Role of Yoga Across the Cancer Care Continuum: From Diagnosis Through Survivorship

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ABSTRACT

Objective: To review the effects of yoga as an adjunct supportive care modality alongside conventional cancer treatment on quality of life (QOL), physical and mental health outcomes, and physiological and biological measures of cancer survivors.

Methods: Nonsystematic review of the literature.

Results: Yoga therapy, one of the most frequently used mind-body modalities, has been studied extensively in cancer survivors (from the time of diagnosis through long-term recovery). Yoga affects human physiology on multiple levels, including psychological outcomes, immune and endocrine function, and cardiovascular parameters, as well as multiple areas of QOL. It has been found to reduce psychological stress and fatigue and improve QOL in cancer patients and survivors. Yoga has also been used to manage symptoms such as arthralgia, fatigue, and insomnia. In addition, yoga offers benefits not only for cancer survivors but also for their caregivers.

Conclusion: As part of an integrative, evidence-informed approach to cancer care, yoga may provide benefits that support the health of cancer survivors and caregivers.

Keywords: fatigue; cancer; proinflammatory cytokines; integrative; mind-body practices; meditation; DNA damage; stress; psychoneuro-immunoendocrine axis; lymphedema; insomnia.

A diagnosis of cancer and adverse effects related to its treatment may have negative effects on quality of life (QOL), contributing to emotional and physical distress in patients and caregivers. Many patients express an interest in pursuing nonpharmacological options, alone or as an adjunct to conventional therapy, to help manage symptoms. The use of complementary medicine approaches to health, including nonpharmacological approaches to symptom management, is highest among individuals with cancer.¹ According to a published expert consensus, integrative oncology is defined as a “patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, QOL, and clinical outcomes across the cancer care continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.”² A key component of this definition, often misunderstood in the field of oncology, is that these modalities and treatments are used alongside conventional cancer treatments and not as an alternative. In an attempt to meet patients’ needs and appropriately use these approaches, integrative oncology programs are now part of most cancer centers in the United States.³–⁶

Because of their overall safety, mind-body therapies are commonly used by patients and recommended by clinicians. Mind-body therapies include yoga, tai chi, qigong, meditation, and relaxation. Expressive arts such as journaling and music, art, and dance therapies also fall in the mind-body category.⁷ Yoga is a movement-based mind-body practice that focuses on synchronizing body, breath, and mind. Yoga has been increasingly used by patients for health benefits,⁸ and numerous studies have evaluated yoga as a complementary intervention for individuals with...
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cancer.9,14 Here, we review the physiological basis of yoga in oncology and the effects of yoga on biological processes, QOL, and symptoms during and after cancer treatment.

Physiological Basis
Many patients may use mind-body programs such as yoga to help manage the psychological and physiological consequences of unmanaged chronic stress and improve their overall QOL. The central nervous system, endocrine system, and immune system influence and interact with each other in a complex manner in response to chronic stress.15,16 In a stressful situation, the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS) are activated. HPA axis stimulation leads to adrenocorticotropic hormone production by the pituitary gland, which releases glucocorticoid hormones. SNS axis stimulation leads to epinephrine and norepinephrine production by the adrenal gland.17,18 Recently, studies have explored modulation of signal transduction between the nervous and immune systems and how that may impact tumor growth and metastasis.19 Multiple studies, controlled for prognosis, disease stage, and other factors, have shown that patients experiencing more distress or higher levels of depressive symptoms do not live as long as their counterparts with low distress or depression levels.20 Both the meditative and physical components of yoga can lead to enhanced relaxation, reduced SNS activation, and greater parasympathetic tone, countering the negative physiological effects of chronic stress. The effects of yoga on the HPA axis and SNS, proinflammatory cytokines, immune function, and DNA damage are discussed below.

Biological Processes

Nervous System
The effects of yoga and other forms of meditation on brain functions have been established through several studies. Yoga seems to influence basal ganglia function by improving circuits that are involved in complex cognitive functions, motor coordination, and somatosensory and emotional processes.21,22 Additionally, changes in neurotransmitter levels have been observed after yoga practice. For instance, in a 12-week yoga intervention in healthy subjects, increased levels of thalamic gamma-aminobutyric acid (GABA) in the yoga group were reported to have a positive correlation with improved mood and decreased anxiety compared with a group who did metabolically matched walking exercise.23 Levels of GABA, an inhibitory neurotransmitter, are decreased in conditions such as anxiety, depression, and epilepsy.24 Yoga therapy has been shown to improve symptoms of mood disorders and epilepsy, which leads to the hypothesis that the mechanism driving the benefits of yoga may work through stimulation of vagal efferents and an increase in GABA-mediated cortical-inhibitory tone.24,25

HPA Axis
Stress activates the HPA/SNS axis, which releases hormones such as cortisol and norepinephrine. These hormones may play a role in angiogenesis, inflammation, immune suppression, and other physiological functions, and may even reduce the effect of chemotherapeutic agents.26,27 Regular yoga practice has been shown to reduce SNS and HPA axis activity, most likely by increasing parasympathetic dominance through vagal stimulation, as demonstrated through increases in heart rate variability.28 One indicator of HPA axis dysregulation, diurnal salivary cortisol rhythm, was shown to predict survival in patients with advanced breast and renal cancer.29-33 Yoga has been shown to lead to less cortisol dysregulation due to radiotherapy and to reductions in mean cortisol levels and early morning cortisol levels in breast cancer patients undergoing radiotherapy.34 This lends support to the hypothesis that yoga helps restore HPA axis balance.

Proinflammatory Cytokines
Cancer patients tend to have increased levels of inflammatory markers such as interleukin (IL)-4, IL-10, tumor necrosis factor (TNF), interferon-γ, and C-reactive protein. This increase in inflammation is associated with worse outcomes in cancer.35 This association becomes highly relevant because the effect of inflammation on host cells in the tumor microenvironment is connected to disease progression.26 Inflammatory cytokines are also implicated in cancer-related symptoms such as fatigue, cognitive dysfunction, peripheral neuropathy, and sleep disturbances.36

Yoga is known to reduce stress and may directly or indirectly decrease inflammatory cytokines. A randomized clinical trial of a 12-week hatha yoga intervention among breast
cancer survivors demonstrated decreases in IL-6, IL-1β, TNF, corticotropin-releasing factor, and cognitive complaints in the yoga group compared with those in the standard care group after 3 months. Furthermore, Carlson et al showed that, after mindfulness-based stress reduction involving a combination of gentle yoga, meditation techniques, and relaxation exercises, breast and prostate cancer patients had reduced levels of proinflammatory cytokines and cortisol. These reductions translated into patients reporting decreased stress levels and enhanced QOL.

**Immune Function**

The effects of yoga practice on the immune system have been studied in both healthy individuals and individuals with cancer. The effects on T and B lymphocytes, natural killer (NK) cells, and other immune effector cells demonstrate that meditation and yoga have beneficial effects on immune activity. Hormones such as catecholamines and glucocorticoids are thought to influence the availability and function of NK cells, and, as noted above, yoga has been shown to modulate stress hormones and lead to reduced immune suppression in patients with early-stage breast cancer undergoing chemotherapy. Additional evidence supports the ability of yoga to reduce immune suppression in the postsurgical setting, with no observed decrease in NK cell percentage after surgery for those in a yoga group compared with a control group. This finding is relevant to patients undergoing surgical management of their cancer and highlights the impact of yoga on the immune system.

**DNA Damage**

Radiation damages DNA in the peripheral blood lymphocytes of patients undergoing treatment. This damage is significant in breast cancer patients undergoing radiotherapy. Stress additionally causes DNA damage and is correlated to impaired DNA repair capacity. In a study conducted by Banerjee et al, breast cancer patients were randomly assigned to a yoga group or a supportive therapy group for 6 weeks during radiotherapy. Prior to the intervention, patients in the study had significant genomic instability. After treatment, patients in the yoga group experienced not only a significant reduction in anxiety and depression levels, but also a reduction in DNA damage due to radiotherapy.

**Yoga in Quality of Life and Symptom Management**

There is evidence showing that yoga therapy improves multiple aspects of QOL, including physical functioning, emotional health outcomes, and the symptoms cancer patients may experience, such as sleep disturbances, fatigue, and pain. Danhauer et al systematically reviewed both nonrandomized trials and randomized controlled trials involving yoga during cancer treatment. They found that yoga improved depression and anxiety as well as sleep and fatigue. Benefits of yoga in cancer based on randomized controlled trials are summarized in the Table. The role of yoga in improving QOL and managing symptoms patients experience during and after treatment is discussed in the following sections.

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Quality of Life
Danhauer et al’s systematic review of trials involving yoga during cancer treatment found that yoga improved multiple aspects of QOL. For example, yoga has been shown to improve QOL in breast cancer patients undergoing radiotherapy. In a study by Chandwani et al, yoga (60-minute sessions twice a week for 6 weeks) was associated with better general health perception and physical functioning scores as well as greater benefit finding, or finding meaning in their experience, after radiotherapy compared with a wait-list group. The yoga group had an increase in intrusive thoughts, believed to be due to a more thorough processing of the cancer experience, which helps to improve patients’ outlook on life. The benefits of yoga extend beyond psychological measures during radiation treatment. Yoga was found to increase physical functioning compared with stretching in breast cancer patients undergoing radiotherapy.

Cognitive Function
Cancer-related cognitive impairment commonly occurs during cancer treatments (e.g., chemotherapy, radiotherapy, surgery, hormone therapy) and persists for months or years in survivors. Impairment of memory, executive function, attention, and concentration are commonly reported. In a trial of a combined hatha and restorative yoga program called Yoga for Cancer Survivors (YOCAS), which was designed by researchers at the University of Rochester, patients in the yoga arm had less memory difficulty than did patients in the standard care arm. However, the primary aim of the trial was to treat insomnia, so this secondary outcome needs to be interpreted with caution. Deficits in attention, memory, and executive function are often seen in cancer-related cognitive impairment, and the meditative aspect of yoga may have behavioral and neurophysical benefits that could improve cognitive functions. More evidence is needed to understand the role of yoga in improving cognitive functioning.

Emotional Health
Psychosocial stress is high among breast cancer patients and survivors. This causes circadian rhythm and cortisol regulation abnormalities, which are reported in women with breast cancer. Yoga is known to help stress and psychosocial and physical functioning in patients with cancer. Yoga was also shown to be equivalent to cognitive behavioral therapy in stress management in a population of patients without cancer. Daily yoga sessions lasting 60 minutes were shown to reduce reactive anxiety and trait anxiety in early-stage breast cancer patients undergoing conventional radiotherapy and chemotherapy compared with patients receiving supportive therapy, highlighting the role of yoga in managing anxiety related to treatment. In a study done by Culos-Reed et al, 20 cancer survivors who did 75 minutes of yoga per week for 7 weeks were compared with 18 cancer survivors who served as a control group. The intervention group reported significant improvement in emotional well-being, depression, concentration, and mood disturbances. In a longitudinal study by Mackenzie et al, 66 cancer survivors completed a 7-week yoga program and were assessed at baseline, immediately after the final yoga session, and at 3 and 6 months after the final session. Participants had significantly improved energy levels and affect. They also had moderate improvement in mindfulness and a moderate decrease in stress. Breast cancer patients who underwent restorative yoga sessions found improvements in mental health, depression, positive affect, and spirituality (peace/meaning). This was more pronounced in women with higher negative affect and lower emotional well-being at baseline. In a study of patients with ovarian cancer receiving chemotherapy, patients were instructed to perform up to 15-minute sessions including awareness, body movement, and breathing. Even with just 1 session of yoga intervention, patients experienced decreased anxiety.

Fatigue
Studies on yoga show improvement in fatigue both during and after treatment. In breast cancer patients undergoing chemotherapy, yoga was shown to benefit cognitive fatigue. Older cancer survivors also seem to benefit from yoga interventions. In a trial of a DVD-based yoga program, the benefits of yoga were similar to those of strengthening exercises, and both interventions helped decrease fatigue and improve QOL during the first year after diagnosis in early-stage breast cancer patients with cancer-related fatigue. Bower et al also showed that, for
breast cancer survivors experiencing persistent chronic fatigue, a targeted yoga intervention led to significant improvements in fatigue and vigor over a 3-month follow-up compared with controls.\textsuperscript{75} Fatigue is commonly seen in breast cancer patients who are receiving adjuvant chemotherapy. In a study by Taso et al, women with breast cancer receiving chemotherapy were assigned to 60-minute yoga sessions incorporating Anusara yoga, gentle stretching, and relaxation twice a week for 8 weeks.\textsuperscript{76} By week 4, patients with low pretest fatigue in the yoga group experienced a reduction in fatigue. By week 8, all patients in the yoga group experienced a reduction in fatigue. Four weeks after the yoga intervention, patients in the group maintained the reduction in fatigue. This study shows the feasibility of an 8-week yoga program for women undergoing breast cancer therapy by improving fatigue. Yoga recently was added to National Comprehensive Cancer Network (NCCN) guidelines for management of cancer-related fatigue (level 1 evidence).\textsuperscript{77} However, the evidence was based on studies in women with breast cancer and survivors; therefore, more studies are needed in men and women with other cancers.

**Surgical Setting/Postoperative Distress**

Distress surrounding surgery in patients with breast cancer can impact postoperative outcomes. Yoga interventions, including breathing exercises, regulated breathing, and yogic relaxation techniques, improved several post-surgical measures such as length of hospital stay, drain retention, and suture removal.\textsuperscript{78} In this study, patients who practiced yoga also experienced a decrease in plasma TNF and better wound healing. Symptoms of anxiety and distress that occur preoperatively can lead to impaired immune function in addition to decreased QOL. In a study of yoga in early-stage breast cancer patients undergoing surgery, the benefit of yoga was seen not only with stress reduction but also with immune enhancement.\textsuperscript{82}

Yoga has been shown to help alleviate acute pain and distress in women undergoing major surgery for gynecological cancer. A regimen of 3 15-minute sessions of yoga, including awareness meditation, coordination of breath with movement, and relaxation breathing, was shown to reduce acute pain and distress in such patients in an inpatient setting.\textsuperscript{79}

**Menopausal Symptoms**

Breast cancer survivors have more severe menopausal symptoms compared with women without cancer.\textsuperscript{80,81} Hot flashes cause sleep disturbances and worsen fatigue and QOL.\textsuperscript{82} Tamoxifen and aromatase inhibitors significantly worsen menopausal symptoms such as hot flashes.\textsuperscript{83} Carson et al conducted a study of yoga that included postures, breathing techniques, didactic presentations, and group discussions.\textsuperscript{83} The yoga awareness regimen consisted of 8 weekly 120-minute group classes. Patients in the yoga arm had statistically significant improvements in the frequency, severity, and number of hot flashes. There were also improvements in arthralgia (joint pain), fatigue, sleep disturbance, vigor, and acceptance.

**Arthralgia**

Joint pain can be a major side effect that interferes with daily functions and activities in postmenopausal breast cancer survivors who receive aromatase inhibitor therapy.\textsuperscript{84} Arthralgia is reported in up to 50% of patients treated with aromatase inhibitors.\textsuperscript{84,85} It can affect functional status and lead to discontinuation of aromatase inhibitor therapy, jeopardizing clinical outcomes.\textsuperscript{86} Yoga as a complementary therapy has been shown to improve conditions such as low back pain\textsuperscript{87} and knee osteoarthritis\textsuperscript{88} in patients who do not have cancer. In a single-arm pilot trial by Galantino et al, breast cancer patients with aromatase inhibitor–related joint pain were provided with twice-weekly yoga sessions for 8 weeks. There were statistically significant improvements in balance, flexibility, pain severity, and health-related QOL.\textsuperscript{89} As noted above, improvement in arthralgia was also found in the study conducted by Carson et al.\textsuperscript{83}

**Insomnia**

Insomnia is common among cancer patients and survivors\textsuperscript{90,91} and leads to increased fatigue and depression, decreased adherence to cancer treatments, and poor physical function and QOL.\textsuperscript{90-92} Management of insomnia consists of pharmacologic therapies such as benzodiazepines\textsuperscript{93,94} and nonpharmacologic options such as cognitive behavioral therapy.\textsuperscript{95}

The first study of yoga found to improve sleep quality was conducted at MD Anderson Cancer Center in lym-
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phoma patients. The effects of Tibetan yoga practices incorporating controlled breathing and visualization, mindfulness techniques, and low-impact postures were studied. Patients in the Tibetan yoga group had better subjective sleep quality, faster sleep latency, longer sleep duration, and less use of sleep medications. Mustian et al conducted a large yoga study in cancer survivors in which patients reporting chronic sleep disturbances were randomly assigned to the YOCAS program, which consisted of pranayama (breath control), 16 gentle hatha and restorative yoga postures, and meditation, or to usual care. The study reported improvements in global sleep quality, subjective sleep quality, actigraphy measures (wake after sleep onset, sleep efficiency), daytime dysfunction, and use of sleep medication after the yoga intervention compared with participants who received standard care.

Yoga to Address Other Symptoms
There is preliminary evidence supporting yoga as an integrative therapy for other symptoms unique to cancer survivors. For example, in head and neck cancer survivors, soft tissue damage involving the jaw, neck, shoulders, and chest results in swallowing issues, trismus, and aspiration, which are more pronounced in patients treated with conventional radiotherapy than in those treated with intensity-modulated radiotherapy. Some late effects of radiotherapy for head and neck cancer—such as pain, anxiety, and impaired shoulder function—were shown to be improved through the practice of hatha yoga in 1 study. Similarly, in a randomized controlled pilot study of patients with stage I to III breast cancer 6 months after treatment, participants in an 8-week yoga program experienced a reduction in arm induration and improvement in a QOL subscale of lymphedema symptoms. However, more evidence is needed to support the use of yoga as a therapeutic measure for breast cancer lymphedema.

Yoga for Caregivers
Along with cancer patients, caregivers face psychological and physical burdens as well as deterioration in their QOL. Caregivers tend to report clinical levels of anxiety, depression, sleep disturbance, and fatigue and have similar or in fact higher levels than those of the patients for whom they are caring. Yoga has been found to help caregivers of patients with cancer. Recently, MD Anderson researchers conducted a trial in patients with high-grade glioma and their caregivers as dyads. Each dyad attended 2 or 3 60-minute weekly Vivekananda yoga sessions involving breathing exercises, physical exercises, relaxation, and meditation. The researchers found that the yoga program was safe, feasible, acceptable, and subjectively useful for patients with high-grade glioma and their caregivers. Preliminary evidence of QOL improvement for both patients and caregivers was noted. An improvement in QOL was also demonstrated in another preliminary study of yoga in patients undergoing thoracic radiotherapy and their caregivers.

Another study by the group at MD Anderson evaluated a couple-based Tibetan yoga program that emphasized breathing exercises, gentle movements, guided visualizations, and emotional connectedness during radiotherapy for lung cancer. This study included 10 patient-caregiver dyads and found the program to be feasible, safe, and acceptable. The researchers also found preliminary evidence of improved QOL by the end of radiotherapy relative to baseline—specifically in the areas of spiritual well-being for patients, fatigue for caregivers, and sleep disturbances and mental health issues such as anxiety and depressive symptoms for both patients and caregivers. This is noteworthy, as QOL typically deteriorates during the course of radiotherapy, and the yoga program was able to buffer these changes.

Conclusion
Yoga therapy has been used successfully as an adjunct modality to improve QOL and cancer-related symptoms.
As a part of an integrative medicine approach, yoga is commonly recommended for patients undergoing cancer treatment. Danhauer et al reviewed randomized controlled trials during and after treatment and concluded that the evidence is clearly positive for QOL, fatigue, and perceived stress.\(^\text{107}\) Results are less consistent but supportive for psychosocial outcomes such as benefit finding and spirituality. Evidence is mixed for sleep, anxiety, and depression. Post-treatment studies demonstrate improvements in fatigue, sleep, and multiple QOL domains. Yoga has been included in NCCN guidelines for fatigue management. Yoga, if approved by a physician, is also included among the behavioral therapies for anticipatory emesis and prevention and treatment of nausea in the recent update of the NCCN guidelines.\(^\text{108}\)

The Society for Integrative Oncology guidelines include yoga for anxiety/stress reduction as a part of integrative treatment in breast cancer patients during and after therapy, which was endorsed by the American Society of Clinical Oncology.\(^\text{109}\)

Because of the strong evidence for its benefits and a low side-effect profile, yoga is offered in group-class settings for patients during and after treatment and/or for caregivers in our institution. We often prescribe yoga as a therapeutic modality for selected groups of patients in our clinical practice. However, some patients may have restrictions after surgery that must be considered. In general, yoga has an excellent safety profile, the evidence base is strong, and we recommend that yoga therapy should be part of the standard of care as an integrative approach for patients with cancer undergoing active treatment as well as for cancer survivors and caregivers.

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