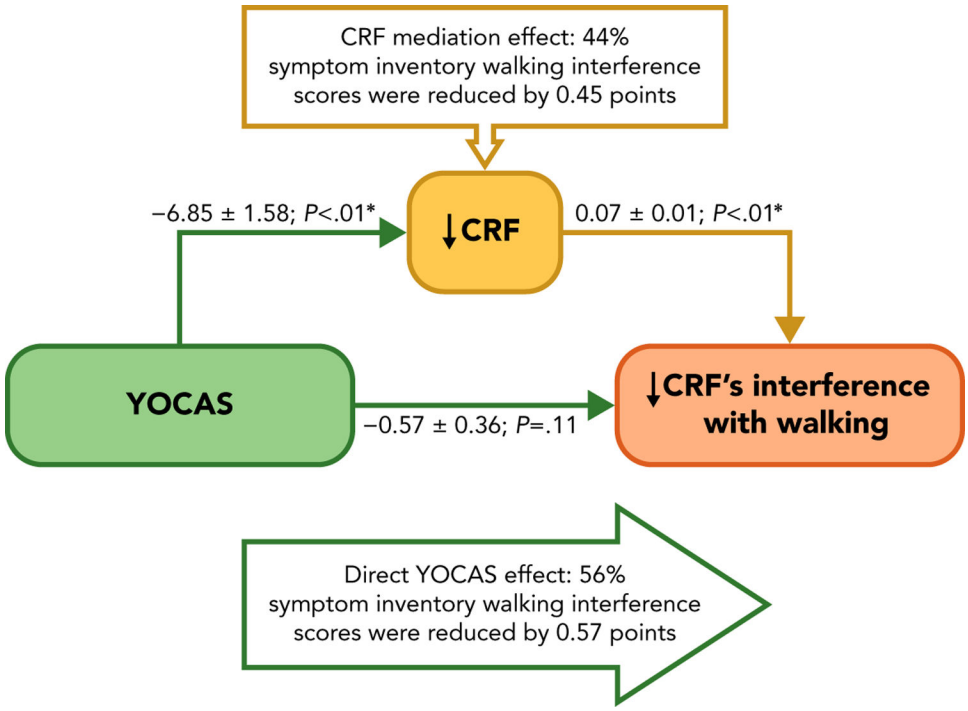

Figure 3.

Mediational effect of CRF on its interference with walking. Data are presented as regression coefficient ±SE.

Abbreviations: CRF, cancer-related fatigue; YOCAS, Yoga for Cancer Survivors.

*$P \leq .05$.

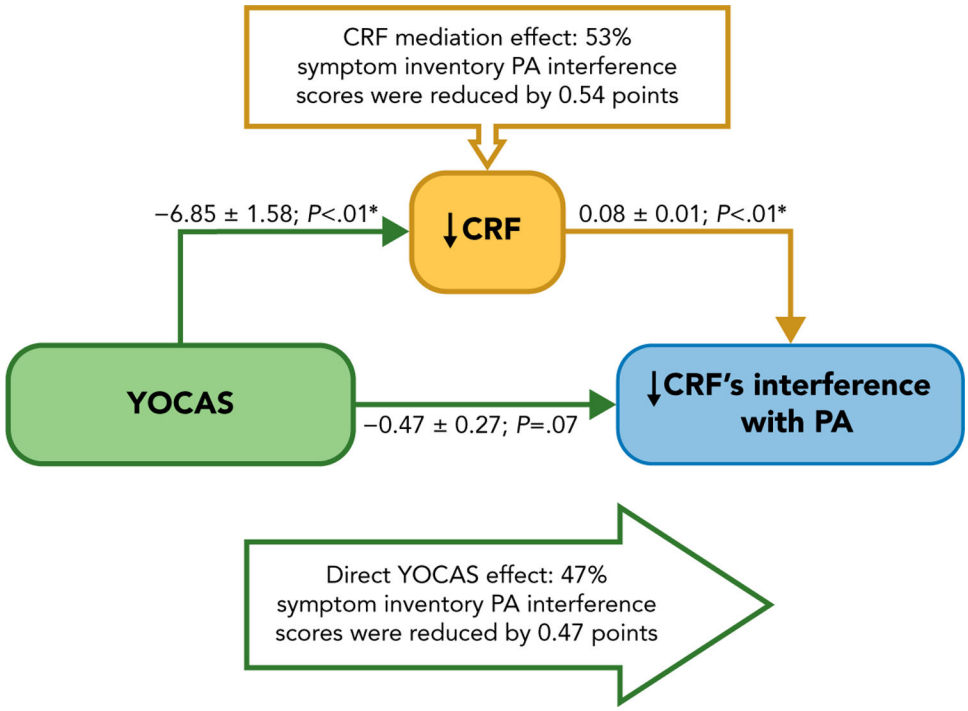

Figure 4.

Mediational effect of CRF on its interference with PA. Data are presented as regression coefficient ±SE.

Abbreviations: CRF, cancer-related fatigue; PA, physical activity; YOCAS, Yoga for Cancer Survivors.

*$P \leq .05$.

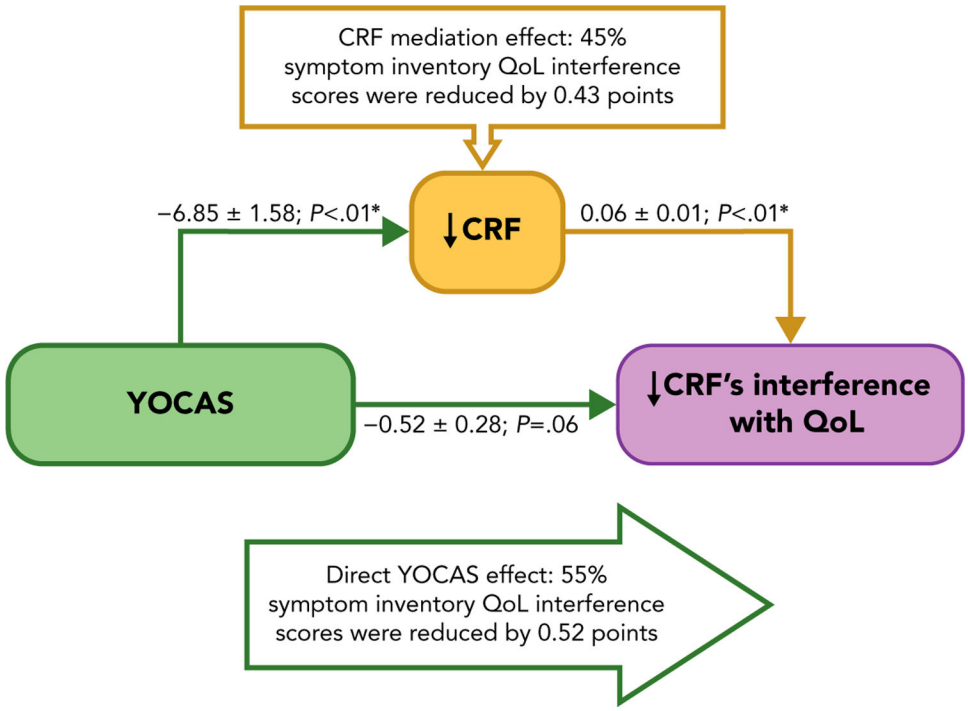

Figure 5.

Mediational effect of CRF on its interference with QoL. Data are presented as regression coefficient ±SE.

Abbreviations: CRF, cancer-related fatigue; QoL, quality of life; YOCAS, Yoga for Cancer Survivors.

*$P \leq .05$.

Table 1.

Demographics and Baseline Characteristics

Characteristic	Total n (%)	YOCAS n (%)	Standard Care n (%)
Total, n	357	176	181
Age, mean [SD], y	54.3 [10.2]	55.0 [11.1]	53.7 [9.3]
Sex			
Female	343 (96)	168 (95)	175 (97)
Male	14 (4)	8 (5)	6 (3)
Race			
White	333 (93)	169 (96)	164 (91)
Black	21 (6)	6 (3)	15 (8)
Other[a]	3 (1)	1 (1)	2 (1)
Marital status			
Married/Committed relationship	260 (73)	125 (71)	137 (75)
Separated/Divorced	52 (15)	25 (14)	27 (15)
Widowed	15 (4)	11 (6)	4 (2)
Single	30 (8)	15 (9)	15 (8)
Education			
Some college or higher	291 (81)	146 (83)	145 (80)
High school graduate	63 (18)	28 (16)	35 (19)
Less than a high school education	3 (1)	2 (1)	1 (1)
Currently employed	291 (81)	149 (85)	142 (78)
Cancer type			
Breast	274 (77)	132 (75)	142 (78)
Hematologic	25 (7)	13 (7)	12 (7)
Alimentary	21 (6)	7 (4)	14 (8)
Gynecologic	16 (4)	10 (6)	6 (3)
Other	21 (6)	14 (8)	7 (4)
Cancer stage			

J Natl Compr Canc Netw. Author manuscript; available in PMC 2023 March 07.

Characteristic	Total n (%)	YOCAS n (%)	Standard Care n (%)
0	17 (5)	9 (5)	8 (4)
I	126 (35)	55 (31)	71 (39)
II	122 (34)	62 (35)	60 (33)
III	57 (16)	28 (16)	29 (16)
IV	10 (3)	7 (4)	3 (2)
Unknown	25 (7)	15 (9)	10 (6)
Previous treatment			
Surgery	323 (90)	159 (90)	164 (91)
Chemotherapy	255 (71)	129 (73)	126 (70)
Radiation therapy	239 (67)	119 (68)	120 (66)
Hormonal therapy	25 (7)	11 (6)	14 (8)
Current hormonal therapy	185 (52)	84 (48)	101 (56)
Months since first cancer treatment, mean [SD]	15.7 [8.2]	14.9 [6.8]	16.4 [9.4]

Abbreviation: YOCAS, Yoga for Cancer Survivors.

[a]Native Hawaiian or Other Pacific Islander, Asian, American Indian, Alaska Native, and unknown.

Table 2.

Changes in CRF's Interference With Walking, Physical Activity, and Quality of Life

	YOCAS				Standard Care				YOCAS vs Standard Care			
Assessment (mean ± SE)	**Baseline (n=176)**	**Postintervention (n = 168)**	**Within-Group Difference (n = 168)**	***t* Test *P* Value**	**Baseline (n = 181)**	**Postintervention (n=160)**	**Within-Group Difference (n = 160)**	***t* Test *P* Value**	**Between-Group Difference**	**Adjusted[a] Between-Group Difference**	**ANCOVA *P* Value**	**Effect Size (95% CI)**
CRF's interference with walking	2.8 ± 0.2	2.2 ± 0.2	−0.6 ± 0.2	.01*	2.7 ± 0.2	3.0 ± 0.2	0.4 ± 0.3	.16	−1.0 ± 0.4	−0.9 ± 0.3	<.01*	−0.33 (−0.54 to −0.11)
CRF's interference with PA	3.8 ± 0.2	2.9 ± 0.2	−0.9 ± 0.2	<.01*	3.5 ± 0.2	3.6 ± 0.2	0.1 ± 0.2	.50	−1.0 ± 0.3	−0.9 ± 0.3	<.01*	−0.33 (−0.52 to −0.15)
CRF's interference with QoL	3.6 ± 0.2	2.5 ± 0.2	−1.0 ± 0.2	<.01*	3.5 ± 0.2	3.4 ± 0.2	−0.1 ± 0.2	.81	−1.0 ± 0.3	−0.9 ± 0.3	<.01*	−0.33 (−0.51 to −0.14)

Abbreviations: CRF, cancer-related fatigue; PA, physical activity; QoL, quality of life; YOCAS, Yoga for Cancer Survivors.

[a]Adjusted for baseline value.

*$P \leq .05$.