

# Antitumor potential of exercise-conditioned human serum: Systematic review of in vitro and clinical findings

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## ABSTRACT

Cancer remains a significant cause of global morbidity and mortality, and non-pharmacological strategies such as exercise are increasingly gaining attention as supportive therapies. One widely studied mechanism is exercise-conditioned human serum, which contains biochemical factors that can potentially suppress cancer cell growth. This study aims to systematically review the clinical and in vitro evidence regarding the antitumor potential of post-exercise serum. Following PRISMA guidelines, the literature search was conducted through PubMed, Scopus, Web of Science, Embase, and the Cochrane Library databases. Of the 1,258 articles identified, only 12 met the inclusion criteria for analysis. The review results indicate that exercise interventions, including high-intensity interval training (HIIT), resistance training, multimodal training, and whole-body electromyostimulation (WB-EMS), consistently improve cardiorespiratory fitness, modulate cancer biomarkers, and suppress tumour cell proliferation. In vitro studies have shown that post-exercise serum can inhibit proliferation, increase apoptosis, and regulate molecular pathways such as Akt/mTOR, IL-6, and other myokines. Meanwhile, clinical studies confirm that structured exercise provides both physiological benefits and biological effects on cancer progression, particularly prostate, breast, colorectal, and pancreatic cancers. Overall, these findings emphasize that exercise has significant potential as a supportive therapy strategy and as part of a multimodal approach to cancer management.

**Keywords:** Exercise, Physical activity, Supplements, Cancer, Exercise therapy.

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## INTRODUCTION

Cancer remains a leading cause of morbidity and mortality worldwide. According to GLOBOCAN 2020, there were an estimated 19.3 million new cancer cases and nearly 10.0 million cancer deaths worldwide (Sung et al., 2021). Cancer prevention and control are critical public health challenges. Implementing comprehensive cancer control programs, including primary, secondary, and tertiary prevention, is crucial for effective management and improving population health outcomes (Davoudi Monfared, 2018). Understanding the effects of cancer informs practices and policies that improve prevention, screening, treatment, and survival, ultimately benefiting millions of people globally (Dee et al., 2023). Therefore, cancer prevention and control efforts have become a crucial public health issue. In addition to medical interventions such as chemotherapy, radiotherapy, and targeted therapy, increasing attention is paid to non-pharmacological approaches, including physical activity. A systematic review emphasized physical activity (PA) as a non-pharmacological approach to optimize health benefits in cancer survivors (Rodrigues et al., 2025).

Numerous experimental and clinical studies have shown that exercise not only benefits cardiovascular, metabolic, and psychological health but also potentially suppresses cancer cell growth. Physical activity is recognized as a key factor in cancer prevention and control (Demark-Wahnefried & Dieli-Conwright, 2022). One mechanism currently being widely studied is the effect of exercise-conditioned human serum, which is human blood serum after physical activity. This serum contains various biochemical factors that can influence cancer cell proliferation, apoptosis, and viability. Exercise-conditioned human serum has been shown to suppress cancer cell growth in vitro by altering key signalling pathways, potentially through changes in circulating proteins, RNA molecules, and metabolites. However, the exact mechanism and duration of the effect require further investigation (Metcalf et al., 2021).

Exercise-conditioned human serum has been shown to reduce growth and proliferation while increasing apoptosis of various cancer cells, including breast, prostate, colorectal, and lung cancers, suggesting its potential as a therapeutic agent in cancer management (Bettariga et al., 2024). In vitro studies have shown that serum conditioned by whole-body electromyostimulation (WB-EMS) inhibits malignant cell proliferation and activates apoptosis in cancer cell cultures, demonstrating its potential to affect various cancer cell types. However, responses vary among individual patients (Ugwoke & Umek, 2021). Exercise-conditioned serum significantly inhibited the growth of breast cancer cells, specifically MCF-7 and MDA-MB-231, reducing cell viability by 11% to 19% in vitro and tumour formation by 50% in vivo, highlighting its potential in cancer suppression (Dethlefsen et al., 2017).

Regular physical activity significantly reduces cancer risk, reduces the side effects of therapy, and improves patients' quality of life. It improves fatigue management, reduces cachexia symptoms, and optimizes metabolic pathways, supporting better overall health and potentially influencing tumour behaviour (Feng et al., 2024). However, integrating laboratory and clinical findings requires a more systematic review to ensure the consistency and strength of the evidence. Systematic reviews and meta-analyses are important methods for summarizing diverse research findings and providing a more comprehensive picture of the effects of exercise on cancer cell growth.

The study aims to systematically review available evidence, both from in vitro and clinical studies, regarding the effects of exercise-conditioned human serum on suppressing cancer cell growth. By integrating data from various studies, it is hoped that this review will provide a deeper understanding of the potential of exercise as a supportive therapy in preventing and treating cancer.

## METHODS

This study uses a literature review method to explore and analyse information from various previous studies. The data used in this review article comes from secondary data relevant to the research topic and was obtained from recent publications within the last 10 years. Source selection was carried out by considering the relevance and novelty of the information to align with the focus of the reviewed research. Search Strategy The databases used in the search in this study were ScienceDirect, Elsevier, Research Gate, Taylor & Francis, and PubMed, which are known as websites that provide access to scientific and health databases. The search strategy for articles in this study included variations of keywords such as "*Exercise-Conditioned Serum*" AND "*Cancer Cell Growth*," "*Physical Activity*" AND "*Oncology*," "*Exercise*" AND "*Cancer*," and "*Exercise-Conditioned Human Serum*." The search in this study followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). PRISMA is a reporting method to avoid fundamental errors in systematic reviews and meta-analysis reports (Haddaway et al., 2022). Article selection follows the PRISMA stages, namely: (1) defining topics and criteria, (2) determining information sources, (3) selecting relevant literature, (4) collecting articles, and (5) analysing articles.

### Procedure

The search strategy in this study was designed to identify relevant studies on the effects of exercise-conditioned human serum on cancer cell growth. The literature search was conducted in several international scientific databases, including PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Keywords used in the search included combinations of: "*Exercise-Conditioned Serum*" AND "*Cancer Cell Growth*," "*Physical Activity*" AND "*Oncology*," "*Exercise*" AND "*Cancer*," and "*Exercise-Conditioned Human Serum*". To increase coverage, synonyms and MeSH (Medical Subject Headings) terms were also used, such as "*post-exercise serum*," "*tumor suppression*," and "*cell proliferation*". All search results were extracted into a Microsoft Excel spreadsheet to facilitate data management and remove duplicate articles. Next, the researchers reviewed the title and abstract of each publication obtained to select relevant studies that met the inclusion criteria. The criteria set were studies examining the relationship between exercise-conditioned human serum and cancer cell growth, both in vitro and clinical studies. Articles not meeting the criteria or unavailable in full text were excluded from further analysis.

### Exclusion and inclusion criteria

This study selected questions, keywords, and search strategies using the PICO format (population, intervention, comparison, and outcomes). Analysis was conducted by dividing the research results into several groups, as shown in the table below. The journal search method used the PICO format to find questions and keywords. Analysis was conducted by grouping the research results. The goal was to gather information regarding the Antitumor Potential of Exercise-Conditioned Human Serum.

Table 1. Article search keywords.

PICO	Information
Population/Problem	Patients with cancer/human cancer cells (both in clinical and in vitro studies)
Intervention	<i>Exercise-conditioned</i> human serum
Comparison	Human serum without exercise (non-exercise serum) / control group
Outcome	Suppressed cancer cell growth

Initially, 1,258 publications were identified through searches of PubMed/MEDLINE, Scopus, Web of Science, Embase, and the Cochrane Library. All retrieved publications were then exported and managed using

reference management software to facilitate the filtering and removing duplicates. After the removal process, 931 unique articles remained for further review.

The next stage was screening based on title and abstract. Most articles were eliminated at this stage because they did not examine the relationship between exercise-conditioned human serum and cancer cell growth. However, they instead only discussed exercise in general or non-oncological biomarkers. A total of 66 articles were then retrieved for full-text review.

From the comprehensive review, 54 articles were excluded for various reasons, including not using post-exercise human serum, not focusing on cancer outcomes, or being review articles without primary data. Ultimately, 12 articles met the inclusion criteria and were included in this systematic analysis.

## RESULTS

Table 1. Characteristics of the studies added.

Author	Participants	Interventions	Outcome Measure	Conclusion
(Kang et al., 2021)	Fifty-two male patients (mean 63.4 ± 7.1 years) were randomized: 26 HIIT, 26 control.	HIIT: 12 weeks of aerobic exercise 3x/week on a treadmill (85–95% VO <sub>2</sub> ). Control: maintain regular exercise.	Peak VO <sub>2</sub> (Bruce modification), PSA, PSA kinetics, LNCaP cell growth, and testosterone.	HIIT improves cardiorespiratory fitness and reduces PSA levels and velocity, prostate cancer cells in men with localized prostate cancer under active surveillance
(Kim et al., 2022)	Twenty-five mCRPC men were randomized: exercise (EX, n = 13) and control (CON, n = 12).	EX: 6 months of supervised multimodal training (aerobic + resistance). CON: self-exercise suggestions according to ACSM guidelines for cancer patients.	Body composition was assessed by DXA, fasting blood was measured (SPARC, OSM, decorin, IGF-1, IGFBP-3), and then serum was tested on DU145 prostate cancer cells for 72 hours with RTCA.	Exercise increases SPARC and OSM and suppresses the growth of DU145 prostate cancer cells, potentially slowing advanced prostate cancer.
(Swain et al., 2022)	58 RCTs met the inclusion criteria; no observational or Mendelian studies were conducted.	Treatment involved a physical activity intervention, which was compared with a control group.	IGF, IGFBP, and insulin resistance markers were analysed through meta-analysis; bias risk was assessed, and evidence quality was determined using the GRADE system.	Physical activity lowers fasting insulin and insulin resistance, increases IGF-1, without effect on IGFBP-3, and reduces the risk of breast cancer.
(Kang et al., 2019)	66 US men with prostate cancer were divided into an exercise group and a control group.	Exercise Group: 12 weeks of supervised HIIT, three sessions/week (28–40 minutes). Control Group: usual care.	Primary: cardiorespiratory fitness. Secondary: immune, cancer biomarkers, psychosocial, physical function. Exploration: clinical indicators of disease progression	This study protocol assessed whether exercise suppresses tumours, reduces cancer fear, and prepares PCa-AS patients for radical treatment, with 80% power to detect differences in VO <sub>2</sub> peak.
(Orange et al., 2022)	Sixteen men with BMI ≥25 kg/m <sup>2</sup> and physically inactive lifestyles, who were at risk of colorectal cancer, were recruited.	This study used acute bouts of moderate aerobic interval training (6 x 5 minutes at 60% heart rate reserve) with a non-exercise control condition. Blood samples were collected before, after exercise, and during the control period.	Participant serum was tested on LoVo colon cancer cells to assess proliferation, IL-6, and γ-H2AX expression; recombinant IL-6 was used to test effects on DNA damage and proliferation further.	Acute post-exercise serum suppresses LoVo cancer cell proliferation, decreases γ-H2AX, increases IL-6, and inhibits colon cancer in vitro through DNA regulation by IL-6.
(Kurgan et al., 2017)	Male subjects were recruited; specific ages were not mentioned.	Blood was collected from men at 4 time points (pre, 5 min, one h, 24 h post exercise) for processing into serum used on NSCLC cells.	Intervention: one session of high-intensity interval training on a cycle ergometer. Outcomes assessed: post-exercise serum effects on NSCLC cells (proliferation & viability). Biomarkers: phosphorylation/activation of Akt,	Post-exercise serum showed anti-cancer effects on NSCLC, inhibiting cell proliferation and survival, and decreasing the phosphorylation of Akt, mTOR, p70 S6K, and Erk1/2 compared to pre-exercise serum.

			mTOR, p70 S6K, and Erk1/2 (cell survival & growth signalling pathways).	
(Agostini et al., 2018)	Healthy volunteers and post-operative cancer patients had their serum collected pre- and post-exercise; patients underwent adjuvant chemotherapy.	MCF-7 and MDA-MB-231 cells were incubated with pre- and post-exercise serum from participants; some experiments used healthy female serum with a specific incubation time (2 hours) and 80 mg/dl glucose.	The viability of MCF-7 and MDA-MB-231 cells was tested after incubation with pre- and post-exercise serum. Tumorigenic potential was assessed in NMRI-FoxN1NU mice with cells incubated with these sera. The role of catecholamines was tested by blocking the $\beta$ -adrenergic pathway to determine their effect on tumour viability and growth.	Post-exercise serum decreased the viability of MCF-7 ( $\downarrow$ 11%) and MDA-MB-231 ( $\downarrow$ 9%) cells, reduced mouse tumours, and suppressed proliferation/tumorigenic potential via catecholamines, including TNBC.
(Metcalfe et al., 2021)	Young, healthy men provide serum for analysis.	Serum was collected before and 2 hours after 65 minutes of aerobic exercise at 50–65% $VO_{2max}$ .	Serum was tested on LNCaP prostate cancer cells for 96 hours, with the primary measure being the number of viable cells.	Post-exercise serum decreased ~30% of prostate cancer cells by suppressing the proliferative pathway, not through apoptosis.
(Schwappacher et al., 2020)	Advanced cancer patients were divided into exercise vs. control: prostate (8 vs. 10) and colorectal (6 vs. 6).	12-week WB-EMS program, 20 minutes per session, 2 $\times$ /week, with a frequency of 85 Hz, a pulse width of 350 $\mu$ s, a cycle of 6 seconds stimulation/4 seconds rest.	Proliferation and apoptosis of prostate and colon cancer cells were measured by BrdU, cell count, and DNA fragmentation; gene expression was analysed by cancer gene array and RT-PCR; electrical stimulation of myotubes mimicked exercise, and myotube media was tested on cancer cell viability.	WB-EMS inhibits proliferation, increases prostate and colon cancer cell apoptosis, and identifies exercise-sensitive genes; even in frail patients, physical activity has a strong anti-oncogenic effect for multimodal therapy.
(Alizadeh et al., 2019)	Participants were randomized to HIIT (n = 26) or control (n = 26); demographic data and medical history were collected via a baseline questionnaire.	The HIIT group performed treadmill training 3 $\times$ /week for 12 weeks, intensity based on maximal heart rate; the control group received standard care.	Body fat was measured by skinfold, $VO_{2max}$ by Rockport Walk Test, blood was drawn before and after exercise; serum was analysed (TNF- $\alpha$ , IL-6, IL-1 $\beta$ , IL-10, HSP70) as well as cytokines IL-4 and IFN- $\gamma$ by ELISA.	HIIT increases $VO_{2max}$ , decreases TNF- $\alpha$ , IL-6, IL-10, and the TNF- $\alpha$ /IL-10 and IL-6/IL-10 ratios, while increasing IL-4 and HSP70 in hormone therapy breast cancer patients.
(KIM et al., 2022)	Ten prostate cancer patients undergoing ADT therapy were recruited.	Participants underwent a 12-week intervention: supervised resistance training, self-paced aerobics, and protein supplementation.	Body composition was measured by DXA, muscle strength by 1RM, fasting blood was analysed (SPARC, OSM, decorin, IGF-1, IGFBP-3), and serum was tested for DU145 prostate cancer cell growth before and after the intervention.	Chronic exercise increases myokines and suppresses prostate cancer cell growth in ADT patients.
(Schwappacher et al., 2021)	Advanced-stage PC patients were recruited.	Treatment: 12 weeks of resistance training with WB-EMS.	Patient blood was analysed after 12 weeks of exercise; an in vitro myotube model was electrically stimulated. Plasma and cultures were analysed for protein/gene expression, and effects on PC cells (proliferation, motility, apoptosis, caspase 3/7, PARP) were evaluated.	Exercise in patients and in vitro models suppresses proliferation, migration, and increases apoptosis of pancreatic cancer cells. The myokines IL-10, CXCL1, and CCL4 released from skeletal muscle after exercise have been shown to inhibit PC cell growth and induce caspase 3/7 and PARP, offering potential supportive cancer therapy.

## DISCUSSION

Despite varying approaches and targets, research on exercise interventions in cancer patients shows fairly consistent benefits. Nearly all studies confirm that exercise—whether in the form of high-intensity aerobic training (HIIT), resistance training, multimodal training, or whole-body electromyostimulation (WB-EMS)—has the potential to improve physical fitness, modulate biomarkers, and suppress cancer cell growth.

The main similarity between these studies is their focus on patients with various types of cancer, particularly prostate, breast, pancreatic, and colorectal cancers. Most used experimental methods, such as randomized controlled trials (RCTs) or in vitro designs, in which patients' post-exercise serum was tested on cancer cell cultures. These findings suggest that exercise not only impacts the patients' physiological state but also has a direct biological effect on cancer cells.

The main differences between studies lie in the type of intervention and the outcomes measured. Kang et al. (2019, 2021) and Alizadeh et al. (2019) emphasized HIIT, which has been shown to increase  $VO_2\text{max}$ , decrease inflammatory markers, and slow the progression of prostate and breast cancer. Kim et al. (2022) also supported these findings, showing that multimodal exercise can increase myokines such as SPARC and OSM, which then suppress the growth of prostate cancer cells. In contrast, studies by Orange et al. (2022), Agostini et al. (2018), Kurgan et al. (2017), and Metcalfe et al. (2021) emphasized molecular mechanisms through in vitro assays. They found post-exercise serum can reduce cancer cell proliferation (prostate, lung, colon, and breast) by modulating signalling pathways such as Akt/mTOR, increasing IL-6, and reducing tumour cell viability.

Meanwhile, Schwappacher et al. (2020, 2021) used the WB-EMS approach in patients with advanced cancer, including prostate, colorectal, and pancreatic cancers. Their results showed that even in patients with limited physical capacity, this intervention could inhibit proliferation, increase apoptosis, and induce the release of myokines that play a role in anti-cancer mechanisms.

Thus, while variations in methods and outcomes have led to inconsistent research findings, a typical pattern emerges that exercise has dual benefits: improving patients' fitness and quality of life, while also exerting significant biological effects on cancer cell control. These findings underscore the important role of exercise as a supportive therapy and potentially a part of a multimodal cancer treatment strategy.

## CONCLUSIONS

Based on a literature review, exercise has been shown to play a crucial role in supporting cancer treatment. Interventions such as HIIT, resistance training, multimodal training, and WB-EMS improve physical capacity and quality of life for patients and contribute to biomarker regulation, suppression of cancer cell proliferation, and induction of apoptosis through complex molecular mechanisms. Although results vary across studies due to differences in populations, intervention types, and measurement methods, a general pattern is that exercise is an effective supportive therapy strategy. These findings reinforce the idea that physical activity should be systematically integrated into rehabilitation and care programs for cancer patients as part of an evidence-based, multimodal approach.

## AUTHOR CONTRIBUTIONS

Gilang Gemilang Muti was responsible for the project's conceptualization, methodology, formal analysis, and initial manuscript writing. Syahrizal Islam contributed to data collection, data curation, and assisted in validating the results. Ardan Raditya Dwi Atmaja focused on data visualization, managed project administration, and participated in reviewing and editing the manuscript.

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## DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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