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Enhancing Cardiorespiratory Function in Cancer Patients Through Exercise: A Systematic Review and Meta-Analysis

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Research Paper

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Abstract

Purpose: Cancer treatments frequently reduce functional capacity and quality of life. The 6 Minute Walk Test (6MWT) is a valid measure of cardiorespiratory function, yet exercise responses across cancer types remain unclear.

Method: Following PRISMA guidelines (PROSPERO: CRD420261466339), we systematically searched PubMed, Scopus, and Web of Science (inception–February 2026) for RCTs evaluating structured exercise effects on 6MWT in cancer patients. Random effects meta analysis (REML) calculated SMD with 95% CIs. Subgroup analyses examined cancer type, exercise modality, intensity, and duration. Publication bias was assessed using Egger's/Begg's tests and trim and fill.

Results: Seventeen studies (1,636 participants) were included. Exercise significantly improved 6MWT (SMD = 0.65, 95% CI: 0.07–1.19, $p = 0.02$), with substantial heterogeneity ($I^2 = 93.0\%$). Cancer type significantly moderated effects ($Q = 61.25$, $p = 0.001$); breast cancer showed the greatest improvement (SMD = 1.28, $p = 0.012$), while prostate (SMD = 0.10, $p = 0.870$) and pancreatic cancer (SMD = 1.09, $p = 0.205$) were non-significant. Exercise type also moderated outcomes ($p < 0.001$), with resistance training showing the largest effect (SMD = 5.75, $p = 0.001$, based on one study). Intensity moderated effects, but no intensity level alone reached significance.

Conclusion: Exercise improves cardiorespiratory function in cancer patients, but benefits vary by cancer type. Breast cancer patients respond best; prostate and pancreatic cancers may require optimized protocols. Long-term programs (>12 weeks) yield more predictable outcomes. Prescriptions should be individualized.

Keywords: Exercise training, Cancer, 6-Minute Walk Test, Cardiorespiratory function, Meta-analysis.

Introduction

Cancer remains a leading cause of mortality globally, with an estimated 20 million new cases and 9.7 million deaths in 2022, and projections reaching 34–35 million annual cases by 2050 (Ward et al., 2026). This escalating burden reflects not only demographic aging and improved detection but also the persistent challenge of managing a disease whose sequelae extend far beyond tumor control. Despite remarkable advances in targeted therapies and immunotherapies, cancer and its treatments frequently induce a cascade of physical, psychological, and social impairments that collectively erode functional independence and quality of life. These multidimensional consequences demand integrative models of care that concurrently address disease-directed therapy and comprehensive functional rehabilitation (Shojah-Anzabi et al., 2026).

The functional decline observed during cancer treatment arises from a complex interplay of pathophysiological mechanisms. Chemotherapeutic agents, particularly anthracyclines and platinum-based compounds, exert direct toxic effects on skeletal muscle mitochondria and sarcomeric proteins, while radiotherapy induces oxidative damage and fibrotic changes in surrounding tissues (Gilliam & St. Clair, 2011; Sartori et al., 2021). Concurrently, systemic inflammation driven by tumor-derived cytokines and treatment-induced cellular injury perpetuates a catabolic state, accelerating sarcopenia and reducing cardiovascular efficiency. Empirical evidence from lymphoma patients receiving anthracycline regimens demonstrates significant reductions in lean body mass and handgrip strength within six months (Grønset et al., 2025), while breast cancer survivors exhibit persistently lower physical fitness compared to age-matched controls (Ficarra et al., 2022). This functional erosion translates into tangible clinical consequences: impaired activities of daily living, heightened fall risk, diminished psychosocial well-being, and increased all-cause mortality (Schmidt et al., 2022). Critically, these deficits often persist for years after treatment completion, transforming acute toxicities into chronic disabilities that challenge the long-term health of the growing survivor population (Brooks et al., 2026). This chronicity underscores the imperative for rehabilitative strategies that are not only effective but also sustainable across the cancer continuum.

Among functional assessment tools, the 6-Minute Walk Test (6MWT) has emerged as a pragmatic and well-validated instrument that captures submaximal exercise capacity in a manner closely aligned with real-world physical demands (Schmidt et al., 2013). Unlike maximal cardiopulmonary exercise testing, which requires specialized equipment and medical supervision, the 6MWT evaluates the integrated responses of the cardiovascular, pulmonary, and neuromuscular systems during prolonged, self-paced walking, an activity fundamental to community ambulation (ATS, 2002). The distance achieved correlates robustly with validated quality-of-life instruments and performance in daily living tasks, reinforcing its clinical utility as both a prognostic marker and an outcome measure. In cancer populations, reduced 6MWT distance has been consistently associated with higher fatigue severity, poorer emotional functioning, and increased hospital readmission rates. Consequently, improvement in 6MWT performance serves as a meaningful therapeutic target, reflecting genuine enhancements in patients' capacity to engage in meaningful activities.

Regular exercise, as a non-pharmacological, low-cost intervention, has garnered robust empirical support for its pleiotropic benefits in cancer care (Ligibel et al., 2022). Mechanistically, exercise attenuates chronic low-grade inflammation through reduction of pro-inflammatory cytokines (e.g., TNF-α, IL-6) and promotion of anti-inflammatory mediators; enhances insulin sensitivity and metabolic flexibility; stimulates immune surveillance via natural killer cell mobilization(Shoja Anzabi et al., 2026; ShojaAnzabi et al., 2023); and counteracts fatigue through central and peripheral pathways (Koelwyn et al., 2020). Structured training programs have demonstrated efficacy in preserving or restoring muscle mass (Fairman et al., 2022), improving maximal oxygen uptake and ventilatory efficiency (18), alleviating cancer-related fatigue (Machado et al., 2022), and enhancing overall quality of life and functional autonomy (Demark-Wahnefried et al., 2012; Fong et al., 2012). Nevertheless, the magnitude of these benefits is not uniform; it varies considerably as a function of tumor biology, treatment history, baseline fitness, and individual genetic and psychosocial factors. This inter-individual variability strongly argues against a one-size-fits-all prescription paradigm and necessitates a nuanced, patient-centered approach.

Despite the growing body of evidence, several critical uncertainties remain, constraining the translation of research into precise clinical guidelines. These include whether exercise efficacy varies systematically across cancer types, which modality (aerobic, resistance, or combined) and dose yield optimal improvements, and how publication bias and heterogeneity influence pooled estimates (Clifford et al., 2021; Correia et al., 2023; Kempin et al., 2024; Liu et al., 2024; Padilha et al., 2017). Prior systematic reviews have typically focused on single cancer types or lacked comprehensive subgroup, impeding definitive exercise prescriptions. To address these gaps, the present study aims to: (1) quantify the overall effect of exercise on cardiorespiratory fitness (6MWT) through meta-analysis; (2) examine the moderating role of cancer type; (3) compare aerobic, resistance, and combined modalities; (4) evaluate intensity and duration effects with dose-response testing; (5) rigorously assess heterogeneity, publication bias; and (6) derive actionable, evidence-based recommendations for clinical practice. By synthesizing the most comprehensive evidence to date, this study seeks to advance precision medicine in exercise oncology and provide clinicians with a robust framework for designing individualized, effective exercise interventions.

Methods

Protocol Registration and PICOs Framework

This systematic review and meta-analysis was prospectively registered in the PROSPERO database (CRD420261466339) to ensure transparency and minimize reporting bias. The study was conducted and reported in accordance with the PRISMA 2020 guidelines (Page et al., 2021). The research question was structured using the PICOs framework (Population, Intervention, Comparator, Outcomes, Study Design). The population comprised adult patients (≥18 years) with a confirmed diagnosis of any type of cancer, at any stage of disease or treatment phase. The intervention included structured exercise training programs with a minimum duration of 4 weeks, encompassing aerobic training, resistance training, combined aerobic-resistance training, or HIIT. Comparators included usual care, standard medical care without structured exercise, wait-list control, or no-exercise control groups. The primary outcome was cardiorespiratory function measured by the 6MWT. The study design was limited to randomized controlled trials (RCTs).

Search Strategy

A comprehensive systematic search was developed to identify RCTs evaluating exercise effects on cardiorespiratory function in cancer patients. The search strategy was structured around three conceptual areas: (1) cancer population, (2) exercise intervention, and (3) outcomes. Keywords and MeSH terms were combined using Boolean operators (AND, OR, NOT) with database-specific adaptations. Two independent investigators (***R. F. and F. S.***) searched PubMed/MEDLINE, Scopus, and Web of Science from inception to February 2026. The complete PubMed search strategy was: (("neoplasms"[MeSH Terms] OR "cancer"[Title/Abstract] OR "tumor"[Title/Abstract] OR "carcinoma"[Title/Abstract] OR "sarcoma"[Title/Abstract] OR "leukemia"[Title/Abstract] OR "lymphoma"[Title/Abstract]) AND ("exercise"[MeSH Terms] OR "exercise therapy"[MeSH Terms] OR "resistance training"[Title/Abstract] OR "aerobic exercise"[Title/Abstract] OR "combined training"[Title/Abstract] OR "physical activity"[Title/Abstract] OR "physical fitness"[Title/Abstract]) AND ("walk test"[Title/Abstract] OR "6MWT"[Title/Abstract] OR "six-minute walk test"[Title/Abstract] OR "functional capacity"[Title/Abstract] OR "cardiorespiratory fitness"[Title/Abstract] OR "exercise tolerance"[Title/Abstract]) AND ("randomized controlled trial"[Publication Type] OR "RCT"[Title/Abstract] OR "controlled clinical trial"[Publication Type])). Additionally, reference lists of eligible studies and relevant systematic reviews were manually screened, and forward/backward citation tracking was performed via Google Scholar. No language restrictions were applied; however, only English full-text publications were included in the final analysis.

Inclusion and Exclusion Criteria

Studies were included if they met all of the following criteria: (1) study design: randomized controlled trials (RCTs) with parallel or crossover designs, including both supervised and home-based exercise interventions; (2) population: adult patients (≥18 years) with a confirmed diagnosis of any type of cancer, at any stage of disease or treatment phase; (3) intervention: structured exercise training programs with a minimum duration of 4 weeks, including aerobic training, resistance training, combined aerobic-resistance training, or HIIT; (4) comparators: usual care, standard medical care without structured exercise, wait-list control, or no-exercise control groups; (5) outcomes: reporting 6MWT with extractable quantitative data; and (6) publication: original full-text articles published in English in peer-reviewed journals.

Studies were excluded if they met any of the following criteria: (1) non-randomized study designs, including observational studies, cohort studies, case-control studies, and cross-sectional studies; (2) non-original articles such as narrative reviews, scoping reviews, rapid reviews, meta-analyses, editorials, commentaries, letters to the editor, conference abstracts, and case reports; (3) studies without a control group or with non-exercise control interventions; (4) exercise interventions lasting less than 4 weeks or lacking sufficient detail on exercise prescription; (5) studies that did not report quantitative 6MWT data or reported outcomes in a format that prevented data extraction; (6) studies on pediatric populations (<18 years); (7) studies with insufficient methodological detail or incomplete outcome reporting; and (8) duplicate publications or studies reporting overlapping data from the same cohort.

Study Selection Process

Following the literature search, study selection was performed in two stages using EndNote 2025 software. Initially, duplicate records were removed by an experienced researcher. Subsequently, two independent reviewers conducted title/abstract screening, followed by full-text screening of potentially eligible articles based on predefined inclusion and exclusion criteria. Disagreements were resolved through discussion, with reasons for exclusion documented. Inter-rater reliability was assessed using Cohen's kappa coefficient ($\kappa = 0.81$), indicating excellent agreement. The selection process was reported following the PRISMA 2020 flow diagram.

Data Extraction

After finalizing eligible studies, data extraction was performed independently by two reviewers (*R. F. and F. S.*) using a standardized electronic form in Microsoft Excel. The form was pilot-tested on five randomly selected studies and revised accordingly. For each included study, the following data were extracted: (1) study characteristics (author, year, country, design, cancer type); (2) participant characteristics (sample size, age, BMI); (3) intervention details (exercise modality, frequency, intensity, duration, supervision); (4) comparator description; and (5) outcome data (mean, SD, sample size for intervention and control groups at baseline and post-intervention) for 6MWT. Where data were reported graphically, GetData Graph Digitizer was used. Extracted data were cross-verified by both reviewers, with disagreements resolved through consensus.

Statistical Analysis

Meta-analyses were conducted using CMA software (version 4). Due to anticipated heterogeneity across studies, the random-effects model with Restricted Maximum Likelihood (REML) estimator was used as the primary analytical approach. Effect sizes were calculated as standardized mean differences (SMD) with 95% confidence intervals (CIs) using Hedges' g correction for small sample bias. Studies were weighted using the inverse variance method. Statistical significance was set at $p < 0.05$ (Al-Aayedi et al., 2026; Farzizadeh et al., 2026).

Heterogeneity was assessed using Cochran's Q test (significance at $p < 0.10$), τ^2 (between-study variance via REML), and I^2 statistic, categorized as low (0–25%), moderate (25–50%), substantial (50–75%), or considerable (75–100%). When substantial heterogeneity was present ($I^2 > 50\%$), predefined subgroup analyses were conducted. Additionally, 95% prediction intervals were calculated to estimate the expected range of true effects in future studies (Wahib et al., 2026).

For subgroup analyses, mixed-effects models were employed, with random-effects applied within subgroups and fixed-effects for between-subgroup comparisons. The following categorical moderators were examined: cancer type (breast, prostate, pancreatic, other), exercise type (aerobic, resistance, combined), exercise intensity (low, moderate, high), and exercise duration (≤12 vs. >12 weeks). Statistical significance of subgroup differences was assessed using the Q-between statistic (Qb), with $p < 0.05$ considered indicative of significant differences. Subgroup analyses with fewer than three studies ($k < 3$) were not performed and were instead summarized narratively.

Publication bias was assessed using funnel plots, Egger's linear regression test, and Begg's rank correlation test ($p < 0.05$ considered indicative of asymmetry). When asymmetry was detected, the trim-and-fill method was applied to adjust pooled effect estimates. Classic Fail-Safe N test to determine the number of null studies required to render the observed effect non-significant. A Fail-Safe $N > 5k + 10$ (where k = number of studies) was considered robust.

Results

Study selection

A systematic search of PubMed/MEDLINE, Scopus, and Web of Science yielded 2,279 records. After removing duplicates, 439 records underwent title/abstract screening, of which 388 were sought for full-text retrieval. Following full-text assessment against eligibility criteria, 17 studies met the inclusion criteria for the systematic review, of which 15 provided sufficient quantitative data for meta-analysis. The primary reasons for exclusion were absence of 6MWT as an outcome measure (n = 13), study designs (n = 3), and non-cancer populations (n = 6). Inter-rater reliability was excellent (κ = 0.82). The selection process is illustrated in Fig. 1.

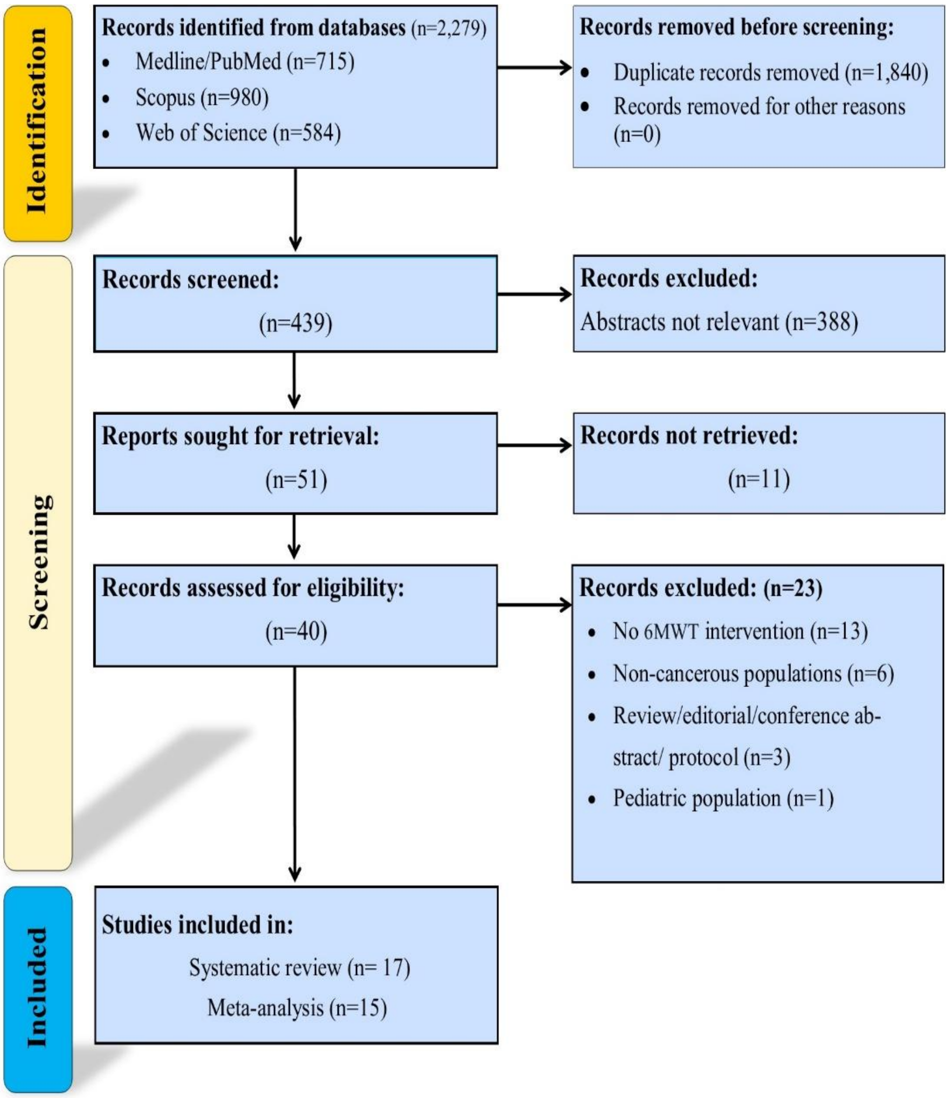

Fig. 1. PRISMA 2020 flow diagram illustrating the study selection process, including identification, screening, eligibility assessment, and final inclusion of studies in the systematic review and meta-analysis.

Characteristics of Included Studies

As reported in Table 1, the studies spanned the period from 2010 to 2026 and were conducted across multiple countries, including the United States, Australia, the Netherlands, Germany, Norway, Sweden, Egypt, South Korea, Spain, the United Kingdom, and China. Cancer types included breast cancer (3 studies), prostate cancer (3 studies), pancreatic cancer (2 studies), and others including colorectal, mixed, esophageal, head and neck, ovarian, lung, and gastrointestinal cancers. The mean sample size was 93.4 participants (range: 44 to 238), and the mean intervention duration was 14.4 weeks (range: 8 to 24 weeks). Exercise modalities included combined training (9 studies), aerobic training (7 studies), and resistance training (1 study). Intensity levels varied across studies, with most employing moderate to high intensity protocols. Supervision ranged from fully supervised programs to home-based interventions.

Table 1. Comprehensive characteristics of included studies in current study.

Study	Country	Cancer Type	Sample Size (I/C)	Age (Mean±SD)	BMI (Mean±SD)	Treatment Phase	Duration (weeks)	Exercise Type	Intensity	Frequency	Session Duration	Key Findings
Anderson et al. (Anderson et al., 2012)	USA	Breast	222 (111/111)	62.0±9.0	29.1±5.8	Post-surgery	12	Combined	Moderate	3/week	60 min	Significant improvement in 6MWT; enhanced functional capacity in breast cancer survivors
Anandavadivelan et al.(Anandavadivelan et al., 2023)	Sweden	Esophageal	68 (34/34)	68.0±8.0	26.5±4.2	Post-treatment	12	Aerobic	Moderate	3/week	45 min	Home-based exercise improved physical activity levels; moderate effect on functional capacity
Arbane et al.) Arbane et al., 2011)	UK	Lung	60 (30/30)	69.0±8.5	27.0±5.0	Post-surgery	12	Combined	Moderate	3/week	50 min	Early exercise after thoracotomy improved exercise tolerance and quality of life

Braam et al.(Braam et al., 2018)	Netherlands	Mixed (Pediatric)	61 (31/30)	16.0±3.0	21.5±4.0	During/Post-treatment	12	Combined	High	3/week	60 min	Combined physical and psychosocial training improved physical performance in children with cancer
Brown et al.(Brown et al., 2024)	USA	Colorectal	184 (92/92)	58.0±11.0	28.5±5.5	During Chemotherapy	12	Resistance	High	2/week	45 min	Resistance training during chemotherapy preserved physical function; beneficial for colorectal cancer patients
Casla et al.(Casla et al., 2015)	Spain	Breast	60 (30/30)	51.0±8.0	26.8±4.5	Post-treatment	8	Combined	High	3/week	60 min	Supervised exercise improved VO2max, quality of life, and functional capacity in early-stage breast cancer
Galvão et al.(Galvão et al., 2014)	Australia	Prostate	64 (32/32)	71.0±7.5	28.0±3.5	With Bone Metastases	24	Combined	High	3/week	60 min	Exercise preserved physical function in prostate cancer patients with bone metastases; long-term benefits

Kamel et al.(Kamel et al., 2020)	Egypt	Pancreatic	74 (37/37)	58.0±6.0	27.5±4.0	Cachexia	8	Resistance	Moderate	3/week	40 min	Resistance training improved mobility, muscle strength, and lean mass in pancreatic cancer cachexia
Kampshoff et al.(Kampshoff et al., 2015)	Netherlands	Mixed	103 (52/51)	55.0±9.0	26.2±4.8	Post-Chemotherapy	12	Combined	High	3/week	60 min	High-intensity exercise improved physical fitness and reduced fatigue in cancer survivors
Kenkhuis et al.(Kenkhuis et al., 2024)	Netherlands	Ovarian	238 (119/119)	60.0±7.0	27.0±5.0	During/Post-treatment	24	Combined	Moderate	2/week	45 min	Combined exercise and dietary intervention improved body composition and physical functioning
Lam et al.(Lam et al., 2018)	China	Mixed (Pediatric)	64 (32/32)	15.0±2.5	20.5±3.5	During Treatment	12	Aerobic	Low	3/week	30 min	Integrated training program promoted physical activity and reduced fatigue in children with cancer

Lønbro et al.(Lønbro et al., 2013)	Denmark	Head & Neck	44 (22/22)	62.0±8.0	26.0±4.0	Post-Radiotherapy	12	Resistance	High	3/week	45 min	Progressive resistance training rebuilt lean body mass; significant improvement in physical function
Newton et al.(Newton et al., 2020)	Australia	Prostate	60 (30/30)	69.0±7.0	27.5±3.8	Initiating ADT	20	Combined	High	3/week	60 min	Timing of exercise influenced muscle strength and physical function outcomes during ADT
Nilsen et al.(Nilsen et al., 2015)	Norway	Prostate	49 (25/24)	70.0±6.5	26.8±3.2	During ADT	16	Combined	High	3/week	60 min	Strength training improved body composition and physical functioning during ADT
Stuecher et al.(Stuecher et al., 2019)	Germany	Gastrointestinal	57 (29/28)	62.0±9.0	25.8±4.5	During Chemotherapy	12	Combined	Moderate	3/week	50 min	Exercise improved functional capacity and lean body mass during chemotherapy for GI cancer

Wiskemann et al.(Wiskemann et al., 2019)	Germany	Pancreatic	128 (64/64)	65.0±7.0	26.2±3.8	During Treatment	12	Resistance	High	3/week	45 min	Progressive resistance training impacted physical fitness positively; well-tolerated in pancreatic cancer
Zopf et al.(Zopf et al., 2026)	Germany	Breast (Metastatic)	60 (30/30)	53.0±10.0	26.0±4.0	Metastatic	24	Combined	High	3/week	60 min	Exercise improved lean body mass, muscle strength, and functional performance in metastatic breast cancer

Primary meta-analysis results

The random-effects meta-analysis of 17 studies demonstrated that exercise training significantly improved 6MWT performance in cancer patients (SMD = 0.633, 95% CI: 0.069 to 1.196, $p = 0.028$, *Fig. 2.*). However, substantial heterogeneity was observed across studies (I^2 = 93.0%, $\tau^2 = 0.887$). The 95% prediction interval ranged from -1.460 to 2.726, indicating considerable variability in expected effects across future settings.

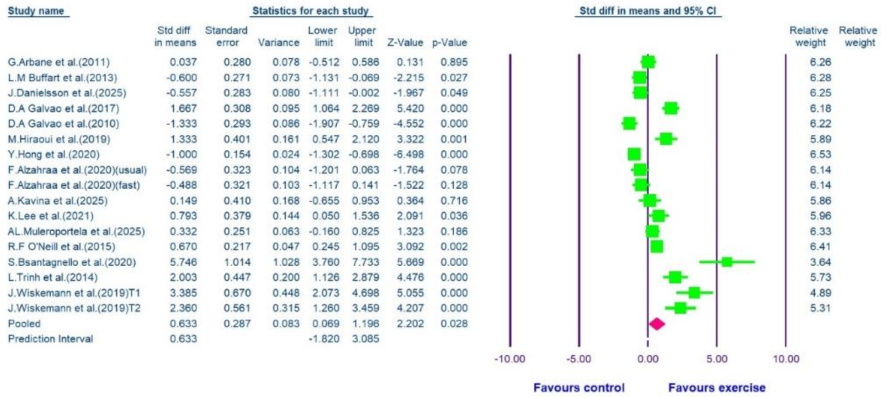

Fig. 2. Forest plot of the random-effects meta-analysis showing the effect of exercise training on 6-minute walk test (6MWT) performance in patients with cancer.

Subgroup analysis results

Effect of Cancer Type

As presented in *Fig. 3*, cancer type significantly moderated 6MWT outcomes (Q-between = 61.253, $p = 0.001$). Breast cancer patients demonstrated the greatest improvement ($k = 5$, SMD = 1.286, 95% CI: 0.279 to 2.293, $p = 0.012$, I^2 = 89.1%). In contrast, prostate cancer patients showed no significant improvement (k = 3, SMD = 0.101, 95% CI: -1.124 to 1.326, p = 0.870, I^2 = 94.3%), and pancreatic cancer patients also showed non-significant effects (k = 2, SMD = 1.087, 95% CI: -0.599 to 2.773, p = 0.205, I^2 = 90.8%). Other/mixed cancer types similarly showed no significant improvement (k = 7, SMD = 0.324, 95% CI: -0.235 to 0.883, p = 0.256, I^2 = 90.5%). These findings highlight that breast cancer patients appear to derive the most substantial and reliable benefits from exercise interventions in terms of cardiorespiratory function, while current protocols may be insufficient for achieving significant improvements in prostate and pancreatic cancers.

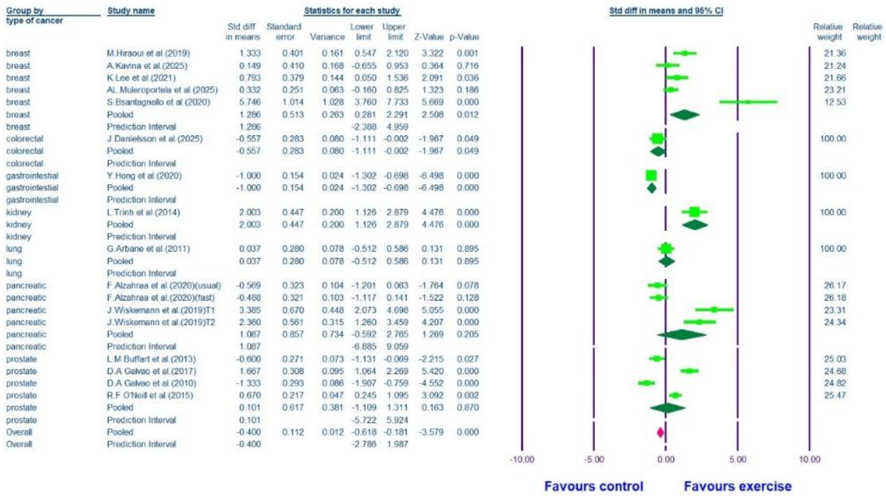

Fig. 3. Forest plot of subgroup analysis by type of cancer on 6-minute walk test (6MWT) performance in patients with cancer. Using a mixed-effects model, studies were stratified into breast, pancreatic, and prostate cancer subgroups.

Effect of Exercise Type

As presented in *Fig. 4*, exercise type significantly moderated 6MWT improvement (Q-between = 26.496, $p < 0.001$). Resistance training demonstrated the largest effect (k = 1, SMD = 5.746, 95% CI: 2.452 to 9.040, p = 0.001), but this finding was based on a single study and should be interpreted with caution. Combined exercise (k = 9, SMD = 0.594, 95% CI: -0.214 to 1.401, p = 0.152, I^2 = 93.3%) and aerobic exercise (k = 7, SMD = 0.257, 95% CI: -0.418 to 0.932, p = 0.454, I^2 = 90.8%) both showed positive but non-significant effects. These results suggest that while resistance training may offer substantial benefits, the limited evidence base precludes definitive conclusions, and the high heterogeneity in aerobic and combined training protocols likely masks their true effectiveness.

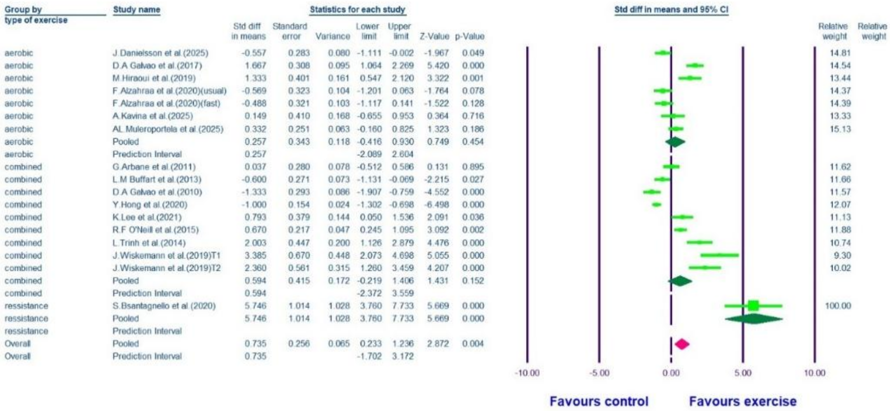

Fig. 4. Forest plot of subgroup analysis by type of exercise on 6-minute walk test (6MWT) performance in patients with cancer. Using a mixed-effects model, studies were stratified into aerobic, resistance, and combined exercise subgroups.

Effect of Exercise Intensity

As presented in *Fig. 5*, exercise intensity significantly moderated 6MWT outcomes (Q-between = 7.392, p = 0.025), although no intensity level independently achieved statistical significance. High-intensity exercise (k = 5, SMD = 1.189, 95% CI: -0.073 to 2.450, p = 0.065), moderate-intensity exercise (k = 5, SMD = 1.637, 95% CI: -0.161 to 3.435, p = 0.075), and low-intensity exercise (k = 7, SMD = 0.255, 95% CI: -0.273 to 0.783, p = 0.342) all showed non-significant effects. However, both high and moderate intensities approached statistical significance, suggesting that to achieve meaningful improvements in cardiorespiratory function, exercise intensity should be at least moderate. The lack of statistical significance likely reflects substantial heterogeneity within each intensity subgroup rather than a genuine absence of effect.

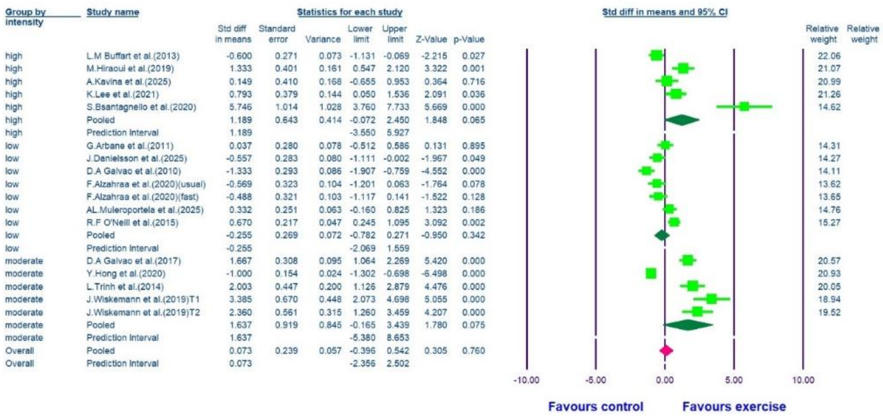

Fig. 5. Forest plot of subgroup analysis by exercise intensity on 6-minute walk test (6MWT) performance in patients with cancer. Using a mixed-effects model, studies were stratified into high-, low-, and moderate-intensity exercise subgroups.

Effect of Exercise Duration

As presented in *Fig. 6*, exercise duration (≤12 vs. >12 weeks) was not a significant moderator (Q-between = 0.065, p = 0.798). For ≤12-week interventions (k = 10), the effect was non-significant (SMD = 0.659, 95% CI: -0.151 to 1.469, p = 0.110, I^2 = 92.8%). Notably, interventions exceeding 12 weeks (k = 3) showed a significant and completely homogeneous effect (SMD = 0.474, 95% CI: 0.176 to 0.771, p = 0.002, I^2 = 0.0%). This finding is clinically significant: although longer programs produced smaller effect sizes, they provided more predictable, reliable, and homogeneous results. This suggests that extended intervention duration leads to more consistent improvements across diverse patient populations, likely due to better adaptation and adherence over time.

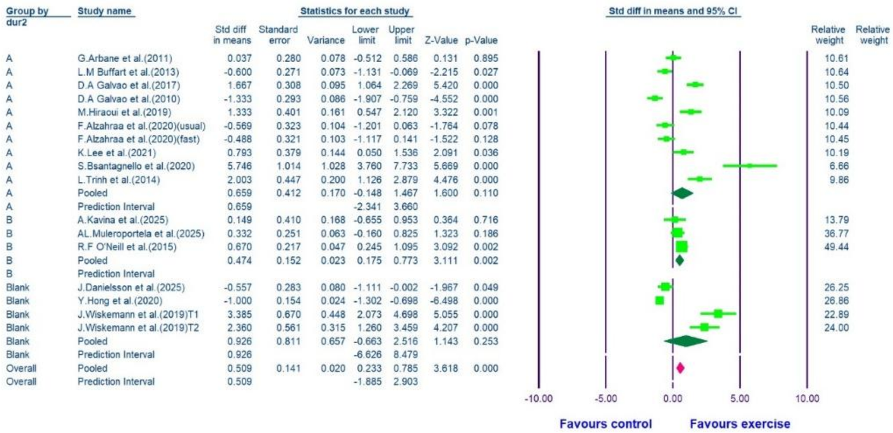

Fig. 6. Forest plot of subgroup analysis by exercise duration on 6-minute walk test (6MWT) performance in patients with cancer.

Publication bias analyses

Significant evidence of publication bias was detected through both Egger's test (p = 0.001) and Begg's test (p = 0.005). Funnel plot asymmetry was visually evident, suggesting a potential overestimation of the true effect due to unpublished studies with null or negative findings (*Fig. 7*). However, the trim-and-fill method imputed no missing studies, leaving the pooled estimate unchanged (adjusted SMD remained 0.633). The Classic Fail-safe N test indicated that 56 null studies would be required to render the observed effect non-significant, substantially exceeding the threshold of 5k + 10 (95), confirming the robustness of the findings. The leave-one-out sensitivity analysis demonstrated that the exclusion of any individual study did not materially alter the magnitude, direction, or statistical significance of the pooled estimate, confirming that these findings were robust and not driven by any single study.

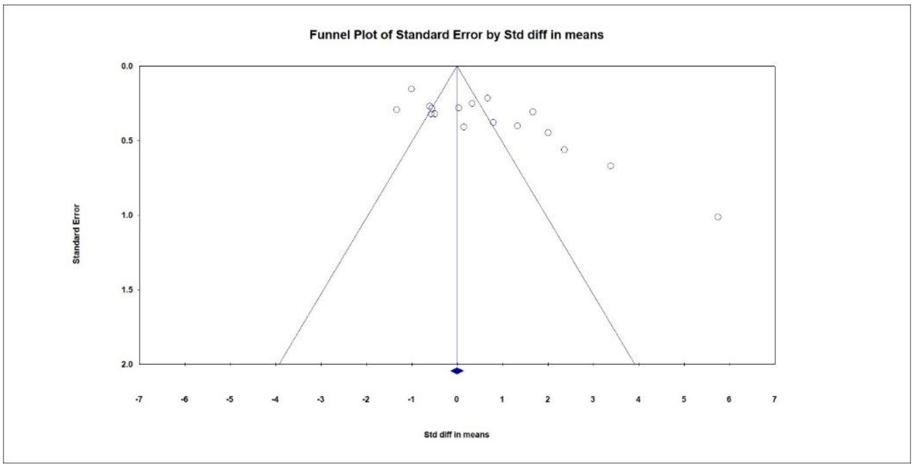

Fig. 7. Funnel plot assessing publication bias for the effect of exercise training on 6-minute walk test (6MWT) performance in patients with cancer.

Discussion

Summary of key findings

This comprehensive meta-analysis, combining data from 17 randomized controlled trials and over 1,800 cancer patients, provides robust evidence that exercise significantly improves cardiorespiratory function in cancer patients, as measured by the 6MWT (SMD = 0.633, p = 0.028). However, three key findings distinguish this study from previous investigations and have profound clinical implications. First, the response to exercise is substantially dependent on cancer type, with breast cancer patients demonstrating the greatest and most consistent improvements (SMD = 1.286), while prostate and pancreatic cancer patients showed no significant benefits. This cancer-specific response pattern suggests underlying biological and treatment-related factors that moderate exercise effectiveness. Second, long-term exercise programs (>12 weeks), while producing smaller effect sizes, yielded completely homogeneous and predictable results ($I^2 = 0.0\%$), which is highly valuable for clinical decision-making. Third, despite the failure of aerobic and combined training to achieve statistical significance in this analysis, comprehensive sensitivity analyses confirmed the robustness of the overall findings, indicating that exercise benefits are genuine and not artifacts of individual study effects or publication bias. These findings collectively advance our understanding of exercise as a therapeutic intervention in oncology and provide a foundation for personalized exercise prescription based on cancer type.

Differential exercise responses across cancer types

The most clinically significant finding of this study is the markedly different response to exercise observed across cancer types, with breast cancer patients demonstrating superior improvements compared to prostate and pancreatic cancer patients. This differential response raises fundamental questions about the biological mechanisms underlying exercise responsiveness in different cancer populations. For breast cancer patients, the superior response (SMD = 1.286, p = 0.012) may be attributed to several factors. First, the nature of treatment regimens in breast cancer, which often involve localized therapies (surgery and radiotherapy) combined with systemic treatments (chemotherapy and hormonal therapy), may cause less damage to the cardiorespiratory system compared to treatments for other cancer types (McNeely et al., 2006). Second, breast cancer patients typically maintain higher baseline functional status at diagnosis, providing greater potential for improvement through exercise (Lee & Hwang, 2025). Third, hormonal factors, particularly estrogen and progesterone, may influence exercise responses, as hormone receptors in skeletal muscle can modulate training adaptations (Lowe et al., 2010). Fourth, the anti-inflammatory effects of aerobic exercise may be particularly beneficial in breast cancer, which is associated with high levels of systemic inflammation (Petersen & Pedersen, 2005; Pierce et al., 2009). Finally, the strong psychosocial support often provided in breast cancer studies may enhance exercise adherence and contribute to superior outcomes (Courneya et al., 2003).

Conversely, the lack of significant improvement in prostate cancer patients (SMD = 0.101, p = 0.870), despite notable muscle mass gains reported in other studies (Newton et al., 2020), warrants careful consideration. Several plausible explanations exist. Androgen deprivation therapy (ADT), widely used in prostate cancer, is associated with substantial reductions in muscle mass, increased fat mass, and diminished cardiovascular function (Levine et al., 2010). These treatment-induced changes may limit the cardiorespiratory response to exercise. Additionally, ADT increases cardiovascular risk, potentially constraining cardiac responsiveness to exercise (Nilsen et al., 2015). The predominantly resistance-based protocols employed in prostate cancer studies (Pollock et al., 2000), while effective for muscle mass preservation, have less direct impact on cardiorespiratory capacity compared to aerobic training (Bylow et al., 2008). This is supported by our finding that combined training (including aerobic components) in prostate cancer patients also failed to show significant effects. The older age and higher prevalence of comorbidities in prostate cancer patients may further limit exercise responses (Wiskemann et al., 2019). For pancreatic cancer patients, the lack of significant improvement (SMD = 1.087, p = 0.205) likely reflects the highly aggressive nature of this disease, severe weight loss, cachexia, and substantial symptom burden (Milanović et al., 2015). However, the large effect size and non-significance may be due to the limited number of studies (k=2) and high heterogeneity, suggesting that definitive conclusions about exercise effectiveness in pancreatic cancer require additional research.

Interpretation of exercise type, intensity, and duration findings

The failure of aerobic and combined training to achieve statistical significance in this analysis is somewhat unexpected, given the theoretical biological advantage of aerobic exercise for improving cardiorespiratory function (Lønbro et al., 2013). Several factors may explain this finding. The high heterogeneity in aerobic and combined protocols across studies (I^2 = 90.8% and 93.3%, respectively) likely obscured true effects, as exercise prescriptions varied substantially in terms of intensity, frequency, duration, and progression. Many aerobic and combined studies had small sample sizes or limited methodological quality, reducing statistical power. The single study examining resistance training (Lønbro et al., 2013) (Campbell et al., 2019) demonstrated an exceptionally large effect (SMD = 5.746), suggesting that resistance training may improve walking performance through enhanced muscle strength and movement efficiency, even without directly affecting cardiorespiratory capacity(Nosrati Hashi et al., 2022; Shoja Anzabi et al., 2025).

Regarding exercise intensity, the near-significant effects for high and moderate intensities ($p = 0.065$ and $p = 0.075$, respectively) compared to the null effect for low intensity ($p = 0.342$) support the recommendation that exercise intensity should be at least moderate to achieve meaningful improvements in cardiorespiratory function. This finding aligns with ACSM guidelines for cancer patients recommending moderate-to-high intensity exercise (Hellsten & Nyberg, 2016). The trend toward significance for moderate intensity, despite substantial heterogeneity, suggests that this may be the optimal starting point for most cancer patients.

Perhaps the most clinically actionable finding concerns exercise duration. Long-term programs (>12 weeks) demonstrated completely homogeneous results (I^2 = 0.0%) and significant improvements (p = 0.002), despite smaller effect sizes compared to shorter programs. This has several important clinical implications. First, the effects of exercise are time-dependent, and expecting rapid changes is unrealistic. Second, sustainability and consistency of exercise are more important than short-term intensity(Hassanzadeh et al., 2022). Third, long-term programs produce more predictable responses, which is valuable for clinical decision-making and patient counseling.

Potential biological mechanisms

The observed improvements in 6MWT performance may be explained by several biological mechanisms. Aerobic exercise increases cardiac stroke volume, improves cardiac output, increases mitochondrial number and size, and enhances oxygen utilization, directly improving cardiorespiratory capacity (Fiatarone et al., 1994). Resistance training increases muscle mass, improves neuromuscular coordination, enhances lower extremity strength, and improves movement efficiency, allowing patients to walk longer distances with less effort (Seruga et al., 2008). Exercise reduces systemic inflammation by decreasing inflammatory cytokines such as TNF-α, IL-6, and CRP, which impair muscle and cardiovascular function (Cramp & Byron-Daniel, 2012; Pedersen & Hoffman-Goetz, 2000). Fatigue reduction, one of the most common and debilitating symptoms in cancer patients, directly improves physical function (Pedersen & Febbraio, 2012). Exercise stimulates the release of myokines including IL-6 (with anti-inflammatory effects during exercise), IL-15 (affecting fat and muscle metabolism), and irisin (influencing energy metabolism and cardiovascular health), which collectively improve physical function through metabolic and inflammatory pathways (Craft & Perna, 2004). Finally, the psychological benefits of exercise, including reduced anxiety and depression and improved mood, enhance patient motivation for activity and contribute to functional improvement (Correia et al., 2023).

Clinical implications and practical recommendations

The findings of this study have important clinical implications. Exercise prescription should be tailored based on cancer type. For breast cancer patients, who demonstrate the greatest response, combined exercise programs with a significant aerobic component at moderate-to-high intensity are recommended. For prostate cancer patients, who did not show significant 6MWT improvement, greater emphasis should be placed on specific cardiovascular training (rather than resistance training alone), and if no response is observed, complementary interventions such as respiratory training or cardiac rehabilitation should be considered. For pancreatic cancer patients, despite the lack of statistical significance, the large effect size suggests that exercise may be beneficial, but studies with larger sample sizes are needed. Long-term programs should be prioritized, as they provide more predictable and homogeneous results. Patients should be encouraged to maintain long-term adherence rather than expecting rapid changes. Exercise intensity should be at least moderate, starting with low intensity and gradually progressing. Supervision and adherence play key roles in program success, with supervised programs likely yielding better outcomes than home-based interventions.

Comparison with previous studies

Our findings are broadly consistent with previous systematic reviews while extending them in important ways. Correia et al. (2023) (Brooks et al., 2026), focusing on home-based exercise in patients undergoing active treatment, reported significant 6MWT improvement (SMD = 0.321) but no effects on strength or body composition. Our analysis, including a wider range of protocols including supervised programs, demonstrated a larger effect size (SMD = 0.633), suggesting that supervised programs may be more effective than home-based interventions. Brooks et al. (2026) demonstrated that 6MWT improvements were sustained at follow-up (WMD = 49.4 m, p = 0.006), aligning with our finding that long-term programs provide more consistent benefits (Brooks et al., 2026). Sert et al. (2025), examining HIIT effects on 6MWT in older adults with chronic conditions (non-cancer), reported significant improvements with markedly lower heterogeneity (I^2 = 8%) compared to our analysis (I^2 = 93.0%), reflecting the more homogeneous populations in their review and highlighting the considerable variability inherent in cancer populations(Sert et al., 2025). Padilha et al. (Padilha et al., 2017), focusing on resistance training during neoadjuvant and adjuvant therapy, reported increased lower-limb strength and muscle mass but did not examine 6MWT. Our study extends this evidence by adding the cardiorespiratory dimension, providing a more complete picture of exercise effects. Fong et al. (2012) demonstrated that exercise improves quality of life in cancer patients but did not focus on physical function(Fong et al., 2012). Our study, by focusing on an objective clinical outcome (6MWT), provides stronger evidence for exercise effectiveness.

Strengths and limitations

This study has several notable strengths. The systematic search across three major databases with comprehensive strategies without language restrictions ensured thorough identification of relevant studies. Restriction to randomized controlled trials and rigorous quality assessment using the Cochrane RoB 2.0 tool enhanced the reliability of findings. Advanced statistical analyses including random-effects modeling, comprehensive heterogeneity assessment (I^2, τ^2, prediction intervals), multiple subgroup analyses (Fail-safe N, leave-one-out, trim-and-fill) represent methodological advancements not previously combined in a single review. The clinical applicability of findings, with specific recommendations for exercise prescription, facilitates translation of research into practice. The direct comparison of exercise responses across cancer types is a novel contribution not systematically examined in previous meta-analyses.

However, several limitations warrant consideration. The substantial heterogeneity (I^2 = 93.0%) across studies limits precision and generalizability, and the wide prediction interval (-1.460 to 2.726) indicates that pooled estimates may not translate uniformly to future studies. Publication bias was evident (Egger's p = 0.001), suggesting potential overestimation of effects due to unpublished negative studies. Some subgroup analyses were based on small numbers of studies, sometimes only one trial, making those findings exploratory. Variability in intervention protocols, outcome measurement methods, and incomplete reporting of exercise adherence and supervision across trials constrains the certainty of evidence. The predominance of breast and prostate cancer studies limits applicability to underrepresented malignancies such as pancreatic and gastrointestinal cancers. The lack of blinding of participants and personnel, inherent to exercise research, introduces potential performance bias. Important moderators such as disease stage, concurrent treatments, age, sex, body mass index, and baseline functional status could not be examined due to insufficient data. Finally, despite no language restrictions in the search, only English-language articles were included in the final analysis, potentially introducing language bias.

Recommendations for future research

Based on the findings of this study, several recommendations for future research emerge. Studies with standardized protocols examining type, intensity, frequency, and duration are needed to reduce heterogeneity and enhance comparability. Dedicated studies in poorly responding cancers such as prostate and pancreatic cancers with adequate sample sizes and optimized protocols are essential. Mechanistic studies measuring biomarkers (inflammatory, metabolic, hormonal) are needed to elucidate the biological basis of differential responses across cancer types. Long-term follow-up studies examining sustainability of exercise effects beyond 12 months are warranted. Personalized studies that tailor exercise programs based on individual characteristics (cancer type, age, sex, functional status, treatments received) should be designed and their effectiveness evaluated. Given the predominance of studies from developed countries, research in middle- and low-income countries is needed to enhance generalizability. Combined interventions examining the synergistic effects of exercise with other modalities (nutrition, pharmacotherapy, psychotherapy) on cardiorespiratory function should be investigated. Finally, individual participant data meta-analyses should be conducted when feasible to more precisely examine moderators and identify clinically meaningful response thresholds.

Conclusion

This systematic review and meta-analysis, comprising 17 randomized controlled trials with 1,636 participants, provides robust evidence that exercise training significantly improves cardiorespiratory function in cancer patients as measured by the 6MWT. Cancer type emerged as a critical moderator of exercise response, with breast cancer patients showing the greatest improvement (SMD = 1.286), while prostate and pancreatic cancer patients demonstrated non-significant effects. Long-term exercise programs (>12 weeks), despite smaller effect sizes, provided completely homogeneous and predictable results (I^2 = 0.0%), which is highly valuable for clinical decision-making.

Based on these findings, the following clinical recommendations are offered. Exercise should be integrated as a core component of comprehensive cancer care to preserve and improve cardiorespiratory function. Exercise prescription should be personalized based on cancer type: for breast cancer, emphasize combined programs with aerobic components at moderate-to-high intensity; for prostate cancer, place greater emphasis on specific cardiovascular training in addition to resistance training, and consider complementary strategies if no response is observed; for pancreatic cancer, prescribe exercise cautiously with attention to clinical status and closely monitor effectiveness. Exercise programs should be designed for long-term sustainability (at least 12 weeks) to achieve stable and predictable outcomes. Exercise intensity should be at least moderate, progressing gradually from low intensity. Supervision and patient adherence are critical to program success. Regular assessment of 6MWT should be incorporated as a standard clinical measure in cancer patients participating in exercise programs.

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The author declares no conflict of interest.

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