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Effects of Yoga on Inflammatory Markers in Cancer: A Systematic Review of Randomized Controlled Trials

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Abstract

Introduction: *Chronic inflammation plays a crucial role in cancer progression and contributes to tumour initiation, growth, and metastasis. Yoga, a mind-body practice, has the potential to modulate inflammatory pathways, reduce stress, and improve the overall well-being of patients with cancer. This systematic review aimed to evaluate the impact of yoga on key inflammatory markers and cortisol levels in cancer patients based on evidence from randomised controlled trials.*

Methods: *A systematic search was conducted across databases, including PubMed, Cochrane Library, Web of Science, and Scopus, encompassing studies published between January 2000 and August 2024. Studies were deemed eligible if they involved cancer patients, utilised yoga as an intervention, and measured inflammatory markers as outcomes. Data on the study characteristics, population, intervention details, and outcomes were extracted. The risk of bias was assessed using the Cochrane Risk of Bias 2 tool.*

Results: *Fourteen randomized controlled trials (RCTs) involving various types of cancer, including breast, prostate, hematologic, and gastrointestinal cancers, were included. These findings demonstrate that yoga significantly reduced pro-inflammatory markers, particularly tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), while increasing the anti-inflammatory cytokine interleukin-10 (IL-10). Cortisol levels have been consistently lowered across multiple studies. However, the effects on C-reactive protein (CRP) levels are heterogeneous, with some studies reporting no significant changes. Despite the inherent challenges in blinding participants and personnel in yoga interventions, the overall risk of bias across studies was evaluated as low to moderate.*

Conclusion: *Yoga appears to be an efficacious complementary intervention for reducing inflammation and improving immune responses in cancer patients. The consistent reduction in pro-inflammatory markers and stress-related hormones underscores the potential benefits of yoga in cancer care. Future research should focus on standardising yoga interventions, exploring their long-term effects, and expanding the scope of the study population to corroborate these findings.*

Keywords: Yoga, Inflammatory Markers, Cancer Care, TNF-α, IL-6, IL-10, Cortisol, C-Reactive Protein (CRP), Complementary Therapy, Randomized Controlled Trials (RCTs)

Abbreviations

- RCT: Randomized Controlled Trial
- YG: Yoga Group
- CG: Control Group
- TNF-α: Tumor Necrosis Factor-alpha
- IL-6: Interleukin-6
- IL-10: Interleukin-10
- CRP: C-Reactive Protein

- IL-1RA: Interleukin-1 Receptor Antagonist
- TNF-R1: Soluble Tumor Necrosis Factor Receptor 1
- NF-κB: Nuclear Factor Kappa B
- IFN-γ: Interferon-gamma
- GM-CSF: Granulocyte-Macrophage Colony-Stimulating Factor
- SOD: Superoxide Dismutas
- CAT: Catalase
- MDA: Malondialdehyde
- NO: Nitric Oxide
- NK Cells: Natural Killer Cells
- LMR: Lymphocyte-to-Monocyte Ratio
- G-CSF: Granulocyte Colony-Stimulating Factor
- MCP-1: Monocyte Chemoattractant Protein
- Flt3L: FMS-like Tyrosine Kinase 3 Ligand

Introduction

Cancer is a complex disease characterised by uncontrolled cell growth and the potential to invade surrounding tissues. The global burden of cancer continues to rise, with the International Agency for Research on Cancer reporting approximately 19.3 million new cancer cases and nearly 10 million cancer-related deaths in 2020 [1]. By 2040, the number of new cases is projected to reach 28.4 million, driven by population growth, aging, and shifting risk factors. Breast cancer accounts for 25.1% of all cancers in women, with over two million new cases reported globally in 2020 [2].

A critical yet often overlooked aspect of cancer progression is the role of chronic inflammation in tumour initiation, promotion, and metastasis. Research has increasingly focused on the complex relationship between cancer and inflammation, underscoring that chronic inflammation is a significant driver of tumour development [3-7]. This process is sustained by inflammatory mediators and immune cells, fostering a tumour-promoting environment. The carcinogenic effects of chronic inflammation are driven by a combination of genetic and epigenetic alterations, cytokine signalling, and immune system evasion, all of which collectively promote tumour growth and metastasis [8].

Key inflammatory cytokines, including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β), play pivotal roles in cancer development by modulating the tumour microenvironment [9-11]. These cytokines enhance tumour survival, stimulate angiogenesis, and suppress anti-tumour immunity, creating conditions conducive to tumour progression. In addition, immune cells recruited during chronic inflammation, such as macrophages and myeloid-derived suppressor cells, can shift to an immunosuppressive state, allowing cancer cells to evade immune detection and destruction [12].

Addressing cancer-related inflammation using non-therapeutic strategies offers promising benefits for improving patient outcomes. Anti-inflammatory diets rich in plant-based foods and healthy fats have been shown to lower pro-inflammatory cytokine levels, while nutraceuticals like curcumin and resveratrol provide complementary anti-inflammatory effects [13,14]. Physical activity and effective weight management also play crucial roles in reducing systemic inflammation, including markers like C-reactive protein (CRP) and IL-6, and can mitigate cancer risks associated with obesity [15-17]. Psychological interventions, such as mindfulness, yoga, and meditation, further help manage stress-induced inflammation, enhancing emotional well-being and quality of life. These holistic, complementary approaches not only address the physiological aspects of inflammation, but also provide psychosocial support, offering a well-rounded strategy for managing inflammation in cancer care.

Yoga, an ancient mind-body practice originating in India, has gained recognition as adjunct therapy in cancer care [18]. Traditionally seen as a holistic practice that enhance physical, emotional, and spiritual well-being, yoga is now being studied for its potential physiological benefits, particularly in modulating inflammation and stress [19,20]. Yoga incorporates physical posture (asanas), breathing exercises (pranayama), and meditation (dhyana), all of which can influence the autonomic nervous system and the endocrine pathways involved in stress regulation.

Chronic stress contributes to inflammation in cancer patients. Persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to elevated cortisol levels, perpetuating inflammation and worsening cancer outcomes. Yoga has been shown to reduce stress-related hormones, such as cortisol, while downregulating pro-inflammatory cytokines such as TNF-α and IL-6. This modulation of inflammatory markers suggests that yoga can improve the overall health outcomes in patients with cancer [21]. Numerous randomised controlled trials (RCTs) have reported reductions in TNF-α, IL-6, and cortisol levels among patients with cancer practising yoga, particularly those with breast cancer. However, the findings of these studies are inconsistent. While some trials reported significant reductions in IL-6 and CRP levels, others have reported no significant changes in these markers [22].

Given the rising interest in non-pharmacological interventions, such as yoga, to improve cancer outcomes, there is a clear need for a systematic review to consolidate existing evidence. This review aimed to assess the impact of yoga on inflammatory markers in cancer care, focusing on cytokines and stress markers, and provide a comprehensive analysis of the physiological mechanisms underlying these effects.

Methods

A comprehensive literature search was conducted to identify studies that examined the effects of yoga on inflammatory markers in cancer patients. The search encompassed multiple databases, including PubMed, Cochrane Library, Web of Science (WOS), and Scopus, covering studies published between January 2000 and August 2024. The search terms comprised combinations of keywords and Medical Subject Headings (MeSH) related to the population (e.g., "cancer", "neoplasm", "tumour"), intervention (e.g., "yoga", "asana", "pranayama"), and outcome (e.g., "inflammatory markers", "cytokines", "TNF-α", "IL-6", "CRP", "cortisol"). Boolean operators (AND, OR) were utilised to ensure comprehensive coverage, and reference lists from selected studies and reviews were screened for additional eligible studies. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)guidelines were adhered to throughout the review process to ensure transparency and completeness [23].

Inclusion and Exclusion Criteria: Studies that met specific eligibility criteria were included in this review. Eligible studies were randomised controlled trials (RCTs), cohort studies, or quasi-experimental studies that focused on cancer patients of any type or stage. The primary intervention had to be yoga, including but not limited to styles such as Hatha, Iyengar, or integrated yoga, delivered as a complementary therapy. Studies are needed to report the effect of yoga on inflammatory markers, such as TNF-α, IL-6, IL-10, IL-1β, C-reactive protein (CRP), and cortisol. Only studies published between January 2000 and August 2024, and those available in English were included in the review. Studies were excluded if they focused on non-cancer populations; did not report inflammatory markers as primary or secondary outcomes; or were case reports, case series, reviews, or editorials without original data.

Study Selection: The search results were screened in two stages. First, articles were assessed for relevance based on their titles and abstracts, followed by full-text screening for potentially eligible studies. Studies that met the inclusion criteria were included in this systematic review. Two independent reviewers conducted the screening and discrepancies were resolved by a third reviewer. Data extraction involved collecting information on study characteristics, population details, type of yoga intervention, outcomes related to inflammatory markers, and key findings comparing the changes in inflammatory markers between the yoga and control groups.

Risk of Bias Assessment: The risk of bias for each included study was assessed independently by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool, which evaluates bias across five domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data or selective reporting [24]. Studies were rated as having a low, high, or unclear risk of bias for each domain, and any disagreement between reviewers was resolved by consensus.

Data Synthesis: Due to the variability in study designs and the different yoga interventions used, a qualitative synthesis of the data was performed. The data were synthesized narratively, with a focus on identifying trends and consistencies in the effects of yoga on inflammatory markers

Results

A total of 637 studies were retrieved from PubMed, Cochrane Library, Web of Science, and Scopus databases. After removing 45 duplicates, 592 articles were screened based on their titles and abstracts. Of these, 545 were excluded as they did not meet the inclusion criteria. The remaining 47 full-text articles were assessed for eligibility, resulting in the inclusion of 14 studies in the final systematic review [24-37]. A PRISMA flow diagram depicting the study selection process is shown in Figure 1. The included studies comprised 1023 cancer patients across various cancer types, including breast, prostate, gastrointestinal, and myeloproliferative neoplasms. The sample sizes of the individual studies ranged from 18 to 200 participants, with the majority of the studies focusing on breast cancer.

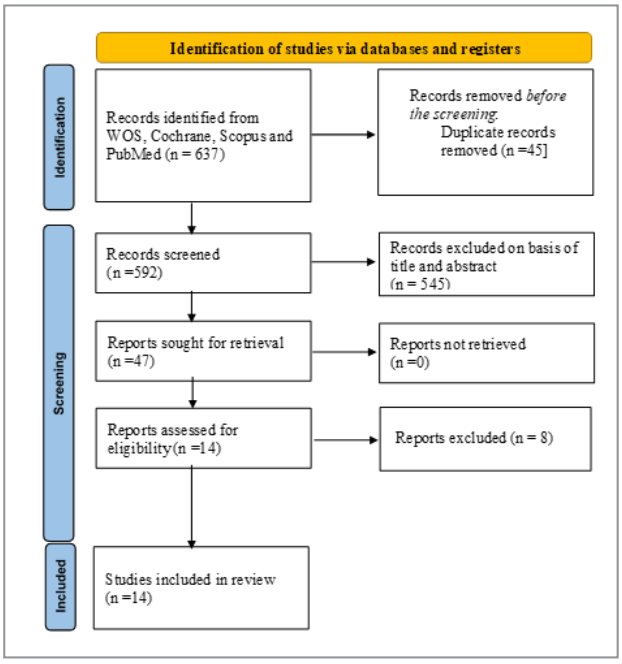

Figure 1: Summarized search strategy (Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram)

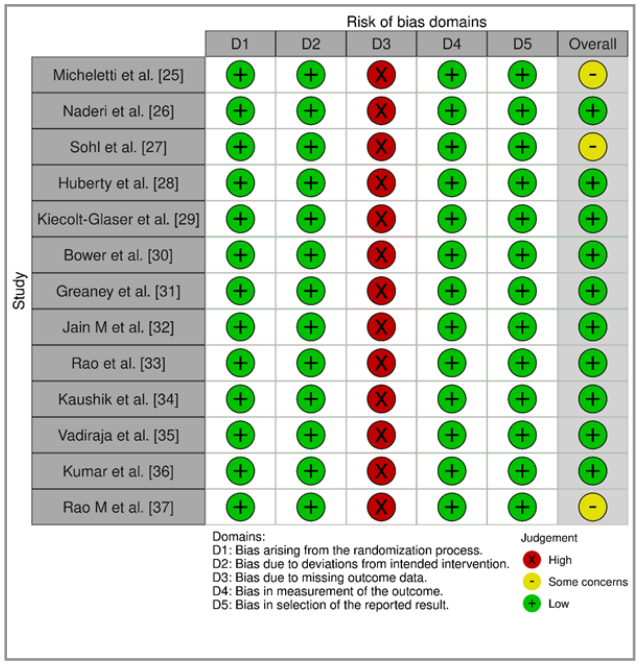

Figure 2: Risk of Bias Chart

The included studies were conducted in various geographical regions, including the USA, India, and Europe. The mean age of the participants ranged from 45 to 65 years old. Yoga interventions varied across studies, with most utilising Iyengar Yoga, Hatha Yoga, or integrated yoga programs, and the duration of the interventions ranged from 4 to 48 weeks. The inflammatory

markers assessed in these studies were primarily cytokines such as IL-6, TNF-α, and IL-10 as well as cortisol and C-reactive protein (CRP). A summary of the study characteristics, including the type of yoga intervention, duration, and primary outcomes, is presented in Table 1.

Table 1: Complete Summary of Study Characteristics and Main findings

Study Author and Year	Study Design	Population (Cancer Type and Stage)	Sample Size	Yoga Intervention (Type, Duration, Frequency)	Inflammatory Markers Assessed	Main Outcomes on Inflammatory Markers
Micheletti et al. [25]	RCT	Patients with stage I to III breast cancer undergoing adjuvant radiotherapy	YG: 12, CG: 12	2 sessions per week during radiotherapy (XRT), Yoga type not specified	IL-6, IL-10, IL-1RA, TNF-α, LMR	Reduction in IL-1β and IL-10 associated with fatigue improvement. Yoga group had lower cortisol levels at end of radiotherapy (p-adj = 0.02)
Naderi et al. [26]	RCT	Breast cancer survivors	30 (HD, YHD, YLD 10 each)	Hatha yoga, 12 weeks, twice per week	IL-10, TNF-α, IL-6	YHD group showed improved cytokine profiles, increased IL-10, decreased TNF-α and IL-6 levels
Sohl et al. [27]	RCT	Adults with GI cancer undergoing chemotherapy	YG: 23, CG: 21	Yoga Skills Training (YST), four 30-minute sessions plus home practice	IL-6, sTNF R1	Larger reductions in IL-6 and sTNF R1 in YST group compared to CG
Huberty et al. [28]	RCT	Patients with Myeloproliferative Neoplasms	YG: 27, CG: 21	Online yoga, 60 min per week for 12 weeks	IL-6, TNF-α	Decrease in TNF-α levels from baseline to week 12 in YG (-1.3 ± 1.5 pg/ml)
Kiecolt-Glaser et al. [29]	RCT	Breast cancer survivors	YG: 100, CG: 100	Hatha yoga, 12 weeks, 90 min sessions, twice per week	IL-6, TNF-α, IL-1β	Lower levels of IL-6, TNF-α, IL-1β in YG at 3 months post-treatment
Bower et al. [30]	RCT	Breast cancer survivors with fatigue	YG: 16, CG: 15	Iyengar yoga, 12 weeks, two sessions per week	NF-κB, sTNF-RII, IL-1RA, CRP, IL-6	Reduction in NF-κB, stable sTNF-RII in YG but increased in CG (p = .028)
Greaney et al. [31]	RCT	Women with early-stage breast cancer	YG: 15, CG: 15	Personalized yoga therapy, average 1.7 sessions per week, 30 mins each	TNF-α, CRP	No significant changes in TNF-α or CRP in YG or CG
Jain et al. [32]	RCT	Stage II/III breast cancer patients undergoing chemo/radiotherapy	YG: 48, CG: 48	Yoga 5 days per week for 48 weeks	TNF-α, IFN-γ, GM-CSF, SOD, CAT, MDA, NO	Significant reduction in TNF-α, IFN-γ, and MDA in YG ($p < 0.05$), NO levels stable in YG but upregulated in CG
Rao et al. [33]	RCT	Metastatic breast cancer patients	YG: 45, CG: 46	Integrated yoga-based stress reduction program, 3 months	NK cell counts, Diurnal cortisol	Improvement in NK cell percentage (p = 0.03), decreased cortisol levels in YG (p = 0.003)
Kaushik et al. [34]	RCT	Localised Prostate Cancer	YG: 14, CG: 15	Yoga for 6 weeks before prostatectomy	G-CSF, MCP-1, Flt3L, CD4+, CD8+, IFN	Decreased G-CSF, MCP-1, Flt3L; increased CD4+ and CD8+ T-cells in YG
Vadiraja et al. [35]	RCT	Stage II and III breast cancer outpatients undergoing radiotherapy	YG: 44, CG: 44	Integrated yoga program before/during radiotherapy	Salivary cortisol	Significant decrease in 6 a.m. cortisol (p = .009) and pooled cortisol (p = .03) in YG
Kumar et al. [36]	RCT	Advanced stage breast cancer patients	YG: 78, CG: 69	Sudarshan Kriya and Pranayama workshop, 18 hours over 3 days, 20 min daily practice	Serum cortisol	Lower cortisol levels in YG (341.2 ng/ml) vs. CG (549.2 ng/ml) ($p \leq 0.002$)
Rao et al. [37]	RCT	Stage II and III breast cancer patients undergoing surgery	YG: 33, CG: 36	Yoga as pre/postoperative intervention	IL-2R, TNF-α, IFN-γ	Significant decrease in TNF-α in YG compared to CG post-surgery ($p < 0.001$)

Effect of Yoga on Inflammatory Markers: Six studies evaluated the effect of yoga on IL-6 levels. [25-29] Most studies have demonstrated a significant reduction in IL-6 levels following yoga intervention. For instance, Kiecolt-Glaser et al. observed significantly lower levels of IL-6 in the yoga group than in the control group three months post-treatment ($p = .027$) [29]. Similarly, Naderi et al. found that breast cancer survivors who practiced yoga exhibited a significant decrease in IL-6 levels, particularly in the high-dose vitamin D and yoga combination group [26].

Eight studies assessed TNF-α levels, with most demonstrating significant reduction in the yoga group [25-29, 31-33]. Micheletti et al. reported lower TNF-α levels in patients with breast cancer who practiced yoga during radiotherapy than in the control group ($p = 0.02$). Additionally, Kaushik et al. found significant reductions in TNF-α levels in patients with prostate cancer who practiced yoga before radical prostatectomy [34]. Three studies examined IL-10, an anti-inflammatory cytokine. [25,26,32] Jain et al. and Naderi et al. reported significant increases in IL-10 levels among cancer patients practising yoga. Notably, Naderi et al. showed that the combination of yoga and high-dose vitamin D supplementation significantly increased IL-10 levels and improved inflammatory cytokine profiles of breast cancer survivors.

Cortisol, a key marker of stress-induced inflammation, was assessed in three studies [35, 36]. Vadiraja et al. reported a significant decrease in morning salivary cortisol levels in patients with breast cancer undergoing adjuvant radiotherapy who practiced yoga compared to those receiving supportive therapy ($p = 0.009$) [35]. Rao et al. also observed a significant reduction in morning waking cortisol levels among patients with metastatic breast cancer following a yoga intervention ($p = 0.003$) [33]. The CRP results showed greater variability. Greaney et al. observed no significant alteration in CRP levels among breast cancer patients engaging in yoga during chemotherapy, whereas other studies did not report CRP as a primary outcome [31]. This suggests that the effect of yoga on CRP levels may be contingent on factors such as cancer type and treatment stage. Several studies have investigated the effects of yoga on immune marker levels. Bower et al. observed reductions in NF-κB activity and increased glucocorticoid receptor activity, indicating an anti-inflammatory effect of yoga on the immune pathways [30]. Kaushik et al. also noted increased numbers of CD4+ and CD8+ T-cells and enhanced interferon-gamma production, suggesting enhanced antitumour immune activity in prostate cancer patients [34].

Summary of Findings: The majority of the included studies indicated that yoga can reduce pro-inflammatory markers, such as IL-6 and TNF-α, while increasing anti-inflammatory markers, such as IL-10. Cortisol levels were consistently reduced in all studies, further supporting the role of yoga in managing stress-induced inflammation. However, the effects on CRP levels were heterogeneous, and further research is required to elucidate the effect of yoga on this marker.

Risk of Bias Assessment: The RoB 2 table indicates that the methodological rigor of these yoga intervention studies was relatively sound in terms of randomisation, allocation concealment, and outcome assessment. However, as is often the case with behavioural interventions, such as yoga, blinding participants and personnel is challenging, posing a risk of performance bias. Additionally, concerns regarding missing outcome data and incomplete reporting of results suggest that certain studies may have been affected by attrition or inconsistent follow-up, potentially affecting their overall credibility.

Discussion

This systematic review expands previous research on the effects of yoga on inflammatory markers in patients with cancer. In contrast to Kaje et al., who focused solely on breast cancer, this review encompasses a broader range of cancers, including prostate, gastrointestinal, and haematological malignancies. This diversity facilitates a more comprehensive understanding of the benefits of yoga for various cancer types [22]. Similarly, while Mishra et al. assessed the effects of yoga on inflammation across a range of chronic conditions, this review focused specifically on cancer [21]. This approach allows for a more in-depth examination of the distinct inflammatory pathways and immune responses involved in oncology, offering insights into how yoga modulates pro-inflammatory cytokines, including TNF-α and IL-6, while reducing cortisol levels and alleviating stress-induced inflammation. These findings also suggest that longer duration yoga interventions may have more pronounced anti-inflammatory effects.

Across the included studies, yoga interventions consistently downregulated pro-inflammatory markers such as TNF-α and IL-6, and in some cases, increased anti-inflammatory markers such as IL-10. Several studies have also reported reductions in cortisol levels, highlighting yoga's potential to mitigate stress-induced inflammation, which is a crucial benefit for patients with cancer who often experience high levels of psychological stress due to their diagnosis and treatment. The longer the duration of yoga intervention, the more significant the reduction in proinflammatory markers, emphasising the importance of sustained practice. Both Kaje et al. and Mishra et al. noted heterogeneity in yoga interventions and study designs, rendering direct comparison challenging. This review expands on these findings by incorporating studies from a broader range of cancers and further elucidating the variability in outcomes contingent upon cancer type, intervention duration, and study design. Although the effects of yoga on TNF-α and IL-6 levels were consistent, the results for CRP levels were heterogeneous, with some studies demonstrating no significant changes. This aligns with the findings of Mishra et al., wherein CRP outcomes exhibited considerable heterogeneity, suggesting that certain markers may be less responsive to yoga or may require longer follow-up periods for detectable changes. Furthermore, studies such as that by Greaney et al. reported no significant effects on inflammatory markers, underscoring the variability in responses based on intervention specifics.

Potential Mechanisms of Action: The anti-inflammatory effects of yoga are likely mediated through its capacity to modulate the hypothalamic-pituitary-adrenal (HPA) axis, thereby reducing cortisol levels and subsequently downregulating pro-inflammatory cytokines [38]. Reduced cortisol levels were observed across diverse cancer types in the studies included in this review, indicating that yoga exerts a beneficial effect on stress-related inflammation. Yoga may also enhance parasympathetic nervous

system activity, alter autonomic balance, and contribute to reduced inflammation, as has been reported by Mishra et al. The pranayama (breathing exercises) and meditation components of yoga likely play crucial roles in this process by promoting relaxation and activating the anti-inflammatory pathways. These mechanisms may explain the reduction in TNF-α and IL-6 levels observed in several studies.

Limitations of the Current Evidence: Notwithstanding the generally positive outcomes, several limitations exist within the current body of evidence. The heterogeneity in yoga interventions, encompassing various forms such as Iyengar and Hatha yoga, with differing frequencies and durations, presents challenges for the standardisation of findings. Kaje et al. and Mishra et al. emphasised similar concerns regarding the variability in intervention types and cancer populations, which influenced the consistency of the results. Furthermore, the majority of studies had a limited sample size, thus restricting the statistical power to detect significant changes in certain markers, such as CRP. The inconsistent findings for CRP and IL-8 levels suggest that these markers may be less responsive to yoga interventions or may require extended follow-up periods to observe changes. Performance bias is another prevalent issue as blinding participants to yoga interventions is inherently problematic, as noted by Kaje et al.

Future Directions: Subsequent research should endeavour to standardise yoga interventions by focusing on specific components, such as pranayama and meditation, and evaluating their individual contributions to reducing inflammation. Larger-scale, longitudinal studies are required to determine the sustained effects of yoga on markers, including CRP, IL-8, and other understudied biomarkers, such as NF-Î B. Moreover, expanding the research to encompass a more diverse range of cancers beyond breast and prostate cancers would provide a more comprehensive understanding of yoga's potential in oncological care.

Clinical Implications: The findings of this review support the integration of yoga as a complementary therapy in cancer care, particularly in the management of stress and inflammation. Although yoga should not supplement conventional treatments, its capacity to reduce key inflammatory markers, such as TNF-α and IL-6, suggests that it can serve as a valuable adjunctive therapy, especially for patients experiencing elevated stress levels. Kaje et al. and Mishra et al. concluded that yoga is a cost-effective, low-risk intervention that enhances quality of life and may modulate cancer-related inflammation.

Conclusion

The findings of this systematic review suggest that yoga is a promising complementary intervention for cancer patients, notably in reducing inflammation and stress markers. Yoga consistently decreased pro-inflammatory cytokines, such as TNF-α and IL-6, while increasing anti-inflammatory cytokine IL-10. Lower cortisol levels further support the role of yoga in mitigating stress, a significant factor in cancer-related inflammation. Although the CRP results varied, the overall evidence indicates a positive impact of yoga on the immune response and inflammatory processes, highlighting its potential to enhance both physiological outcomes and quality of life in cancer patients. Future studies should address these methodological limitations, standardise yoga practices, and explore their long-term effects. Expanding research to include diverse cancer types and larger sample sizes is crucial for validation. Yoga shows significant promise as a cost-effective, non-invasive strategy that complements traditional cancer treatments by modulating inflammation and reducing stress.

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None

Ethical Statement

Ethical approval was not required for this study, as it was a review article whose data were obtained through a literature search.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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