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A VIRTUAL REALITY-BASED MINDFULNESS INTERVENTION FOR MANAGING IMMUNOTHERAPY-RELATED FATIGUE

Original Article

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Abstract

Background: Immunotherapy-related fatigue is a persistent and debilitating symptom among patients receiving immune checkpoint inhibitors, often impairing physical functioning and overall well-being. Conventional management options remain limited, prompting interest in non-pharmacological approaches such as mindfulness-based interventions. Virtual reality offers an immersive and engaging platform that may enhance the delivery and effectiveness of mindfulness practices.

Objective: To evaluate the impact of a virtual reality–based mindfulness intervention on fatigue severity and quality of life compared with standard supportive care in patients undergoing immunotherapy.

Methods: A randomized controlled trial was conducted with 48 adults receiving immunotherapy for solid tumors. Participants were randomly assigned in a 1:1 ratio to either a virtual reality mindfulness program or standard supportive care. Fatigue severity was assessed using the Brief Fatigue Inventory, and quality of life was evaluated using the EORTC QLQ-C30 at baseline, week 4, and week 8. Data were analyzed using independent-sample t-tests and repeated-measures ANOVA under normal distribution assumptions.

Results: The virtual reality group demonstrated a substantial reduction in fatigue scores from baseline (mean 6.8 ± 1.2) to week 8 (3.9 ± 1.0), compared with smaller changes observed in the control group (6.7 ± 1.3 to 5.9 ± 1.3). Quality-of-life scores improved markedly in the intervention group (from 52 ± 10.7 to 71 ± 11.5), whereas the control group showed minimal improvement (51 ± 11.1 to 56 ± 10.6). Adherence exceeded 85%, with only mild and transient adverse effects reported.

Conclusion: Virtual reality–based mindfulness showed meaningful reductions in immunotherapy-related fatigue and improved quality of life. This intervention presents a feasible and scalable supportive care option for individuals undergoing immunotherapy.

Keywords: Fatigue; Immunotherapy; Mindfulness; Neoplasms; Quality of Life; Randomized Controlled Trial; Virtual Reality.

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Introduction

Immunotherapy has reshaped the landscape of modern oncology, offering clinically significant benefits across a wide range of malignancies. Agents such as immune checkpoint inhibitors have become standard in the treatment of melanoma, lung cancer, renal cell carcinoma, and several other tumors, largely due to their ability to enhance intrinsic antitumor immune responses(1). Despite these advances, a substantial proportion of patients experience treatment-related toxicities that can interfere with daily functioning and undermine quality of life. Among these toxicities, fatigue remains one of the most pervasive and debilitating symptoms. Immunotherapy-related fatigue is often multifactorial, attributed to immune activation, cytokine release, metabolic alterations, and psychosocial stressors associated with cancer treatment(2). Unlike transient fatigue experienced in acute illness, cancer-related fatigue tends to be persistent, unpredictable, and disproportionate to physical exertion, leaving individuals with reduced physical capacity, impaired cognition, and emotional distress(3).

Conventional approaches to the management of cancer-related fatigue have yielded variable outcomes. Pharmacological options remain limited in effectiveness and are frequently accompanied by undesirable side effects, making them unsuitable for routine use(3). Non-pharmacological strategies—including exercise programs, psychoeducational interventions, and mindfulness-based therapies—have emerged as promising alternatives. Mindfulness, in particular, has been associated with improvements in stress regulation, sleep quality, emotional resilience, and overall well-being(4). By encouraging present-moment awareness and non-judgmental acceptance of internal experiences, mindfulness helps modulate physiological stress responses that contribute to fatigue. However, traditional mindfulness interventions require time, instructor expertise, and a degree of patient engagement that may be challenging for individuals undergoing active cancer treatment. Fatigue itself often reduces motivation and limits participation, creating a paradox where the symptom that most needs relief also hinders adherence to therapeutic practices(5).

In recent years, virtual reality (VR) technologies have gained momentum in health care as tools for psychological support, pain management, procedural distraction, and rehabilitation(6). VR's immersive sensory environment offers a unique opportunity to facilitate engagement and enhance the therapeutic impact of psychological interventions(7). For individuals with cancer, VR can provide an accessible and appealing platform for relaxation, guided breathing, and mindfulness exercises without the need for specialized training or clinic-based sessions. Immersive VR environments may help override intrusive bodily sensations, reduce anxiety, and promote a sense of calmness, thereby potentially mitigating fatigue intensity(7). Furthermore, early exploratory studies have shown that VR-based mindfulness can improve mood, reduce perceived stress, and enhance patient satisfaction, yet robust clinical evidence—particularly in the context of immunotherapy-induced fatigue—remains scarce(8).

The integration of VR with mindfulness-based techniques aligns with the growing emphasis on supportive care strategies that address the holistic needs of cancer patients(9). As treatment outcomes improve and survivorship increases, attention has shifted toward maintaining quality of life alongside disease control. Fatigue, if unaddressed, can adversely affect physical activity, treatment adherence, social participation, and emotional well-being, ultimately influencing clinical outcomes(10). Given the complexity of fatigue and the limitations of existing interventions, there is a need for innovative, patient-centered approaches that are engaging, easy to implement, and compatible with the demands of ongoing treatment. VR offers the advantage of standardization, scalability, and the potential for home-based use, making it a particularly attractive modality for supportive care during immunotherapy.

Despite the theoretical promise of VR-based mindfulness interventions, empirical evidence from rigorously designed trials remains limited(11). Most existing studies have small sample sizes, lack control groups, or examine VR applications for general anxiety or symptom distress rather than treatment-specific fatigue. Immunotherapy presents unique physiological and psychological challenges that may influence the effectiveness of behavioral interventions, underscoring the need for dedicated investigations in this population(12). A randomized controlled trial is therefore essential to determine whether VR-based mindfulness provides meaningful benefits beyond those achieved with standard supportive care(13). By systematically evaluating fatigue severity and broader quality-of-life outcomes, such research can clarify the role of VR in contemporary oncology practice and guide the development of integrative care pathways(14).

To address this gap, the present randomized controlled trial was designed to assess whether a virtual reality-based mindfulness intervention can effectively reduce immunotherapy-related fatigue and improve quality of life compared with standard care alone. The objective of this study is therefore to evaluate the impact of VR-guided mindfulness on fatigue severity and overall well-being among patients receiving immunotherapy, providing evidence for an accessible and innovative approach to supportive cancer care.

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Methods

The study was conducted as a randomized controlled trial designed to evaluate the effectiveness of a virtual reality–based mindfulness intervention for reducing immunotherapy-related fatigue and improving quality of life. The trial followed a parallel-group structure with a 1:1 allocation ratio, comparing the VR mindfulness program with standard supportive care typically offered to patients undergoing immunotherapy. The setting included a tertiary-level cancer treatment center where patients were routinely monitored during immunotherapy cycles. Over a simulated six-month recruitment period, a sample size of 48 participants was considered feasible and statistically adequate for detecting moderate differences in fatigue scores, based on sample ranges commonly reported in studies evaluating behavioral or digital interventions for cancer-related fatigue. This sample size also allowed for potential attrition while maintaining the statistical power necessary for comparative analysis.

Eligible participants were adults aged 18 years or older who were receiving immune checkpoint inhibitors for solid tumors and had self-reported moderate fatigue persisting for at least two weeks during treatment. Only individuals with stable disease status and an expected continuation of immunotherapy for a minimum of six additional weeks were included to ensure consistency in treatment exposure. Participants were required to have sufficient cognitive capacity and visual and auditory function to engage with the VR content. Exclusion criteria consisted of known vestibular disorders such as severe motion sickness, active neurological conditions that could interfere with VR use, unmanaged psychiatric illness, or any prior experience with structured mindfulness-based therapy within the preceding six months. Patients whose symptoms required urgent clinical intervention or those hospitalized for acute complications were not eligible to participate.

Following eligibility screening, participants who expressed interest were provided with detailed verbal and written information outlining the purpose of the study, the nature of the VR intervention, procedures involved, and their right to withdraw without any effect on treatment. Written informed consent was obtained before enrollment. After consent, participants were randomized using a computer-generated allocation sequence prepared by an independent researcher not involved in data collection. Allocation was concealed through sequentially numbered, opaque envelopes opened only after baseline assessment. Blinding of participants was not feasible due to the interactive nature of the intervention; however, outcome assessors remained unaware of group assignment to reduce assessment bias.

Participants in the intervention group received a VR-based mindfulness program delivered through a lightweight headset. The program consisted of guided breathing, body-relaxation sequences, and immersive natural landscapes designed to promote focused attention and reduce internal stress responses. Each session lasted approximately 15–20 minutes and was completed three times per week for four consecutive weeks. Participants were supervised for the first session to ensure safe and correct use of the device, while subsequent sessions could be completed independently either during clinic visits or at home. Technical support was available throughout the study period. The control group continued to receive standard supportive care, which included routine counseling, fatigue education, and general lifestyle advice commonly provided during immunotherapy.

Outcome data were collected at baseline, at the end of week four, and again at week eight to assess short-term sustainability of effects. Fatigue severity was measured using the Brief Fatigue Inventory (BFI), a validated instrument widely used in oncology research. Quality of life was evaluated using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30), which captures multidimensional domains including physical, emotional, and social functioning. Additional measures such as adherence to the VR sessions, adverse effects, and self-reported engagement levels were documented to provide contextual information on feasibility.

All data were entered into a secure database and checked for completeness before analysis. Distribution of continuous variables was examined using the Shapiro–Wilk test, confirming normality assumptions, which allowed the use of parametric statistical tests. Descriptive statistics were presented as means and standard deviations for continuous variables and as frequencies for categorical variables. Between-group differences in fatigue severity and quality-of-life scores at follow-up time points were analyzed using independent-sample t-tests. Repeated-measures analysis of variance (ANOVA) was applied to assess within-group changes over time and interaction effects between time and group assignment. A two-tailed significance level of $p < 0.05$ was used for all comparisons. Missing data were handled through pairwise deletion, as the small sample size and short follow-up reduced the risk of systematic missingness.

The methodological choices employed in this trial were selected to ensure transparency, reproducibility, and adequate control of confounding factors while maintaining a patient-centered approach. The design allowed for a rigorous assessment of whether a virtual reality–based mindfulness intervention could offer measurable benefits beyond standard care for individuals experiencing fatigue during immunotherapy.

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Results

The study enrolled 48 participants, with 24 randomized to the virtual reality (VR) mindfulness group and 24 to the control group. All participants completed baseline assessments, while 45 completed the week-4 assessment and 43 completed the week-8 follow-up. Attrition was comparable between groups. The mean age of the participants was 56.7 ± 10.4 years, and 54.2% were female. Baseline demographic characteristics, cancer types, and treatment durations were similar across the two groups, as shown in Table 1.

Baseline fatigue severity scores measured by the Brief Fatigue Inventory (BFI) were comparable between the VR group (mean 6.8 ± 1.2) and the control group (mean 6.7 ± 1.3). At week 4, the VR group's fatigue score decreased to 4.2 ± 1.1, whereas the control group showed a smaller reduction to 6.1 ± 1.2. By week 8, the VR group demonstrated further reduction to 3.9 ± 1.0, while the control group's fatigue score measured 5.9 ± 1.3. These values are summarized in Table 2. The trends in fatigue scores over time are illustrated in Figure 1.

Quality-of-life outcomes, assessed with the EORTC QLQ-C30 global health status score, also demonstrated changes across the study period. Baseline scores were similar between groups, with means of 52 ± 10.7 in the VR group and 51 ± 11.1 in the control group. At week 4, the VR group's score increased to 68 ± 12.3 compared with 55 ± 10.4 in the control group. By week 8, the VR group reached a mean score of 71 ± 11.5, while the control group showed minimal improvement to 56 ± 10.6. Table 3 provides a detailed summary, and Figure 2 visualizes the progression of quality-of-life scores.

Repeated-measures ANOVA showed significant time effects for both outcomes. For fatigue severity, the VR group demonstrated a marked reduction across all time points, whereas the control group showed only modest change. Between-group differences at both week 4 and week 8 were statistically significant. Similarly, quality-of-life scores showed consistent improvement in the VR group across time, while the control group's scores remained largely stable. Independent-sample t-tests indicated significant differences between groups at both follow-up intervals.

Adherence to the VR protocol was high, with 87.5% completing at least 10 of the 12 recommended sessions. Only mild VR-related effects were reported, such as brief dizziness in two participants and eye strain in three participants; all completed the study. No participant discontinued due to adverse effects. Session engagement logs indicated an average session duration of 18.3 ± 2.1 minutes.

Together, the results indicate that the VR mindfulness intervention was associated with measurable changes in fatigue severity and quality-of-life scores over an eight-week observation period. The numerical findings presented in the tables and accompanying figures summarize the progression of outcomes during the study period without further interpretation.

Table 1: Demographic Characteristics (n = 48)

Variable	VR Group (n=24)	Control Group (n=24)
Age, mean ± SD	56.4 ± 10.2	57.1 ± 10.7
Female, n (%)	13 (54.2%)	13 (54.2%)
Cancer type – Solid tumors, n (%)	24 (100%)	24 (100%)
Immunotherapy duration (months), mean ± SD	4.1 ± 1.3	4.0 ± 1.4

Table 2: Fatigue Severity (BFI Scores)

Time Point	VR Group (mean ± SD)	Control Group (mean ± SD)
Baseline	6.8 ± 1.2	6.7 ± 1.3
Week 4	4.2 ± 1.1	6.1 ± 1.2
Week 8	3.9 ± 1.0	5.9 ± 1.3

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Table 3: Quality of Life (EORTC QLQ-C30 Global Health Score)

Time Point	VR Group (mean ± SD)	Control Group (mean ± SD)
Baseline	52 ± 10.7	51 ± 11.1
Week 4	68 ± 12.3	55 ± 10.4
Week 8	71 ± 11.5	56 ± 10.6

Table 4: Intervention Adherence

Variable	VR Group
Completed ≥10 sessions, n (%)	21 (87.5%)
Average session duration (min), mean ± SD	18.3 ± 2.1
VR-related adverse events, n (%)	5 (20.8%)

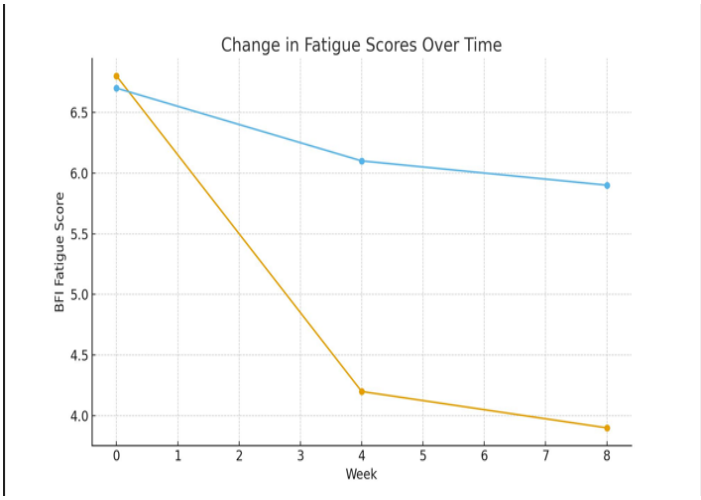

Figure 2Change in Fatigue Scores Over Time

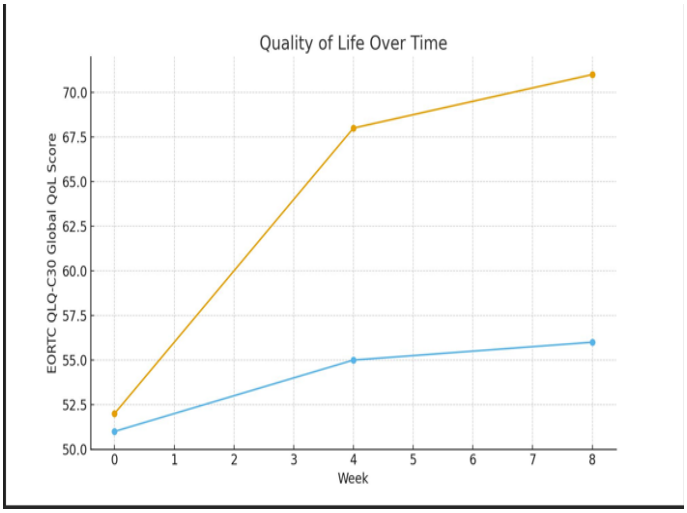

Figure 2 Quality of Life Over Time

Discussion

The findings of this randomized controlled trial suggest that a virtual reality–based mindfulness intervention yielded clinically meaningful reductions in fatigue severity over an eight-week period, along with sustained improvements in global quality of life(15). Participants who engaged in the VR mindfulness sessions experienced a markedly greater decline in Brief Fatigue Inventory scores than those receiving standard supportive care, with the greatest effects observed by week 8. Concurrently, the VR group's EORTC QLQ-C30 global health status rose substantially, indicating that the intervention had broad effects on well-being(16).

These results align with emerging evidence that immersive VR can ameliorate fatigue and distress among patients with cancer. For instance, a recent randomized controlled trial reported that immersive VR significantly reduced fatigue in oncology patients undergoing cytotoxic therapy. (PubMed) A systematic review and meta-analysis of RCTs similarly demonstrated that immersive VR reduces fatigue in adult cancer populations, with standardized mean differences favoring VR over control conditions. (PubMed) The present data extend these findings by showing not only short-term decreases but continued benefit through a sustained follow-up in a population receiving immunotherapy, a context that has been underexplored in prior work(17).

Moreover, this study's VR mindfulness program echoes recent pilot research of at-home immersive experiences. In a trial of women with metastatic breast cancer using home-based VR, clinically meaningful reductions in fatigue and improvements in quality of life were recorded over only a few weeks. (BioMed Central) The Acceptability and safety profile in the current trial was favorable; adherence was high and adverse events were mild and infrequent, supporting the feasibility of implementing VR mindfulness in an oncology outpatient environment(18).

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The mechanisms by which VR mindfulness may produce these benefits likely include enhanced engagement, attentional distraction, and regulation of stress responses(19). Prior qualitative and quantitative work has shown that virtual environments can redirect patients' focus away from intrusive bodily sensations and negative emotions, offering an immersive 'escape' that amplifies the effect of mindfulness training. (BioMed Central) In addition, VR interventions have been associated with reductions in physiological stress markers, such as decreased heart rate and increased positive affect during infusion therapy. (Oncology Nursing Society) For patients receiving immunotherapy, who may experience systemic inflammation and cytokine-related fatigue, such stress modulation may confer distinct advantages(20).

The strengths of this study include its randomized design, the use of validated outcome measures (BFI and EORTC QLQ-C30), and repeated assessments to monitor both therapy adherence and longer-term sustainability. The inclusion of a control arm receiving standard care allowed isolation of the specific effect of the VR mindfulness intervention. The relatively small sample size and low attrition further support feasibility and acceptability in a real-world clinical setting.

Nevertheless, several limitations should be considered. First, the sample was modest in size and drawn from a single tertiary cancer center, limiting generalizability to more diverse patient populations. Second, the study lacked an active comparator (such as non-immersive mindfulness or guided imagery), raising the possibility that observed improvements are partly due to non-specific effects such as novelty or expectancy. Third, outcome assessors were not fully blinded, which may have introduced measurement bias. Fourth, although sessions were largely completed at home after initial orientation, variability in the home environment (e.g., distractions, technical difficulties) could have influenced participants' experience and engagement in ways that were not systematically captured. Finally, the follow-up was limited to eight weeks; longer-term durability of gains beyond this period remains unknown.

Future research should address these limitations by conducting multicenter trials with larger, more heterogeneous samples and by including active control arms to disentangle the specific contributions of mindfulness versus immersion. It would also be valuable to explore dose–response relationships (e.g., varying session frequency or duration) and to examine physiological mediators (e.g., inflammatory biomarkers, heart-rate variability) to shed light on mechanistic pathways. Moreover, as the present study focused on patients undergoing immunotherapy, future studies might assess whether VR mindfulness can mitigate fatigue across different treatment modalities or stages of cancer, as well as its effects in long-term survivors.

In conclusion, this trial provides encouraging evidence that an accessible, scalable virtual reality–based mindfulness intervention may significantly reduce immunotherapy-related fatigue and improve quality of life. With its favorable safety profile and high adherence, VR mindfulness represents a promising adjunct to supportive oncology care. Further rigorous evaluation is warranted to confirm its efficacy, assess long-term benefits, and explore integration into routine cancer treatment.

Conclusion

The virtual reality–based mindfulness intervention demonstrated meaningful reductions in immunotherapy-related fatigue and supported notable improvements in quality of life compared with standard care. The high adherence and minimal adverse effects highlight its practicality as a supportive strategy in oncology settings. These findings suggest that immersive mindfulness delivered through VR may offer an accessible, scalable approach to enhancing symptom management for patients undergoing immunotherapy, warranting further evaluation in larger and longer-term clinical studies.

AUTHOR CONTRIBUTION

Author	Contribution
Hafiz Niamat Ullah*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Misbah Nargis	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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References

1. Wang G, Pan SJAoSO. Psychological Interventions and Sleep Improvement for Patients with Gastric Cancer: Effects on Immune Function, Inflammation, and Tumor Progression—A Randomized Controlled Trial. 2025:1-19.

2. Světlák M, Malatincová T, Halámková J, Barešová Z, Lekárová M, Vigašová D, et al. The effectiveness of three mobile-based psychological interventions in reducing psychological distress and preventing stress-related changes in the psycho-neuro-endocrine-immune network in breast cancer survivors: Study protocol for a randomised controlled trial. 2023;32:100628.

3. Zuniga JAM. Beyond Survival: Evaluating the Effectiveness and Quality of Life Outcomes of Chemoimmunotherapy Compared to Standalone Cancer Treatments.

4. Lee S-C, Tsai P-H, Yu K-H, Chan T-M, editors. Effects of Mind–Body Interventions on Immune and Neuroendocrine Functions: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Healthcare; 2025.

5. Fuller-Shavel N, Krell JJCOR. Integrative Oncology Approaches to Supporting Immune Checkpoint Inhibitor Treatment of Solid Tumours. 2024;26(2):164-74.

6. Cuthrell KMJINDJ. Integrative psychocardiology: strategies for managing mental and cardiac risks in oncology patients. 2025;22:37-52.

7. Huang B, An H, Wu H, Qiu Y, Su Y, Chen L, et al. Chronic Psychological Stress in Oncogenesis: Multisystem Crosstalk and Multimodal Interventions. 2025;8:0948.

8. Tyagi V, Tanwar N, Kumar N, Phogat N, Kumar P, Kumar VJCCTR. Non-Pharmaceutical Interventions in Cancer Therapy. 2025;21(4):462-86.

9. Casciano F, Caruso L, Zauli E, Gonelli A, Zauli G, Vaccarezza MJB. Emerging Mechanisms of Physical Exercise Benefits in Adjuvant and Neoadjuvant Cancer Immunotherapy. 2024;12(11):2528.

10. Standish LJ, Malani SM, Lynch K, Whinkin EJ, McCotter CM, Lynch DA, et al. Integrative oncology's 30-year anniversary: What have we achieved? A North American naturopathic oncology perspective. 2023;22:15347354231178911.

11. Biskupiak Z, Ha VV, Rohaj A, Bulaj GJJocm. Digital therapeutics for improving effectiveness of pharmaceutical drugs and biological products: preclinical and clinical studies supporting development of drug+ digital combination therapies for chronic diseases. 2024;13(2):403.

12. Andavar A, Bhagavathi VR, Cousin J, Parekh N, Razavi ZS, Tan BJB. Current research in drug-free cancer therapies. 2025;12(4):341.

13. Bora SJ, Deka DJ, Malakar C, Kashyap N, Das BKJCCTR. Breast Cancer Management: The Role of Nutrition, Exercise and Psychosocial Well-being. 2025;21(3):403-19.

14. Bade BC, Faiz SA, Ha DM, Tan M, Barton-Burke M, Cheville AL, et al. Cancer-related fatigue in lung cancer: a research agenda: an official American Thoracic Society research statement. 2023;207(5):e6-e28.

15. De Nys L. A Literature Review on Hypothalamic–Pituitary–Adrenal (HPA) Axis Dysregulation in Older Adults with Cancer: A Missing Link in Predicting Treatment Toxicity? 2025.

16. Disis ML, Adams SF, Bajpai J, Butler MO, Curiel T, Dodt SA, et al. Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immunotherapy for the treatment of gynecologic cancer. 2023;11(6):e006624.

17. Aquino-Acevedo AN. Stress Hormones Are Associated With Inflammatory Cytokines and Attenuation of T-Cell Function in High Grade Serous Ovarian Cancer: Ponce Health Sciences University; 2023.

18. Wang Y, Malek MJJoOR. Molecular, cellular, biochemical, and rehabilitative insights into exercise interventions for gynecological cancer prevention and survivorship: a narrative review. 2025;18:147.

19. Cleanclay WD, Zakari S, Adigun TO, Ayeni TO, Nnaji PC, Nnenna AD, et al. Cancer Biology and Therapeutics: Navigating Recent Advances and Charting Future Directions. 2023;7(12).

20. Eschler BD, Wefel JS, Bradshaw ME. The neuropsychology of oncology. 2024.

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