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The impact of exercise on prostate-specific antigen and testosterone in prostate cancer: a systematic review and meta-analysis

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ABSTRACT

Background: Exercise prescription can promote the rehabilitation of patients with prostate cancer (PCa). However, the effect of exercise intervention on serum levels of prostate-specific antigen (PSA) and testosterone remains unclear.

Methods: The primary outcome was the effect of exercise prescription on PSA level. The secondary outcome was the effect of exercise training on testosterone level. The pooled standardized mean difference (SMD) with 95% confidence interval (CI) was selected as the indicator. Meta-regression was conducted to assess the relationship between covariates and outcomes. Publication bias was evaluated using funnel plots and Egger's test.

Results: The data of 594 patients from 8 randomized controlled trials (RCTs) were included and analyzed. Pooled effect of exercise intervention on PSA was 0.13 (95% CI: -0.04 to 0.29, $I^2 = 0.0\%$, $p = 0.984$), while the pooled effect on testosterone was 0.19 (95% CI: -0.00 to 0.39, $I^2 = 0.0\%$, $p = 0.435$). The meta-regression showed there was no significant association of age, body mass index, and the exercise duration with PSA or testosterone. No significant publication bias was detected in meta-analysis.

Conclusions: Although many benefits were documented, exercise intervention have no significant effect on PSA and testosterone levels in PCa patients.

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KEYWORDS

Prostate cancer; treatment; exercise; prostate-specific antigen; testosterone

Introduction

Prostate cancer (PCa) is the most common carcinoma in men at USA [1]. It is estimated that 299,010 new PCa cases were diagnosed with 35,250 deaths in 2024 [2]. Currently, a multidisciplinary team of oncologists and urologists could provide treatment plans for PCa patients based on clinical and pathological features, including active surveillance, androgen deprivation therapy (ADT), radical prostatectomy (RP), radiotherapy, and other adjuvant management [3]. In the process, prostate-specific antigen (PSA) and testosterone are considered as crucial biomarkers for evaluating the efficacy and prognosis [4]. However, it is reported that these biomarkers might be influenced by interventions, lifestyles and other factors, which may interfere the strategy making and clinical practice [5,6].

In recent years, lifestyle interventions have emerged as an important strategy for prevention and treatment of many conditions due to the safety and effectiveness [7]. Among them, exercise intervention can reduce blood lipids, increase energy consumption, and regulate psychological balance, providing benefits in the rehabilitation [8,9]. Meanwhile, physical activity has become an effective strategy of

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The Fourth Military Medical University is also named Air Force Medical University.

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improving cardiorespiratory fitness, emotional state, and quality of life in cancer patients [7]. In this regard, a growing body of research has revealed that exercise prescription could promote the recovery of PCa patients, in terms of improving cardiopulmonary capacity, body composition, fatigue symptom, and treatment-related side effects [10]. However, the effect of exercise prescription on serum levels of PSA and testosterone remains unclear.

In this study, we reviewed the studies focusing on the relationship between exercise and PCa treatment or prognosis, aiming to investigate the effect of exercise on PSA and testosterone.

Methods

Literature search

This meta-analysis was conducted according to the PRISMA guidelines [11]. The protocol of this meta-analysis was registered in PROSPERO (CRD42025649037). Included studies were searched and selected by using PubMed, Embase, and Cochrane Library. The latest search was performed on February 2025. The search terms included “Prostate neoplasms” (MeSH Terms) OR “Prostatic neoplasm” OR “Prostate cancer” OR “Cancer of prostate” OR “Prostatic neoplasm” OR “Prostatic cancer” AND “Exercises (MeSH Terms)” OR “Exercise” OR “Physical exercise” OR “Aerobic exercise” OR “Exercise training” OR “Physical activity.” The search was not limited on date. Additional studies were searched and selected manually according to search terms, and any existed disagreements were resolved through consensus.

Literature selection and data extraction

The inclusion criteria of this meta-analysis are: (a) enrolled patients were diagnosed with PCa based on pathological examination; (b) enrolled patients underwent treatment, including active surveillance, ADT, RP, and radiotherapy; (c) studies were randomized controlled trials (RCTs) containing exercise intervention group and control group; (d) all included study reported PSA and testosterone levels before and after exercise intervention; (e) studies were published in English. Non-RCTs, case reports, commentaries, letters, reviews, and unpublished data were excluded. Two authors (ZL and QX) independently reviewed and extracted the data of included RCTs, and the third author (YX) was designated to resolve any disagreements in this section.

The extracted data included first author, publication information, exercise protocols, patients characteristics, and serum level of biomarkers regardless of the concentration unit. If two studies from a same RCT reported the outcomes, both were included. If a study designed two arms receiving exercise intervention with one control group, data from the two intervention group were extracted and pooled separately.

Outcomes

The effect of exercise intervention on total PSA level was chosen as the primary outcome due to PSA density was reported rarely. The secondary outcome was the effect of exercise on total testosterone level. Because no significant differences between groups at the baseline, PSA and testosterone after intervention were pooled to assess the effect of exercise on them. The concentration units of PSA and testosterone were defined by the respective trials according different test methods, which were not converted in analyses.

Quality assessment

The quality assessment of selected articles was performed by two independent reviewers (FZ and YX) basing on Cochrane Collaboration’s Risk of Bias (RoB) tool of Review Manager software. Domains were evaluated using the RoB tool, including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Reviewers assessed the risk in each bias by categorizing as low, unclear, or high. Any discrepancies in this section were discussed until an agreement was reached. RCTs were

classified as high risk of selection bias if the evidence of randomization and allocation concealment was insufficient. RCTs were categorized as high risk of performance and detection bias if blinding and consistent measures were not applied by participants or investigators.

Statistical analysis

All analyses were performed basing on an intention-to-treat (ITT) principle. The pooled standardized mean difference (SMD) with 95% confidence intervals (CI) was selected as the evaluation indicator. The random-effects model was used through this meta-analysis. The SMD was calculated from the mean value with standard deviation (SD), which was measured using Cohen's d standard [12]. Pooled estimates at 0.2, 0.5, and 0.8 were cut-off values for small, medium, and large effect sizes, respectively, as well as very large effect size was defined as the estimate more than 0.8 [13]. If valuables were not reported, such as SD or difference between groups, they were estimated *via* mean, range, and sample size. Heterogeneity was evaluated by the Cochran's Q test and I^2 test. $I^2 \leq 30\%$ was regarded as a trend toward homogeneity. Subgroup and sensitivity analyses were used to detect heterogeneity source and remove unqualified studies. Meta-regression was conducted to visualize the impact of clinically significant variables on outcomes. Publication bias was assessed by funnel plots and computed using Egger's test. The Review Manager software and STATA software were used in this meta-analysis.

Results

Characteristics of the included studies

The process of literature search and selection process was showed in Figure 1. There were 1281 records after duplicates removed, and 172 studies were assessed for eligibility. After the exclusion of 164 studies, 8 studies from 2009 to 2021 were included and the data of 594 patients were synthesized eventually [14–21]. The characteristics of included studies are shown in Table 1. RoB summary of included studies are showed in Figure S1. Of all, exercise intervention was prescribed as an adjuvant therapy of ADT (four studies), active surveillance (two studies), and radical prostatectomy or radiotherapy (two studies). Meanwhile, exercise protocol included resistance training, aerobic exercise or combination of both. Among included studies, one study designed two intervention arms with different exercise protocol (resistance training or aerobic exercise) to compare with control group.

The effect of exercise intervention on PSA and testosterone levels

The pooled SMD with 95% CI was applied to assess the effect of exercise on biomarkers. Primarily pooled effect of exercise intervention on PSA was 0.03 (95% CI: -0.18 to 0.24 , $I^2 = 38.1\%$, $p = 0.115$) (Figure S2). Due to the significant heterogeneity was detected, subgroup and sensitivity analysis were performed subsequently (Figure S3 and S4). After the heterogenous study removed, pooled effect size was 0.13 (95% CI: -0.04 to 0.29), while the heterogeneity of pooled data was decreased obviously ($I^2 = 0.0\%$, $p = 0.984$), suggesting that exercise prescription had no significant effect on PSA levels (Figure 2). Although pooled effective size was small in the overall population, combined aerobic exercise with resistance training had same effective directions in subgroup analyses, indicating that this exercise prescription may increase PSA level marginally (Effective size: 0.16, 95% CI: -0.12 to 0.44 , $I^2 = 0.0\%$, $p = 0.954$) (Figure 2). No significant subgroup differences were detected ($p = 0.869$).

Pooled SMD with 95% CI of exercise intervention on testosterone was 0.19 (95% CI: -0.00 to 0.39 , $I^2 = 0.0\%$, $p = 0.435$) (Figure 3). In different subgroups, pooled estimates of aerobic exercise on testosterone was 0.32 (95% CI: -0.03 to 0.66 , $I^2 = 0.0\%$, $p = 0.404$) (Figure 3). Although individuals in this subgroup were small, pooled data suggested that aerobic exercise may increase the testosterone level. . No significant subgroup differences were detected ($p = 0.696$).

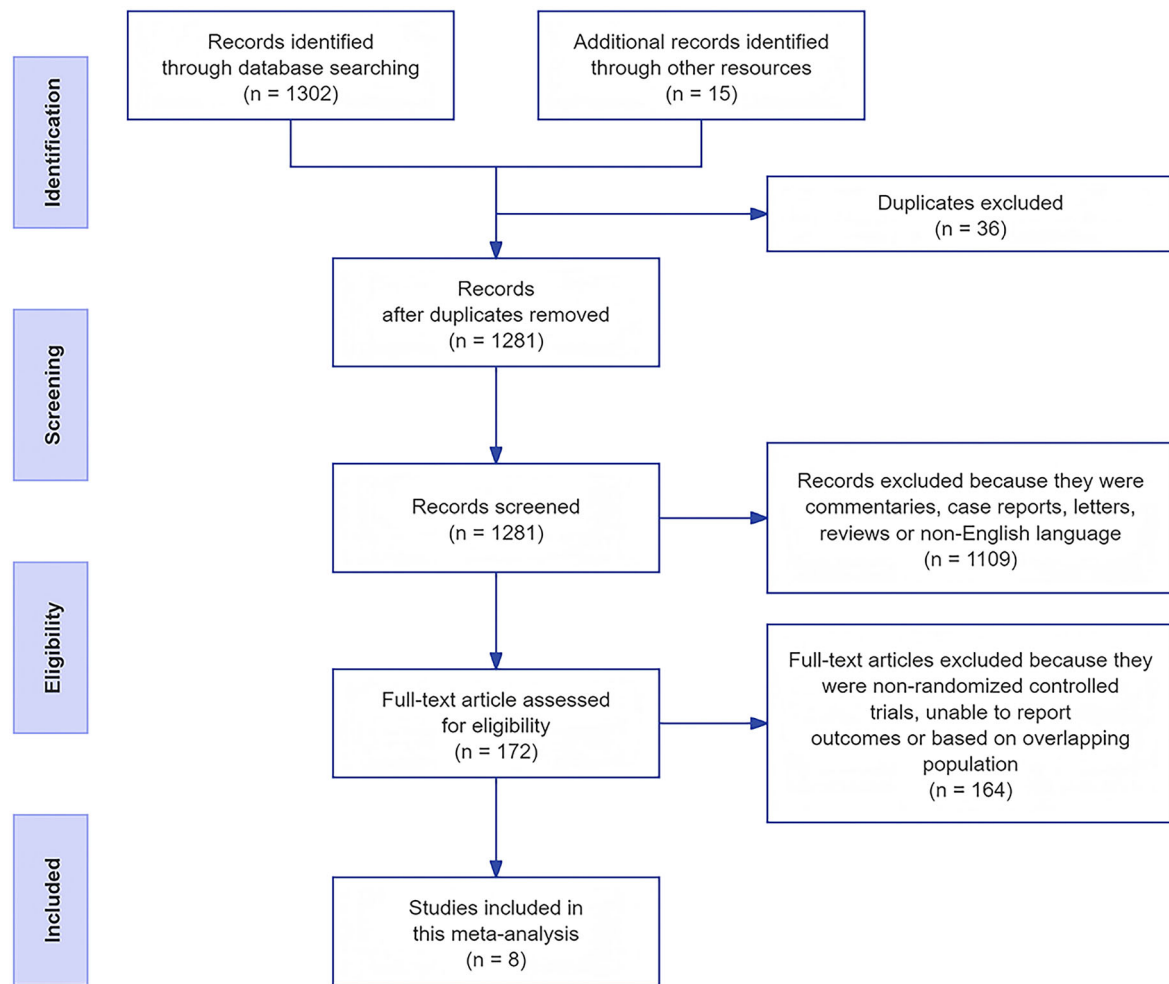


Figure 1. Flowchart of searching literature.

Meta-regression

Meta-regression was conducted to assess the association between outcomes and covariates, including age, body mass index (BMI), and the duration of exercise intervention. The meta-regression revealed that no significant association of those covariates with PSA or testosterone levels existed (All $p > 0.05$) (Figure 4). Among them, although the trend was not significant, exercise duration seems more likely to affect testosterone levels (Figure 4f).

Publication bias

No significant publication bias was detected in pooled effects of exercise intervention on PSA and testosterone using funnel plot (Figure 5a and b). Similarly, Egger's test did not detect the publication bias (Figure 5c and d).

Discussion

The exercise training as an adjuvant treatment for various diseases has gathered increasing attention in recent years [22]. Exercise interventions, including aerobic exercises, resistance training, and combination of both, have been shown to improve overall physical health, quality of life, and mental well-being in appropriate patients group [7]. One of the primary advantages in exercise interventions is low cost and non-invasive nature, making it an appealing option for both patients and healthcare systems [23]. Meanwhile, exercise strategy can be tailored to individual and integrated into daily life at home, offering

Table 1. Baseline characteristics of included studies.

Author	Journal	Title	Publication date	Study period
Segal et al. [14]	J Clin Oncol	Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer	2009	2003–2006
Galvão et al. [15]	J Clin Oncol	Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial	2010	2007–2008
Culos-Reed et al. [16]	Support Care Cancer	Physical activity for men receiving androgen deprivation therapy for prostate cancer: benefits from a 16-week intervention	2010	2004–2006
Hébert et al. [17]	Cancer Epidemiol	A diet, physical activity, and stress reduction intervention in men with rising prostate-specific antigen after treatment for prostate cancer	2012	2004–2006
Antwi et al. [18]	Cancer Epidemiol	Plasma carotenoids and tocopherols in relation to prostate-specific antigen (PSA) levels among men with biochemical recurrence of prostate cancer	2015	2004–2006
Wall et al. [19]	Med Sci Sports Exerc	Exercise improves VO2max and body composition in androgen deprivation therapy-treated prostate cancer patients	2017	2009–2011
Demark-Wahnefried et al. [20]	Br J Cancer	Presurgical weight loss affects tumour traits and circulating biomarkers in men with prostate cancer	2017	2012–2015
Kang et al. [21]	JAMA Oncol	Effects of exercise on cardiorespiratory fitness and biochemical progression in men with localized prostate cancer under active surveillance: the ERASE randomized clinical trial	2021	2018–2020

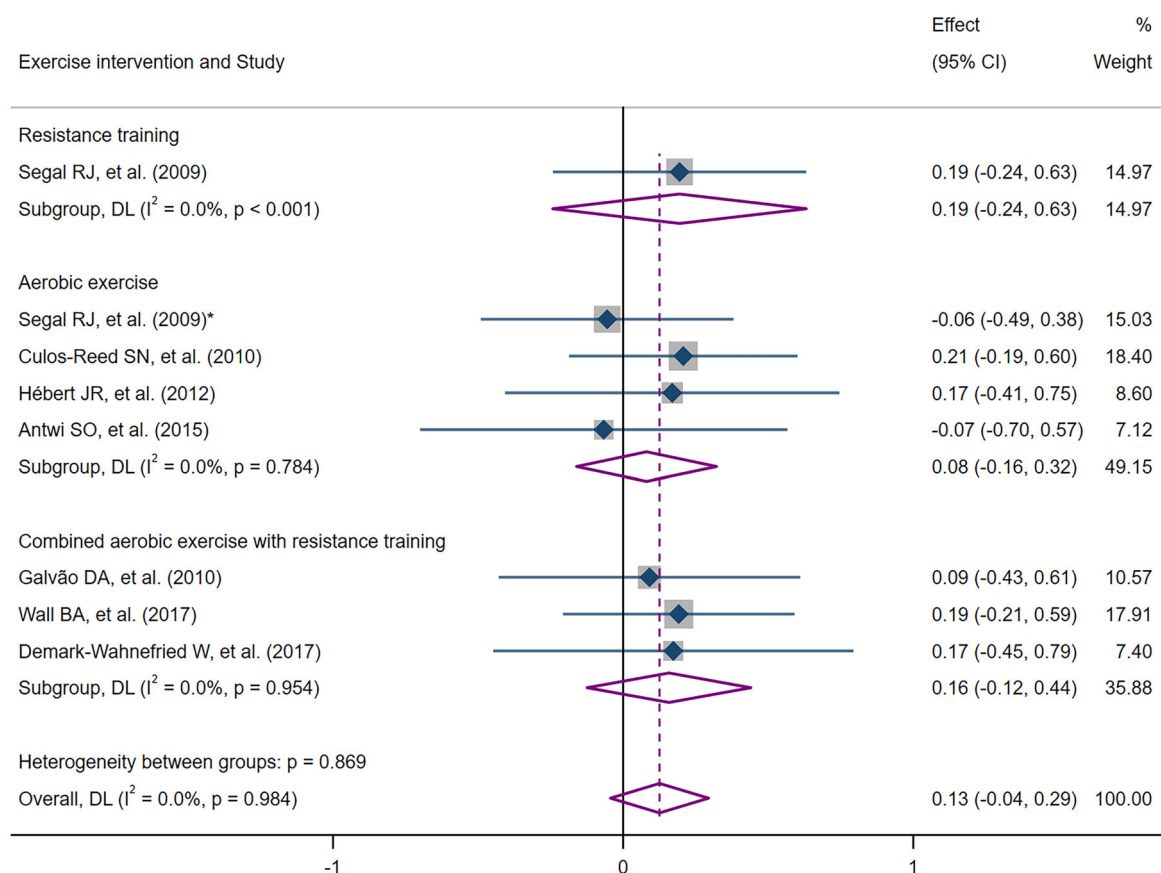
Exercise parameters				
Author	Primary management strategy	Type	Duration (week)	Frequency
Segal et al.	Androgen deprivation therapy with or without radiation therapy	Resistance training	24	Thrice-weekly
Galvão et al.	Androgen deprivation therapy with or without radiation therapy	Combined aerobic exercise with resistance training	12	NR
Culos-Reed et al.	Androgen deprivation therapy	Aerobic exercise	16	Three to five times per week
Hébert et al.	Radical prostatectomy or radiation therapy	Aerobic exercise	24	Moderate intensity exercise on ≥ 5 days per week
Antwi et al.	Radical prostatectomy or radiation therapy	Aerobic exercise	24	Moderate intensity exercise on ≥ 5 days per week
Wall et al.	Androgen deprivation therapy with or without radiation therapy	Combined aerobic exercise with resistance training	24	Twice weekly
Demark-Wahnefried et al.	Active surveillance, and scheduling for radical prostatectomy	Combined aerobic exercise with resistance training	6	Two to five times per week
Kang et al.	Active surveillance	Aerobic exercise	12	Thrice-weekly

(continued)

Table 1. Continued

Author	Control group post-intervention profile				Intervention group post-intervention profile			
	ITT (n)	VO ₂ max (L/min)	PSA (ng/mL)	Testosterone	ITT (n)	VO ₂ max (L/min)	PSA(ng/mL)	Testosterone
Segal et al.	41 (Intervention group 1)	2.38 ± 0.44	0.57 ± 3.07	5.50 ± 7.30 pmol/L	40	2.51 ± 0.57	1.19 ± 3.31	6.08 ± 7.61 pmol/L
	41 (Intervention group 2)	2.38 ± 0.44	0.57 ± 3.07	5.50 ± 7.30 pmol/L	40	2.55 ± 0.55	0.40 ± 3.10	6.97 ± 7.38 pmol/L
Galvão et al.	28	NR	0.70 ± 2.10	1.00 ± 0.60 nmol/L	29	NR	0.90 ± 2.30	2.10 ± 2.90 nmol/L
Culos-Reed et al.	47	NR	0.74 ± 2.51	NR	53	NR	1.27 ± 2.60	NR
Hébert et al.	21	NR	0.77 ± 1.54	NR	26	NR	1.09 ± 2.13	NR
Antwi et al.	17	NR	5.27 ± 80.30	NR	22	NR	4.26 ± 53.4	NR
Wall et al.	47	1.94 ± 0.33	0.20 ± 0.40	1.80 ± 2.60 pmol/L	50	2.16 ± 0.55	0.40 ± 1.40	1.60 ± 2.10 pmol/L
Demark-Wahnefried et al.	20	2.53 ± 0.22	4.95	320.80 ± 119.60 ng/dL	20	2.31 ± 0.49	5.40	366.40 ± 222.50 ng/dL
Kang et al.	26	2.46 ± 0.64	8.60 ± 4.20	12.00 ± 3.70 nmol/L	26	2.60 ± 0.58	5.70 ± 1.70	13.90 ± 3.90 nmol/L

Abbreviation: ITT, intention to treat; NR, non-reported; PSA, prostate-specific antigen; VO₂max, maximum oxygen uptake.



NOTE: Weights and between-subgroup heterogeneity test are from random-effects model

Figure 2. Pooled effect of exercise intervention on PSA level grouped by different exercise interventions after the heterogenous study removed.

Abbreviations: PSA, prostate-specific antigen. *means this arm from same study.

a sustainable and safe treatment unlike medication that require supervision [24]. Moreover, emerging evidence suggests that exercise could enhance cardiovascular health, boost immune function, and improve psychological well-being [25]. Taken together, exercise interventions have gained wide acceptance as part of disease rehabilitation programs across various health conditions, including cancer.

Currently, exercise has revealed promising effects in the rehabilitation of cancer patients, in terms of improving physical function, alleviating fatigue, and managing some treatment-related side effects such as muscle wasting and weight loss [26]. Increasing evidence suggests that exercise prescription can improve cardiorespiratory fitness, body composition, and overall physical performance in cancer survivors, contributing to a better quality of life [27]. However, few studies have investigated whether exercise might influence biomarkers that are crucial for diagnosing and treatment evaluation [28]. Moreover, it remains unclear that specific effects of exercise on tumor-related biomarkers, such as PSA and testosterone, particularly in patients with PCa. Given the significance of PSA and testosterone surveillance in the management of PCa, exploring the influences of exercise on these biomarkers should be investigated further.

Thus, we aimed to address this issue by pooling published RCTs to assess the effect of exercise interventions on PSA and testosterone levels in PCa patients. Interestingly, the pooled effective sizes were small, indicating that exercise prescription has no meaningful influence on PSA and testosterone levels. Although the findings from our meta-analysis did not reveal significant alterations of PSA or testosterone levels following exercise, these negative results also carry clinical importance. It suggests that exercise may not directly impact tumor-related or hormonal biomarkers typically used to evaluate PCa management when providing benefits of improving physical fitness and overall well-being. These results highlights the complexity of the relationship between lifestyle interventions and biomarkers, and further research to explore underlying mechanism is required.

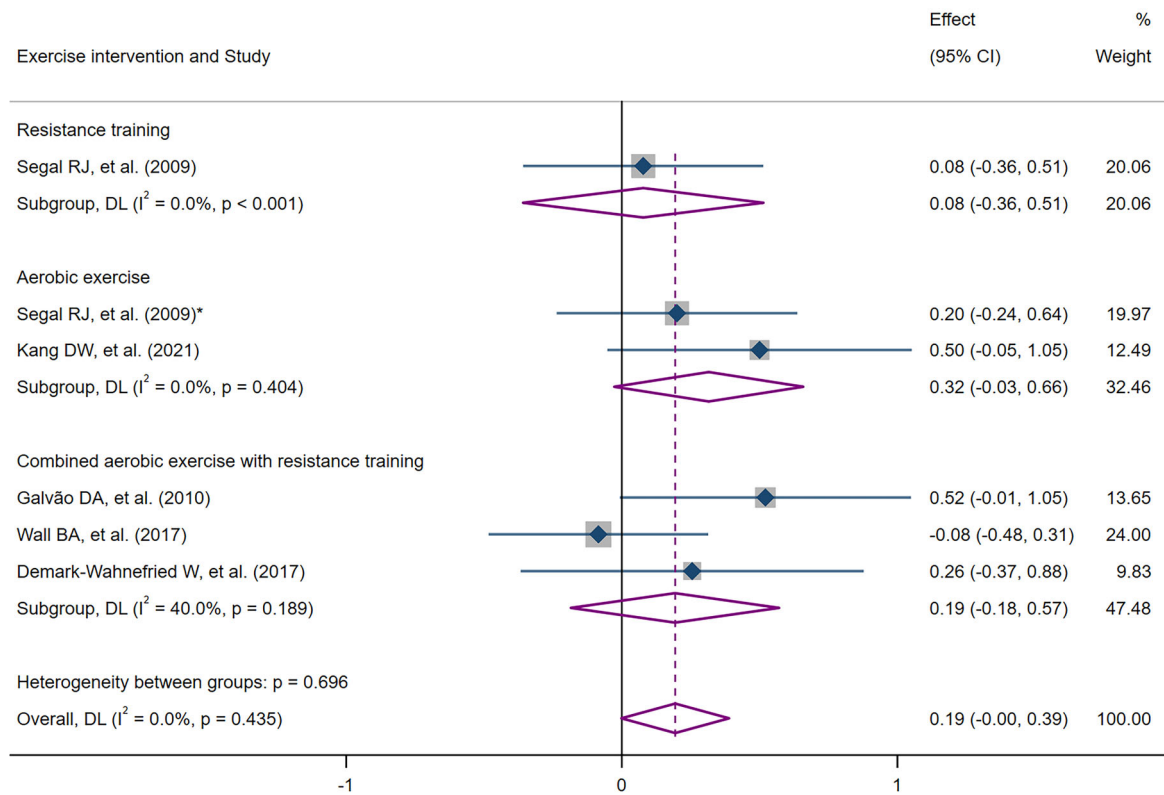


Figure 3. Pooled effect of exercise intervention on testosterone level grouped by different exercise interventions.
*means this arm from same study.

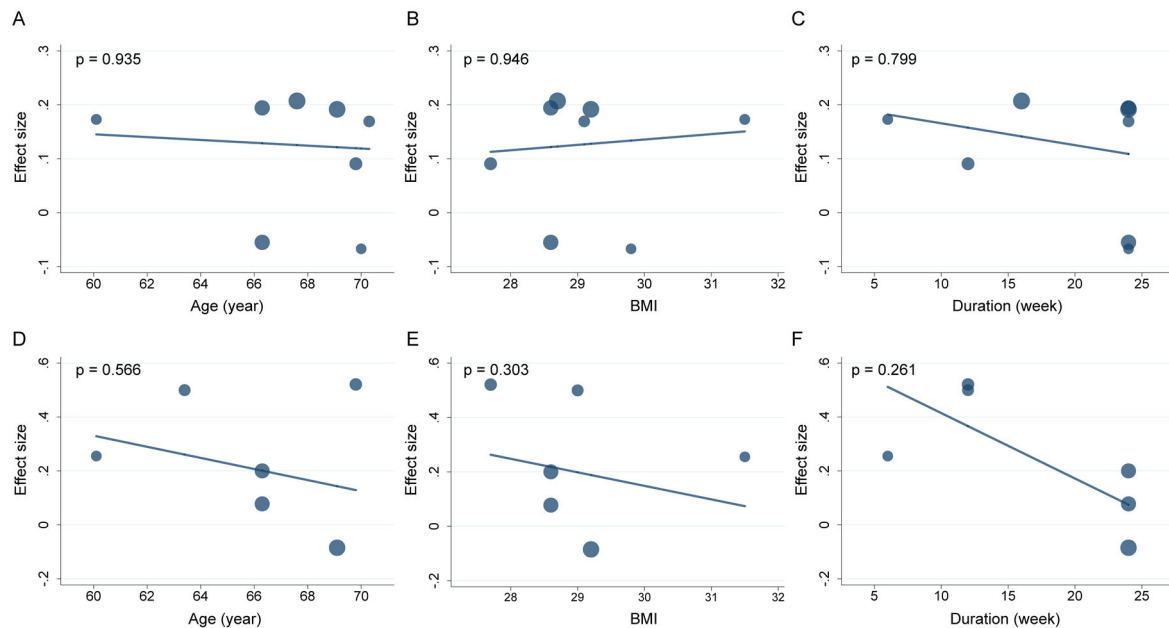


Figure 4. Meta-regression to evaluate the association of age (a), BMI (b), and exercise duration (c) with PSA level. Meta-regression to evaluate the association of age (d), BMI (e), and exercise duration (f) with testosterone level. Abbreviations: BMI: body mass index; PSA, prostate-specific antigen.

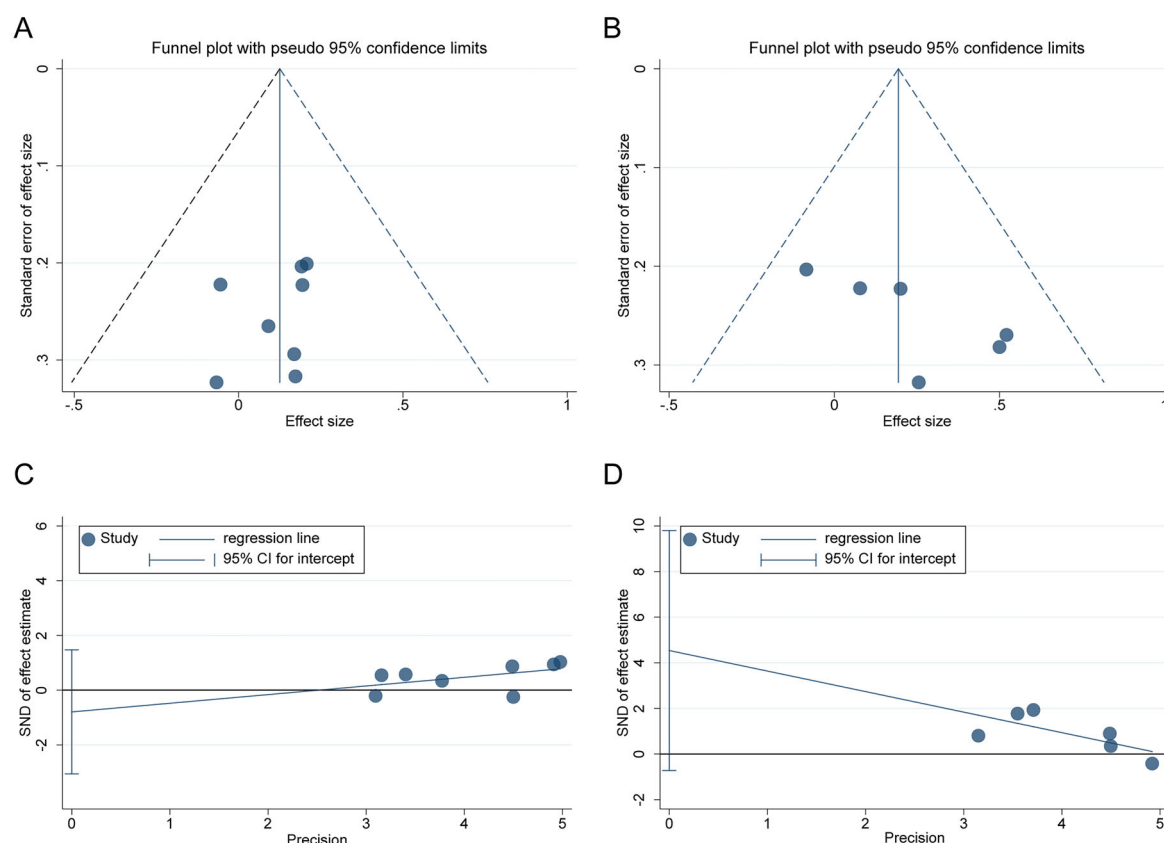


Figure 5. Funnel plot to assess the publication bias in pooling effects of exercise on PSA level (a) and testosterone level (b). Egger's test to assess the publication bias in pooling effects of exercise on PSA level (c) and testosterone level (d). Abbreviations: PSA, prostate-specific antigen.

Despite the lack of significant changes in PSA and testosterone levels, our findings are different with previous literature, which has mixed results regarding the impact of exercise on biomarkers [29,30]. Meanwhile, several studies have reported small effects of exercises on testosterone, particularly with aerobic exercise, while others have found no significant change [31,32]. The variability may be attributed to differences in exercise protocols, study designs, and patient populations. Moreover, although exercise prescription may not directly influence PSA and testosterone levels, it still have benefits for PCa recovery or rehabilitation, such as reducing fatigue, enhancing physical function, and improving mental health. Therefore, exercise should be considered as an important adjunct therapy for PCa treatment, even in the absence of significant effects on these specific biomarkers.

There are several limitations in this study. Firstly, this meta-analysis is subject to the inherent limitations of combining data from various studies. Variability in study designs, exercise protocols, and patient populations may have contributed to the heterogeneity and uncertainty in the results. Secondly, the small number of studies included in our analysis limits the power of our findings. More well-powered studies are necessary to better understand the potential effects of exercise on tumor and hormonal biomarkers in PCa patients. Finally, the inclusion of only English-language studies may introduce a language bias, potentially excluding relevant research published in other languages.

Conclusions

Exercise interventions, including aerobic exercise, resistance training and combination of both, have no significant effect on PSA and testosterone levels in PCa patients. However, given the well-documented benefits, exercise prescription remains a meaningful component of PCa rehabilitation programs. Further investigation on the mechanism linking exercise and cancer biomarkers should be conducted, and the potential of combining exercise with other interventions in cancer management should be explored.

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Ethical statement

This article does not contain any studies with human participants or animals performed by any of the authors.

Authors contributions

CRediT: **Fuxun Zhang**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **Zhirong Luo**: Conceptualization, Data curation, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing; **Qi Xue**: Data curation; **Xuyan Guo**: Data curation; **Wei Zhang**: Data curation, Formal analysis, Writing – review & editing; **Yang Xiong**: Data curation, Formal analysis, Investigation; **Yong Jiao**: Funding acquisition, Supervision, Writing – review & editing; **Uzoamaka Adaobi Okoli**: Conceptualization, Supervision, Visualization, Writing – original draft, Writing – review & editing; **Geng Zhang**: Funding acquisition, Project administration, Resources, Supervision, Writing – review & editing.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Data availability statement

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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