The role of physical activity in modulating immune biomarkers and oxidative stress among cancer patients: a systematic review

El papel de la actividad física en la modulación de biomarcadores inmunológicos y del estrés oxidativo en pacientes con cáncer: una revisión sistemática

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Abstract

Introduction: physical activity (PA) is recognized as a safe and beneficial intervention for individuals diagnosed with cancer. It is recommended that all cancer patients engage in regular physical activity as an integral component of a comprehensive treatment plan.
Objective: to critically evaluate the role of physical activity in modulating immune and oxidative stress biomarkers in cancer patients.
Methodology: A comprehensive search across several prominent academic databases—including ScienceDirect, PubMed, Springer, Scopus, Taylor & Francis, Sage, Google Scholar, and Wiley—resulted in the identification of 1,447 relevant articles. A total of eleven studies that satisfied the inclusion criteria were incorporated into the narrative review, followed by an assessment of the risk of bias for each study using the RoB 2.0 tool.
Results: of the eleven studies analyzed, 36.4% had low bias risk, 18.2% had potential bias concerns, and 45.5% had high bias risk.
Discussion: PA has been repeatedly demonstrated to influence the regulation of immune responses and oxidative stress indicators in individuals with cancer. It aids in boosting the function of immune cells, including $CD8^+$ T lymphocytes and NK cells, and promotes the activation of antioxidant enzymes such as SOD, CAT, and GPX. Additionally, it reduces pro-inflammatory markers and supports gene and cytokine expression related to immune regulation, making it a promising adjuvant to improve cancer therapy outcomes.
Conclusions: PA has been demonstrated to enhance immune system performance and mitigate oxidative stress among cancer patients, concurrently augmenting the cytotoxic capabilities of NK cells and $CD8^+$ T lymphocytes in targeting and destroying malignant cells.

Keywords

Physical activity; immune biomarker; oxidative stress; cancer.

Resumen

Introducción: Introducción: La PA es reconocida como una intervención segura y beneficiosa para las personas diagnosticadas con cáncer. Se recomienda que todos los pacientes con cáncer realicen PA de forma regular como parte integral de un plan de tratamiento integral.
Objetivo: Evaluar críticamente el papel de la PA en la modulación de biomarcadores inmunológicos y de estrés oxidativo en pacientes con cáncer.
Metodología: Una búsqueda exhaustiva en varias bases de datos académicas destacadas —incluyendo ScienceDirect, PubMed, Springer, Scopus, Taylor & Francis, Sage, Google Scholar y Wiley— permitió identificar 1,447 artículos relevantes. Once estudios que cumplieron con los criterios de inclusión fueron incorporados a la revisión narrativa, seguida de una evaluación del riesgo de sesgo de cada estudio mediante la herramienta RoB 2.0.
Resultados: De los once estudios analizados, el 36.4% presentó bajo riesgo de sesgo, el 18.2% mostró preocupaciones potenciales respecto al sesgo, y el 45.5% presentó alto riesgo de sesgo.
Discusión: La PA ha demostrado repetidamente influir en la regulación de las respuestas inmunológicas y de los indicadores de estrés oxidativo en individuos con cáncer. Contribuye a mejorar la función de células inmunitarias, incluidos los linfocitos T $CD8^+$ y las células NK, y promueve la activación de enzimas antioxidantes tales como SOD, CAT y GPX. Además, reduce los marcadores proinflamatorios y favorece la expresión génica y de citocinas relacionadas con la regulación inmunitaria, posicionándola como un adyuvante prometedor para mejorar los resultados de la terapia contra el cáncer.
Conclusiones: Se ha demostrado que la PA mejora el desempeño del sistema inmunológico y mitiga el estrés oxidativo en pacientes con cáncer, aumentando simultáneamente la capacidad citotóxica de las células NK y los linfocitos T $CD8^+$ para identificar y destruir células malignas.

Palabras clave

Actividad física; biomarcador inmunológico; estrés oxidativo; cáncer.

Introduction

Physical activity is widely recognized as safe and is strongly recommended for individuals diagnosed with cancer. It is considered a fundamental component of comprehensive cancer care, with guidelines encouraging all patients to remain physically active throughout the treatment continuum. Physical activity (PA) refers to any form of bodily movement that involves skeletal muscles and requires energy expenditure, encompassing structured exercise, household tasks, regular sports, as well as activities performed during work or leisure (Longobucco et al., 2022). As cancer therapies continue to advance, PA-based interventions have become increasingly integral to holistic rehabilitation and survivorship programs. While several clinical trials have demonstrated the protective effects of physical activity against cancer development and progression, the results have not always been consistent. This variability is largely attributed to the heterogeneity of cancer types, diverse participant characteristics, and a wide range of biological and psychosocial variables influencing individual responses (Spanoudaki et al., 2023 & Codima et al., 2021).

Cancer remains one of the leading causes of death in more than 57 countries. It is characterized by the uncontrolled growth of abnormal cells, which may remain localized at the site of origin or spread to other organs through the process of metastasis (Bray et al., 2021). In Indonesia, cancer rates are steadily increasing, with 409,000 new cases reported in 2022 and a projected rise to 434,000 by 2025 (Globocan, 2022). Globally, approximately 1.4 billion adults have not achieved the recommended levels of physical activity necessary to support overall health.

Based on data from the World Health Organization (WHO), the most commonly detected types of cancer in 2022 were breast, lung, colorectal, prostate, cervical, skin, and stomach cancers (Siegel et al., 2024). Notably, physical activity levels vary significantly across socioeconomic contexts, with 39.5% of individuals in high-income countries meeting activity guidelines compared to only 26.3% in low-income settings. In Indonesia, national indicators reflect persistently low physical activity levels. The sports participation index declined from 0.284 in 2022 to 0.254 in 2023, and the physical fitness index dropped from 0.185 to 0.179. In Indonesia, only approximately 20% of children aged 6 to 17 years engage in physical activity for 60 minutes daily, in accordance with recommended guidelines. Moreover, the average daily step count among Indonesians is lower than that of other Asian populations (Mempora, 2023). Recent research has identified a strong association between low levels of physical activity and sedentary behavior with a range of adverse health outcomes, including overweight, reduced cardiovascular fitness, elevated blood cholesterol levels, and various non-communicable diseases (Wang et al., 2022, Saudi & Lameky, 2025). According to data from the World Health Organization, approximately 64% of adults remain seated for more than four hours per day. According to WHO data, 64% of adults sit for more than four hours daily. Prolonged periods of physical inactivity significantly contribute to the global prevalence of non-communicable diseases, accounting for approximately 10% of breast and colorectal cancer cases (Lee et al., 2012).

Various epidemiological studies, including retrospective, prospective, and case-control designs, have demonstrated that physical activity plays a crucial role in reducing the risk of developing cancer (Wang & Zhou, 2021). The habit of engaging in regular exercise has been proven to reduce the risk of developing several types of cancer, including bladder, breast, renal, colorectal, prostate, endometrial, lung, pancreatic cancers, renal, esophageal adenocarcinoma, gastric cancers (McTiernan et al., 2019). Newton and Galvão (2008) reported that regular physical activity may reduce overall cancer risk by up to 40%. Sedentary behavior or physical inactivity significantly increases the relative risk of developing colorectal cancer by twofold and breast cancer by 1.5 times. Meanwhile, high-intensity physical activity has been shown to reduce the risk of breast cancer by up to 75% and colorectal cancer by up to 22% (Bray et al., 2021). This is further supported by data from the U.S. Centers for Disease Control and Prevention (CDC), which indicate that individuals who regularly engage in physical activity exhibit lower incidence rates of breast, colorectal, lung, and endometrial cancers (Idorn & Hojman, 2016).

Beyond safety, physical activity has shown beneficial effects during active cancer treatment, contributing positively to disease progression and overall patient well-being. Exercise not only improves muscle strength and physical function but also supports mental health outcomes. Several biological mechanisms are believed to mediate these benefits, including enhanced vascularization, improved tissue perfusion, modulation of the immune system, alterations in tumor metabolism, and molecular interactions

between muscle and cancer cells (Pedersen & Saltin, 2015). Nevertheless, further research is required, particularly well-structured intervention studies, to establish a clear causal relationship between these mechanisms and tumor growth regulation (Lu et al., 2024).

Systematic reviews have highlighted a broad range of benefits associated with physical activity in oncology. The benefits obtained include improved quality of life, reduced levels of depression and anxiety, enhanced cognitive function, decreased chronic pain and cancer-related fatigue, alleviation of swallowing difficulties following radiotherapy, and overall improvement in physical functioning (Tauda et al., 2025 & Tauda & Bravo, 2025). Moreover, PA has been linked to reduced risks of cachexia, sarcopenia, chemotherapy-induced toxicity, and sleep disturbances (Lu et al., 2024, Geng et al., 2023, Caru et al., 2023, Zhu et al., 2022, Tsitkanou et al., 2022, Atoui et al., 2021, Causar et al., 2020, Mclaughlin et al., 2021, & Codima et al., 2021). Despite the growing recognition of physical activity's advantages in cancer treatment, research specifically examining its impact on immune biomarkers and oxidative stress is still comparatively scarce.

Given this background, the present systematic review aims to comprehensively evaluate the role of physical activity in modulating immune biomarkers and oxidative stress in individuals with cancer. The goal is to strengthen the scientific understanding of these mechanisms and support the integration of exercise into multidisciplinary therapeutic approaches in oncology.

Method

Study Design

This systematic review aims to comprehensively evaluate the role of physical activity in modulating immune and oxidative stress biomarkers in cancer patients. The main objective of the study is to integrate pertinent research evidence to elucidate the underlying biological pathways connecting physical activity with immune system function and oxidative stress within the cancer context.

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework to guarantee transparency in methodology, promote reproducibility, and uphold rigorous standards during the processes of study identification, selection, data extraction, and analysis (Shamseer et al., 2015). By adhering to this framework, the review aimed to generate high-quality evidence that could inform the development of physical activity-based interventions as adjunctive therapeutic strategies for cancer patients.

Data Sources and Literature Search

The literature search was carried out in December 2024 using a range of academic databases, including ScienceDirect, PubMed, Springer, Scopus, Taylor & Francis, SagePub, Google Scholar, and Wiley. A combination of search terms and Boolean operators was used to maximize the retrieval of relevant literature. Keywords included: physical AND activity, exercise AND physical, oxidative AND stress, biomarkers, children, adolescents OR youth, and cancer OR neoplasm OR tumor. The search was restricted using filters to include only open-access research articles that have undergone peer review, were published in English between January 2019 and December 2024, and involved human subjects exclusively.

An example of the search syntax used was: [[All: physical] AND [All: activity;]] OR [[All: exercises] AND [All: physical;] AND [All: oxidative] AND [All: stress;]] OR [[All: biomarkers;] AND [All: children;]] OR [All: adolescents] OR [[All: youth] AND [All: cancer;]] OR [All: neoplasm] OR [All: tumor] AND [All Subjects: Oncology]]

The initial screening phase involved reviewing titles and abstracts based on predefined inclusion and exclusion criteria. Detailed counts of eligible studies included in this process are presented in Table 1.

Study Selection Criteria

To maintain relevance and uphold methodological standards, studies were selected according to the following criteria: (1) publication in English between 2019 and 2024; (2) availability of full-text articles; (3) original research using either experimental or randomized controlled trial (RCT) designs; (4) human participants of any age or gender; (5) investigation of any type of cancer and any form of physical activity

intervention; and (6) inclusion of immune or oxidative stress biomarkers as outcome measures. Studies were excluded if they were published only in abstract form, were study protocols, or were not available in English. These criteria were applied systematically to include only studies with comprehensive and scientifically robust data.

Screening, Data Extraction, and Synthesis

Following the literature search, duplicate references were identified and removed using the reference management software Mendeley©. The remaining documents were then independently screened by two reviewers, who separately assessed titles and abstracts to determine topic relevance. After the initial screening, the reviewers compared their results and resolved any discrepancies through discussion until reaching consensus. Articles that met the initial screening criteria were subsequently examined through a comprehensive full-text review to confirm their relevance and eligibility for inclusion. The article assessment process is illustrated in Figure 1.

Data extraction was performed by three reviewers and later cross-checked by two independent reviewers to guarantee the consistency and accuracy of the gathered data. The collected data encompassed information such as the authors' names, study design, patient diagnosis, treatment sample characteristics, specifics of the intervention (including the type, intensity, and duration of physical activity), evaluated biomarkers, and outcomes relevant to the impact of physical activity on immune function and oxidative stress markers in individuals with cancer. This data was then organized into a Microsoft Excel spreadsheet for further analysis.

Conducting a meta-analysis was not possible due to substantial heterogeneity across the included studies, particularly in terms of intervention types, cancer classifications, outcome measures, and study settings. As a result, the findings were synthesized and reported using a narrative approach.

Risk of Bias Assessment in Research

Four expert reviewers (LS, FP, ANS, and YNS) independently evaluated the methodological rigor of the studies that satisfied the inclusion criteria. For studies utilizing experimental or randomized controlled trial (RCT) designs, the Cochrane Risk of Bias 2.0 (RoB 2.0) tool was employed (Higgins et al., 2011). This tool assesses several key domains, including the randomization procedure, allocation concealment, blinding of participants and study personnel, completeness of outcome data, blinding of outcome evaluators, selective outcome reporting, and potential bias from other sources.

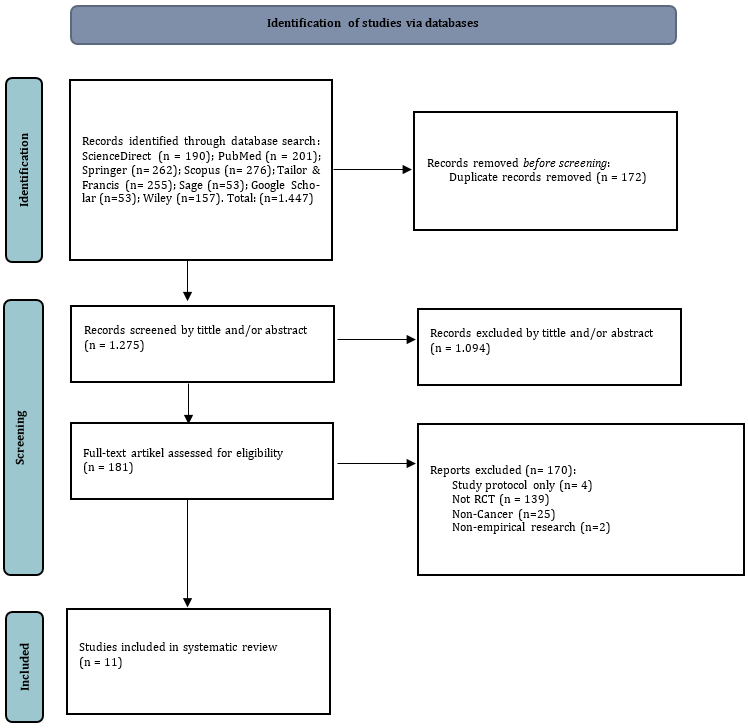
Each domain was rated as 'yes' (indicating low risk of bias), 'no' (indicating high risk of bias), or 'unclear' (indicating insufficient information or ambiguity regarding the risk of bias). Any discrepancies among reviewers (LS, FP, ANS, and YNS) in the quality assessment were resolved through discussion and consensus.

Results

Search Results

An initial search across databases yielded 1,447 articles. Following the removal of 172 duplicates, 1,275 unique records were subjected to title and abstract screening. From this, 1,094 articles were excluded for not fulfilling the inclusion criteria, resulting in 181 articles being assessed in full-text form. Of these, 170 were excluded due to non-compliance with the established eligibility criteria. Consequently, 11 studies were deemed suitable and included in the final analysis of this systematic review. The detailed selection procedure is presented in the PRISMA flow chart (Figure 1).

Figure 1. Flowchart of the study selection process



Study Selection

A total of eleven studies were selected for inclusion in the final analysis, aiming to investigate the influence of physical activity on immune system function and oxidative stress biomarkers in patients diagnosed with cancer. All studies involved human participants. Of these, five focused on the impact of resistance training on oxidative stress biomarkers, three examined the effects of aerobic exercise, two assessed combined resistance and aerobic training, and one investigated the influence of whole-body electromyostimulation (WB-EMS) on oxidative stress.

Risk of Bias

Among the eleven studies reviewed, 36.4% were identified as having a low risk of bias, while 18.2% presented potential concerns that should be considered. The remaining 45.5% were found to carry a high risk of bias. Specifically, three studies displayed a high risk in terms of outcome measurement, and two others were notably affected by issues related to randomization procedures, incomplete outcome data, and the evaluation methods used. Two further studies were found to have potential bias in outcome assessment, primarily due to unclear randomization procedures and insufficient information regarding assessor blinding. Although some concerns were noted, the reported results are still considered objective and unlikely to be significantly affected by bias. Six additional studies were assessed to be free from serious risk of bias (see Figure 2).

Figure 2. Risk bias assessment chart of the included literature

The Role of Physical Activity on Biomarkers

This review included a total of 11 studies to examine the role of physical activity as a potential anti-cancer catalyst. Various biomarkers were identified to be correlated with physical activity, including CAT, SOD, GPX, NADPH oxidase in leukocytes, plasma MPO, leukocyte MPO, 8-OHdG, AOPP, MDA, cytotoxic NK cells ($CD56^{dim}$ $CD16^{+}$), $CD57^{+}$, $NKG2D^{+}$, $CXCR3^{+}$, $TIM\text{-}3^{+}$, $CD45^{+}$, $CD8^{+}$ T cells, $CD19^{+}$ B cells, $CD56^{+}CD16^{+}$ cells, $CD14^{+}CD16^{+}$ monocytes, leptin, IGF-1, LNCaP, DU145, PC3, HT29, DNA fragmentation, calcium, β2-microglobulin, IgM, serum LDH, IP-10, IL-15, ICAM-1, VCAM-1, bFGF, Eotaxin-3, SOD2, L3MBTL1, TET1, DNMT3B, $CD20^{+}$, CD16 (ADCC), IL-6, IL-17, and the SII.

Table 1. Summary of Interventions

Study	Design	Diagnosis	Sample	Treatment	Intervention			Control Group	Assessed biomarkers
					Physical activity	Dosages	Duration		
Delrieu et al., 2021; France	Non-RCTs	Breast cancer	Age 18-78	Chemotherapy, radiotherapy	Home-based walking, assessed using the Six-	1,000 steps per week were	6 weeks	Without a control group	Antioxidant enzymes: CAT ($\mu mol \cdot min^{-1} \cdot L^{-1}$)

			years; n= 49	, hormonal therapy, and/or targeted therapy	Minute Walk Test (6MWT). The level of physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ)	increased every two weeks until reaching a maximum of 10,000 steps per day			, SOD ($\mu mol \cdot min^{-1} \cdot L^{-1}$) , GPX. Pro-oxidant enzymes: NADPH oxidase in leukocytes ($\mu mol \cdot min^{-1} \cdot mg^{-1}$ of protein), MPO in plasma ($\mu mol \cdot min^{-1} \cdot L^{-1}$) , MPO in leukocytes ($\mu mol \cdot min^{-1} \cdot mg^{-1}$ of protein). Oxidative stress markers: 8-OHdG ($\mu g \cdot L^{-1}$), AOPP ($\mu mol \cdot L^{-1}$), MDA
Parent-Roberge, et al., 2024; Canada	Non-RCTs	Breast cancer, Colorectal cancer, Esophagus cancer, Prostate cancer, Lung cancer	Age 45-65 years MOD: n = 6; HIIE: n = 7	Chemotherapy regimen: 5-Fluorouracil-based, Taxane, Miscellaneous.	Moderate-intensity continuous aerobic exercise session (MOD) & high-intensity interval exercise (HIIE); Measured using a submaximal incremental exercise test.	HIIE: 10 high-intensity sessions lasting 1 minute each MOD: performed at a steady work rate	30 minutes	Without a control group	Lymphocytes (T cells and B cells). NK cells: ($CD3^{-}CD56^{+}$), Regulator NK cells ($CD56^{bright}$ $CD16^{-}$), Cytotoxic NK cells ($CD56^{dim}$ $CD16^{+}$). Regulatory Subset of B cells: $CD56^{bright}$ $CD16^{-}$ $CD57^{+}$, $CD56^{bright}$ $CD16^{-}$ $NKG2D^{+}$, $CD56^{bright}$ $CD16^{-}$ $CD158a^{+}$. Cytotoxic Subset of NK cells: $CD56^{dim}$ $CD16^{+}$ $CXCR3^{+}$, $CD56^{dim}$ $CD16^{+}$ $CXCR4^{+}$, $CD56^{dim}$ $CD16^{+}$ $CCR2^{+}$, and $CD56^{dim}$ $CD16^{+}$ $TIM\text{-}3^{+}$
Koivula, et al., 2023; Finlandia	Non-RCTs	Breast cancer	The average age is 58 ± 11 years; n = 20	New patient	Bicycle ergometer; measured using the Borg scale	10 minutes per session.	10 minutes	Without a control group	Total leukocytes ($CD45^{+}$), T cells $CD8^{+}$ (cytotoxic), B cells $CD19^{+}$, Total NK cells: $CD56^{+}CD16^{+}$, Intermediate monocytes: $CD14^{+}CD16^{+}$
Cartmel, et al., 2022; Amerika serikat	RCTs	Ovarian cancer	Age 18-75 years; EG: n = 74; CG: n = 70	Has completed adjuvant therapy at least one month prior to sample randomization	Walking, assessed using the Modifiable Physical Activity Questionnaire	150 minutes/week	6 months	Discussion on topics related to ovarian cancer patient survival	Metabolic hormones: Insulin, Leptin, Adiponectin. Tumor and inflammatory markers: CA-125, CRP. Growth factors and cytokines: IGF-1, IL-6, TNFα measured with ELISA kits. VEGF
Schwappacher, et al., 2020; Jerman	RCTs	Prostate cancer & Colorectal cancer	Age > 18 years. Prostate cancer: CG: n = 10; EG:	Chemotherapy, hormonal therapy	Whole-body electromyostimulation (WB-EMS).	WB-EMS uses low-frequency electrical impulses (<100 Hz) and low	12 weeks	Not undergoing Whole-Body Electromyostimulation (WB-EMS) training	Prostate cancer cells: LNCaP, DU145, PC3, Colon cancer cells: HT29, and DNA fragmentation

			n = 8. Colorectal cancer: CG: n = 6; EG: n = 6			current intensity (<100 mA)			
Wang, et al., 2023; China	Non-RCTs	Multiple myeloma (MM)	Age > 50 years. EG: n = 17; CG: n = 13	No information	Walking, household chores, or activities considered as moderate physical activity	No information	17 days	Not engaging in physical activity	Metabolic and physiological biomarkers: Total proteins, calcium, creatine. Immunological biomarkers: β2-microglobulin. Immunoglobulins: IgG, IgD, IgM. Free light chains. Cancer progression and inflammatory markers: Serum LDH and IL-6
Kennedy, et al., 2021; China	RCTs	Esophagogastric cancer	Age 63-67 years CG: n = 17; EG: n = 20	Has completed chemotherapy.	Aerobic exercise and resistance training. Monitored using the Polar FT7 heart rate monitor and exercise logs.	Aerobics: progressing from 30-40% HRR to 45-60% HRR. Resistance: progressing from 12-17 reps max, with 2-6 sets.	12 weeks	Receiving standard treatment.	Inflammatory mediators: IP-10, IL-27, IL-15. Vascular injury biomarkers: ICAM-1, VCAM-1. Angiogenesis marker: bFGF. Chemokine: Eotaxin-3
Moulton, et al., 2024; Italia	RCTs	Breast cancer stadium I-III	Age 45-65 years. CG: n = 10; EG: n = 10.	Chemotherapy, radiotherapy, hormone-therapy, alone or in combinations	Resistance exercises and aerobic training. Measured using the IPAQ, 6MWT, Borg CR10 scale, muscle strength test, and flexibility	Strength training: circuit with light weights. Aerobic exercise: aerobic steps at ~70% HRR	60 minutes per session, once a week, for 16 weeks.	Receiving standard medical care	DNA methylation on the promoter genes related to oxidative stress: SOD1, SOD2, & CAT. DNA methylation on the promoter genes related to breast cancer: BRCA1, L3MBTL1, & RASSF1A. Enzymes involved in the DNA methylation and demethylation mechanisms: TET1, & DNMT3B
Collier-Bain, et al., 2024; Inggris	Non-RCTs	CLL	Age > 18 years; n = 20	New patient	Cycling, assessed using a bicycle ergometer	10–15% above the individual's anaerobic threshold with a pedaling cadence of 60–80 RPM	20–30 minutes	Without a control group	B cells ($CD19^+$) and their subtypes: $CD19^+$ (B cells), $CD20^+$, CD49d, CD38, $CD5^{brigh}CXCR4^{dim}$, $CD5^{dim}CXCR4^{brigh}$. Natural Killer (NK) cells: $CD3^-CD56^+$, $CD56^{dim}$ and $CD56^{brigh}$, CD57 and CD16 (involved in ADCC), $CD158a^-NKG2A^+$, $CD158^+NKG2A^-$. Monocytes and their subtypes:

								CD14 and CD16 ($CD14^+CD16^-$, $CD14^+CD16^+$), $HLA\text{-}DR^+$, CD32 (involved in ADCC). Myeloid-Derived Suppressor Cells (MDSCs): $HLA\text{-}DR^-CD33^+$ (including monocytic and polymorphonuclear subtypes).
Leite, et al., 2021; Brasil	Non-RCTs	Breast cancer	Age 40-65 years; n = 22.	Undergoing tamoxifen treatment.	Resistance training (RT)	Week 1-4: ~60% of 1-RM, 15–20 repetitions per set. Week 5-8: ~70% of 1-RM, 8–12 repetitions per set. Week 9-12: ~85% of 1-RM, 4–6 repetitions per set.	50 minutes per session, 3 sessions per week, for 12 weeks.	Without a control group	Inflammatory and metabolic blood markers: IL-4, IL-6, IL-10, IL-17, IFN-γ, TNF-α, Adiponectin, TGC, t-C, HDL-C, LDL-C. Oxidative stress markers: Thiobarbituric Acid Reactive Substances (TBARS), Carbonyl, Thiols, Catalase activity, SOD.
Winker, et al, 2022; Jerman	RCTs	AL, TCL, & CNS	Age 4-17 years. EG: n = 11 CG: n = 14	Undergoing chemotherapy treatment.	Strength and endurance training, measured using the 6-minute walking test.	3 training sessions per week, each lasting 45-60 minutes.	6-8 weeks	Receiving standard anti-cancer treatment.	Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), Systemic Immune-Inflammation Index (SII)

Table 2. Summary of Outcomes

Study	Design	Physical activity intensity	Biomarkers involved	Findings
Delrieu et al., 2021; France	Non-RCTs	Resistance training – Light to moderate physical activity (home-based walking)	Antioxidant enzymes: CAT, SOD, GPX. Prooxidant enzymes: MPO plasma, MPO leucocytes. Oxidative stress markers: 8-OHdG, AOPP, MDA	↑GPX (+17%), ↑MDA (+9%), respondents with metastatic cancer ↑MDA (+20%), ↓AOPP (-46%), ↑CAT, ↓SOD, ↑MPO plasma, ↑MPO leucocytes, ↑8-OhdG. A significant association was observed between physical activity levels and changes in oxidative stress markers, particularly evidenced by a correlation in 8-OHdG concentration changes (r = 0.32; p = 0.03).
Parent-Roberge, et al., 2024; Canada	Non-RCTs	Aerobic exercise – Moderate to high-intensity physical activity.	NK cells: Cytotoxic NK cells ($CD56^{dim}$ $CD16^+$). Regulatory NK cell subset: $CD57^+$, $NKG2D^+$. Cytotoxic NK cell subset: $CXCR3^+$, $TIM\text{-}3^+$	MOD and HIIE both increase the number of cytotoxic NK cells ($CD56^{dim}$ $CD16^+$). They exhibit tumor infiltration responses and have high cytotoxic potential, such as $CD57^+$, $NKG2D^+$, $CXCR3^+$, and $TIM\text{-}3^+$. HIIE shows changes in the median fluorescence intensity (MFI) for the NKG2D and CXCR4 receptors, indicating potential alterations in migration or cytotoxic activity.
Koivula, et al., 2023; Finlandia	Non-RCTs	Aerobic exercise – Low-intensity (Cycle ergometer)	Total leukocytes ($CD45^+$), $CD8^+$ T cells (cytotoxic), $CD19^+$ B cells, Total NK cells: $CD56^+CD16^+$ and Intermediate monocytes: $CD14^+CD16^+$	↑Leukocytes (29%), ↑CD8 T cells (34%), ↑CD19 B cells (18%), ↑CD56 CD16 NK cells (130%), and ↑$CD14^+$CD16 monocytes (51%). Leukocyte mobilization ($CD45^+$, $CD8^+$, $CD19^+$, $CD56^+$, $CD56^+CD16^+$) positively correlates with systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate during exercise. Low-intensity exercise can effectively mobilize cytotoxic immune cells.
Cartmel, et al., 2022; Amerika serikat	RCTs	Resistance training – Moderate intensity (Walking)	Metabolic hormone: Leptin. Growth factors and cytokines: IGF-1	↓IGF-1 levels (mean difference between groups: -14.2 ng/mL; 95% CI: -26.1 to -2.3; p = 0.02) and ↓leptin (-8.9 ng/mL; 95% CI: -16.5 to -1.4; p = 0.02) in the exercise group. The 6-month exercise program resulted in a significant reduction in IGF-1 and leptin levels, but did not affect other biomarkers.

Schwappacher, et al., 2020; Jerman	RCTs	Low intensity (WB-EMS)	Prostate cancer cells: LNCaP, DU145, PC3. Colon cancer cells: HT29. DNA fragmentation	Proliferation of prostate cancer cells ↓LNCaP by 10.9% (p = 0.014), ↓DU145 by 7.0% (p = 0.048), and ↓PC3 by 10.4% (p = 0.011) after 96 hours. Colon cancer cells (HT29) proliferation ↓9.1% (p = 0.031) after 96 hours and 13.2% (p = 0.021) after 48 hours. ↑Apoptotic cells in LNCaP from 17.6% to 28.1% (p = 0.001) and ↑DNA fragmentation (+21.2%) (p = 0.035). WB-EMS exercise is effective as an adjunct therapy for advanced cancer patients, reducing cancer cell proliferation and increasing apoptosis.
Wang, et al., 2023; China	RCTs	Resistance training – Moderate intensity (Walking, household chores).	Metabolic and physiological biomarkers: Calcium. Immunological biomarker: β2-microglobulin. Immunoglobulin: IgM. Cancer progression and inflammation markers: Serum LDH and IL-6	↑IL-6 significantly in the MM+PA group, indicating the role of physical activity in enhancing the anti-inflammatory response. ↑IgM significantly in the MM+PA group, but no significant changes in IgD, IgG, kappa, or lambda chains. ↓LDH, ↓calcium, and ↓beta-2 microglobulin significantly decreased in the physical activity (MM+PA) group compared to the control group ($p \leq 0.05$). ↓LDH, calcium, and β2-microglobulin were associated with improvements in biochemical function. ↑IgM indicating increased immune stimulation.
Kennedy, et al., 2021; China	RCTs	Low intensity (Aerobic exercise and Resistance training).	Inflammatory mediators: IP-10, IL-27, IL-15. Vascular injury biomarkers: ICAM-1, VCAM-1. Angiogenesis marker: bFGF. Chemokine: Eotaxin-3	↑IP-10 at T1 (MD: 38.02, 95% CI: 0.69-75.35, p = 0.05). ↑IL-27 at T1 (MD: 249.48, 95% CI: 22.43-476.53, p = 0.03). ↑ICAM-1 at T1 (Ratio of Means: 1.05, 95% CI: 1.07-1.66, p = 0.02). ↑VCAM-1 at T1 (Ratio of Means: 1.51, 95% CI: 1.04-2.14, p = 0.02). ↑Eotaxin-3 at T2 (MD: 2.59, 95% CI: 0.23-4.96, p = 0.03). ↑IL-15 at T2 (MD: 0.27, 95% CI: 0.00-0.54, p = 0.05). ↓bFGF at T2 (MD: -1.62, 95% CI: -2.99 to -0.26, p = 0.02).
Moulton, et al., 2024; Italia	RCTs	Low intensity (Resistance exercises and aerobic training).	DNA methylation on the promoter of oxidative stress-related gene: SOD2. DNA methylation on the promoter of breast cancer-related gene: L3MBTL1. Enzymes involved in DNA methylation and demethylation mechanisms: TET1 & DNMT3B	Modulating DNA methylation and gene expression: SOD2. ↓Promoter methylation (~20%) and ↑mRNA expression (~77%) & L3MBTL1. ↓Promoter methylation (~25%) and ↑mRNA expression (~43%). ↑TET1 mRNA (~15%) and ↓DNMT3B mRNA expression (~28%).
Collier-Bain, et al., 2024; Inggris	Non-RCTs	Aerobic exercise – High intensity (Cycling)	B cells: $CD19^+$ and its subtype: $CD20^+$. NK cells: CD16 (ADCC)	↑Effector NK cells $CD16^+$ (254%), ↑CLL cells $CD20^+$ (67%). Rituximab can enhance ADCC efficacy against CLL cells by 129% after exercise.
Leite, et al., 2021; Brasil	Non-RCTs	Resistance training – Moderate to high intensity.	Inflammatory and metabolic blood markers: IL-6, IL-17. Oxidative stress markers: TBARS, Carbonyl, catalase activity, SOD activity, plasma Thiols	↑IL-6, ↓IL-17, adiponectin remained unchanged after resistance training (RT) but increased after detraining. ↓TBARS, ↓Carbonyl, ↓catalase activity, ↓SOD activity, and no changes in plasma Thiols. Resistance training for 12 weeks was effective in improving lipid profiles and reducing oxidative stress in postmenopausal breast cancer survivors.
Winker, et al, 2022; Jerman	RCTs	Resistance training – Moderate intensity (Strength and endurance training).	Systemic Immune Inflammation Index (SII)	Exercise significantly reduced the systemic inflammatory index (SII) in pediatric cancer patients compared to controls (p = 0.036), indicating its anti-inflammatory effect.

Types and Characteristics of Interventions

Among the eleven studies reviewed, three primary categories of physical activity interventions were identified: (1) resistance training, (2) aerobic exercise, and (3) machine-assisted training using Whole-Body Electromyostimulation (WB-EMS). The characteristics of each study—including intervention type, cancer diagnosis, intervention duration and frequency, and outcome measures—are detailed in Tables 1 and 2.

A range of assessment tools was used to measure physical activity levels across the included studies. Several tools were employed in the assessment. The Six-Minute Walk Test (6MWT) was used to evaluate functional capacity. The International Physical Activity Questionnaire (IPAQ) collected self-reported data on physical activity levels. Submaximal graded exercise tests assessed endurance performance. Perceived exertion was measured using the Borg Scale. Additionally, customized Physical Activity Questionnaires were utilized. Physiological monitoring was conducted with the Polar FT7 heart rate monitor. Exercise logs documented the frequency and duration of training sessions.

Regarding treatment status, six studies included participants undergoing active cancer treatment, two enrolled newly diagnosed individuals yet to begin therapy, two involved participants who had completed treatment, and one study did not report treatment status. The reviewed studies encompass a diverse range of cancer types, including breast, prostate, colorectal, esophageal, lung, ovarian cancers, multiple myeloma, esophagogastric cancer, chronic lymphocytic leukemia, acute leukemia, T-cell lymphoma, and cancers of the central nervous system.

The dosage and frequency of the physical activity interventions varied based on the exercise type, intensity, and the clinical condition of the participants (see Table 1). In terms of study design, six studies employed non-randomized controlled trials (non-RCTs), while five used randomized controlled trial (RCT) designs.

1. Resistance Training

Five of the eleven studies implemented resistance training interventions (Delrieu et al., 2021; Cartmel et al., 2022; Wang et al., 2023; Leite et al., 2021; Winker et al., 2022). These interventions included walking (Cartmel et al., 2022; Wang et al., 2023), home-based walking programs (Delrieu et al., 2021), and strength or endurance exercises (Winker et al., 2022). Exercise intensity ranged from low (Delrieu et al., 2021), to moderate (Cartmel et al., 2022; Wang et al., 2023; Leite et al., 2021; Winker et al., 2022), to high (Delrieu et al., 2021; Leite et al., 2021).

Physical activity assessment tools included the IPAQ (Delrieu et al., 2021), 6MWT (Winker et al., 2022; Delrieu et al., 2021), and the Modifiable Physical Activity Questionnaire (Cartmel et al., 2022). Intervention durations varied across studies.

Participants in these trials were diagnosed with breast cancer (Delrieu et al., 2021; Leite et al., 2021), ovarian cancer (Cartmel et al., 2022), multiple myeloma (Wang et al., 2023), and hematologic or central nervous system malignancies, including acute leukemia, T-cell lymphoma, and CNS tumors (Winker et al., 2022). Treatment status ranged from active therapies such as chemotherapy (Winker et al., 2022; Delrieu et al., 2021), radiotherapy, hormonal therapy, and targeted therapies (Delrieu et al., 2021), to post-treatment care (Cartmel et al., 2022), including patients taking tamoxifen (Leite et al., 2021).

2. Aerobic Training

Three studies focused on aerobic exercise as the primary intervention (Parent-Roberge et al., 2024; Koivula et al., 2023; Collier-Bain et al., 2024). The modalities included cycling on a stationary ergometer (Koivula et al., 2023), traditional cycling (Collier-Bain et al., 2024), while Parent-Roberge et al. (2024) did not specify the aerobic modality. Exercise intensities ranged from low (Koivula et al., 2023) to moderate and high (Parent-Roberge et al., 2024; Collier-Bain et al., 2024).

Outcome assessments included the submaximal incremental exercise test (Parent-Roberge et al., 2024; Collier-Bain et al., 2024) and the Borg Rating of Perceived Exertion Scale (Koivula et al., 2023). Training durations varied and are provided in Table 1.

Participants had diagnoses of breast (Parent-Roberge et al., 2024; Koivula et al., 2023), colorectal, esophageal, prostate, and lung cancers (Parent-Roberge et al., 2024), as well as chronic lymphocytic leukemia (CLL) (Collier-Bain et al., 2024). Most were undergoing chemotherapy regimens, including FOLFIRI, FOLFOX, capecitabine, taxanes (docetaxel, paclitaxel), carboplatin-gemcitabine, or vinorelbine (Parent-Roberge et al., 2024), while the remaining studies involved pre-treatment participants (Collier-Bain et al., 2024; Koivula et al., 2023).

3. Machine-Assisted Training (WB-EMS)

One study applied whole-body electromyostimulation (WB-EMS) as a physical activity intervention (Schwappacher et al., 2020). This approach was used with patients diagnosed with prostate and colorectal cancers who were receiving chemotherapy and hormonal therapy.

4. Combined Resistance and Aerobic Training

Two studies utilized combined low-intensity resistance and aerobic training protocols (Kennedy et al., 2021; Moulton et al., 2024). One study involved participants diagnosed with esophagogastric cancer (Kennedy et al., 2021), whereas another focused on breast cancer patients at stages I to III (Moulton et

al., 2024). The interventions were applied during chemotherapy, radiotherapy, and hormonal therapy (Moulton et al., 2024), or following the completion of treatment (Kennedy et al., 2021).

Assessment instruments included the Polar FT7 heart rate monitor and exercise logs (Kennedy et al., 2021), as well as the IPAQ, 6MWT, Borg CR10 Scale, muscle strength evaluations, and flexibility tests (Moulton et al., 2024). Intervention durations varied and are detailed in Table 1.

5. Impact of Intervention on Immune Biomarkers and Oxidative Stress

Both resistance and aerobic exercise interventions have demonstrated positive effects on immune function and oxidative stress markers in cancer patients. Resistance training has been shown to significantly enhance the activity of key antioxidant enzymes such as CAT, SOD, and GPX, thereby providing protection against oxidative damage induced by free radicals (Delrieu et al., 2021). However, the observed increase in oxidative damage biomarkers, including 8-OHdG and MDA (with MDA rising by approximately 20%) following exercise, indicates that oxidative stress persists despite the upregulation of antioxidant defenses.

Resistance training also led to reductions in biomarkers associated with cancer cell proliferation, including IGF-1 and LDH, implying a potential role in tumor growth suppression (Cartmel et al., 2022; Wang et al., 2023). Aerobic exercise, particularly when performed continuously at moderate intensity or as high-intensity intervals, has been shown to enhance both the quantity and function of cytotoxic immune cells, such as natural killer (NK) cells and $CD8^+$ T cells. Furthermore, this type of training increases the expression of key molecules including NKG2D, CXCR3, and TIM-3, which facilitate the immune system's recognition and destruction of cancer cells (Koivula et al., 2023; Parent-Roberge et al., 2024).

Exercise also impacted epigenetic regulation, particularly in genes involved in antioxidant defense and tumor suppression. Physical activity decreased DNA methylation in genes such as SOD2 and L3MBTL1, while concurrently increasing their mRNA expression—an effect associated with enhanced immune function and oxidative stress resilience (Moulton et al., 2024). Additionally, a structured rehabilitation program in esophagogastric cancer patients showed favorable modulation of inflammatory, angiogenic, and vascular injury biomarkers, supporting the role of exercise as a valuable adjunct to standard cancer therapies (Kennedy et al., 2021).

Discussion

Physical activity (PA) has been widely recognized for its capacity to modulate key biomarkers associated with immune function and oxidative stress in cancer patients. PA influences the function and distribution of various immune cell types, including $CD8^+$ T cells, $CD19^+$ B cells, and natural killer (NK) cells, while modulating biological pathways that inhibit cancer cell growth. Key biomarkers frequently examined in these studies include antioxidant enzymes such as CAT, SOD, and GPX; pro-oxidant enzymes like NADPH oxidase and MPO; as well as oxidative damage markers to DNA and lipids, including 8-OHdG and MDA. Additionally, cytotoxic markers such as $CD56^{dim}$ $CD16^+$, $CD57^+$, and $NKG2D^+$ are also considered due to their roles in inflammation and immune system regulation.

Regular physical activity can increase the population of natural killer (NK) cells characterized by the $CD56^{dim}$ $CD16^+$ phenotype, which possess cytotoxic capabilities. It also enhances the expression of surface molecules such as CD57, NKG2D, CXCR3, and TIM-3, all of which play crucial roles in the NK cell-mediated destruction of tumor cells (Farley et al., 2023 & Campbell et al., 2024). Elevated $CD45^+$ expression suggests improved immune responsiveness, whereas a reduction in $CD14^+CD16^+$ monocytes, typically linked to tumor-promoting inflammation, indicates a favorable shift in immune profiles (Chiarotto et al., 2017). Physical activity also enhances both the proliferation and cytotoxic function of $CD8^+$ T cells. This activation is stimulated by adrenaline released during exercise and myokines such as IL-6 and IL-15. IL-15, predominantly produced by skeletal muscle, supports the growth and maturation of NK and T cells, while IL-6 contributes to tumor suppression by inducing DNA damage in cancer cells and activating the immune system (Farley et al., 2023 & Kirkham et al., 2020).

Physical activity increases the activity of antioxidant enzymes including CAT, SOD (notably SOD2), and GPX, which play a protective role against reactive oxygen species (ROS) that may damage DNA and pro-

mote cancer progression (Gomez-Cabrera et al., 2021). Delrieu et al. (2021) identified a positive correlation between GPX activity and fitness levels, underscoring the critical role of GPX in bodily protection. Several studies have also reported significant reductions in the oxidative DNA damage biomarker 8-OHdG following combined exercise programs, indicating improved genomic stability through DNA repair mechanisms (Repka & Hayward, 2018, Guinan et al., 2016, & Powers et al., 2020). Nonetheless, inconsistencies across studies highlight the necessity for standardized methodologies in future research.

Lipid peroxidation marker MDA is often elevated in cancer patients, particularly those with progressive disease, yet exercise interventions consistently lower MDA levels, indicating reduced lipid membrane damage (Guedes, et al., 2025). Similarly, advanced oxidation protein products (AOPP), byproducts of protein oxidation, decrease following exercise, reflecting improved oxidative balance. Reductions in NADPH oxidase activity in leukocytes and MPO levels in plasma further suggest lower systemic inflammation and ROS production (Delrieu, et al., 2021 & Bettariga, et al. 2023). PA has also been shown to inhibit the growth of various cancer cell types, including LNCaP, DU145, PC3, and HT29, by modulating hormone levels and growth factors. This effect is particularly evident through the reduction of leptin and IGF-1 levels. The decrease in IGF-1 subsequently suppresses the PI3K/Akt/mTOR signaling pathway, which is critical for cell proliferation, while the increased activity of AMPK facilitates the induction of programmed cell death, or apoptosis (Xia et al., 2021).

PA also reduces markers of cellular damage such as DNA fragmentation, β2-microglobulin, and serum lactate dehydrogenase (LDH), all of which are associated with cancer progression. In patients with multiple myeloma, decreased serum calcium levels post-exercise indicate improved bone metabolism (Cheng et al., 2021). The exercise-induced increase in IgM levels is likely a result of immune system activation or alterations in immune cell distribution (Campbell et al., 2016). Furthermore, physical activity promotes the upregulation of proteins such as IP-10/CXCL10, IL-27, and adhesion molecules including ICAM-1 and VCAM-1, which play a crucial role in guiding immune cells toward tumor sites (Kennedy et al., 2021 & Fabbi et al., 2017). Although some biomarkers like bFGF and eotaxin-3 may have ambiguous roles, exercise has been shown to reduce bFGF levels in certain contexts, potentially limiting angiogenesis (Babina et al., 2017).

From an epigenetic perspective, physical exercise has been shown to modulate the expression of key regulatory genes such as TET1, L3MBTL1, and DNMT3B, which are critically involved in DNA methylation processes and the regulation of gene expression pathways implicated in cancer progression. While research in this area remains limited, existing findings suggest that exercise may help establish a gene expression profile less conducive to tumor growth. Furthermore, exercise reduces the SII, indicating a more balanced immune state and reduced systemic inflammation (Chiarotto et al., 2017). Donovan et al. (2021) reported that physical activity mitigates T cell exhaustion and senescence caused by chronic activation, thereby preserving immune functionality and extending anti-tumor activity—a promising implication for long-term cancer therapy.

Despite these encouraging results, the current literature is limited by small sample sizes, diverse study designs, and inconsistent biomarker measurements, which hinder the generalizability of findings. Therefore, well-designed randomized controlled clinical trials are necessary to scientifically validate and confirm the specific effects of exercise on immune system modulation in cancer patients. Among the immune cell types influenced by exercise, NK cells are particularly pivotal. Physical activity promotes NK cell infiltration into tumors, delays tumor growth, and enhances NK cytotoxicity via adrenaline and IL-6 (Pedersen et al., 2016 & Abdalla et al., 2014). Combining exercise with radiotherapy has also been shown to enhance NK cell infiltration and improve treatment outcomes (Wennerberg et al., 2020).

In addition to affecting the innate immune system, physical activity also enhances the adaptive immune response. Studies using breast cancer mouse models have demonstrated that exercise can increase the number and improve the efficacy of $CD8^+$ T cells in targeting and destroying cancer cells (Gomes-Santos et al., 2021). These cells infiltrate tumors more effectively and exhibit improved energy efficiency, strengthening the overall anti-tumor immune response. Exercise also enhances the efficacy of standard treatments such as immunotherapy and radiation (Kurz et al., 2022 & Wennerberg et al., 2020). In addition to T cells and NK cells, antioxidant enzymes such as SOD and GPX also play a critical role in mitigating damage caused by reactive oxygen species (ROS), which can contribute to cancer progression and recurrence (Delrieu et al., 2021). Elevated MDA levels in patients with progressive cancer suggest its

utility as a negative prognostic marker (Dejeans et al., 2012), whereas lower AOPP levels post-exercise may reflect a more favorable oxidative profile (Lefèvre et al., 1998)

Engagement in physical activity influences the regulation of adhesion molecules such as ICAM-1 and VCAM-1, which play crucial roles in blood vessel restoration as well as skeletal muscle remodeling and recovery (Kennedy et al., 2021). It also alters circulating levels of cytokines and growth factors, including IP-10, IL-15, and bFGF. For instance, elevated IP-10 may promote lymphocyte infiltration into tumors (Mendelson et al., 2015), while increases in IL-27 and eotaxin-3 have been reported, although their specific roles in cancer remain unclear (Fabbi et al., 2017 & Lan et al., 2018).

β2-microglobulin is another exercise-responsive biomarker potentially involved in anti-tumor immunity, warranting further study (Kim et al., 2022). In multiple myeloma, physical activity also appears to lower serum LDH levels, a marker associated with disease progression (Terpos et al., 2010). Overall, exercise promotes beneficial shifts in cancer-related immune responses by enhancing NK and $CD8^+$ T cell activity, reducing oxidative stress, and modulating key cytokines and growth factors. Mechanistic studies with rigorous methodologies are needed to clarify these complex interactions. Nonetheless, current evidence supports the incorporation of physical activity into cancer care regimens to enhance therapeutic efficacy and improve patient outcomes.

Consistent physical activity has been shown to effectively reduce inflammation and oxidative stress levels in individuals who have successfully completed cancer treatment. The SII, a commonly used marker of immune-inflammatory status, significantly declines in patients who engage in regular physical activity (Pagola et al., 2020 & Yeh et al., 2011), reinforcing its anti-inflammatory potential. Exercise also strengthens the body's antioxidant system by stimulating increased activity of enzymes such as SOD, GPX, and CAT, which play a crucial role in combating oxidative stress caused by treatment, thereby helping to maintain the overall health and quality of life of patients

Immunologically, exercise promotes the proliferation of NK cells, $CD8^+$ T cells, and $CD19^+$ B cells. Increases in $CD56^+CD16^+$ and $CD57^+$ NK cells following exercise suggest enhanced cytotoxic potential. Additionally, exercise improves antibody-dependent cellular cytotoxicity (ADCC), a key defense mechanism mediated by $CD16^+$ NK cells (Emery et al., 2022; Vermi et al., 2018). High-intensity cycling has been found to mobilize $CD19^+$ and $CD20^+$ B cells, potentially enhancing monoclonal antibody-based therapies such as rituximab (Calissano et al., 2011 & Pasikowska et al., 2016). These findings suggest a supportive role for exercise in optimizing immunotherapy.

Exercise also alters DNA methylation in gene promoters involved in oxidative stress response, such as SOD2 and L3MBTL1. PA in breast cancer patients has been shown to be associated with decreased methylation levels and increased expression of the SOD2 gene, which may contribute to a reduction in reactive oxygen species (ROS) production (Petersen et al., 2005; Pedersen et al., 2015). Similarly, hypomethylation of L3MBTL1 may enhance its tumor-suppressive activity (Abel et al., 2018; Bigley et al., 2014).

Finally, exercise influences circulating growth factors and hormones. Reductions in IGF-1 and leptin levels—both implicated in tumor growth—were observed in ovarian cancer patients post-exercise, supporting a shift toward anti-proliferative signaling (Khalafi et al., 2021). Increased VEGF levels may indicate improved tissue oxygenation, although the clinical relevance remains to be fully understood (Schink et al., 2018).

Conclusions

Overall, the findings of this review indicate that physical activity exerts beneficial effects on biomarkers associated with oxidative stress and immune function. Engaging in physical activity can improve the ability of natural killer (NK) cells and $CD8^+$ T cells to destroy harmful cells, lower oxidative stress by boosting antioxidant enzyme production, and modulate systemic biomarkers that play a role in cancer progression. Despite these promising outcomes, several limitations—such as heterogeneity in study designs and variability in biomarker assessment methods—underscore the need for further research employing robust methodologies, particularly randomized controlled trials (RCTs) with standardized protocols. Continued investigation into the underlying biological mechanisms is essential to fully elucidate

the immunomodulatory effects of exercise. Such insights could support the integration of physical activity as an adjunctive strategy in cancer treatment, with the potential to enhance therapeutic efficacy and improve patient quality of life.

Disclosure statement

The authors declare that there are no conflicts of interest related to this study.

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