

Research Article

Protective effect of regular physical activity on prostate cancer complications

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Abstract

Prostate cancer (PCa) is one of the leading causes of cancer-related mortality and morbidity among men worldwide. Although the number of deaths from this cancer has decreased over the past decade, the incidence of PCa continues to rise globally. In addition to non-modifiable risk factors, modifiable risk factors such as diet, tobacco and alcohol consumption, obesity, and physical inactivity play a significant role in the development of PCa. Daily physical activity is an important factor in PCa risk, and incorporating it into the daily routine of healthy individuals can substantially reduce the likelihood of developing PCa, while in affected individuals, it can significantly slow disease progression. Reviewing the results of studies investigating the effects of various exercise programs on PCa demonstrates that regular physical activity can markedly reduce the negative impacts of PCa. These changes occur both at the prostate tumor level, slowing tumor growth, and can also modulate treatment-related side effects such as quality of life (QoL), physical function capacity, muscle mass, sexual function, and fatigue. Regular physical activity exerts its protective effects in PCa patients through improving metabolic status, enhancing antioxidant defense capacity, increasing tumor growth-inhibiting myokines, and a range of other biological mechanisms. Based on the findings of this study, it is recommended that regular physical activity, particularly a combination of aerobic and resistance training, be integrated as an essential component of the management process for individuals with PCa.

Received: 3 October 2025

Accepted: 9 November 2025

Keywords:

Aerobic exercise,
Resistance exercise,
Prostate cancer

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1. Introduction

Prostate cancer (PCa) is one of the most common malignancies affecting men. Statistics from the World Health Organization indicate that PCa is the second most frequently diagnosed cancer in men and the fifth leading cause of cancer-related death worldwide. It accounts for approximately 15% of all diagnosed cancers among men (1,2). Although PCa mortality has declined over the past decade (3), its global incidence continues to rise (4), imposing a considerable burden on healthcare systems, families, and affected individuals (5,6). Several factors contribute to the development of PCa. In addition to uncontrollable risk factors such as age, family history, and ethnicity, modifiable risk factors—including lifestyle factors such as diet, tobacco and alcohol consumption, obesity, and physical inactivity, as well as environmental exposures like harmful chemicals and ionizing radiation—play major roles in the onset of PCa (7). Unlike uncontrollable risk factors, modification of controllable factors such as diet and physical activity has a significant impact on reducing the risk of PCa (8,9). Accordingly, growing evidence suggests that modifiable lifestyle factors—including diet, physical activity, and weight management—can influence the risk of developing PCa. Furthermore, daily physical activity levels affect both the incidence and progression of PCa; post-diagnosis exercise has been strongly associated with a marked reduction in PCa-related mortality. This highlights the importance of incorporating structured physical activity interventions into oncologic care to improve long-term patient outcomes (10,11,12). The findings of studies on the effects of regular physical activity in managing the side effects of prostate cancer (PCa) and its treatment have been promising.

Available evidence indicates that physical activity is a safe and beneficial strategy for individuals with PCa (13,14,15). Data from various studies show that regular exercise improves quality of life (QoL), cardiorespiratory fitness, functional capacity, lean body mass, and reduces fatigue (16). Overall, regular physical activity has the potential to mitigate and even prevent many adverse effects associated with androgen deprivation therapy, thereby improving survival outcomes in men with PCa. Incorporating structured exercise programs into the treatment plans of PCa patients can yield significant health and economic benefits by enhancing QoL and reducing complications (17). Given the crucial role of regular physical activity in PCa management, this review examines its protective effects against PCa-related complications.

The effect of aerobic exercise on PCa

Regular physical activity has been widely studied due to the high prevalence of prostate cancer (PCa) among men, focusing on its effects on various aspects of the disease. One such aspect includes physical performance capacity, body composition, and fatigue. Radiotherapy is one of the most common treatments for PCa, and more than half of men undergoing therapy for the disease choose this approach (18). However, radiotherapy can impair physical performance and contribute to the development of fatigue. It has been suggested that rest and reduced physical activity during the course of radiotherapy may be detrimental. To evaluate the efficacy of regular physical activity in mitigating radiotherapy-induced fatigue, a study investigated the effects of aerobic exercise performed before radical radiotherapy in patients with localized PCa.

The control group, which was advised to rest and take things easy, exhibited a slight decline in physical performance and a marked increase in fatigue at the end of radiotherapy. In contrast, moderate-intensity walking performed at home led to a significant improvement in physical performance without causing a notable increase in fatigue. Enhancing physical performance may therefore be essential for counteracting fatigue associated with radiotherapy (19). It has been reported that eight weeks of aerobic training performed three times per week in men with prostate cancer (PCa) undergoing radiotherapy, compared with a control group (no aerobic training), led to significant improvements in cardiorespiratory fitness, leg strength, flexibility, fatigue, quality of life (QoL), and the Functional Assessment of Cancer Therapy–Prostate (FACT-P) score (20). Segal et al. (2009) also demonstrated in their study that aerobic and resistance training reduced fatigue, body fat percentage, and blood triglyceride levels, and improved QoL in patients initiating radiotherapy, with or without androgen-deprivation therapy (21). Similarly, combined aerobic and resistance exercise has been shown to enhance QoL, increase upper- and lower-body strength, improve aerobic performance, and reduce fatigue and C-reactive protein levels in men with PCa (22). Findings from a cohort study conducted by Galvão et al. (2009) involving 370 men with PCa undergoing radiotherapy revealed that six months of regular aerobic exercise improved cardiovascular performance, QoL, physical function, and reduced psychological distress, insulin resistance, and abdominal obesity (23). In another study, the same authors examined the effects of twelve months of regular aerobic exercise in men treated with androgen-deprivation and radiation therapy, and reported similar outcomes, further confirming the efficacy of regular physical activity in improving QoL and physical performance in PCa patients (24). Ndjavera et al. (2020) found that a three-month combined aerobic and resistance training program improved QoL, cardiovascular capacity, and reduced fatigue in men newly diagnosed with prostate cancer initiating androgen-deprivation therapy (25). Comparable findings, including improvements in QoL and hematological markers (white blood cells,

red blood cells, hemoglobin, and hematocrit) without serious adverse events, were observed after six months of combined aerobic and resistance exercise in men with PCa undergoing androgen-deprivation and radiotherapy (26). Since both radiotherapy and androgen-deprivation therapy can reduce muscle mass and consequently impair physical performance, combining aerobic and resistance exercises may theoretically counteract these adverse effects. Indeed, one study demonstrated that in PCa patients receiving radiotherapy and androgen-deprivation therapy, combined aerobic and resistance training improved skeletal muscle mass without interfering with the treatment process (27). Although aerobic exercise has been shown to alleviate PCa-related side effects, the characteristics of the training program appear to influence the extent of its effectiveness. Martin et al. (2015) investigated the effect of aerobic exercise intensity on cardiorespiratory performance in prostate cancer survivors. Their results indicated that eight weeks of aerobic training at both low and high intensities improved VO_2 peak, with greater gains observed following high-intensity training, underscoring the critical role of exercise intensity (28). However, the findings of Xiong et al. (2022) demonstrated that among prostate cancer (PCa) survivors undergoing radiotherapy, regular physical activity is an effective and safe intervention for reducing cancer-related fatigue and improving quality of life (QoL). The authors suggested that such activity should be prescribed as a rehabilitation option in clinical management. Regarding the types of exercise, regular moderate-intensity aerobic or resistance training appear to be the most effective interventions for alleviating cancer-related fatigue, enhancing QoL, and mitigating treatment-related symptoms (29).

Evidence indicates that different exercise modalities and baseline physical fitness may also moderate the effects of aerobic and other exercise programs on health outcomes in patients with PCa. Twelve months of aerobic or combined aerobic and resistance training in 163 prostate cancer patients were reported to reduce fatigue and improve QoL, with the greatest benefits observed in those exhibiting the highest fatigue and lowest vitality levels at baseline (30). The efficacy of both aerobic and resistance exercise in improving QoL and sleep quality has also been documented in men with metastatic castrate-resistant prostate cancer (31). Radical prostatectomy is considered a standard treatment for localized PCa but can result in decreased QoL (32). Supporting the beneficial effects of regular physical activity on complications associated with PCa and its standard treatments, Swain et al. (2020) examined postoperative recovery following radical prostatectomy in a 65-year-old endurance-trained man. Their findings showed that the patient's aerobic fitness returned to, and even exceeded, pre-surgery levels within just seven weeks after radical prostatectomy (33). Similarly, improved aerobic capacity, muscular strength, and QoL without adverse effects were reported following ten weeks of elastic-band training after robot-assisted radical prostatectomy (34). Consistent with these findings, Singh et al. (2023) investigated the effects of aerobic and resistance training on physical performance in patients with PCa undergoing prostatectomy, both before and after surgery. The results revealed that preoperative exercise enhanced upper- and lower-body strength, improved performance in 400-meter walk, chair rise, six-meter fast walk, and backward walk tests. While early postoperative declines in strength and physical function were observed, these impairments were mitigated by continued aerobic and resistance exercise. The authors recommended that, although postoperative exercise is valuable for recovery, preoperative training should also be considered to minimize surgical complications in men scheduled for prostatectomy (35).

Among men with prostate cancer on active surveillance, sixteen weeks of home-based walking training improved VO_2peak , reduced urinary obstruction/irritation, and diminished fear of recurrence. These results suggest that moderate- to vigorous-intensity aerobic exercise enhances cardiorespiratory fitness and QoL in men under active surveillance for PCa (36). One of the major challenges faced by men with PCa is sexual dysfunction. A six-month combined aerobic and resistance training intervention in 112 men with PCa was reported to reduce fat mass, improve chair-rise performance, enhance upper- and lower-body muscle strength, and improve sexual function—highlighting the importance of regular physical activity in this population (37). Given the growing number of studies investigating the effects of regular physical activity as an adjunct therapy in patients with prostate cancer (PCa), researchers have published several systematic reviews and meta-analyses based on these findings. A meta-analysis incorporating data from forty studies (2,929 cancer survivors) involving physical activity interventions demonstrated that regular exercise significantly reduced overall depressive symptoms among cancer survivors, and this reduction increased in a dose-dependent manner with higher weekly volumes of aerobic exercise (38). Evidence indicates that PCa is often associated with reduced social and cognitive function. Fang et al. (2020), based on a pooled analysis of clinical trial data, found that aerobic and resistance training improved social and cognitive performance in men with PCa compared with control groups (no aerobic or resistance training) (39). Regarding the effects of physical activity on fatigue, Ahmadi and Daneshmand (2013) reported that a combined resistance/aerobic exercise program produced significant improvements in fatigue, sexual function, and cognitive performance in PCa patients undergoing androgen-deprivation therapy. Additionally, both home-based and group exercise programs improved fatigue and adverse metabolic outcomes (40). In a systematic review of randomized controlled trials, Teleni et al. (2016) suggested that regular physical activity enhances both disease-specific and general health-related QoL in men with PCa undergoing androgen-deprivation therapy (41).

Similarly, the meta-analysis by Yunfeng et al. (2017), which included data from fifteen studies involving 1,135 participants, showed that aerobic and resistance training significantly improved upper- and lower-body muscle strength, increased exercise tolerance as an index of fatigue, and helped patients control body fat mass and BMI while preserving sexual function. Notably, the fatigue associated with androgen-deprivation therapy was influenced by the duration of the exercise program, and no significant differences were observed between aerobic and resistance exercise modalities (42). Andersen et al. (2022), following meta-analysis of data from 33 clinical trials including 2,567 participants, reported that regular physical activity effectively improves metabolic health in men with PCa, identifying aerobic exercise as the most beneficial modality (43). Nevertheless, another meta-analysis by Shao et al. (2022) demonstrated that regular physical activity can alleviate the adverse effects of androgen-deprivation therapy on body composition. The authors concluded that combined training programs—including resistance training at intensities of 8–12 repetitions maximum (RM), extended program duration, and performing exercise sessions immediately after treatment—were associated with superior improvements (44). Supporting these results, Ussing et al. (2022), in their analysis of eighteen clinical trials involving 1,477 participants, reported that supervised exercise therapy likely enhances disease-specific QoL and walking performance in PCa patients receiving androgen-deprivation therapy compared with controls. This effect was consistent across all cancer stages, underscoring the necessity of supervised exercise therapy for managing the side effects of androgen-deprivation therapy (45). Furthermore, Lee et al. (2024) analyzed data from six clinical trials including 332 participants with PCa and concluded that regular physical activity improves cardiorespiratory fitness, QoL, and prostate-specific antigen (PSA) levels in men undergoing active surveillance for PCa (46).

Similarly, another study reported that serum obtained following twelve weeks of regular physical activity—including supervised resistance training and self-directed aerobic exercise—suppressed prostate tumor growth, suggesting that upregulated myokine expression induced by consistent physical activity may exert tumor-suppressive effects (51). An increased plasma estradiol/testosterone ratio, insulin levels, and IGF-I concentration are recognized as major molecular contributors to the development of benign prostatic hyperplasia (BPH). Evidence indicates that aerobic exercise can reduce these plasma factors, thereby attenuating the progression of BPH (52). Supporting these findings, it has been reported that home-based exercise in men with PCa undergoing androgen-deprivation therapy reduced serum IGF-1 levels, which was associated with decreased prostate cancer progression (53). Another study reported significant improvements in plasma triglycerides, adiponectin, IGF-1, IGFBP-1, and fasting glucose levels following 24 months (three sessions per week) of home-based endurance training in out-clinic patients with biochemical recurrence after radical prostatectomy. Moreover, improvements in physical fitness were correlated with an increase in prostate-specific antigen (PSA) doubling time, a surrogate endpoint for disease progression, suggesting a potential link between exercise and slower PCa progression (54). One proposed molecular mechanism explaining how physical activity may modulate PCa control involves the production of natural antibodies that react with vasoactive intestinal peptide (VIP). Regular physical activity has been shown to stimulate the generation of natural anti-VIP antibodies, potentially leading to suppression of VIP activity. This suppression may exert a

Molecular Mechanisms Underlying the Reduction of PCa Complications Following Regular Physical Activity

Analysis of data from numerous clinical and epidemiological studies provides compelling evidence that regular physical activity may reduce the risk of developing prostate cancer (PCa). Despite this progress, the precise biological mechanisms through which habitual physical activity prevents PCa progression remain incompletely understood. To elucidate the molecular mechanisms by which regular physical activity influences cancer development, serum samples from sedentary individuals and men who engaged in aerobic exercise five days per week were applied in vitro to lymph node carcinoma of the prostate (LNCaP) tumor cells. The results showed that aerobic exercise inhibited prostate tumor growth by reducing serum insulin-like growth factor (IGF) axis components and promoting mitochondrial-dependent apoptotic signaling (48). In another study, serum collected from healthy individuals before and after nine weeks of high-intensity interval training (HIIT), both at rest and following high-intensity endurance cycling, was introduced to PCa cell lines. The findings demonstrated that sera obtained after exercise significantly suppressed proliferation and microtumor formation in prostate cancer cells, whereas sera collected at rest had no such effect. The antitumor potential of post-exercise serum appeared to be mediated through the modulation of Hippo and Wnt/ β -catenin signaling pathways (49). Additionally, it was observed that the application of post-exercise serum to androgen-sensitive human prostate adenocarcinoma cells (LNCaP) exerted inhibitory effects on cell survival via the cancer-suppressive myokines oncostatin M and osteonectin (50).

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This suppression may exert a protective effect against prostate cancer (55). Another proposed molecular pathway underlying the beneficial effects of regular physical activity in mitigating PCa development is through modulation of oxidative stress. Regular aerobic exercise may delay PCa progression by reinforcing the antioxidant defense system and reducing oxidative stress (56). Ashcraft et al. (2016), in a critical systematic review of 53 studies, summarized the molecular mechanisms through which aerobic exercise may prevent or attenuate cancer development. The studies reviewed were categorized into three domains: prevention, progression, and metastasis. Preventive studies revealed that aerobic exercise modulates local immune responses, tumor metabolism, and tumor physiology or angiogenesis. Studies focused on cancer progression showed that aerobic exercise exerts beneficial effects via multiple mechanisms, including apoptosis induction, improved perfusion, and immune cell infiltration. Under metastatic conditions, aerobic training was found to help control disease progression primarily by promoting apoptotic pathways (57).

Δ. Conclusion

The findings from the reviewed studies—including clinical trials, narrative reviews, systematic reviews, and meta-analyses—indicate that regular physical activity exerts substantial effects in suppressing the progression of prostate cancer (PCa). Physical activity can mitigate the adverse effects of PCa, such as reduced quality of life (QoL), impaired physical performance, muscle mass loss, and increased fatigue, in patients undergoing radiotherapy, androgen-deprivation therapy, radical prostatectomy, and in prostate cancer survivors. Moreover, it contributes to improvements in sexual, psychological, and social health outcomes. At the molecular level, regular physical activity exerts its protective effects in PCa patients by improving metabolic regulation, reducing oxidative stress, enhancing the secretion of tumor-suppressive myokines, and promoting apoptosis. Based on the collective evidence, incorporating regular exercise—consisting of aerobic, resistance, or combined training—should be recommended as an adjunct or complementary approach within the therapeutic regimens of individuals with prostate cancer.

Acknowledgements

This article is based on a doctoral thesis in exercise physiology. It was conducted at the Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences, Islamic Azad University, Central Tehran Branch. The authors of this article would like to thank the officials of the Faculty of Physical Education for their invaluable assistance in conducting this study.

Funding

This study did not have any funds.

Compliance with ethical standards

Conflict of interest None declared.

Ethical approval the research was conducted with regard to the ethical principles.

Informed consent Informed consent was obtained from all participants.

Author contributions

Conceptualization: F.J, H.M.H, M.A.A ; Methodology: F.J, H.M.H, M.A.A ; Software: F.J, H.M.H, M.A.A ; Validation: F.J, H.M.H, M.A.A ; Formal analysis: F.J, H.M.H, M.A.A ; Investigation: F.J, H.M.H, M.A.A ; Resources: F.J, H.M.H, M.A.A ; Data curation: F.J, H.M.H, M.A.A ; Writing - original draft: F.J, H.M.H, M.A.A ; Writing - review & editing: F.J, H.M.H, M.A.A ; Visualization: F.J, H.M.H, M.A.A ; Supervision: F.J, H.M.H, M.A.A ; Project administration: F.J, H.M.H, M.A.A ; Funding acquisition: F.J, H.M.H, M.A.A .

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