Review Article

A systematic review evaluating the effectiveness of exercise training on physical condition in prostate cancer patients undergoing androgen deprivation therapy

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Background: Androgen deprivation therapy (ADT) is an effective prostate cancer (PCa) treatment strategy that can curb the development or progression of the disease. This review aimed to examine and summarize available systematic reviews/meta-analyses (SRs/MAs) of exercise training on physical condition of PCa patients undergoing ADT.

Methods: A comprehensive search of 8 databases was conducted for relevant literature published before April 25, 2022 with the language restrictions of Chinese and English. Two reviewers independently assessed the methodological quality, risk of bias, reporting quality, and evidence quality of the included SRs/MAs using a range of evaluation tools, including A Measurement Tool to Assess Systematic Reviews (AMSTAR) 2, Risk of Bias in Systematic Reviews (ROBIS), the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA), and Grades of Recommendations, Assessment, Development and Evaluation (GRADE).

Results: This review included 8 SRs/MAs which included a total of 94 studies. Ultimately, A total of 51 outcomes was included, regarding 11 different outcome categories. The AMSTAR-2 tool showed that 3 SRs/MAs had moderate methodological quality, 4 SRs/MAs had very low quality, and the remaining 1 had low quality. According to the ROBIS scale, 3 SRs/MAs had a high risk of bias. The PRISMA checklist showed that the primary reporting faults were protocol registration and funding source. The GRADE system was used to analyze the evidence quality of the 51 outcomes, and no high-quality evidence was found. However, moderate-quality evidence indicated that exercise training may improve body composition [by lowering body fat mass (BFM) and body fat rate (BFR)], muscular strength, and quality of life (QoL) in PCa patients undergoing ADT. Low-quality evidence demonstrated that exercise training could improve such symptoms as fatigue, depression, sexual function, and cardiometabolic changes.

Conclusions: Available evidence suggests that exercise training may be used as an adjuvant treatment for PCa patients undergoing ADT to improve several aspects of general health. Studies with more rigorous designs and larger sample sizes are needed to support our findings with more robust evidence.

Keywords: Exercise; prostate cancer (PCa); systematic review (SR)

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Introduction

Androgen deprivation therapy (ADT) is an effective prostate cancer (PCa) treatment strategy that can curb the development or progression of the disease (1). However, ADT may cause hypogonadism and other adverse effects such as obesity, sarcopenia, metabolic syndrome, cardiovascular diseases, osteoporosis, sexual function failure, diabetes mellitus, and gynecomastia (2-11). Apart from these well-established complications, there is data showing that between 5–50% of PCa patients receiving ADT exhibit some form of cognitive dysfunction (12,13). Recent papers suggest that ADT may be a risk factor of major depression disorder and suicidal behavior (14).

Several studies have demonstrated that exercise training is helpful in preventing the negative effects of ADT on physical health, as well as in improving quality of life (QoL) in men with PCa (15-17). Oncology exercise guidelines recommend all cancer patients engage in 20–30 minutes of moderate-intensity, aerobic, and resistance exercise 3–5 times per week (18). Resistance exercise training (RET) and aerobic exercise training (AET) are practicable and well-tolerated therapies for patients with PCa to improve their physical condition, including body composition, muscular strength, cardiorespiratory fitness, physical function, and fatigue (19).

Notably, how exercise training improves the physical condition of PCa patients undergoing ADT has become a focus of research (20). PCa cells are predisposed to oxidative stress, which is required for the aggressive phenotype (21). Oxidative stress can promote the occurrence and progression of PCa by activating androgen receptor (AR) signaling, and PCa patients undergoing ADT produce a large amount of reactive oxygen species (ROS) (22). Excessive generation of ROS disrupts the mechanisms of cancer suppression, leading to cell damage and death. Moreover, numerous data demonstrate that PCa is associated with the development of oxidative stress (23). Simultaneously, ADT-induced osteoporosis, cardiovascular diseases, and body composition changes are also correlated with oxidative stress (24). Exercise training is a fundamental form of therapy for treating diseases. Antioxidant indicators increase after exercise training, while prooxidant indicators tend to decline, regardless of exercise volume, intensity, type, or population. Thus, physical activity has an antioxidant effect (25), and regular AET enhances the brain's antioxidant capacity (26).

There is a growing body of systematic reviews/meta-analyses (SRs/MAs) on exercise training for PCa patients undergoing ADT. For evidence users, there are many systematic reviews that need to be retrieved and read for different clinical issues of the same disease, which is time-consuming and laborious. On the other hand, summarizing the existing SRs/MAs, can comprehensively present the high-quality research results about a specific subject, save time, and obtain a higher level of evidence resources, which is timelier and more feasible to solve clinical problems. The quality of the methodology and evidence has not been evaluated, and whether the results can offer reliable evidence for clinicians is still under debate. Hence, the purpose of this study was to assess the methodological

Highlight box

Key findings

- Moderate-quality evidence indicated that exercise training may improve body composition [lower body fat mass (BFM) and body fat rate (BFR)], muscular strength, and quality of life (QoL) in prostate cancer (PCa) patients undergoing androgen deprivation therapy (ADT). Meanwhile, low-quality evidence demonstrated that exercise training could improve such symptoms as fatigue, depression, sexual function, and cardiometabolic changes.

What is known and what is new?

- Exercise training is helpful in preventing the negative effects of ADT and improving QoL in men with PCa. In addition, exercise training improves muscular strength, body composition, and physical performance in PCa patients receiving ADT.
- This study assessed the evidence level of the systematic evaluation of the effect of exercise on QoL of PCa patients receiving ADT. No evidence of high quality was found.

What is the implication, and what should change now?

- Exercise training can be used to manage adverse effects in PCa patients treated with ADT.

quality, risk of bias, reporting quality, and evidence quality of available SRs/MAs on exercise training and physical condition for PCa patients receiving ADT. We present this article in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-23-272/rc).

Methods

Eligibility criteria

Type of studies

The present study summarized available SRs/MAs on exercise training for PCa patients undergoing ADT. We excluded meeting summaries, case reports, SR/MA protocols, comment updates, studies with inadequate data, duplicate records, and network MAs of the effects of various exercise training programs.

Type of participants

Participants were diagnosed with PCa and underwent ADT. No restrictions were imposed on age, race, course of disease, and pathological type.

Type of interventions

PCa patients undergoing ADT were assigned to a treatment group and control group. The treatment group received exercise training in addition to routine care. No restrictions were placed on the exercise type, frequency, and intervention time.

Type of comparison

The control group only received routine treatment (usual or standard care) with no exercise training.

Type of outcomes

The primary outcome measure was body composition. The secondary outcomes included mood, QoL, physical function, cardiometabolic changes, bone mineral density (BMD), and sexual function.

Search strategy

A comprehensive search in Web of Science, Embase, PubMed, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Databases, VIP Journals Database, and Chinese Biomedical Databases (CBM) was conducted for SRs/MAs on exercise training for PCa patients undergoing ADT. The retrieval was as of April 25, 2022 with the language restrictions of Chinese and English. Both subject headings and free words were used in the search. The search terms included prostatic neoplasms, prostate neoplasm, prostate cancer, androgen deprivation therapy, exercise, physical activity, meta-analysis, and systematic review. The search strategy is summarized in Table S1 in the supplementary materials.

Data extraction and management

Three reviewers (MJ, ZM, and PZ) participated in literature screening, data extraction, and quality evaluation of the included SRs/MAs. Article screening and data extraction were done by 2 reviewers (XZ and DC) independently.

The searched studies were imported into Endnote X9 for management. After removing duplicate records, we screened the titles and abstracts to exclude irrelevant studies. Based on a full-text review, 8 SRs/MAs with 51 outcomes were included in this study. Two reviewers independently extracted data and cross-checked the results. Extracted data included the author, year of publication, quality assessment methods, duration of intervention, intervention measures, number of patients, number of included studies, outcome indicators, data analysis methods (whether sensitivity analysis and subgroup analysis were used), and conclusions. Any disagreements were discussed with a third researcher (YY) for a final consensus.

Assessment of methodological quality

A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) was adopted to assess the methodological quality of the included SRs/MAs (27). This scale comprises 16 items, 7 of which are critical items that can affect the validity of a review. The evaluation items are answered as yes, partial yes, or no. Based on methodological flaws in the critical items, the overall confidence in the results of a review is rated as critically low, low, moderate, or high. A study with no flaws or only 1 noncritical weakness was rated as high quality. If a review contained more than 1 weakness but no critical defects, it was classified as moderate quality. A review with 1 critical flaw was graded as low quality. A review with more than 1 critical defect was considered critically low quality.

Assessment of risk of bias

The risk of bias of the included SRs/MAs was assessed using Risk of Bias in Systematic Reviews (ROBIS) (28). The risk of bias assessment involves 3 phases: evaluating relevance, determining concerns about the review process, and grading the overall risk of bias. In addition, phase 2 covers 4 domains: research inclusion criteria, literature selection, data extraction and study assessment, and synthesis and findings. The overall risk of bias in the included studies was graded as low, unclear, or high.

Assessment of reporting quality

The PRISMA statement was used to evaluate the reporting quality of the included studies (29). PRISMA consists of a 27-item checklist involving the title, abstract, introduction, methods, results, and discussion sections. Each item received a response of either yes (full report), partial report, or no (no report) according to the integrity of information in the SRs/MAs.

Quality assessment of evidence

The quality of evidence in the included literature was assessed using the Grades of Recommendations, Assessment, Development and Evaluation (GRADE) system (30). This system describes 5 quality-compromising factors: limitations, indirectness, imprecision, inconsistency, and publication bias. There are also 3 confidence-increasing factors in the GRADE system: large effect quantity, dose-effect relationship, and negative bias. Two researchers (MJ and PZ) thoroughly evaluated the quality of evidence in the included studies and classified them as high, moderate, low, or very low quality. If there were no compromising factors, the evidence would be graded as high quality. If 1 compromising factor was found, the evidence was rated as moderate quality. When there were compromising factors, the quality of evidence was considered low. When there were 3 or more compromising factors, the evidence was rated as very low quality.

Data synthesis

Dichotomous data are presented as risk ratio (RR) or odds ratio (OR), and continuous data are reported as standard mean difference (SMD) or weighted mean difference (WMD) with 95% confidence intervals (CIs). The study selection process, the characteristics and results of the included SRs/MAs, and the results of the evaluation tools are summarized in tables or figures.

Results

Study selection

We retrieved 265 articles from the databases and imported them into Endnote for management. After removing 83 duplicates, the titles and abstracts were screened, and 160 articles were excluded. Based on a full-text review, 14 studies were further excluded. Finally, 8 articles (31-38) were included in the present study. The study selection process is shown in *Figure 1*.

Study characteristics

The included studies were published between 2015 and 2022. Five articles were from China, 2 from Australia, and 1 from Denmark. The 8 eligible studies involved 7,483 patients and 100 trials in total, but only 92 randomized controlled trials with 7,146 patients were finally included in the present study.

The intervention in the treatment group was exercise training (RET or AET) plus routine care, while the intervention in the control group was only usual or standard care. The intervention duration was more than 3 months. Most eligible SRs/MAs used the Cochrane risk of bias tool to assess the quality of their original studies, but 1 MA (32) adopted the Physiotherapy Evidence Database (PEDro) quality assessment scale. The effect of exercise training on body composition in PCa patients undergoing ADT was reported in 6 SRs/MAs (31-35,38), changes in physical function were reported in 3 SRs/MAs (31,33,36), improvement in fatigue was reported in 3 SRs/MAs (31,37,38), and patients' QoL was reported in 4 SRs/MAs (35-38). Meanwhile, some SRs/MAs reported on BMD and sexual health. Additionally, 3 SRs/MAs performed sensitivity and subgroup analyses (36-38). All 8 eligible SRs/MAs showed that exercise training improved physical conditions in PCa patients undergoing ADT. Three SRs/MAs (32,33,35) proposed that larger studies were needed to verify their results due to their small sample sizes. The basic characteristics of the included SRs/MAs are presented in *Table 1*.

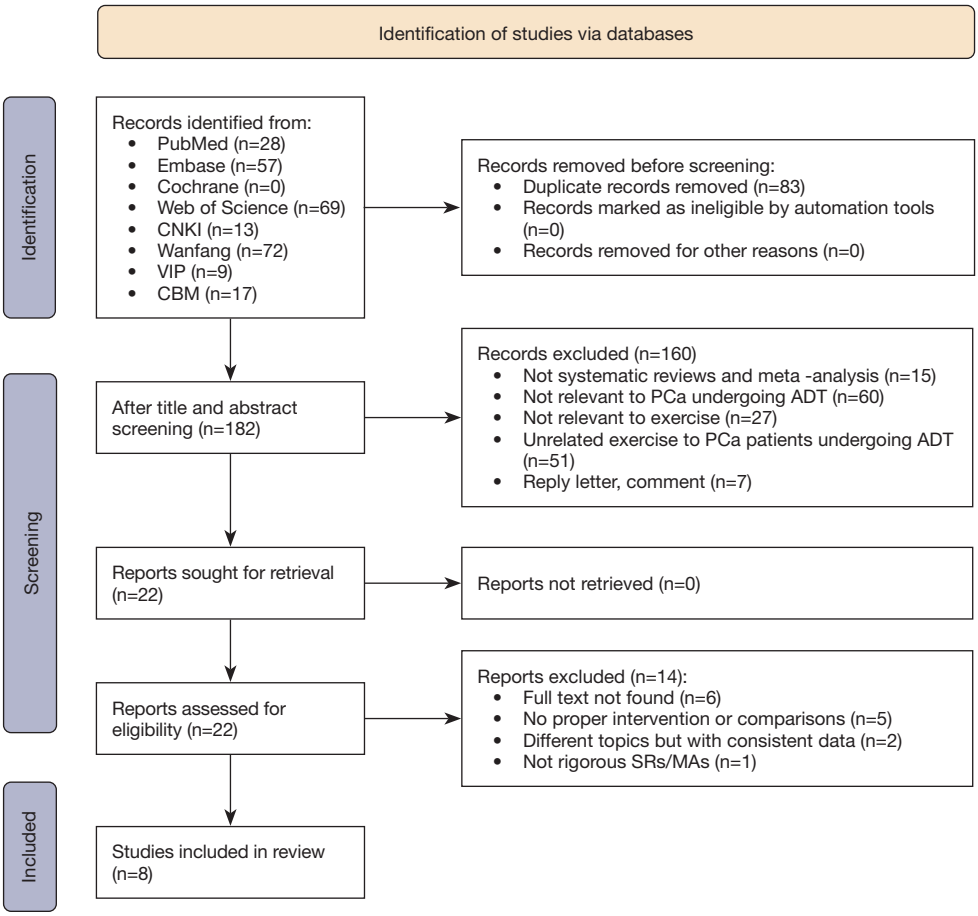

Figure 1 Flow chart of study selection. CNKI, China National Knowledge Infrastructure; VIP, VIP Journals Database; CBM, Chinese Biomedical Databases; PCa, prostate cancer; ADT, androgen deprivation therapy; SR, systematic review; MA, meta-analysis.

Methodological quality of the included SRs/MAs

The methodological quality of the included SRs/MAs was assessed using the AMSTAR-2 tool. Due to various methodological defects in critical (2,7,13,15) and noncritical items (10,12,14,16), 3 SRs/MAs (32,35,36) were of moderate methodological quality, 4 SRs/MAs (31,34,37,38) were of very low methodological quality, and 1 SR/MA (33) was of low methodological quality. The methodological quality of the included SRs/MAs is shown in Table S2.

Risk of bias of the included SRs/MAs

The risk of bias in the included SRs/MAs was evaluated utilizing the ROBIS tool. The assessment results showed that all SRs/MAs had a low risk in phase 1 of the ROBIS scale. In terms of the 4 domains in phase 2, all eligible SRs/MAs had a low risk in domain 1, 6 SRs/MAs (31-36) had a low risk of bias in domain 2, 5 SRs/MAs (32,34-37) had a low risk of bias in domain 3, and 4 SRs/MAs (32,35,36,38) had a low risk in domain 4. Furthermore, 5 SRs/MAs (31,34,36-38) were rated as having a low overall risk of bias in phase 3. The risk of bias assessment of the included SRs/MAs is presented in Table S3.

Reporting quality of the included SRs/MAs

The reporting quality of the included SRs/MAs was assessed using the PRISMA tool. Five studies (32-36) received a yes (full report) to item 5 (protocol and registration), 6 studies (31,33-37) received a yes (full report) to item 12 (risk of bias), and 6 studies (32,34-38) received a yes (full report) to item 23 (additional analysis). The reporting quality is presented in Table S4.

Table 1 Basic characteristics of the included SRs/MAs

Author [year]	Country	No. of included studies [sample size]	Type of included studies	Intervention	Control	Intervention duration (months)	Outcome	Quality assessment tool	Data analysis methods	Sensitivity/ subgroup analysis	Results summary	Financial support
Yunfeng G, *et al.* [2017]	China	15 trials [1,135], 14 RCTs [1,063]	RCT [14] + CT [1]	RET/AET	Usual care	4–12	①②③④⑤⑥	Cochrane Risk of Bias Tool	MA	No/yes	Effective	No mention
Bigaran A, *et al.* [2021]	Australia	18 trials [1,204], 11 RCTs [2 groups, 939] in this overview	RCT (14, 11 RCTs consist of 2 groups, 3 RCTs consist of 3 groups) + NRS [4]	Exercise	Usual care	3–13	①③⑦⑧⑨	Cochrane Risk of Bias Tool; PEDro quality assessment scale	SR/MA	No/yes	Effective (limited evidence)	No mention
Chen Z, *et al.* [2019]	China	7 [468]	RCT	Supervised Exercise	Usual care	3–12	①②	Cochrane Risk of Bias Tool	SR/MA	No/yes	Effective (limited evidence)	No mention
Shao W, *et al.* [2022]	China	12 [715]	RCT	Exercise; AET/RET/ impact exercise	Usual care	3–12	①⑤	Cochrane risk of bias tool	SR/MA	No/yes	Effective	No support
Teleni L, *et al.* [2016]	Australia	9 [738]	RCT [7]	AET/RET	Standard care or no treatment	3–6	①③⑧⑩	Cochrane Risk of Bias Tool	MA	No/yes	Effective (limited evidence)	Yes
Ussing A, *et al.* [2022]	Denmark	18 [1,477]	RCT	Supervised exercise	No exercise therapy	3–12	②⑩⑪	Cochrane Risk of Bias tool; GRADE	SR/MA	Yes/yes	Effective	Yes
Yang B, *et al.* [2017]	China	10 [841]	RCT	Exercise	Usual care	3–6	④⑩	Cochrane Risk of Bias tool	MA	Yes/yes	Effective	No mention
Ying M, *et al.* [2018]	China	1 [905]	RCT	Exercise	Usual care	3–6	①④⑩⑪	Cochrane Risk of Bias tool	MA	Yes/yes	Effective	No support

Outcomes: ①, body composition; ②, physical function; ③, cardiometabolic changes; ④, fatigue; ⑤, BMD; ⑥, sexual health; ⑦, exercise capacity; ⑧, blood pressure; ⑨, inflammatory markers; ⑩, quality of life; and ⑪, depression. SR, systematic review; MA, meta-analysis; RCT, randomized controlled trial; CT, controlled trial; NRS, non-randomized studies; AET, aerobic exercise training; RET, resistance exercise training; PEDro quality assessment scale: Physiotherapy Evidence Database quality assessment scale; GRADE, Grades of Recommendations, Assessment, Development and Evaluation; BMD, bone mineral density.

Efficacy of exercise for PCa patients undergoing ADT

The eligible SRs/MAs involved 13 types of outcome measures. The effect of exercise training on body composition in PCa patients on ADT was analyzed in 6 SRs/MAs (31-35,38), fatigue was reported in 3 SRs/MAs (31,37,38), QoL was discussed in 4 SRs/MAs (35-38), depression was reported in 2 SRs/MAs (36,38), and physical function was reported in 3 SRs/MAs (31,33,36). Simultaneously, cardiometabolic changes, BMD, sexual health, exercise capacity, blood pressure, and inflammatory markers were also discussed. The outcome measures in the included SRs/MAs are summarized in Table S5.

Body composition

Body composition comprises body mass index (BMI), lean body mass (LBM), body fat rate (BFR), and body fat mass (BFM). Six SRs/MAs (31-35,38) reported on body composition. Nonetheless, only 1 of them (38) comprehensively investigated the effect of exercise interventions on body composition in PCa patients undergoing ADT, showing that an exercise-dominated lifestyle significantly improved body composition in PCa patients on ADT (SMD =–0.1, 95% CI: –0.19, –0.01, I^2=0%, P=0.03). The remaining 5 papers (31-35) analyzed their outcome indicators statistically.

BMI was reported in 2 SRs/MAs (31,38). Yunfeng *et al.* (31) analyzed the BMI index with a cutoff of 6 months and found that exercise training improved BMI (SMD =–0.33, 95% CI: –0.55, –0.12, I^2=38%, P=0.002, <6 months; SMD =–0.59, 95% CI: –1.01, 0.17, I^2=25%, P=0.006, >6 months). In contrast, Ying *et al.* (38) found no significant improvement in BMI (SMD =–0.11, 95% CI: –0.32, 0.10, I^2=9%, P=0.30).

LBM was discussed in 6 SRs/MAs (31-35,38). Three SRs/MAs (31,33,38) revealed that exercise training did not significantly improve LBM in PCa patients undergoing ADT [Yunfeng *et al.* (31): SMD =–0.08, 95% CI: –0.20, 0.30, I^2=0%, P=0.57; Chen *et al.* (33): MD=–0.49 kg, 95% CI: –0.76, 1.74, I^2=0%, P=0.44; Ying *et al.* (38): SMD =–0.01, 95% CI: –0.24, 0.22, I^2=0%, P=0.91]. However, 2 SRs/MAs (32,34) found that exercise training significantly improved LBM in PCa patients receiving ADT [Bigaran *et al.* (32): MD =0.70 kg, 95% CI: 0.39, 1.01, I^2=0%, P<0.0001; Shao *et al.* (34): MD =0.88, 95% CI: 0.40, 1.36; I^2=0%, P=0.0003]. One MA (34) showed that RET alone did not significantly improve LBM compared to usual care (MD =1.43, 95% CI: –0.29, 3.14, I^2=58%, P=0.10), but RET combined with other exercises such as AET improved LBM (MD =0.86, 95% CI: 0.16, 1.56, I^2=0%, P<0.05). In addition, its subgroup analysis showed that exercise training improved LBM regardless of intervention intensity (8–12 repetition maximum or 6–12 repetition maximum), exercise duration (>6 or ≤6 months), immediate exercise after ADT, or delayed exercise after ADT (MD =2.61, 95% CI: 0.89, 4.32, I^2=0%, P<0.01; MD =0.83, 95% CI: 0.12, 1.55, I^2=0%, P<0.05; MD =0.75, 95% CI: 0.23, 1.28, I^2=0%, P<0.01; MD =1.60, 95% CI: 0.37, 2.83, I^2=0%, P<0.05; MD =0.93, 95% CI: 0.18, 1.67, I^2=0%, P<0.05; MD =1.02, 95% CI: 0.08, 1.96, I^2=0%, P<0.05). Another SR/MA (35) did not conduct heterogeneity analysis and showed that exercise did not significantly improve LBM (MD =–0.20, 95% CI: –1.72, 1.32).

BFM was described in 5 SRs/MAs (31,32,34,35,38). Two of them (31,38) suggested that exercise training did not significantly lower BFM in PCa patients undergoing ADT (P>0.05). One MA (32) found that exercise training improved whole-BFM and trunk fat mass (MD =–0.67 kg, 95% CI: –1.08, –0.27, I^2=51%, P=0.001; MD =–0.49 kg, 95% CI: –0.87, –0.12, I^2=51%, P=0.01). Another SR (34) suggested that exercise training improved BFM (MD =–0.60, 95% CI: –1.10, –0.10, I^2=0%, P=0.02). Moreover, RET combined with other exercises such as AET (MD =–0.21, 95% CI: –0.85, 0.44, I^2=0%, P=0.53) showed greater improvement in LBM than RET alone (MD =–1.19, 95% CI: –1.99, –0.40, I^2=0%, P<0.01). It also revealed that high frequency (6–12 repetition maximum) training (MD =–1.15, 95% CI: –1.97, –0.34, I^2=0%, P<0.01) and immediate exercise after ADT (MD =–1.37, 95% CI: –2.25, –0.49, I^2=0%, P<0.01) had more beneficial effects on BFM. Another study (35) did not perform heterogeneity analysis, and its results revealed that exercise improved BFM (MD =–0.61, 95% CI: –2.48, 1.26).

BFR was reported in 5 SRs/MAs (31,32,34,35,38), all of which revealed that exercise training was beneficial to BFR [Yunfeng *et al.* (31): SMD =–0.22, 95% CI: –0.42, –0.01, I^2=0%, P=0.04; Bigaran *et al.* (32): MD =–0.79, 95% CI: –1.16, –0.42, I^2=59%, P<0.0001; Shao *et al.* (34): MD =–0.93, 95% CI: –1.39, –0.47, I^2=15%, P<0.0001; Teleni *et al.* (35): MD =–0.71, 95% CI: –1.96, 0.55; Ying *et al.* (38): SMD =–0.21, 95% CI: –0.40, 0.03, I^2=0%, P=0.03]. One SR/MA (34) performed subgroup analysis and found that RET with 8–12 repetition maximum, prolonged exercise duration, and immediate exercise after ADT significantly improved BFR (P<0.05), but delayed exercise after ADT did not improve BFR (MD =–0.97, 95% CI: –1.97, 0.04, I^2=35%, P=0.06).

Fatigue

Two SRs/MAs (37,38) demonstrated that exercise training significantly alleviated fatigue (Yang *et al.*: SMD =–0.32, 95% CI: –0.45, –0.18, I^2=35%, P<0.00001; Ying *et al.*: SMD =0.17, 95% CI: 0.00, 0.34, I^2=0%, P=0.05). Another MA (31) found that exercise training for more than 6 months significantly improved fatigue (SMD =–9.3, 95% CI: –16.22, –2.39, I^2=49%, P=0.003), while exercise training for fewer than 6 months did not improve fatigue (SMD =0.84, 95% CI: –1.43, 3.10, I^2=51%, P=0.85). Its subgroup analysis showed no difference in the effects of AET and RET on fatigue (SMD =0.09, 95% CI: –0.27, 0.44, I^2=51%, P=0.63).

QoL

Four SRs/MAs (35-38) analyzed the effects of exercise training on QoL in PCa patients undergoing ADT. One of them (36) revealed that exercise training improved disease-specific QoL in PCa patients undergoing ADT (SMD =0.43, 95% CI: 0.29, 0.58, I^2=11%, P<0.00001). Its subgroup analysis showed that AET/RET significantly improved disease-specific QoL (P=0.00001), but football training did not improve disease-specific QoL (P=0.64). Meanwhile, Ying *et al.* (38) found that simple exercise training significantly improved patients' QoL (SMD =0.17, 95% CI: 0.00, 0.34, I^2=0%, P=0.05), while exercise training combined with dietary advice did not improve patients' QoL (SMD =0.45, 95% CI: –0.17, 1.08, I^2=80%, P=0.15).

Depression

Depression was reported in 2 SRs/MAs (39,40). One article (36) showed that exercise training mitigated depression (SMD =–0.23, 95% CI: –0.54, 0.08). In contrast, the other (38) revealed that there was no statistical difference in the improvement of depression between the exercise training group and usual care group (MD =–0.18, 95% CI: –0.67, 0.31, I^2=46%, P=0.47). However, the results had a high risk of bias due to the small sample sizes in the 2 reviews.

Physical function

Physical function was reported in 3 studies (40-42). Physical function consists of chest press, leg press, and VO_2 peak. One MA (31) found that exercise training significantly improved physical function (P<0.05), including leg press (SMD =0.78, 95% CI: 0.57, 0.99, I^2=0%, P<0.00001), chest press (SMD =0.71, 95% CI: 0.50, 0.92, I^2=0%, P<0.00001), and VO_2 peak regardless of intervention duration (SMD =0.35, 95% CI: 0.04, 0.66, I^2=0%, P=0.03, <6 months; SMD =0.59, 95% CI: 0.16, 1.03, I^2=0%, P=0.007, >6 months). However, its subgroup analysis showed no statistically significant difference in the improvement of VO_2 peak between the AET and RET groups (SMD =–0.12, 95% CI: –0.44, 0.21, I^2=0%, P=0.63). Chen *et al.* (33) found that exercise training significantly improved leg press and chest press (P<0.0001). Meanwhile, Ussing *et al.* (36) found that exercise training significantly improved VO_2 peak (MD =1.76, 95% CI: 0.82, 2.69), muscle strength (SMD =0.47, 95% CI: 0.28, 0.65), walking performance (SMD =–0.41, 95% CI: –0.60, –0.22, I^2=29%, P<0.0001), and sit-to-stand performance (SMD =0.35, 95% CI: 0.14, 0.56).

Other outcomes

Cardiometabolic changes were reported in 1 MA (31), which showed that exercise training significantly improved total serum cholesterol (SMD =0.35, 95% CI: 0.1, 0.61, I^2=0%, P=0.007), but there was no significant improvement in triglycerides, high-density lipoprotein (HDL), and fasting glucose (SMD =0.27, 95% CI: –0.5, 1.03, I^2=87%, P=0.5; SMD =0.21, 95% CI: –0.13, 0.55, I^2=0%, P=0.08; SMD =–0.30, 95% CI: –0.64, 0.04, I^2=0%, P=0.30). Fasting blood glucose was reported in 1 review (32), which revealed that exercise training improved fasting blood glucose (MD =–0.38 mmol/L, 95% CI: –0.65, –0.11, I^2=0%, P=0.006).

BMD change was discussed in 2 SRs/MAs (43,44). One MA (31) found no significant difference in BMD change between the exercise training group and usual care group (SMD =–0.03, 95% CI: –0.07, 0.01, I^2=0%, P=0.12). The other (34) indicated that exercise training did not significantly inhibit the loss of whole-body BMD, lumbar BMD, total hip BMD, and femoral neck BMD (MD =–0.00, 95% CI: –0.01, 0.01, I^2=0%, P=0.74; MD =0.00, 95% CI: –0.00, 0.01, I^2=0%, P=0.16; MD =0.00, 95% CI: –0.00, 0.01, I^2=0%, P=0.09; MD =0.00, 95% CI: –0.00, 0.00, I^2=0%, P=0.74).

Notably, 1 MA (31) concluded that exercise training improved sexual health in PCa patients undergoing ADT (SMD =0.66, 95% CI: 0.35, 0.97, I^2=2%, P<0.00001). Another study (32) reported that exercise training had a beneficial effect on 400-m-walk performance (MD =–10.11 s, 95% CI: –14.34, –5.88, I^2=0%, P<0.00001), but had no significant effect on 6-min-walk performance (MD =52.57, 95% CI: –3.03, 108.16, I^2=0%, P=0.06).

Blood pressure was reported in 2 SRs/MAs (32,35). One of them (32) revealed that exercise training significantly improved diastolic blood pressure (MD =–2.22 mmHg, 95% CI: –3.82, –0.61, I^2=0%, P=0.007). In contrast, the other (35) reported that exercise did not significantly

improve systolic blood pressure (MD =1.72, 95% CI: –2.47, 5.90). C-reactive protein level was reported in one MA (32), which indicated that exercise training could reduce the level of C-reactive protein (mg/L) (MD =–1.16 mg/L, 95% CI: –2.11, –0.20, I^2=47%, P=0.02).

Evidence quality of the included SRs/MAs

The GRADE system was adopted to evaluate the evidence quality of the 51 outcomes extracted from the 8 eligible SRs/MAs. Based on the evidence quality assessment, 8 outcomes had moderate evidence quality (15.69%), 23 had low evidence quality (45.10%), and 20 had very low evidence quality (39.22%). There was no high-quality evidence. The most important factor for the compromised quality of evidence was the publication bias (40/51, 78.43%) caused by a lack of funnel plots or a limited number of original studies. The secondary factors were imprecision (35/51, 68.63%) and risk of bias (33/51, 64.71%). The evidence quality of the included SRs/MAs is shown in *Table 2*.

Discussion

Summary of main findings

The current overview summarized available SRs/MAs on exercise training for PCa patients undergoing ADT to elucidate the effectiveness of exercise therapy. The quality of the included SRs/MAs was assessed. All eligible studies were published in the past 5 years, except 1 (35) published in 2016, 2 studies (31,37) published in 2017. The relative novelty of the articles suggests that using exercise training as an intervention method for PCa patients, especially those undergoing ADT treatment, has gained traction from clinical workers in recent years.

The methodological quality of the 8 included SRs/MAs was evaluated using the AMSTAR-2 tool. Three of the studies (31,34,35) were rated as moderate quality, 4 (30,33,36,37) were graded as very low quality, and 1 (32) was considered low quality. According to the ROBIS tool, the primary causes for a high risk of bias were an insufficient literature search, inappropriate study selection, unsuitable data collection and synthesis methods, and an inadequate discussion on the risk of bias. The high risk of bias may have made the current evidence less reliable. Based on the PRISMA checklist, we found that protocol and registration, risk of bias, additional analyses, and funding sources were not properly reported in the included reviews. The defects mentioned above may have affected the clarity and transparency of the included SRs/MAs.

Six articles (30-34,37) analyzed changes in body composition in PCa patients undergoing ADT, showing that exercise training could improve BMI (30), LBM (31,33,34), BFM (31,33,34), and BFR (30,31,33,34,37). Three articles (30,36,37) found that exercise training could significantly alleviate fatigue symptoms. The duration of exercise regime appears important, and Yunfeng *et al.* (31) highlighted that a longer-term exercise regime beyond 6 months significantly improve fatigue. Four articles (34-37) reported that exercise training could improve the QoL of patients. One article (35) showed that exercise training could relieve depression, while another (37) reported that exercise training did not improve depression. Three articles (30,32,35) suggested that exercise training significantly improved physical function. In addition, exercise training was also reported to improve physical changes (30,31), physical health (30), exercise capacity (31), blood pressure (31), and C-reactive protein (31). In short, exercise training could improve body composition (BMI, LBM, BFM, and BFR), physical function, QoL, and other factors. These findings are in line with earlier research. Exercise has been reported to bring psychological and physical benefits to PCa patients undergoing ADT, including relieving fatigue, reducing depression, enhancing cardiopulmonary function, and increasing muscle strength (45,46). These benefits may be correlated with the fact that exercise training can enhance the antioxidation system and reduce oxidative stress. Several studies have reported that oxidative stress and prooxidant–antioxidant imbalance play a key role in the development of PCa, which may be associated with increased ROS and damaged antioxidation systems (23,41,43,47-49). PCa patients undergoing ADT may produce a large amount of ROS, including superoxide anion (O_2^-), hydroxyl radical (OH^-), and hydrogen peroxide (H_2O_2), destroying the balance between prooxidant and antioxidant enzymes and aggravating oxidative stress. Routine exercise can regulate redox signaling and enhance antioxidant defense, thus curbing the onset and development of PCa (39,40,42,44,50).

However, there were differences in the effect of exercise training on BMI, LBM, fatigue, depression, and cardiometabolic indexes. The main factors for the different results are as follows: (I) the number of included studies was small, and the sample size was insufficient; (II) because PCa patients are generally older, the influence of basic diseases such as diabetes, hypertension, and hyperlipidemia may have caused different results; and (III) the type, intensity,

Table 2 Results of evidence quality evaluation

Outcomes	References	Studies [participants]	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence
Body composition								
BMI	Yunfeng G, *et al.* [2017]							
	<6 months	5 [346]	−1①	0	0	−1④	0	Low
	>6 months	2 [91]	−1①	0	0	−1④	−1⑥	Very low
	Ying M, *et al.* [2018]	6 [452]	−1①	0	0	0	−1⑤	Low
LBM	Yunfeng G, *et al.* [2017]	4 [196]	−1①	0	0	−1④	−1⑥	Very low
	Bigaran A, *et al.* [2021]	5 [372]	0	0	0	−1④	0	Moderate
	Chen Z, *et al.* [2019]	7 [490]	−1①	0	0	0	0	Moderate
	Shao W, *et al.* [2022]	9 [562]	−1①	0	0	0	−1⑤	Low
	Teleni L, *et al.* [2016]	4 [335]	0	0	0	−1④	−1⑥	Low
	Ying M, *et al.* [2018]	5 [292]	−1①	0	0	−1④	−1⑤	Very low
The percentage fat mass	Yunfeng G, *et al.* [2017]	5 [398]	−1①	0	0	−1④	−1⑥	Very Low
	Bigaran A, *et al.* [2021]	4 [275]	0	−1②	0	−1④	0	Low
	Shao W, *et al.* [2022]	8 [428]	−1①	0	0	0	0	Moderate
	Teleni L, *et al.* [2016]	4 [335]	0	0	0	−1④	−1⑥	Low
	Ying M, *et al.* [2018]	5 [393]	−1①	0	0	−1④	−1⑤	Very low
BFM	Bigaran A, *et al.* [2021]	5 [372]	0	−1②	0	−1④	0	Low
	Shao W, *et al.* [2022]	9 [549]	−1①	0	0	0	0	Moderate
Physical function								
Leg press	Yunfeng G, *et al.* [2017]	5 [417]	−1①	0	0	0	−1⑥	Low
	Chen Z, *et al.* [2019]	4 [235]	−1①	0	0	−1④	−1⑥	Very low
Chest press	Yunfeng G, *et al.* [2017]	6 [428]	−1①	0	0	0	0	Moderate
	Chen Z, *et al.* [2019]	5 [335]	−1①	0	0	−1④	0	Low
VO_2 peak	Yunfeng G, *et al.* [2017]							
	<6 months	3 [202]	−1①	0	0	−1④	−1⑥	Very low
	>6 months	2 [105]	−1①	0	0	−1④	−1⑥	Very low
	Ussing A, *et al.* [2022]	6 [406]	0	−1②	0	−1④	−1⑤	Very low
Cardiometabolic changes								
Total serum cholesterol	Yunfeng G, *et al.* [2017]	4 [238]	−1①	0	0	−1④	−1⑥	Very low
Triglyceride	Yunfeng G, *et al.* [2017]	4 [238]	−1①	0	0	−1④	−1⑥	Very low
	Teleni L, *et al.* [2016]	3 [300]	0	0	0	−1④	−1⑥	Low
HDL	Yunfeng G, *et al.* [2017]	3 [138]	−1①	0	0	−1④	−1⑥	Very low

Table 2 *(continued)*

Table 2 *(continued)*

Outcomes	References	Studies [participants]	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence
Fasting glucose	Yunfeng G, *et al.* [2017]	4 [238]	–1①	0	0	–1④	–1⑥	Very low
	Bigaran A, *et al.* [2021]	3 [217]	0	0	0	–1④	–1⑥	Low
	Teleni L, *et al.* [2016]	3 [300]	0	0	0	–1④	–1⑥	Low
Fatigue	Yunfeng G, *et al.* [2017]							
	<6 months	5 [433]	–1①	–1②	0	0	0	Low
	>6 months	3 [321]	–1①	0	0	–1④	–1⑥	Very low
	Yang B, *et al.* [2017]	9 [784]	–1①	0	0	0	–1⑤	Low
	Ying M, *et al.* [2018]	9 [737]	–1①	0	0	0	–1⑤	Low
Depression	Ying M, *et al.* [2018]	2 [163]	–1①	0	0	–1④	–1⑥	Very low
BMD	Yunfeng G, *et al.* [2017]	3 [171]	–1①	0	0	–1④	–1⑥	Very low
	Shao W, *et al.* [2022]							
	The whole-body BMD	4 [329]	–1①	0	0	–1④	–1⑥	Very low
	The lumbar BMD	7 [426]	–1①	0	0	0	–1⑤	Low
	The total hip BMD	6 [406]	–1①	0	0	0	–1⑤	Low
	The femoral neck BMD	5 [259]	–1①	0	0	–1④	–1⑤	Very low
Sexual health	Yunfeng G, *et al.* [2017]	3 [220]	0	0	0	–1④	–1⑥	Low
QoL	Yang B, *et al.* [2017]	10 [841]	–1①	0	0	0	–1⑤	Low
	Ying M, *et al.* [2018]	6 [554]	–1①	0	0	0	–1⑤	Low
Health-related QoL								
	Teleni L, *et al.* [2016]	5 [427]	0	0	0	0	–1⑤	Moderate
	Ussing A, *et al.* [2022]	4 [246]	0	–1②	0	–1④	–1⑥	Very low
Disease-specific QoL								
	Teleni L, *et al.* [2016]	3 [271]	0	0	0	–1④	–1⑥	Low
	Ussing A, *et al.* [2022]	12 [894]	0	0	0	0	–1⑤	Moderate
Exercise capacity	Bigaran A, *et al.* [2021]							
	The 400-m-walk test, s	3 [222]	0	0	0	–1④	–1⑥	Low
	6-min walk test, m	3 [180]	0	0	0	–1④	–1⑥	Low
Diastolic blood pressure, mmHg	Bigaran A, *et al.* [2021]	5 [357]	0	0	0	–1④	0	Moderate
C-reactive protein, mg/L	Bigaran A, *et al.* [2021]	3 [217]	0	0	–1③	–1④	–1⑥	Very low

①, most data are extracted from the studies at a moderate or high risk of bias, which have serious limitations in concealment, randomization, allocation and blinding; ②, few confidence intervals overlap, or the I^2 values are relatively large (medium and high heterogeneity); ③, the population, intervention measures, and measurement outcomes in original studies are quite different, or the intervention measures cannot be directly compared; ④, the sample size is small; the confidence intervals are wide (the sample size of continuous variables <400, the sample size of binary variables <300); or the 95% CI crosses the invalid line; ⑤, the funnel diagram is asymmetry; ⑥, few studies are included, and the results are positive and may result in publication bias. BMI, body mass index; LBM, lean body mass; BFM, body fat mass; VO_2, oxygen consumption; HDL, high-density lipoprotein; BMD, bone mineral density; QoL, quality of life.

and duration of exercise training, as well as probability in PCa patients on ADT were inconsistent.

In addition, the differences in the outcomes are due to the low-quality methodologies and evidence in the included SRs/MAs. The AMSTAR-2 tool was used for the methodological quality assessment, and the included SRs/MAs were rated as either low or very low quality. The main reasons for the low quality were as follows: (I) some SRs/MAs did not list the excluded studies in detail or describe the rationality of the exclusion, which might have affected the credibility and transparency of the results; (II) except for 1 study, none of the included SRs/MAs investigated publication bias, and no funnel diagram (51) was drawn due to there being less than 10 included randomized controlled trials (RCTs); and (III) some studies failed to identify the funding sources or conflicts of interest, making it difficult to assess their impact on the results.

Eight cases of moderate-quality evidence (8/51, 15.69%) suggested that exercise training might help PCa patients on ADT prevent adverse events. Exercise training could reduce BFM and BFR in body composition, increase muscle strength, and improve QoL. Subgroup analysis found that AET and RET had better performance in improving adverse reactions. The credibility of other outcomes was impaired as a result of several limitations, most notably a lack of description of the randomization, allocation concealment, and blind methods in original RCTs, as well as a potential risk of selective reporting. In a word, the quality of evidence included in this overview was low.

Implications for future study

Our overview is the first to comprehensively focus on exercise training in PCa patients receiving ADT. The methodological quality of original studies was highly correlated with the overall quality of SRs/MAs. Therefore, a significant number of multicenter, large-scale RCTs on the effects of exercise training for PCa patients on ADT are required to increase the quality of evidence. In this overview, there was no unified standard for evaluating the efficacy of exercise training. Thus, future research should be based on the efficacy evaluation indicators that have been recognized in the guidelines, recommended by expert consensus, or accepted by experts in the industry, such as body composition, QoL, and BMD. In addition, longer follow-up is required in future research to investigate the long-term effect of exercise training on PCa men undergoing ADT. Also, some areas appear to be under-investigated in regard to a potential effect of physical exercise on non-cancer health aspects in those patients, mainly the sexual and mental health.

Additionally, given the observed relatively high rate of methodological concerns, we believe that SRs/MAs should be registered in advance. Protocols should be published to enhance the objectivity and authenticity of research, improve the level of documentary evidence, and reduce the risk of bias. AMSTAR-2, PRISMA, and ROBIS should be utilized to reduce subjective bias and improve research quality. Subgroup and sensitivity analyses should be conducted when there is high heterogeneity in the data. Moreover, funding sources and conflicts of interest in original studies should be described in detail to avoid the impact of researchers on the objective evaluation of evidence quality.

Limitations

This overview has some limitations. Firstly, inconsistent evaluation results in the methodological quality assessment may have been due to the low quality of the included literature, low credibility of evidence, and the different opinions of the researchers. Secondly, the languages of the included SRs/MAs were mainly Chinese and English. Lack of articles in other languages may have resulted in omission of included studies. Thirdly, the importance of exercise in advanced cancer has always been overlooked, and the few limited studies that attempt to evaluate this aspect could not committed to a homogenous clinical outcome, which was highlighted in the SR/MA. Moreover, this overview did not analyze the type, intensity, duration of exercise training, and stage of PCa patients undergoing ADT. Lastly, there was a risk of publication bias for a limited number of RCTs included in some SRs/MAs, and no funnel charts were drawn.

Conclusions

Exercise training is a potential adjunctive therapeutic strategy for PCa patients undergoing ADT. Nevertheless, due to a lack of high-quality evidence in this overview, more well-designed and large-scale studies are required to support our findings with more robust evidence.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-23-272/rc

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Supplementary

Table S1 Search strategies for each database

PubMed

Number	Search items	Number of retrieved articles
#1	"Exercise"[MeSH Terms]	229542
#2	"exercis*"[Title/Abstract] OR "physical activit*"[Title/Abstract] OR "physical exercis*"[Title/Abstract] OR "acute exercis*"[Title/Abstract] OR "isometric exercis*"[Title/Abstract] OR "aerobic exercis*"[Title/Abstract] OR "exercise training*"[Title/Abstract]	438,665
#3	#1 OR #2	522,518
#4	"Prostatic Neoplasms"[MeSH Terms]	141,509
#5	"prostate neoplasm*"[Title/Abstract] OR "prostatic neoplasm*"[Title/Abstract] OR "prostate cancer*"[Title/Abstract] OR "prostatic cancer*"[Title/Abstract]	140,535
#6	"PCa"[Title/Abstract] OR "Castration-Resistant Prostate Cancer"[Title/Abstract] OR "CRPC"[Title/Abstract] OR "Metastatic castration resistant prostate cancer"[Title/Abstract] OR "mCRPC"[Title/Abstract]	59,994
#7	"ADT"[Title/Abstract] OR "androgen deprivation therapy"[Title/Abstract]	9181
#8	(#4 OR #5 OR #6) AND #7	7501
#9	#3 AND #8	2,128
#10	"systematic review"[Title/Abstract] OR "Clinical Trial Overviews"[Title/Abstract]	241759
#11	#9 AND #10 AND "Meta-Analysis"[Publication Type]	28

Embase

Number	Search items	Number of retrieved articles
#1	'prostate neoplasm'/exp	243611
#2	'prostate neoplasm*':ab,ti OR 'prostatic neoplasm*':ab,ti OR 'prostate cancer':ab,ti OR 'prostate cancer*':ab,ti OR 'prostatic cancer*':ab,ti OR 'PCa':ab,ti OR 'Castration-Resistant Prostate Cancer':ab,ti OR 'CRPC':ab,ti OR 'Metastatic castration resistant prostate cancer':ab,ti OR 'mCRPC':ab,ti	255192
#3	'Exercise'/exp	401401
#4	'exercis*':ab,ti OR 'physical activit*':ab,ti OR 'physical exercis*':ab,ti OR 'acute exercis*':ab,ti OR 'isometric exercis*':ab,ti OR 'aerobic exercis*':ab,ti OR 'exercise training*':ab,ti	287231
#5	'Androgen deprivation therapy'/exp	14909
#6	'ADT':ab,ti	9896
#7	#1 OR #2	325938
#8	#3 OR #4	563123
#9	#5 OR #6	18813
#10	#7 AND #9	16572
#11	#8 AND #10	493
#12	#11 AND 'meta-analysis'/de	57

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Cochrane Library

Number	Search items	Number of retrieved articles
#1	MeSH descriptor: [Prostatic neoplasms] explode all trees	6216
#2	(“Prostate Neoplasm*”):ti,ab,kw OR (“Prostatic Neoplasm*”):ti,ab,kw OR (“Prostate Cancer*”):ti,ab,kw OR (“Prostatic Cancer*”):ti,ab,kw OR (“PCa”):ti,ab,kw	19929
#3	(“Castration-Resistant Prostate Cancer”):ti,ab,kw OR (“CRPC”):ti,ab,kw OR (“Metastatic castration resistant prostate cancer”):ti,ab,kw OR (“Mcrpc”):ti,ab,kw	2344
#4	#1 OR #2 OR #3	19965
#5	MeSH descriptor: [Exercise] explode all trees	28782
#6	(“Exercises”):ti,ab,kw OR (“Physical Activit*”):ti,ab,kw OR (“Physical Exercis*”):ti,ab,kw OR (“Acute Exercis*”):ti,ab,kw OR (“Isometric Exercis*”):ti,ab,kw	28339
#7	(“Aerobic Exercis*”):ti,ab,kw OR (“Exercise Training*”):ti,ab,kw	9859
#8	#5 OR #6 OR #7	59756
#9	(“Androgen deprivation therapy”):ti,ab,kw OR (ADT):ti,ab,kw	3178
#10	#4 AND #8 AND #9	96
#11	Cochrane Reviews	0

Web of Science

Number	Search items	Number of retrieved articles
#1	((((((((((TS=(“prostate cancer”)) OR TS=(“Prostatic Neoplasms”)) OR TS=(“Prostate Neoplasm*”)) OR TS=(“Prostatic Neoplasm*”)) OR TS=(“Prostate Cancer*”)) OR TS=(“Prostatic Cancer*”)) OR TS=(“PCa”)) OR TS=(“Castration-Resistant Prostate Cancer”)) OR TS=(“CRPC”)) OR TS=(“Metastatic castration resistant prostate cancer”)) OR TS=(“mCRPC”)	179094
#2	(((((((TS=(“Exercise”)) OR TS=(“Exercises”)) OR TS=(“Physical Activit*”)) OR TS=(“Physical Exercis*”)) OR TS=(“Acute Exercis*”)) OR TS=(“Isometric Exercis*”)) OR TS=(“Aerobic Exercis*”)) OR TS=(“Exercise Training*”)	309213
#3	(TS=(“Androgen deprivation therapy”)) OR TS=(“ADT”)	10042
#4	#3 AND #1 AND #2	442
#5	((TS=(“Meta-Analysis”)) OR TS= (“Clinical Trial Overviews”)) OR TS= (“systematic review”)	293641
#6	#4 AND #5	69

CNKI

SU=(‘前列腺癌’+’前列腺肿瘤’+’去势抵抗性前列腺癌’+’PCa’+’CRPC’) AND SU=(‘运动’+’体育锻炼’+’锻炼’+’抗阻训练’) AND SU=(‘系统评价’+’荟萃分析’+’Meta’) 13

Wanfang

主题:(前列腺癌 or 前列腺肿瘤 or 去势抵抗性前列腺癌 or PCa or CRPC) and 主题:(运动 or 体育锻炼 or 锻炼 or 抗阻训练) and 主题:(系统评价 or 荟萃分析 or Meta) 72

VIP

任意字段 U=(前列腺癌 OR 前列腺肿瘤 OR 去势抵抗性前列腺癌 OR PCa OR CRPC) AND U=(运动 OR 体育锻炼 OR 锻炼 OR 抗阻训练) AND U=(系统评价 OR 荟萃分析 OR Meta) 9

CBM

(“系统评价”[全部字段:智能] OR “荟萃分析”[全部字段:智能] OR “Meta”[全部字段:智能]) AND ((“前列腺癌”[全部字段:智能] OR “前列腺肿瘤”[全部字段:智能] OR “去势抵抗性前列腺癌”[全部字段:智能] OR “PCa”[全部字段:智能]) OR “CRPC”[全部字段:智能] OR “mCRPC “[全部字段:智能]) OR “前列腺癌”[不加权:扩展])) AND ((“运动”[全部字段:智能] OR “体育锻炼”[全部字段:智能] OR “锻炼”[全部字段:智能] OR “抗阻训练”[全部字段:智能]) OR (“运动”[不加权:扩展])) 17

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Table S2 Results of the AMSTAR-2 assessments (27)

Item	Yunfeng, G., *et al.* (2017)	Bigaran, A., *et al.* (2021)	Chen, Z, *et al.* (2019)	Shao, W., *et al.* (2022)	Teleni, L., *et al.* (2016)	Ussing, A., *et al.* (2022)	Yang, B., *et al.* (2017).	Ying, M., *et al.* (2018)
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Y	Y	Y	Y	Y	Y	Y	Y
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	N	Y	Y	Y	Y	Y	N	N
3. Did the review authors explain their selection of the study designs for inclusion in the review?	Y	Y	Y	Y	Y	Y	Y	Y
4. Did the review authors use a comprehensive literature search strategy?	Y	Y	PY	Y	Y	Y	Y	PY
5. Did the review authors perform study selection in duplicate?	Y	Y	Y	Y	Y	Y	Y	Y
6. Did the review authors perform data extraction in duplicate?	Y	Y	Y	Y	Y	Y	Y	Y
7. Did the review authors provide a list of excluded studies and justify the exclusions?	N	Y	Y	PY	Y	PY	PY	N
8. Did the review authors describe the included studies in adequate detail?	Y	Y	Y	Y	Y	Y	Y	Y
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Y	Y	Y	Y	Y	Y	Y	Y
10. Did the review authors report on the sources of funding for the studies included in the review?	N	Y	N	N	Y	N	N	N
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	Y	Y	Y	Y	Y	Y	Y	Y
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	N	N	Y	Y	PY	Y	Y	N
13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?	Y	Y	Y	N	Y	Y	Y	N
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Y	N	Y	Y	Y	Y	Y	Y
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	N	Y	N	N	Y	Y	N	Y
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	N	Y	N	N	Y	Y	N	N
Overall Quality	Very low	Moderate	Low	Very low	Moderate	Moderate	Very low	Very low

Y, yes; PY, partially yes; N, no. The contents of the table can be publicly referenced.

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Table S3 Results of the ROBIS assessments (28)

Review	Phase 1	Phase 2				Phase 3
	ASSESSING RELEVANCE (participants, interventions, comparisons, outcomes)	Domain 1: Study ELIGIBILITY CRITERIA	Domain 2: identification and selection of studies	Domain 3: DATA COLLECTION AND STUDY APPRAISAL	Domain 4: SYNTHESIS AND FINDINGS	RISK OF BIAS IN THE REVIEW
Yunfeng, G., *et al.* (2017)	☺	☺	☺	☹	?	☺
Bigaran, A., *et al.* (2021)	☺	☺	☺	☺	☺	☹
Chen, Z., *et al.* (2019)	☺	☺	☺	☹	☹	☹
Shao, W., *et al.* (2022)	☺	☺	☺	☺	?	☺
Teleni, L., *et al.* (2016)	☺	☺	☺	☺	☺	☹
Ussing, A., *et al.* (2022)	☺	☺	☺	☺	☺	☺
Yang, B., *et al.* (2017).	☺	☺	☹	☺	☹	☺
Ying, M., *et al.* (2018)	☺	☺	☹	☹	☺	☺

☺ Low risk; ☹ High risk; ? Unclear risk.

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Table S4 Results of the PRISMA (29)

Section/Topic	Items	Yunfeng, G, *et al.* (2017)	Bigaran, A., *et al.* (2021)	Chen, Z., *et al.* (2019)	Shao, W., *et al.* (2022)	Teleni, L., *et al.* (2016)	Ussing, A., *et al.* (2022)	Yang, B., *et al.* (2017).	Ying, M., *et al.* (2018)
TITLE	1. Title	Y	Y	Y	Y	Y	Y	Y	Y
ABSTRACT	2. Structured summary	Y	Y	Y	Y	Y	Y	Y	Y
INTRODUCTION	3. Rationale	Y	Y	Y	Y	Y	Y	Y	Y
	4. Objectives	Y	Y	Y	Y	Y	Y	Y	Y
METHODS	5. Protocol and registration	N	Y	Y	Y	Y	Y	N	N
	6. Eligibility criteria	Y	Y	Y	Y	Y	Y	Y	Y
	7. Information sources	Y	Y	Y	Y	Y	Y	Y	Y
	8. Search	Y	Y	Y	Y	Y	Y	Y	Y
	9. Study selection	Y	Y	Y	Y	Y	Y	Y	Y
	10. Data collection process	Y	Y	Y	Y	Y	Y	Y	Y
	11. Data items	Y	Y	Y	Y	Y	Y	Y	Y
	12. Risk of bias in individual studies	Y	N	Y	Y	Y	Y	Y	N
	13. Summary measures	Y	Y	Y	Y	Y	Y	Y	Y
	14. Synthesis of results	Y	Y	Y	Y	Y	Y	Y	Y
	15. Risk of bias across studies	Y	Y	Y	Y	Y	Y	Y	N
	16. Additional analyses	N	PY	PY	Y	PY	Y	Y	PY
RESULTS	17. Study selection	Y	Y	Y	Y	Y	Y	Y	Y
	18. Study characteristics	Y	Y	Y	Y	Y	Y	Y	Y
	19. Risk of bias within studies	N	Y	Y	Y	Y	Y	Y	N
	20. Results of individual studies	Y	Y	Y	Y	Y	Y	Y	Y
	21. Synthesis of results	Y	Y	Y	Y	Y	Y	Y	Y
	22. Risk of bias across studies	Y	Y	Y	Y	Y	Y	Y	N
	23. Additional analysis	N	PY	N	PY	PY	Y	PY	Y
	24. Summary of evidence	N	Y	Y	Y	Y	Y	Y	Y
DISCUSSION	25. Limitations	Y	Y	N	Y	Y	PY	Y	Y
	26. Conclusions	Y	Y	Y	Y	Y	Y	Y	Y
FUNDING	27. Funding	N	N	N	N	Y	Y	N	N

Y, yes; PY, partially yes; N, no.

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Table S5 Summary of evidence

SR/MA	Intervention measures	Outcomes	Synthesis of results	No. of studies (sample size)
Yunfeng, G, *et al.* (2017)	Exercise *VS.* Usual care	Body composition		11 (826)
		BMI	SMD=−0.33, 95%CI [−0.55, −0.12], I^2=38%, P=0.002, <6 months	5 (346)
			SMD=−0.59, 95%CI [−1.01, 0.17], I^2=25%, P=0.006, >6 months	2 (91)
		LBM	SMD=−0.08, 95%CI [−0.20, 0.30], I^2=0%, P=0.57	4 (196)
		Total body fat (%)	SMD=−0.22, 95%CI [−0.42, −0.01], I^2=0%, P=0.04	5 (398)
		Physical function		8 (544)
		Leg press	SMD=0.78, 95%CI [0.57, 0.99], I^2=0%, P<0.00001	5 (417)
		Chest press	SMD=0.71, 95%CI [0.50, 0.92], I^2=0%, P<0.00001	6 (428)
		VO_2 peak	SMD=0.35, 95%CI [0.04, 0.66], I^2=0%, P=0.03, <6 months	3 (202)
			SMD=0.59, 95%CI [0.16, 1.03], I^2=0%, P=0.007, >6 months	2 (105)
		Cardiometabolic changes		5 (401)
		Total serum cholesterol	SMD=0.35, 95%CI [0.1, 0.61], I^2=0%, P=0.007	4 (238)
		Triglyceride	SMD=0.27, 95%CI [−0.5, 1.03], I^2=87%, P=0.5	4 (238)
		HDL	SMD=0.21, 95%CI [−0.13, 0.55], I^2=0%, P=0.08	3 (138)
		Fasting glucose	SMD=−0.30, 95%CI [−0.64, 0.04], I^2=0%, P=0.30	4 (238)
		Fatigue	SMD=0.84, 95%CI [−1.43, 3.10], I^2=51%, P=0.85, <6 months	5 (433)
			SMD=−9.3, 95%CI [−16.22, −2.39], I^2=49%, P=0.003, >6 months	3 (321)
		BMD	SMD=−0.03, 95%CI [−0.07, 0.01], I^2=0%, P=0.12	3 (171)
		Sexual health	SMD=0.66, 95%CI [0.35, 0.97], I^2=2%, P<0.00001	3 (220)
	AET *VS.* RET	Fatigue	SMD=0.09, 95%CI [−0.27, 0.44], I^2=51%, P=0.63	3 (350)
		Body fat mass	SMD=−0.14, 95%CI [−0.47, 0.18], I^2=51%, P=0.60	2 (187)
		VO_2 peak	SMD=−0.12, 95%CI [−0.44, 0.21], I^2=0%, P=0.63	2 (187)
Bigaran, A., *et al.* (2021)	Exercise *VS.* Usual care	Exercise capacity		
		The 400-m-walk test, s	MD=−10.11 s, 95% CI [−14.34, −5.88]; I^2=0%, P<0.00001	3 (222)
		6-min walk test, m	MD=52.57, 95% CI [−3.03, 108.16]; I^2=0%, P=0.06	3 (180)
		Blood pressure		
		Diastolic blood pressure, mmHg	MD=−2.22 mmHg, 95% CI [−3.82, −0.61]; I^2=0%, P=0.007	5 (357)
		Fasting blood glucose, mmol/L	MD=−0.38 mmol/L, 95% CI [−0.65, −0.11]; I^2=0%, P=0.006	3 (217)
		Inflammatory markers		
		C-reactive protein, mg/L	MD=−1.16 mg/L, 95% CI [−2.11, −0.20]; I^2=47%, P=0.02	3 (217)
		Body composition		
		Whole-body lean mass, kg	MD=0.70 kg, 95% CI [0.39, 1.01]; I^2=0%, P<0.0001	5 (372)
		Appendicular lean mass, kg	MD=0.59 kg, 95% CI [0.43, 0.76]; I^2=0%, P<0.00001	3 (178)
		Whole-body fat mass, kg	MD=−0.67 kg, 95% CI [−1.08, −0.27]; I^2=51%, P=0.001	5 (372)
		Whole-body fat percentage, %	MD=−0.79, 95% CI [−1.16, −0.42]; I^2=59%, P<0.0001	4 (275)
		Trunk fat mass, kg	MD=−0.49 kg, 95% CI [−0.87, −0.12]; I^2=51%, P=0.01	4 (275)
Chen, Z., *et al.* (2019)	Supervised Exercise *VS.* Usual care	Lean Mass, kg	MD=−0.49 kg, 95% CI [−0.76, 1.74]; I^2=0%, P=0.44	7 (490)
		Chest press	MD=3.15 kg, 95% CI [2.46, 3.83]; I^2=0%, P<0.00001	5 (335)
		Leg press	MD=27.46 kg, 95% CI [15.05, 39.87]; I^2=0%, P<0.0001	4 (235)
Shao, W., *et al.* (2022)	Exercise *VS.* Usual care	Body composition		
		LBM	MD=0.88, 95% CI [0.40, 1.36]; I^2=0%, P=0.0003	9 (562)
		BFM	MD=−0.60, 95% CI [−1.10, −0.10]; I^2=0%, P=0.02	9 (549)
		BFR	MD=−0.93, 95% CI [−1.39, −0.47]; I^2=15%, P<0.0001	8 (428)
		Bone mineral density		
		The whole-body BMD	MD=−0.00, 95% CI [−0.01, 0.01]; I^2=0%, P=0.74	4 (329)
		The lumbar BMD	MD=0.00, 95% CI [−0.00, 0.01]; I^2=0%, P=0.16	7 (426)
		The total hip BMD	MD=0.00, 95% CI [−0.00, 0.01]; I^2=0%, P=0.09	6 (406)
		The femoral neck BMD	MD=0.00, 95% CI [−0.00, 0.00]; I^2=0%, P=0.74	5 (259)
	RET *VS.* Usual care	LBM	MD=1.43, 95% CI [−0.29, 3.14]; I^2=58%, P=0.10	3 (127)
		BFM	MD=−0.21, 95% CI [−0.85, 0.44]; I^2=0%, P=0.53	2 (78)
		BFR	MD=−1.48, 95% CI [−3.48, 0.52]; I^2=69%, P=0.15	3 (127)

Table S5 *(continued)*

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Table S5 *(continued)*

SR/MA	Intervention measures	Outcomes	Synthesis of results	No. of studies (sample size)
	RET and other exercise (AET) *VS.* Usual care	LBM	MD=0.86, 95% CI [0.16, 1.56]; I^2=0%, P<0.05	6 (435)
		BFM	MD=−1.19, 95% CI [−1.99, −0.40]; I^2=0%, P<0.01	7 (471)
		BFR	MD=−1.08, 95% CI [−1.53, −0.62]; I^2=69%, P<0.01	5 (301)
	Intensity of resistance exercise			
	8–12 RM	LBM	MD=2.61, 95% CI [0.89, 4.32]; I^2=0%, P<0.01	2 (69)
		BFM	MD=−1.69, 95% CI [−7.36, 3.98]; I^2=0%, P=0.56	2 (56)
		BFR	MD=−2.52, 95% CI [−4.13, −0.91]; I^2=0%, P<0.01	3 (105)
	6–12 RM	LBM	MD=0.83, 95% CI [0.12, 1.55]; I^2=0%, P<0.05	5 (385)
		BFM	MD=−1.15, 95% CI [−1.97, −0.34]; I^2=0%, P<0.01	5 (385)
		BFR	MD=−1.09, 95% CI [−1.56, −0.62]; I^2=0%, P<0.01	3 (224)
	Duration of exercise			
	<6 months	LBM	MD=0.75, 95% CI [0.23, 1.28]; I^2=0%, P<0.01	4 (228)
		BFM	MD=−0.75, 95% CI [−1.60, 0.09]; I^2=36%, P=0.08	4 (228)
		BFR	MD=−0.78, 95% CI [−1.20, −0.36]; I^2=10%, P<0.01	4 (219)
	≥6 months	LBM	MD=1.60, 95% CI [0.37, 2.83]; I^2=0%, P<0.05	5 (334)
		BFM	MD=−0.54, 95% CI [−2.28, 1.19]; I^2=0%, P=0.54	5 (321)
		BFR	MD=−2.01, 95% CI [−3.23, −0.78]; I^2=0%, P<0.01	4 (309)
	Duration of ADT			
	Immediate exercise after ADT	LBM	MD=0.93, 95% CI [0.18, 1.67]; I^2=0%, P<0.05	4 (237)
		BFM	MD=−1.37, 95% CI [−2.25, −0.49]; I^2=0%, P<0.01	4 (237)
		BFR	MD=−1.12, 95% CI [−1.60, −0.64]; I^2=20%, P<0.01	3 (187)
	Delayed exercise after ADT	LBM	MD=1.02, 95% CI [0.08, 1.96]; I^2=0%, P<0.05	5 (325)
		BFM	MD=−0.23, 95% CI [−0.83, 0.38]; I^2=0%, P=0.47	5 (312)
		BFR	MD=−0.97, 95% CI [−1.97, 0.04]; I^2=35%, P=0.06	5 (241)
Teleni, L., *et al.* (2016)	Exercise *VS.* Usual care	Quality of life		
		Health-related QoL	SMD=0.29, 95%CI [0.10, 0.49], I^2=0%, P=0.003	5 (427)
		Disease-specific QoL	SMD=0.36, 95%CI [0.11, 0.61], I^2=0%, P=0.04	3 (271)
		Metabolic risk factors		
		Total body weight	MD=0.26, 95% CI [−2.40, 2.93]; I^2=0%	4 (310)
		Waist circumference measures	MD=−0.38, 95% CI [−2.97, 2.22]; I^2=0%	2 (200)
		Body composition		
		LBM	MD=−0.20, 95% CI [−1.72, 1.32]	4 (335)
		Total fat mass	MD=−0.61, 95% CI [−2.48,1.26]	3 (214)
		Percentage fat mass	MD=−0.71, 95% CI [−1.96, 0.55]	4 (335)
		Blood pressure		
		Systolic blood pressure	MD=1.72, 95% CI [−2.47, 5.90]	3 (300)
		Blood lipids and glucose metabolism		
		Blood glucose levels	MD=0.13, 95% CI [−0.16, 0.43]	3 (300)
		Total cholesterol	MD=0.13, 95% CI [−0.18, 0.44]	3 (300)
		Triglycerides	MD=−0.06, 95% CI [−0.27, 0.15]	3 (300)
		LDL cholesterol	MD=−0.06, 95% CI [−0.20, 0.32]	3 (300)
		HDL cholesterol	MD=−0.06, 95% CI [−0.05, 0.16]	3 (300)
Ussing, A., *et al.* (2022)	Supervised Exercise *VS.* no exercise therapy	Diagnose-specific QoL	SMD=0.43, 95% CI [0.29, 0.58], I^2=11%, P<0.00001	12 (894)
		Health-related QoL	MD=1.34, 95% CI [−1.99, 4.67] SF-36, physical component Scale from: 0 to 100	4 (246)
			MD=3.30, 95% CI [0.87, 5.74], SF-36, mental component	3 (198)
		Physical performance measured by walking performance	SMD=−0.41, 95% CI [−0.60, −0.22], I^2=29%, P<0.0001	11 (667)
		Physical performance, sit to stand	SMD=0.35, 95% CI [0.14, 0.56]	8 (463)
		Muscle strength	SMD=0.47, 95% CI [0.28, 0.65]	15 (968)
		VO_2 peak	MD=1.76, 95% CI [0.82, 2.69]	6 (406)
		Prevalence of depression	SMD=−0.23, 95% CI [−0.54, 0.08]	3 (195)
	AET/RET *VS.* no exercise therapy	Diagnose-specific QoL	SMD=0.47, 95% CI [0.33, 0.62], I^2=0%, P<0.00001	11 (807)

Table S5 *(continued)*

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Table S5 *(continued)*

SR/MA	Intervention measures	Outcomes	Synthesis of results	No. of studies (sample size)
	Football training *VS.* no exercise therapy	Diagnose-specific QoL	SMD=0.43, 95% CI [0.29, 0.58], P=0.64	1 (46)
Yang, B., *et al.* (2017)	Exercise *VS.* Usual care	CRF	SMD=−0.32, 95% CI [−0.45, −0.18], I^2=35%, P<0.00001	9 (784)
		QoL	SMD=0.21, 95% CI [0.08, 0.34], I^2=0%, P=0.002	10 (841)
Ying, M., *et al.* (2018)	Exercise *VS.* Usual care	QoL	SMD=0.17, 95% CI [0.00, 0.34], I^2=0%, P=0.05	6 (554)
		Fatigue	SMD=0.17, 95% CI [0.00, 0.34], I^2=0%, P=0.05	9 (737)
		Depression	SMD=−0.18, 95% CI [−0.67, 0.31], I^2=46%, P=0.47	2 (163)
	Exercise + dietary advice *VS.* Usual care	QoL	SMD=0.45, 95% CI [−0.17, 1.08], I^2=80%, P=0.15	3 (244)
	Lifestyle intervention *VS.* Usual care	Body composition	SMD=−0.1, 95% CI [−0.19, −0.01], I^2=0%, P=0.03	
		LBM	SMD=−0.01, 95% CI [−0.24, 0.22], I^2=0%, P=0.91	5 (292)
		Fat mass	SMD=−0.17, 95% CI [−0.39, 0.04], I^2=0%, P=0.12	5 (322)
		The percentage of fat mass	SMD=−0.21, 95% CI [−0.40, 0.03], I^2=0%, P=0.03	5 (393)
		Body weight	SMD=0.02, 95% CI [−0.17, 0.20], I^2=1%, P=0.86	6 (480)
		BMI	SMD=−0.11, 95% CI [−0.32, 0.10], I^2=9%, P=0.30	6 (452)

BMI, body mass index; LBM, lean body mass; BFM, body fat mass; BFR, body fat rate; VO_2, oxygen consumption; HDL, high-density lipoprotein; BMD, bone mineral density; RET, resistance exercise training; AET, aerobic exercise training; MD, Mean differences; SD, standard deviation; SMD, Standard mean difference; ES, Cohen's d effect size; RM, Repetition maximum, to evaluate the load intensity of resistance exercise; 1RM is defined as the maximum load; 6RM is defined as the load that repeated six times to reach the maximum load; 6RM≈R5% of 1RM; 8RM≈80% of 1RM; 12RM≈67% of 1RM; CRF, Cancer-Related fatigue.

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