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# Yoga as a Complementary Therapy for Cancer Patients: From Clinical Observations to Biochemical Mechanisms

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## Keywords

Cancer · Yoga · Integrative oncology · Complementary therapy · Randomized clinical trials · Biochemical mechanisms

## Abstract

**Background:** Integrative oncology combines conventional and complementary, or integrative, therapies for a holistic treatment of cancer patients. Yoga is increasingly used as a complementary therapy for cancer patients, but there is no direct evidence for its effect on cancer pathophysiology like tumor response, or patient outcome like overall survival. **Summary:** In this narrative review, we present in detail published studies from randomized clinical trials on complementary yoga therapy for cancer patients, including details about the biochemical mechanisms involved. Medicinal hatha yoga with breathing, postures, meditation, and relaxation enhances the quality of life of cancer patients by providing both psychological and physiological health benefits, highlighting the interconnectedness of mind and body. Yoga therapy reduces stress levels improving heart rate variability, leading to changes in hormonal regulation (e.g., cortisol), reduced oxidative stress, and improved immune function with reduced inflammation. Still, the biochemical effects of yoga on the cancer disease itself are unrevealed. **Key Messages:** More clinical and basic research is needed for further establishment of yoga as complementary therapy in oncology.

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## Yoga als Komplementärtherapie für Krebspatienten: Von klinischen Beobachtungen bis zu biochemischen Mechanismen

## Schlüsselwörter

Krebs · Yoga · Integrative Onkologie · Komplementärtherapie · Randomisierte klinische Studien · Biochemische Mechanismen

## Zusammenfassung

**Hintergrund:** Die integrative Onkologie verbindet konventionelle und komplementäre, oder integrative, Therapien zu einem ganzheitlichen Behandlungsansatz für Menschen mit Krebs. Yoga findet zunehmend Verbreitung als Komplementärtherapie bei Krebs, doch es liegt keine direkte Evidenz für seine Wirkung auf den Verlauf der Krebserkrankung, zum Beispiel das Tumoransprechen, oder auf Patienten-Outcomes wie das Gesamtüberleben vor. **Zusammenfassung:** In dieser narrativen Übersichtsarbeit stellen wir ausführlich Publikationen über randomisierte klinische Studien zu komplementärer Yogatherapie bei Krebspatienten vor und gehen dabei auch auf die beteiligten biochemischen Mechanismen ein. Medizinisches Hatha-Yoga mit Atmung, Stellungen, Meditation und Entspannung erhöht die Lebensqualität von Krebspatienten durch sowohl psychische als auch physische gesundheitliche Vorteile, was die Verbundenheit von Geist und Körper unterstreicht. Yogatherapie verringert die Stressbelastung

und verbessert die Herzfrequenzvariabilität und führt so zu Veränderungen der hormonellen Regulation (z. B. von Cortisol), geringerem oxidativem Stress und verbesserter Immunfunktion mit vermindertem Entzündungsgeschehen. Die biochemischen Effekte von Yoga auf die Krebserkrankung selbst bleiben jedoch weiterhin ungeklärt. **Kernaussagen:** Weitere klinische und Grundlagenforschung ist erforderlich, um den Platz von Yoga als Komplementärtherapie in der Onkologie weiter zu festigen.

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## Introduction

Integrative oncology is a patient-centered, evidence-informed field of oncology, which promotes the use of traditional, complementary, and integrative medicine (TCIM) alongside conventional cancer treatments [1]. TCIM approaches are increasingly used to support the patient's healing process in conjunction with conventional cancer treatments to eradicate the tumor, by means of surgery, radiotherapy, chemotherapy, immunotherapy, and hormone therapy. TCIM approaches are divided into mind-body practices (e.g., yoga), natural products (e.g., herbs), and lifestyle modifications (e.g., diet) [2]. According to a 2012 systematic review covering over 65,000 patients surveyed across 18 countries, the number of cancer patients using complementary and alternative medicine has increased from about 25% in the 1970s to 49% after 2000 [3]. Also, yoga therapy is increasingly used as a complementary therapy for cancer patients and survivors [4].

Yoga originated in India, and its development goes back 5,000 years. Yoga is the Sanskrit word for “yoke” or “unite” encompassing the mind, body, and spirit. Yoga intends to bring balance within and in between the mental (mind), emotional (heart/spirit), and physical (body) aspects of our human being. Yoga is therefore referred to as a “mind-body-breath” discipline and considered a mind-body intervention (another example is tai-chi) or a body-based therapy (another example is massage). Yoga comprises seven paths all rooted in the same moral and ethical principles (yamas and niyamas), ultimately leading to enlightenment. One path is Raja Yoga, which is based upon Patanjali's yoga sutras consisting of eight limbs: yamas (ethics), niyamas (self-observation), asanas (postures), pranayama (breathing), pratyahara (sense withdrawal), dharana (concentration), dhyana (meditation), and freedom/bliss (samadhi). Another path is hatha yoga – translated as “stubborn,” and called for “yoga of forceful effort.” Hatha yoga was born through a new and mentally challenging approach to practicing Raja Yoga. Around early 15th century, some

yoga practitioners from the Natha lineage became in-patient and began practicing asanas before yamas and niyamas. As the mind was not ready for practice, they had to work harder (therefore “stubborn” or “force”). Thus, in hatha yoga, only six limbs are present (omitting yamas and niyamas). Swami Swatmarama compiled the document called “hatha yoga pradipika.” The idea is to first start with asanas, as mastering the body makes it easier to master the mind. In this way, yoga became more accessible to people, leading to a rapid increase in its practice in the West. It was only in the end of the 18th century that hatha yoga made its breakthrough in the West. In the early 20th century, T. Krishnamacharya (the father of modern yoga) and his students established various forms of yoga based on hatha yoga, such as therapeutic yoga or Viniyoga, Iyengar yoga, and Ashtanga-Vinyasa yoga. Today, hatha yoga is the most popular in the West, referring to an umbrella of various yoga styles that emphasizes physical postures.

Yoga therapy is well regarded for its stress-reducing effects and is a key component of the mindfulness-based stress reduction program [5, 6]. Many patients experience chronic stress related to the diagnosis of cancer and its treatment, which can negatively influence their healing journey by aggravating disease progression and treatment effects [7, 8]. Chronic stress causes abnormal activation of the hypothalamus-pituitary-adrenal axis and sympathetic nervous system (SNS). Dysfunction of these neuroendocrine networks results in the excessive release of glucocorticoids (i.e., cortisol) and catecholamines (i.e., epinephrine and norepinephrine). These stress-related hormones contribute to increased oncogene expression, exacerbate chronic inflammation, and impair immunologic function [9]. Thus, chronic stress exposure may negatively influence most hallmarks of cancer known to facilitate tumorigenesis and progression [8]. For example, in an orthotopic ovarian cancer mouse model, chronic stress was observed to result in higher levels of tissue catecholamines and increased tumor growth. Increased norepinephrine levels primarily activated the cyclic AMP-protein kinase A signaling pathway by  $\beta_2$ -receptor activation in ovarian cancer cells, triggering an increase in the expression of the vascular endothelial growth factor gene. This resulted in enhanced tumor vascularization and aggressive growth and spread of malignant cells [10]. Chronic stress also results in dysfunction and exhaustion of the T cells located in the tumor microenvironment [11]. Yoga mainly dampens the SNS and stimulates the parasympathetic nervous system, supporting a balanced autonomic nervous system (ANS) [12]. Yoga practices lead to the inhibition of the sympathetic area of the hypothalamus, which in turn induces the anterior pituitary gland to produce less adrenocorticotropic hormone, reducing the production of cortisol in the adrenal glands [13]. Several studies have reported a

decrease in cortisol levels upon yoga practice [13, 14]. Stress hormones, such as cortisol, are known to compromise the immune system and modulate inflammatory markers [14].

Medicinal hatha yoga (*aka* yoga in the further manuscript) combines postures, breathing, meditation, and relaxation and intends to prevent and/or treat medical conditions like cancer [15]. Multiple meta-analyses report on the positive effects of yoga therapy for cancer patients and survivors with improvements in quality of life (QOL) (i.e., emotional, social, functional well-being), and psychological (i.e., anxiety, depression, distress, cognition) and physiological (i.e., fatigue, sleep disturbance, inflammation, and weakened immunity) symptoms [16–20]. The physical, psychological, and spiritual well-being are interconnected whereby yoga is focused on calming the mind leading to a harmonious state of being that positively affects physical health. While there is an abundance of research and evidence for the psychological health and mental QOL of the cancer patients, the effect of yoga therapy on the physiological health and physical QOL of cancer patients is underexplored and less well understood. This may reflect the holistic nature of yoga with the physical benefits being secondary to the primary goal of mental and spiritual well-being. Furthermore, the interconnectedness of psychological, spiritual, and physiological health benefits through yoga remains underexplored. Particularly, there is still the question as to whether and how yoga therapy influences the pathophysiology of cancer and its response to conventional treatments. Insights into the clinical significance and underlying biochemistry of yoga could help us better understand the healing force of yoga therapy for cancer patients [21].

In this narrative review, we present the existing clinical evidence from randomized clinical trials (RCTs) on yoga therapy given to cancer patients during conventional treatment period with special attention to its effects on QOL, psychological and physiological health including biomarkers. In addition, we offer our perspectives of yoga therapy on the pathophysiology of cancer and treatment outcomes. Overall, our study aims to give an overview of the current state of yoga therapy in oncology, and to guide future research required for further implementation of yoga therapy in cancer care.

### **Yoga as a Complementary Therapy for Cancer Patients**

We researched the scientific literature for RCT studies on the effects of yoga practice, including postures, breathing, meditation, and relaxation exercises, in comparison to a control group (no yoga/standard care, or active control group) on the QOL, psychological and/or physiological health (with special attention for known treatment-induced side effects) of a variety of cancer patients while undergoing

specific conventional treatments, being surgery, chemotherapy, and/or radiotherapy (Table 1: details on study objects, interventions, and outcome results; online suppl. Table S1: details on yoga practice, measured outcomes, in- and exclusion criteria, and follow-up; for all online suppl. material, see <https://doi.org/10.1159/000540213>).

Men diagnosed with prostate cancer scheduled for radical prostatectomy were randomized into either a control group receiving standard care or a yoga group receiving yoga therapy for 6 weeks before surgery and for 6 weeks starting 3–6 weeks after surgery. The perioperative yoga therapy, consisting of biweekly 1 h in-person sessions that included meditation and gentle joint mobilization postures, improved the patients' QOL in several areas: sexual function, fatigue, prostate cancer-specific QOL, and physical, social, and functional well-being. Additionally, it boosted the immune response by increasing the number of peripheral CD4+ and CD8+ T cells, enhancing interferon-gamma (IFN $\gamma$ ) and increasing the expression of Fc receptor III (FcRIII) (*aka* CD16) by natural killer (NK) cells. The yoga therapy also attenuated inflammation by reducing the levels of regulatory T cells and inflammatory cytokines, including granulocyte colony-stimulating factor, monocyte chemoattractant protein-1, and FMS-like tyrosine kinase-3 ligand [22].

Breast cancer (stages II and III) patients received concurrent with their chemotherapy yoga therapy or supportive therapy and coping preparation as control for nonspecific effects such as attention, support, and sense of control. The yoga therapy consisted of 30-min relaxation and meditation practice at the bedside just before each chemotherapy cycle and daily 1 h home practice with a set of postures done with awareness, voluntarily nostril breathing, meditation, and relaxation with imagery, which improved the overall QOL, reduced anxiety, depression and distressful symptoms, and reduced treatment-related toxicity and chemotherapy-induced nausea and vomiting (CINV). Notably, CINV measures correlated positively with anxiety, depression, toxicity, and distressful symptoms and inversely with QOL [23]. Women undergoing chemotherapy for early-stage or locally advanced breast cancer over a period of 12–20 weeks were complementary attributed to yoga therapy, consisting of 3 sessions of 30 min per week of mindful movements, mindful breathing, and mindful moments at home under supervision of a yoga therapist, or received the standard care. The yoga therapy improved the overall QOL, reduced fatigue, and improved weight maintenance without changes in blood levels of the inflammatory markers C-reactive protein and TNF $\alpha$  (tumor necrosis factor- $\alpha$ ) [24]. Breast cancer patients (stages I–III) receiving anthracycline-based chemotherapy were randomized into either a standard care control group or a yoga therapy group. The yoga therapy consisted of 40-min sessions, 5 days per week, involving loosening exercises, postures, breathing exercises, meditation, and relaxation, with an

**Table 1.** Summary of RCT studies on medicinal hatha yoga therapy for cancer patients undergoing conventional treatment

Cancer Treatm PatNr	Yoga (Y): program (P), schedule (S), location (L), control (C)	Outcomes (Y vs. C)	Ref
Prostate Surgery 29	P: meditation, postures S: 2× 60 min/w, 6 w pre- and 6 w post-OP L: in person C: standard care	↑QOL: sexual, fatigue, functional, physical, social ↑Immunity: ↑CD T cells, ↑IFN $\gamma$ production, and FcRIII (CD16) expression by NK cells ↓Inflammation: ↓G-CSF, MCP-1, Flt-3 ligand	22
Breast CT 98	P: In person: relaxation, meditation and Home: postures, breathing, relaxation, meditation S: 30 min before CT and 60 min, 6 d/w L: in person 1-on-1 and home (audio) C: standard care and supportive therapy	↑Overall QOL ↓Anxiety, depression, distress ↓Treatment-related toxicity and CINV !Positive correlation for CINV and anxiety, depression, and distress; inverse correlation for CINV and QOL	23
Breast CT 30	P: postures, breathing, meditation S: 3× 30 min/w (12–20 w) L: home (manual) C: standard care	↑Overall QOL ↓Fatigue ↑Weight maintenance No change: CRP and TNF $\alpha$	24
Breast CT 68	P: postures, breathing, meditation, relaxation S: 40 min 5d/w (18 w) L: in person 1-on-1 and home (video) C: standard care	↓CAD ↓RHR, ↑HRV ↑Parasympathetic, ↓sympathetic indices	25
Breast RT 52	P: breathing, postures, relaxation, meditation S: 2× 75 min/w (5 w) L: in person C: standard care	↓Distress: ↓cortisol ↓Inflammation: ↓IL1Ra (no change: IL-6 and IL-10) No change: QOL, sleep disturbance, fatigue	26
Breast RT 178	P: postures, breathing, meditation, relaxation S: 3× 60 min/w (6 w) L: in person C: stretching (S) or waitlist (W)	Y versus W: ↑GH, PF, PCS Y versus S/W: ↑GH, PF Y/S versus W: ↓cortisol, ↓fatigue No change: MH, depression, sleep quality	27
Breast RT 88	P: postures, breathing, meditation, relaxation S: 3× 60 min/w (6 w) L: in person 1-on-1 C: supportive therapy	↓Anxiety, depression, stress perception ↓Cortisol: at 6 a.m. and for pooled mean levels !Negative correlation for morning cortisol and anxiety and depression	28
Prostate RT 68	P: breathing and centering, postures, relaxation S: 2× 75 min/w (6–9 w) L: in-person group C: standard care	↑SWB No changes: FWB, EWB, and PWB ↓Fatigue ↑Sexual health, ↑urinary function	29
Breast CT/RT 96	P: breathing, postures, meditation, relaxation S: 5 days/w (48 w) L: in-person 1-on-1 and home C: standard care	↑QOL ↓Symptoms: nausea, fatigue, pain, insomnia ↓Inflammation: ↓IFN $\gamma$ and TNF $\alpha$ (no change: GM-CSF) ↓Oxidative stress: ↓MDA levels, NO not increased	30

CAD, coronary artery disease; CD, cluster of differentiation; CINV, chemotherapy-induced nausea and vomiting; CRP, C-reactive protein; CT, chemotherapy; D, day; EWB, emotional well-being; GH, general health; FcR III, Fc receptor III; Flt-3, FMS-like tyrosine kinase-3; FWB, functional well-being; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; HRV, heart rate variability; IFN $\gamma$ , interferon gamma; IL1Ra, interleukin-1 receptor antagonist; IL-6, interleukin-6; IL-10, interleukin-10; MCP-1, monocyte chemoattractant protein-1; MDA, malonaldehyde; MH, mental health; Min, minutes; NK, natural killer; NO, nitric oxide; PatNr, patient number; PCS, physical component score; PF, physical functioning; PWB, psychological well-being; QOL, quality of life; RHR, resting heart rate; RT, radiotherapy; W, week; SWB, social well-being; TNF $\alpha$ , tumor necrosis factor alpha; Treatm, treatment.

emphasis on maintaining an exhalation time twice as long as the inhalation time promoting relaxation. The yoga therapy appeared to prevent a commonly observed adverse effect of anthracycline-based treatment, namely cardiac autonomic dysfunction, by balancing the ANS, as reflected

by a decrease in resting heart rate and an increase in the heart rate variability (HRV) [25].

Breast cancer patients (stages 0–III) who practiced yoga during their radiotherapy in person at the radiotherapy facility for 75 min twice weekly, incorporating

warm-up exercises, yogic postures, breath control exercises, meditation, and deep relaxation experienced reduced psychological distress (reduced cortisol levels) and inflammation (reduced interleukin-1 receptor antagonist, with no change in interleukin 6 [IL-6] and interleukin 10 [IL-10] levels) compared to those receiving standard care only. However, there was no significant change in QOL, sleep disturbance, and fatigue [26]. Another study with breast cancer patients (stages 0–III) practicing yoga during their radiotherapy period 3 times 1 h weekly in person at the radiotherapy facility with yogic postures, nadi shodhana pranayama (alternative nostril breathing), meditation, and relaxation showed improved QOL (general health and physical functioning), and physiological changes, e.g., reduced cortisol levels indicating reduced stress levels, but no difference in mental health outcomes or sleep disturbances in comparison to stretching practice only. Reduced fatigue was only identified in patients from the yoga group when compared to waitlist control group and not in the stretching control group [27]. Early-stage breast cancer patients (stages II–III) undergoing an integrated yoga program with supportive therapy during their adjuvant radiotherapy managed stress better than those receiving standard care with brief supportive therapy alone. The yoga program, consisting of 1-h sessions 3 times per week in person at the radiotherapy facility with postures, breathing exercises, meditation, and relaxation with imaginary, led to reduced levels of psychological distress (anxiety, depression, and stress) and lower stress hormone levels (cortisol). Additionally, a positive correlation was found between morning salivary cortisol levels, and both anxiety and depression [28]. Men with prostate cancer undergoing radiotherapy were randomized to either Eischens yoga practice or standard care. Eischens yoga is rooted in Iyengar yoga and was held twice weekly for 75 min, including mainly yogic postures with 5 min of breathing and centering before, and 5 min of relaxation with savasana or corpse pose after. Patients receiving Eischens yoga therapy experienced reduced fatigue and less urinary and sexual dysfunction, though the results for QOL were mixed with only an increase in social well-being, and no change in emotional, physical, or functional well-being [29]. Long-term yoga practice, consisting of loosening exercises, breathing exercises, postures, meditation, and relaxation for 1 h, 5 days a week over 48 weeks, reduced levels of pro-inflammatory cytokines TNF $\alpha$  and IFN $\gamma$  (but not granulocyte macrophage colony-stimulating factor) and levels of oxidative stress markers malondialdehyde and nitric oxide in breast cancer patients undergoing chemotherapy and/or radiotherapy. Though, this practice improved QOL and alleviated symptoms [30].

## Impact of the Individual Components of Yoga on Cancer Patients

To further understand the mechanistic actions of yoga, we reviewed literature on RCTs that explored the psychological and physiological effects of the individual components of yoga on cancer patients undergoing conventional treatments (see Table 2 for the list of studies with details on the study objects, interventions, and outcome results). We found, and present here, RCT studies with breathing exercises (pranayama), meditation, and relaxation, but not for yogic postures.

Lu et al. [31] investigated the effect of pranayama alone or pranayama based upon a problem-solving model in perioperative outcomes of lung cancer patients undergoing surgical resection. The effect of pranayama alone reduced patients' dyspnea (i.e., shortness of breath) and anxiety, while pranayama based upon a problem-solving model also improved exercise capacity, in comparison to usual care only. No changes were observed for the other outcomes, namely, depression and indwelling time of the thoracic drainage tube. Dhruva et al. [32] reported a pilot randomized study on yogic breathing practices among cancer patients (primarily breast cancer) receiving chemotherapy and found that performing a combination of breath observation, ujjayi, kapalabhati (skull-shining breath or breath of fire), and nadi shodana 10–15 min twice daily reduced sleep disturbance and anxiety, while improving mental QOL. Chakrabarty et al. [33] studied the effects of pranayama practice in breast cancer patients undergoing radiotherapy. Patients practicing 18 min of nadi shodana, sheethali (cooling breath), and bhamari (bee breath) twice daily during the 6 weeks of radiotherapy had significantly higher levels of glutathione and protein thiols. This indicates a stronger antioxidant defense, which may reduce radiotherapy-induced toxicities. Two additional studies were published by Chakrabarty et al. [34] using the same RCT. The first study demonstrated that the pranayama practices also reduced fatigue in the breast cancer patients undergoing radiotherapy. The second study showed that these practices reduced impatience, worry, anxiety, and frustration in the same patient population [35]. Kaur et al. [36] studied the effect of pranayama on fatigue among cancer patients undergoing radiotherapy. Daily 40 min pranayama practice, including Sahaj (natural breathing), Nadi Sodhana, Sheethali, Bhamari, Ujjayi, Chandra bhedana (left nostril breathing), Surya bhedana (right nostril breathing), and Bhastrika (bellows breath), during the 12 days of radiotherapy reduced fatigue.

Wren et al. [37] studied the effects of a meditation practice focused on cultivating unconditional compassion called loving-kindness meditation (compared to music or usual care) on anxiety and physical symptoms in breast

**Table 2.** Summary of RCT studies on individual components of medicinal hatha yoga therapy for cancer patients undergoing conventional treatment

Yoga comp	Cancer Treatm PatNr	Yoga (Y): program (P), schedule (S), location (L), control (C)	Outcomes (Y vs. C)	Ref
Breathing	Lung Surgery 108	P: breathing w/o (Y1) or w/ problem-solving (Y2) C: standard care	↑Dyspnea, ↓anxiety, for Y1 Additionally, ↑exercise capacity, for Y2 No change: depression or indwelling time of thoracic drainage tube	31
	Cancer (breast) CT 23	P: breath observation, Ujjayi, Kapalabhati, Nadi Shodhana S: 60 min/w; ×2 10–15 min/d L: in person weekly; home daily C: waitlist	↑Mental QOL No effect on physical QOL ↓Anxiety, ↑sleep	32
	Breast RT 160	P: Nadi Shodhana, Sheethali, Bhramari S: 2× 18 min/d (6 w) L: home C: standard care	↓Anxiety, worry, impatience, frustration ↓Fatigue ↑Antioxidant defense: ↑protein thiols and GSH	35 34 33
	Cancer (HN, ESCA, CC) RT 84	P: Sahaj, Nadi Sodhana, Sheethali, Bhramari, Ujjayi, Chandra and Surya Bhedana, Bhastrika S: 40 min/d (12 d) L: home C: standard care	↓Fatigue	36
Meditation	Breast Surgery 138	P: loving kindness (LKM) D: 20 min/d L: home (audio) C: music (M) or standard care	↓Pain, ↑compassion, ↓heart rate, for LKM ↓Pain, for M Trend for ↓anxiety, for LKM	37
	Breast CT 92	P: mindfulness (MM) D: 20 min/d (12 w) L: 40 min in person; home (audio) C: progressive muscle relaxation (PMR) or cancer education	No change: QOL ↓Fatigue, ↑coping, for MM and PMR	38
	Colorectal CT 57	P: mindful body scan D: 12 min (one CT session) L: in hospital (audio-video) C: cancer education or standard care	↑Cortisol reactivity (within 60 min after start) Cortisol uncorrelated with biobehavioral measures !Inverse correlation between mindfulness, and fatigue and distress	39
	Breast RT 102	P: BWV D: 2× 60 min/w (6 w) L: in person C: standard care	↑Global QOL ↓Anxiety and fatigue No change: depression	40
Relaxation	Prostate RT 54	P: relaxation response therapy (RRT) S: weekly (8 w) L: in person C: Reiki or waitlist	↑Emotional QOL, for RRT ↓Anxiety in anxious patients, for RRT and Reiki No change: total scores for anxiety, depression, or QOL	41
	Breast CT/RT 96	P: relaxation therapy (Rt) S: 90 min/w (5 w) L: in person C: CBT or health education	↓Distress, for Rt and CBT ↓Inflammation: ↓NF-κB, for Rt and CBT Correlation between distress and NF-κB	42

CBT, cognitive behavior therapy; CC, cervical cancer; Comp, component; CT, chemotherapy; D, day; ESCA, esophageal cancer; Min, minutes; GSH, glutathione; HN, head and neck; LKM, loving-kindness meditation; M, music; MM, mindfulness meditation; NF-κB, nuclear factor kappa B; PatNr, patient number; PMR, progressive muscle relaxation; QOL, quality of life; RRT, relaxation response therapy; RT, radiotherapy; Rt, relaxation therapy; Treatm, treatment; W, week.

cancer patients undergoing needle breast biopsy, receiving their diagnosis, and undergoing breast surgery. Multilevel modeling analysis demonstrated that loving-

kindness meditation significantly improved pain, self-compassion, and heart rate compared to standard care only. There was a trend for reduced anxiety upon

meditation practice. Music therapy significantly improved pain only. Metin et al. [38] reported that early breast cancer patients practicing 20 min mindfulness meditation daily or followed a progressive muscle relaxation program while undergoing paclitaxel chemotherapy experienced less fatigue and demonstrated better coping strategies. However, these interventions did not result in improved QOL compared to patients who received usual care with attention-matched education on breast cancer. Black et al. [39] studied the effect of meditation delivered during 1 session of 60-min active chemotherapy administration on the acute salivary cortisol response and on the biobehavioral measures distress, fatigue, and mindfulness in colorectal cancer patients. A 12-min mindful body scan meditation (+8 min rest + 20 min education + 20 min rest), in comparison to standard care (60 min rest) or attention control (20 min cancer education + 40 min rest), led to increased cortisol reactivity (less cortisol blunting), which was uncorrelated with the biobehavioral measures. However, mindfulness was inversely related to fatigue and distress. Kim et al. [40] demonstrated that brain wave vibration (BWV) meditation, a practice with focus on the senses of the body while relaxing the mind and body and relieving negative thoughts in the body through natural rhythmic movements, supports breast cancer patients undergoing radiotherapy. Biweekly 60 min BWV meditation sessions during the 6 weeks of radiotherapy were found to reduce anxiety and fatigue, and improve general QOL in breast cancer patients, though without effect on depression.

Beard et al. [41] reported in a pilot RCT study that men with prostate cancer receiving relaxation response therapy weekly in combination with radiotherapy achieved improved emotional well-being and less anxiety, compared to Reiki or standard care only. Reiki only showed a trend for reduced anxiety. No significant effects of either relaxation response therapy or Reiki were measured for total scores for anxiety, depression, and QOL. Diaz et al. [42] demonstrated that a 5-week intervention consisting of 90-min weekly sessions of in-person relaxation therapy (Rt) or cognitive behavior therapy, compared to health education (HE), resulted in reduced stress and lower levels of the inflammation marker NF- $\kappa$ B for up to 12 months after intervention in breast cancer patients who had undergone surgery and were receiving radiotherapy and/or chemotherapy.

## Discussion

Complementary yoga therapy supports cancer patients and improves their QOL during and after conventional treatments, alleviating mental and physical health problems arising after disease diagnosis and/or conventional treatments [4]. The main advantages of yoga

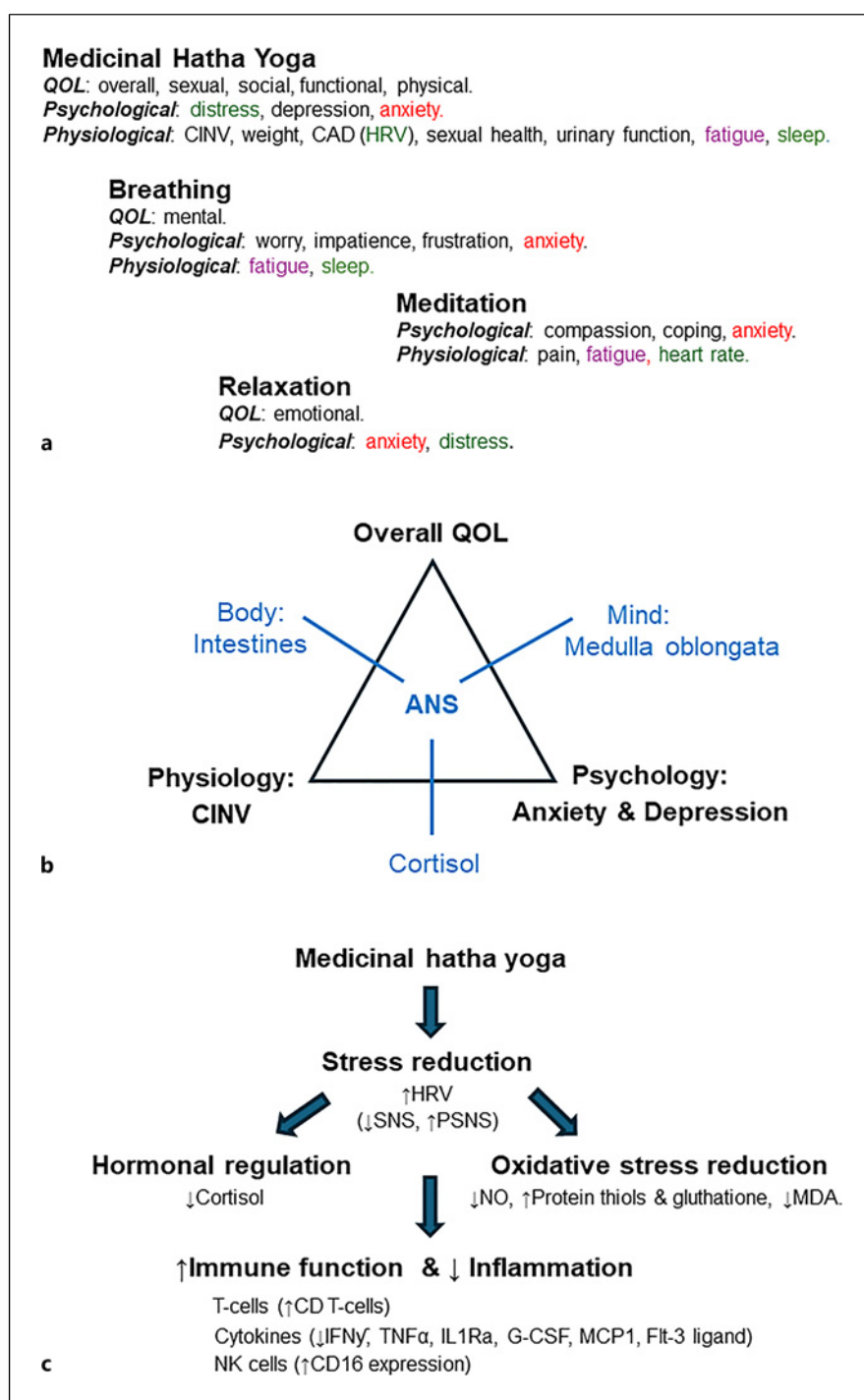
therapy, in comparison to other physical activities, are that: (1) yoga practice is generally safe with only minor adverse events, such as strains and sprains [43], (2) yoga practice is highly flexible and adaptable; namely, yoga postures can easily be modified to accommodate functional impairments or limited mobility [44], and (3) lactic acid accumulation related to postexercise fatigue is usually not observed [45].

Our literature study confirms the positive effects of medicinal hatha yoga practice on QOL, psychological and physiological health of cancer patients undergoing conventional treatments. Yoga practice consisting of breathing, postures, meditation, and relaxation improves QOL, including sexual, social, functional, and physical well-being, psychological health with less stress, distress, anxiety, and depression, and physiological health with reduced fatigue, sleep disturbance, pain, less CINV, better weight maintenance, increased HRV and reduced cardiac autonomic dysfunction, improved sexual health, and enhanced urinary function. Furthermore, RCT studies with yoga therapy applied to cancer patients after completing conventional treatment confirm yoga's beneficial effects on inflammation and fatigue [46, 47], sleep disturbance [48, 49], depression and anxiety, and add on the beneficial effects on chemotherapy-induced peripheral neuropathy [50], cognitive issues [51], and menopausal symptoms [52, 53].

Study results with meditation practice only for cancer patients undergoing conventional treatments indicated better global QOL for BWV meditation that includes gentle movements but no change in QOL for mindfulness meditation, suggesting effects of movements on QOL, better psychological health with more self-compassion, better coping strategies and less anxiety, and better physical health with less pain, less fatigue, and lower heart rate. Breathing practice only resulted in better mental QOL, better psychological health with less anxiety, worry, impatience, frustration, and better physiological health with less fatigue and sleep disturbance. Relaxation therapies showed improvements in emotional QOL and in levels of the psychological symptoms of anxiety and distress. Thus, both the full yoga practice and individual ingredients meditation, breathing, and relaxation helped the cancer patients to deal with anxiety. Reduction in distress was observed upon full yoga practice as well as upon relaxation therapy. Regarding QOL, the entire yoga practice improved overall QOL (incl. physical), breathing mental QOL, relaxation emotional QOL, and meditation with no change in QOL. The physical symptom heart rate was positively influenced by full yoga practice and meditation only (see Fig. 1a). Notably, our study suggests that only the entire yoga practice has potential to improve overall QOL (incl. physical well-being), with one exception reported in the study by Chandwani et al. [27] where only improvement in physical well-being but not in mental well-being was observed upon full yoga practice



**Fig. 1. a** Overview of health parameters affected by the full medicinal hatha yoga practice or the individual components breathing, meditation, and relaxation. Red color marks symptoms addressed in all 4 groups, purple for 3 groups, green for 2 groups, and black for 1 group. **b** Diagram illustrating the potential role of medicinal hatha yoga practice in the overall QOL of breast cancer patients undergoing chemotherapy. The overall QOL is supported by psychological and physiological improvements, being reduced levels of anxiety and depression and CINV, respectively. In particular, the vomiting response is regulated by the intestines (body) and the medulla oblongata (mind) both regulating the ANS, which is influenced by stress through the production of cortisol. **c** Illustration of the biochemical mechanisms for medicinal hatha yoga in cancer patients undergoing conventional cancer treatment. ANS, autonomic nervous system; CAD, coronary artery disease; CD, cluster of differentiation; CINV, chemotherapy-induced nausea and vomiting; FcR, immunoglobulin Fc receptor; Flt-3, FMS-like tyrosine kinase-3; G-CSF, granulocyte colony-stimulating factor; HRV, heart rate variability; IFN $\gamma$ , interferon-gamma; IL1Ra, interleukin-1 receptor antagonist; MCP-1, monocyte chemoattractant protein-1; NO, nitric oxide; NK, natural killer; QOL, quality of life; SNS, sympathetic nervous system; TNF $\alpha$ , tumor necrosis factor-alpha; MDA, malondialdehyde; PSNS, parasympathetic nervous system.



in breast cancer patients undergoing radiotherapy. The individual ingredients meditation, breathing, and relaxation may improve some aspects of QOL only by reducing anxiety, improving heart rate variability, and reducing fatigue. Altogether, our study results illustrate the interconnectedness of mind (psychology) and body (physiology) in the QOL of cancer patients undergoing yoga therapy during conventional treatments. Hereby, the yogic postures seem essential in improving the physical well-being and QOL of cancer patients under-

going conventional treatments. Despite the known interconnectedness of mind and body, we noticed that only few studies measured the direct correlation between psychological and physiological effects of yoga therapy. Raghavendra et al. [23] demonstrated a positive correlation between CINV and anxiety, depression, and distressful symptoms in breast cancer patients receiving yoga therapy during their chemotherapy treatment period. These observations are in line with the pathophysiology of CINV involving both a peripheral path

initiated in the gastrointestinal tract and a central path initiated in the vomiting center in the brain (medulla oblongata) whereby vagal afferents and the vagus nerve are subsequently affected, respectively [54] (see Fig. 1b).

Our study of biochemical mechanisms observed in RCT involving yoga for cancer patients undergoing conventional treatments demonstrates significant health benefits. The practice of medicinal hatha yoga reduces stress levels reflected in reduced SNS and increased parasympathetic nervous system activity, leading to improved HRV. This change in ANS balance correlates with lower cortisol levels, reduced oxidative stress with no increase in nitric oxide levels, and increased protein thiols and glutathione levels. Furthermore, yoga positively impacted immune function and inflammation. Yoga practitioners showed an increase in CD T cells, a reduction in pro-inflammatory cytokines (IFN $\gamma$ , TNF $\alpha$ , malondialdehyde, interleukin-1 receptor antagonist), and an increase in FcRIII expression by NK cells (see Fig. 1c). In addition, Kochupillai et al. [55] demonstrated that lung cancer patients who practiced Sudarshan kriya and pranayama after conventional treatment had higher NK cell levels after 12 and 24 weeks of practice compared to baseline, indicating a better immune function. Furthermore, breathing practices are known to affect systematic levels of oxygenation, which may tackle hypoxia in cancer [56], reduce reactive oxygen species, and improve oxidation status [57]. Meditation may possibly lead to tumor regression as supported in several case studies by Meares et al. [58–61]. Meditation has been found to modulate the expression of inflammatory cytokines in various diseases, including cancer. Meditation resulted in reduced TNF $\alpha$  and IL-6 levels and increased IFN $\gamma$  levels in early breast cancer patients [62]. TNF $\alpha$  and IL-6 levels appeared to be also elevated after meditation among breast cancer survivors [63]. Moreover, long-term meditation could result in epigenetic changes related to common human diseases like cancer [64], and it has been reported that meditation can result in elevated telomerase activity in patients with prostate cancer [65].

While yogic postures have not been studied separately in RCT studies for cancer patients, it is relevant to address their mechanisms of actions. One aspect of postures is stretching. Interestingly, stretching is known to affect the systematic process of inflammation [45, 66, 67] and has been shown to reduce tumor growth in a breast cancer mouse model [68]. Note that asanas are more than physical exercise as the exercises are done with focused awareness touching the mental aspect of the yoga practice. The study results reported by Chandwani et al. [27], with comparison of the effects of yoga and purely stretching exercises in breast cancer patients undergoing radiotherapy, demonstrated that the improved QOL and physiological changes for the yoga group are beyond the benefits of stretching (i.e., steepest cortisol slope and greatest increase in physical functioning [while the same effect on fatigue]). Furthermore, Francis et al. [69] addressed the involvement of the musculoskeletal system in yoga's

influence on stress through body posture, embodied cognition, and mind-body connection.

Multiple clinical guidelines have been established to guide healthcare practitioners in the application of yoga therapy for cancer patients and survivors. Guidelines from the Society for Integrative Oncology (SIO) and the American Society of Clinical Oncology (ASCO) indicate that yoga may be considered to manage depression, anxiety, and mood disturbances, decrease stress, and enhance overall QOL in cancer patients and survivors [70, 71]. Greenlee et al. [70] reported guidelines for the therapeutic use of yoga for breast cancer patients to address the following clinical outcomes: anxiety/stress reduction, depression/mood disturbance, fatigue, QOL, and sleep disturbance. Mao et al. [72] presented SIO-ASCO guidelines with the recommendation of yoga as integrative therapy for cancer patients for general cancer pain or musculoskeletal pain and for aromatase inhibitor-related joint pain (although only low quality of evidence and thus weak strength of recommendation). Carlson et al. [73] reported an SIO-ASCO guideline on the use of yoga therapy for anxiety and depression symptoms in adults with cancer or history of cancer. According to the National Comprehensive Cancer Network (NCCN) guidelines, yoga may be considered for improving some survivorship issues, such as distress, cognitive functioning, menopausal symptoms, and pain [74]. Yoga is also listed in the NCCN guidelines for addressing cancer-related fatigue (CRF) and anticipatory nausea/vomiting [75, 76]. In addition, mind-body practices like yoga are recommended in the European Society for Medical Oncology (ESMO) guidelines for treatment of breathlessness in cancer patients [77] and for improvement of CRF in cancer survivors and QOL [78].

Evidence-based standardized medical yoga therapy programs promote the integration of yoga therapy in healthcare systems. One example is MediYoga<sup>®</sup> (MOSI<sup>®</sup>) (<https://mediyoga.se/>), which is a medicinal and therapeutic yoga program established in Sweden. Another example is the Yoga4Cancer methodology established in the USA (<https://yoga4cancer.com/>). Interestingly, MediYoga<sup>®</sup> is based upon Kundalini yoga and primarily focusses on balancing the ANS, while the Y4C method is based on Vinyasa yoga and is classified as a moderate physical activity touching more bodily systems like the musculoskeletal system and lymphatic system. Importantly, ASCO recommends 150 min of moderate physical activity per week for cancer disease prevention. We also noted that it is important to investigate yoga practices that do increase the pulse (mimicking aerobic exercise) stimulating physical fitness, strength, and endurance in contrast to how yoga is mostly implemented in medical care being gentle and low impact, focused on promoting flexibility, balance, and relaxation [79]. Especially, aerobic exercise has been reported to reduce the risk of mortality for breast, colon, and prostate cancers by an estimated 40–50%. Moreover, it has been shown that running

reduces tumor growth in mice due to increased levels of a specific type of immune cell, the CD8+ T cell, circulating in the blood [80].

Also, there is a rise of online or virtual yoga programs since the COVID-19 pandemic. Online yoga may increase accessibility and facilitate participation for patients susceptible to infection and those living far from organized rehabilitation opportunities. One study is ongoing, called DigiYoga CaRe (<https://clinicaltrials.gov/search?term=NCT04812652>), where a 12-week digital yoga program is evaluated on CRF and stress, health-related quality of life, and pro-inflammatory and metabolic markers of breast cancer patients [81]. Another clinical pilot study (IM@home) was recently reported by Mao et al. [82], demonstrating that online mind-body fitness classes may have important benefits such as reducing the risk of being hospitalized for treatment-related problems. Overall, virtual yoga can be vital for cancer patients and survivors to improve access and consistency and reduce risk on a compromised immune system. Recently, the YOCAN-PREFER clinical study was initiated in Sweden with comparison of in-person versus online yoga therapy (<https://classic.clinicaltrials.gov/ct2/show/NCT06248450>).

## Concluding Remarks

Although yoga has not been shown to directly affect cancer pathophysiology, substantial evidence supports its impact on the body's stress levels, inflammation levels, and immunity with known roles in cancer progression and treatment response. Notably, dysregulation of the hypothalamus-pituitary-adrenal axis, as indicated by diurnal salivary cortisol rhythm, is a significant predictor of survival in patients with advanced breast cancer [83]. Thus, it is reasonable to suggest that yoga therapy may affect the progression as well as the treatment outcome of cancer patients.

To advance the integration of yoga therapy in oncology, we need more clinical studies with large, well-defined populations, adequate controls, randomized treatment allocation, and adequate duration [84]. Limitations of current evidence-based research, including available RCTs (among other study types), include: (1) lack of active control groups, (2) coverage of few cancer types (majority in breast cancer patients), (3) heteroge-

neity among yoga as an intervention (e.g., types of yoga), and (4) wide variety in yoga teacher training. In addition, such high-quality clinical studies not only with the examination of the standard clinical endpoints (survival, relapse, etc.) but also with molecular and cellular investigations (immune cell infiltration, tumor matrix remodeling, etc.) are needed to document the effects of yoga therapy on the pathophysiology of cancer. To date, no study has yet identified the effective "ingredients" of yoga. Therefore, future trials must consider the effects of yogic techniques and types as well as patient and disease characteristics (e.g., stages of cancer). When establishing future research, we should also consider the reversed research model for complementary and alternative medicine suggested by Fönnebo et al. [85]. This model highlights the most urgent clinical research questions to guarantee safety and stresses that the investigation of beliefs and attitudes should precede the exploration of effectiveness [86]. Knowing the potential benefits of yoga therapy for cancer patients and survivors, it is important to continue with major efforts in basic and clinical research to further establish yoga therapy in integrative oncology.

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## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

S.B. conceptualized the manuscript, researched the literature, and wrote the manuscript. P.W.S. has been involved in critical revising. Both authors read and approved the manuscript.

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