

The impact of yoga practice on cortisol levels in breast cancer patients — a comprehensive review

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Abstract

Breast cancer is one of the most prevalent cancers in women worldwide, often accompanied by significant psychological distress and hormonal imbalances, including elevated cortisol levels. Cortisol, as a crucial hormone secreted in response to physical and psychological stress, plays an important role in regulation of numerous human body systems. A vast number of studies showed that chronic stress and prolonged hypersecretion of cortisol promote carcinogenesis and tumor growth. Because of the known relaxing effects of yoga and its ability to lower cortisol levels, complementary therapies including integrated yoga programs have gained attention due to their potential to mitigate the adverse effects of cancer and its treatment. To this day, multiple studies to evaluate the positive impact of yoga on lowering cortisol levels in breast cancer patients have been carried out. This review aims to shed light on how cortisol level impacts cancer development and progression as well as summarize the beneficial effect of yoga on cortisol levels in breast cancer patients and its potential as an adjunctive therapy.

Keywords: yoga, mindfulness, neoplasms, breast neoplasms, glucocorticoids, hydrocortisone, trauma and stressor-related disorders

Introduction

Breast cancer

Breast cancer is a major problem worldwide. According to statistics, breast cancer is the most common female malignancy as well as the most common cancer overall. At the end of 2020, there were nearly 8 million women alive who had received breast cancer diagnosis in the past 5 years. In the same year, the disease caused 685 000 deaths globally [1, 2]. According to Waks and Winer, over 90% of breast cancers are not metastatic at the point of diagnosis. In those patients, therapy involves surgical resection, with consideration of postoperative radiation if lumpectomy is performed [3]. In some cases, it is also advisable to include systemic therapy before surgery. Besides that, patients can receive endocrine therapy and/or chemotherapy, depending on the presence of hormone receptors [4].

Taking into consideration the complexity and invasiveness of cancer treatment, it is no surprise that cancer patients must learn to endure great emotional distress, which imposes substantial burdens on one's emotional welfare and happiness [5]. Patients undergoing radiotherapy have been shown to have higher levels of stress, anxiety, and depression, which simultaneously are negatively correlated with resilience [6].

Breast cancer patients have turned out to be the most severely distressed subgroup among cancer patients, with the highest stress test scores. The major source of distress was fear of disease progression [7]. Introducing practices that aim to help cancer patients manage their stress can be especially helpful in this group of patients and should be more often considered as part of disease management.

Cortisol

Response to stress, challenge, and threat is regulated by several hormones, with cortisol being among the most crucial. Cortisol is a glucocorticoid hormone produced mainly by the adrenal cortex, and its levels vary between individuals and fluctuate at different

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times of the day, i.e. they are higher in the morning and lower at night [8]. Control of diurnal cortisol production lies with the hypothalamic-pituitary-adrenal (HPA) axis neuroendocrine system [9]. Activation of the HPA axis allows the organism to adapt to stressors [10]. However, its hyperstimulation, leading to prolonged higher cortisol levels, has been associated with numerous negative effects [11]. Elevated cortisol in blood has been linked to impairment in the immune, neuroendocrine, and musculoskeletal systems, as well as the central nervous system and cognitive functions [12, 13]. Higher secretion of cortisol has for many years turned out to be an impactful factor in developing various metabolic disorders and cardiovascular diseases [14]. In the general population, people experiencing chronic stress are also at higher risk of developing malignant tumors since stress hormones and mediators facilitate neoplasm initiation and progression [15]. Chronic stress, as a result of prolonged or continuously repeated exposure to physiological or psychological stressors, heavily impairs the signaling pathways in the sympathetic nervous system and disturbs the secretion of a wide variety of hormones [16].

Especially for oncological patients, the stress associated with diagnosis, invasive and aggressive treatment as well as predicted survivorship can lead to dysregulation of the HPA axis, resulting in increased cortisol production [17]. Fear of cancer progression or, in survivors, fear of recurrence are among the most common stressors in cancer patients [18, 19]. In addition, patients tend to worry about body changes, like chemotherapy-induced hair loss, their sudden functional disability, and missing out on social interactions [20–22]. Cancer patients, regardless of sex, suffer from having significantly diminished satisfaction from their physical appearance [23].

Psychological distress after cancer diagnosis includes high levels of anxiety before introducing oncological treatment as well as depressive thoughts, fatigue, and low-performance status after medical intervention [24]. Moreover, recent studies have shown that cancer survivors experience post-traumatic stress disorder more often than people in the general population [25].

Throughout recent years, numerous studies provided strong evidence of the influence of chronic stress on tumor growth and progression, emphasizing the role of psychological distress in cancer evolution [26–28]. Besides that, several studies focused specifically on breast cancer development and progression, demonstrating that cortisol and other glucocorticosteroids play an important factor in breast cancer progression since they are capable of altering biological processes and influencing disease progression [29]. Moreover, high glucocorticoid receptor expression

has been associated with increased risk of disease progression in early-stage untreated triple-negative breast cancers [30].

Flaherty et al. [31] demonstrated that acute exposure to cortisol led to exacerbated production of reactive oxygen and reactive nitrogen species, thus inducing DNA damage. The study was conducted on breast cancer cell lines and *in vivo* using mouse models, suggesting the influence of stress and cortisol on breast cancer progression and treatment. Patients with metastatic breast cancer whose diurnal cortisol rhythms were flattened, which indicated a lack of normal diurnal variation, suffered from earlier mortality. Flatter diurnal cortisol slopes predicted a significantly shorter survival time of up to 7 years after assessment [32].

Glucocorticoids have been demonstrated to be able to promote changes in breast-cancer-associated signal transduction pathways. These changes include regulation of growth factors, transcription factors, expression of oncogenes, tumor suppressor genes, survival genes, proliferation, and apoptosis-related genes and proteins, cytokines, and other intracellular secondary messengers, which, in turn, contribute to glucocorticoid-induced resistance to chemotherapy in breast cancer patients [33]. In glandular cells, such as the mammary gland epithelia, glucocorticoids protect against apoptotic signals evoked by cytokines, cyclic adenosine monophosphate (cAMP), tumor suppressors, and death genes.

The anti-apoptotic effect of glucocorticoids is exerted by modulation of several survival genes and affects breast cancer cells by increasing their survival and decreasing apoptosis [34]. Moreover, Giudice et al. [35] demonstrated that high levels of cortisol, associated both with chronic psychosocial stress and therapeutic use of glucocorticoids, promote breast cancer progression. The cortisol-mediated inhibition of the transcription factor Nrf2 (NF-E2-related factor 2) decreased the cellular defense against oxidative stress, thus promoting breast carcinogenesis and poor disease prognosis [35].

Given the multitude of negative, cancer-related effects of high cortisol levels, it is imperative to introduce practices that might improve the underlying cause, i.e. stress.

Methods

A thorough literature search was conducted using databases such as PubMed, Google Scholar, and Web of Science. Keywords included “yoga,” “cortisol,” “breast cancer,” and related terms. Studies published up to September 2023 were considered. The inclusion criteria encompassed clinical trials reporting cortisol measurements in breast cancer patients who participated in yoga interventions.

Yoga

Yoga is the Sanskrit concept, literally meaning “union” since it comprises both physical and spiritual practice. It originated in ancient India and is a traditional Hindu philosophy [36]. There is a vast variety of yoga practices, schools, and courses. Classical yoga is based on performing asanas, which are postures done mindfully, and synchronized with breath [37]. Thanks to focusing one’s mind on movement and breath control, yoga helps to increase awareness and release muscle tension; it gives one a feeling of relaxation and inner peace [38]. Yoga is said to be a form of meditation in motion, so its main goal is to let go of all the anxiety and stressful thoughts to achieve a blissful state [39]. Sessions usually begin with a didactic lecture about mindfulness and self-confidence, followed by chanting Om, a sacred sound of Indian religion [40].

The first research on beneficial effects of yoga in medicine was conducted on patients suffering from severe airway obstruction and was published in 1978. The intervention of yoga and yogic breathing exercises were compared to the control group who received physiotherapy breathing exercises. Patients who trained in yoga experienced a significant increase in mean maximum work, whereas no such rise occurred after physiotherapy training [41]. Since then, an increasing number of scientists have decided to further explore the potential of yoga in numerous chronic diseases and conditions, which resulted in the recognition of a wide variety of today’s known benefits of regular yoga practice. It has been shown that yoga has a positive effect on physical well-being, as well as spiritual and mental well-being [42]. Yoga is known for its ability to decrease stress and promote relaxation, relieve anxiety, and reduce inflammation [38, 43]. It can also improve overall health by lowering blood pressure and pulse rate [10]. Studies on yoga demonstrated that finding at least 20 minutes a few times per week to practice yoga may be enough to see a noticeable difference in health and overall well-being [36].

Yoga and cortisol in breast cancer patients

Yoga has been practiced for thousands of years to help improve both emotional and physical health. Several studies on cancer patients have shown that introduction of yoga practice has a positive impact on stress perception, mood, and disease prognosis, all of which have been linked to a decrease in cortisol levels.

A randomized controlled trial explored the effects of yoga on cortisol rhythm in early breast cancer patients undergoing adjuvant radiotherapy. The patients were assigned to two equal groups: one undertook

a yoga program and the other brief supportive therapy. Both interventions lasted 6 weeks and were conducted simultaneously with the course of radiotherapy. The yoga program consisted of a set of postures (asanas), breathing exercises, meditation, and relaxation techniques. The group was required to attend at least 3 in-person sessions per week, while on other days, they practiced at home. The trial showed a significant decrease in 0600h salivary cortisol and pooled mean cortisol in the yoga group compared to controls. The results correlated with a reduction in anxiety and perceived stress reported by patients practicing yoga [44]. Similar results were achieved in a 2022 trial conducted on breast cancer patients undergoing adjuvant radiotherapy, with cortisol concentration measured in blood samples. The participants in the yoga intervention group attended up to two 75-minute yoga classes each week during their 5 weeks of radiotherapy. All classes were conducted by a trained yoga teacher. The yoga group showed significantly lower cortisol levels on the last day of radiotherapy compared to the control group [45].

During a study on metastatic breast cancer patients, the intervention group attended yoga sessions consisting of a set of asanas, breathing exercises, and mindful meditation, while the control group received standard education and supportive therapy sessions. After 3 months, the yoga group demonstrated a considerable decrease in early morning salivary cortisol levels [46]. Similarly, in a recent trial, 91 patients with metastatic breast cancer were randomized to receive additive therapy, which was either an integrated yoga program or supportive therapy and education over 3 months. The yoga group showed a significant positive correlation between changes in fatigue severity with a decrease in 9 a.m. cortisol levels, indicating that yoga intervention contributed to lower cortisol levels and less fatigue [47].

In addition to the results described above, a large randomized controlled trial compared serum cortisol concentration in two groups of advanced-stage breast cancer patients: one received standard care and the other standard care accompanied by Sudarshan kriya Yoga and Pranayam (controlled breath practice). The yoga group showed significantly lower cortisol levels after 3 and 6 months compared to the control group [48].

Another trial evaluated the effects of yoga and stretching on saliva cortisol levels in women with breast cancer undergoing radiotherapy. Patients were assigned to three groups: yoga, stretching, and waitlist. The cortisol levels have been presented in the form of a slope which was significantly steeper in the yoga group than in the stretching and waitlist groups at the end of the treatment as well as the one-month follow-up [49]. Similar intervention randomizing patients to yoga, stretching, and waitlist groups

compared saliva cortisol levels at baseline, end of treatment, and 1, 3, and 6 months later [50]. Both yoga and stretching interventions were conducted 3 times a week during a course of 6-week radiotherapy. The results showed the steepest slope for the yoga group in comparison to stretching and waitlist groups, which indicated that the effects of yoga proved to be more beneficial than simple stretching, social support, or other indirect effects.

Similar methods and procedures were used in another trial, during which women with breast cancer treated with a 6-week course of radiotherapy were assigned to 3 groups: yoga, stretching, and waitlist control groups. Assessments were performed at baseline, end-of-treatment, and 1, 3, and 6 months after treatment. The cortisol levels were measured from 5 saliva samples obtained at different times of day (waking, 45 minutes later, approximately 8 and 12 hours after waking, and at bedtime) for 3 following days at each assessment. The trial demonstrated a steeper cortisol slope in the yoga group compared with the stretching and waitlist groups immediately after completing the course of radiotherapy. Moreover, yoga intervention was linked to a steeper cortisol slope compared with the waitlist at one-month follow-up [51].

The trials comparing yoga to other interventions or no intervention showed a clear effect on cortisol levels; however, a study by Witek-Janusek et al. [52] investigated the cortisol level changes in breast cancer patients assigned to yoga intervention compared to cancer-free women. The breast cancer patients included in the study had been treated surgically while some also subsequently received radiotherapy. The 8-week intervention was based on mindfulness taught through breath awareness, meditation, and mindful yoga. The session was performed once a week for 2.5 hours. The control group consisted of breast cancer patients who received assessment only and a group of healthy, cancer-free women. The study found that cancer women who did not receive the stress reduction program had significantly higher serum cortisol levels, compared to the study group. Interestingly, cancer-free women turned out to have significantly lower cortisol concentrations than women in the cancer groups, both those who received the program and those who only participated in assessment [52].

Another study on breast cancer survivors aimed to evaluate the effects of Iyengar yoga practice on fatigue and diurnal salivary cortisol. The study group attended yoga practice for 90 min twice a week for 8 weeks while the control group received no intervention. Results showed that the yoga group had significantly lower morning and 5 p.m. salivary cortisol levels. The lower cortisol levels in the yoga group aligned with better mood and emotional well-being, and lower fatigue scores [53].

A trial on breast cancer patients and prostate cancer patients aimed to evaluate the relationship between mindfulness-based stress-reduction meditation program and quality of life, mood states, stress symptoms, as well as levels of salivary cortisol, dehydroepiandrosterone-sulfate (DHEAS), and melatonin. The stress reduction program consisted of relaxation, meditation, gentle yoga, and daily home practice. Patients were not assigned to the study or control groups — all the participants were introduced to the eight-week stress reduction program. The analysis of parameters performed pre- and post-intervention showed a decrease in afternoon cortisol levels after eight weeks of intervention [54].

It is important to note that not all studies report a lowering of the cortisol level in breast cancer patients practicing yoga. A trial on breast cancer survivors compared the impact of twelve-week restorative Iyengar yoga intervention and health education on saliva cortisol concentration at baseline, post-intervention, and at three-month follow-up, showing no significant differences in the magnitude of change in cortisol slope or total daily cortisol output from baseline to the average of both follow-up time points. However, a major limitation of this trial was the small size of the study ($n = 16$) and control ($n = 15$) groups [55].

Conclusions

Elevated cortisol levels in breast cancer patients have been the subject of significant research interest. Numerous studies suggest a potential link between high cortisol levels and disease progression, highlighting the need for further investigation into its impact on the course of breast cancer and potential therapeutic interventions. For many years, yoga has been shown to have a positive impact on cortisol levels. Regular practice of yoga, with its emphasis on controlled breathing, mindfulness, and physical postures, can help reduce the body's stress response. This reduction in cortisol levels can contribute to improved overall well-being, reduced anxiety, and better management of stress-related health conditions in breast cancer patients, who were shown to be among the most stressed cancer patients. The prevalence of breast cancer, along with the well-documented impact of high cortisol on the development of the disease, makes it a priority to find a good strategy for lowering stress and its hormones in breast cancer patients. The impact of yoga on cortisol levels in breast cancer patients is a subject of growing interest within the realm of complementary and integrative medicine. Several studies have suggested that incorporating yoga into the care regimen of breast cancer patients can have a positive influence on cortisol levels. Research in this area is ongoing, with a focus on gaining a deeper understanding of

the specific mechanisms through which yoga exerts its beneficial effects on cortisol and overall health in breast cancer patients. Further research in this area is needed to provide a more comprehensive understanding of the underlying mechanisms through which yoga contributes to lowering cortisol in breast cancer patients. Different breast cancer patients may respond differently to yoga practices. Furthermore, it is crucial to identify which types of yoga, frequencies, and durations of practice are most beneficial for individual patients, allowing for personalized treatment plans. In this way, healthcare professionals could understand how to integrate yoga into the comprehensive care of their breast cancer patients. This includes identifying the ideal timing and combination of yoga with other medical treatments.

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Author contributions

A.W.B.: literature review, preparation of the work concept, preparation of the original version of the manuscript, preparation of table; I.P.: preparation of the final version of the manuscript, supervision of the team.

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Conflict of interest

Authors declare no conflict of interest.

Supplementary material

Summary table S1.

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SUPPLEMENTARY MATERIAL

Table S1. Summary

Author, Year	Title	Study group	Control group	Duration of intervention	Results
H. S. Vadiraja et al., 2009	Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: A randomized controlled trial.	Yoga program — 3 sessions in person per week, home practice on remaining days	Brief supportive therapy	6 weeks during the course of radiotherapy	A significant decrease in 0600h salivary cortisol and pooled mean cortisol in the yoga group, correlated with reduction of anxiety and perceived stress reported by patients practicing yoga
Micheletti et al., 2022	Effects of yoga practice on physiological distress, fatigue and QOL in patients affected by breast cancer undergoing adjuvant radiotherapy	Up to two 75 min yoga classes each week	Usual care	5 weeks during radiotherapy	Yoga group showed significantly lower serum cortisol levels at the last day of radiotherapy
Rao et al., 2017	Effect of Yoga on Sleep Quality and Neuroendocrine Immune Response in Metastatic Breast Cancer Patients	30-minute yoga sessions in person, at least 2 times a week, home practice on remaining days	Standard education and supportive therapy sessions	12 weeks	Yoga group demonstrated a considerable decrease in early morning salivary cortisol levels
H. Vadiraja et al., 2017	Effects of Yoga in Managing Fatigue in Breast Cancer Patients: A Randomized Controlled Trial	60-minute yoga sessions daily	Supportive therapy and education every 10 days	12 weeks	A decrease in 9 a.m. Cortisol levels in yoga group, correlated with lower fatigue severity
Kumar et al., 2013	Randomized Controlled Trial in Advance Stage Breast Cancer Patients for the Effectiveness on Stress Marker and Pain through Sudarshan Kriya and Pranayam	Standard care accompanied by Sudarshan kriya Yoga and Pranayam — 3 days of workshops and following daily home practice for 20 min	Standard care	12 weeks	Yoga group showed significantly lower serum cortisol levels after 3 and 6 months
Chandwani et al., 2014	Randomized, Controlled Trial of Yoga in Women With Breast Cancer Undergoing Radiotherapy	Two intervention groups - one attended stretching, the second — yoga, up to three 60-minute sessions a week	Waitlist	6 weeks during radiotherapy	Steeper cortisol slope in the yoga group than in the stretching and waitlist groups at the end of the treatment and at the one-month follow up
Cohen et al., 2011	Effect of yoga on QOL, cortisol rhythm, and HRV for women with breast cancer undergoing radiotherapy	Two intervention groups - one attended stretching, the second — yoga, 3 times a week	Waitlist	6 weeks during radiotherapy	Steepest cortisol slope in the yoga group in comparison to stretching and waitlist groups
Ratcliff et al., 2016	Examining Mediators and Moderators of Yoga for Women With Breast Cancer Undergoing Radiotherapy	Two intervention groups — one attended stretching, the second — yoga, up to three 60-minute classes per week	Waitlist	6 weeks during radiotherapy	Steeper cortisol slope in the yoga group compared with stretching and waitlist groups immediately after completing the course of radiotherapy, steeper cortisol slope in yoga group compared with waitlist at one-month follow-up

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Table S1 cont. Summary

Author, Year	Title	Study group	Control group	Duration of intervention	Results
Witek-Janusek et al., 2008	Effect of Mindfulness Based Stress Reduction on Immune Function, Quality of Life and Coping In Women Newly Diagnosed with Early Stage Breast Cancer	Women with breast cancer attending 2.5-hour session of mindfulness and yoga once a week	Women with breast cancer receiving assessment only and a group of cancer-free women	8 weeks	Women with cancer who did not receive the yoga program had significantly higher serum cortisol levels, compared to the study group; cancer free women had significantly lower cortisol concentration than women in cancer groups
Banasik et al., 2011	Effect of Iyengar yoga practice on fatigue and diurnal salivary cortisol concentration in breast cancer survivors	Yoga practice for 90 min twice a week	No intervention	8 weeks	Yoga group had significantly lower morning and 5 p.m. Salivary cortisol levels and better mood, emotional well-being and lower fatigue scores
Carlson et al., 2004	Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients	Breast cancer and prostate cancer patients receiving stress reduction program based on yoga and relaxation techniques	No control group	8 weeks	A decrease in afternoon cortisol levels after eight weeks of intervention
Bower et al., 2014	Yoga reduces inflammatory signaling in fatigued breast cancer survivors: A randomized controlled trial	90-minute yoga classes twice a week	Health education once a week for 120 min	12 weeks	No significant differences in the magnitude of change in cortisol slope or total daily cortisol output