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REVIEW ARTICLE

The effects of resistance exercise on physical performance and health-related quality of life in prostate cancer patients: a systematic review

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Abstract
Purpose Physical exercise has been shown to be an effective, safe, and quite inexpensive method to reduce cardiovascular and metabolic risk factors and is currently in the process of establishing its relevance for cancer specific morbidity and mortality. The aim of this systematic review was to focus on specific effects of resistance exercise (RE) in the adjuvant therapy and rehabilitation of prostate cancer patients (PCaPs) receiving or having received androgen deprivation therapy (ADT).
Methods A systematic literature search focusing on relevant and peer-reviewed studies published between 1966 and September 2014, using PubMed, EMBASE, MEDLINE, SCOPUS, and Cochrane Library databases, was conducted.
Results The majority of studies demonstrated RE as an effective and safe intervention to improve muscular strength and performance, fatigue and quality of life (QoL) in PCaPs, while there is inconclusive evidence concerning cardiovascular performance, body composition, blood lipids, bone mineral density (BMD), and immune response.
Conclusion Existing evidence leads to the conclusion that RE seems to be a safe intervention in PCaPs with beneficial effects on physical performance capacity and QoL. Nevertheless, further research in this field is urgently needed to increase understanding of exercise interventions in PCaPs.

Keywords Prostate cancer · Resistance exercise · Muscular strength · Androgen deprivation therapy · Physical performance · Quality of life

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Introduction

During the last two decades, the perception of physical exercise interventions in cancer patients has gone through a significant change process. Therefore, the recommendation of regular physical activity is a rather new option for cancer patients [1, 2].

Especially in prostate cancer patients (PCaPs) receiving androgen deprivation therapy (ADT), the treatment side effects often have massive negative implications on the well-being and quality of life of the patients [3, 4]. Overcoming these side effects is of major interest for both the attending health care team and their patients. Many PCaPs are undergoing long-term ADT, and therefore, its side effects unfold over a long period of time [5].

Known ADT side effects including loss of muscle mass [6, 7] and strength [7], increased fat mass [6–8], alterations both in the lipolytic profile [9, 11] and the insulin metabolism [8, 10, 11], together with an increased arterial stiffness [10, 11] lead to an increased risk of developing type II diabetes [12] and an enhanced cardiovascular risk [11, 12]. A decrease in bone mineral density leads to osteoporosis and to fracture risk [7, 13], whereas the loss of muscular strength, physical performance, and sexual functioning has substantial effects on QoL and is often considered to be a considerable contributor in the development of mental disorders like anxiety or depression [14, 15].

Many of those side effects and especially the predictors of QoL are positively affected by actively participating in exercise programs [2–4, 11, 16–21]. The majority of the exercise intervention studies up to the present primarily focused on the question if exercise is a safe option with beneficial effects on PCaPs receiving ADT. Only a few studies focused on the specific effects of different types of exercise.

The aim of this systematic review was to determine of how resistance exercise (RE) specifically impacts PCaPs—referring primarily to the management of treatment-related side effects.

Methods

A systematic review of the existing scientific literature was performed including the following databases: PubMed, EMBASE, MEDLINE, SCOPUS, and Cochrane Library.

The search strategy included the terms and key words "resistance training," "resistance exercise," "strength training," "prostate cancer," "androgen deprivation therapy," "androgen suppression therapy," and their possible variations.

A total of 945 studies were found and screened for eligibility by title and abstract. Eight hundred ninety-three studies did not meet the criteria due to a lack in inclusion criteria [including insufficient representation of RE in the intervention branch, inapplicable type of cancer (non-PCa), unsuitable type of study (review, study protocol, conference abstracts, etc.), or being represented multiple times]. After this, 52 studies were selected for full-text analysis, of which 13 met the study inclusion criteria [22, 24–32, 34–36]. Of the full text publications analyzed, only six studies focused only on RE [22, 24–27, 30] and another seven included combined RE and other exercise modalities [28, 29, 31, 32, 34–36].

Of the reported six studies that provided adequate data to evaluate the effect of the RE intervention alone in PCaPs [22, 24–27, 30], Galvao et al. [22] and Hanson et al. [24] lacked of a control group and therefore are graded to be of evidence level IIb.

The four very high-quality randomized controlled trials (RCTs) with evidence level Ib, of Segal et al. [26, 27], Santa Mina [25], as well as of Cormie [30] remain in this field of expertise. Unfortunately, the latter have some weaknesses, e.g., they were either suffering from a high dropout rate [25] or a small sample size and therefore limited power [30]. In addition, Santa Mina et al. [25] had no inactive control group. These facts lead us to modify the inclusion criteria and to include both, papers of lesser quality [22, 24] and papers with RE combined with other exercise modalities [28, 29, 31, 32, 34–36]. Furthermore, the results of eight later additional publications [23, 33, 37–42]—all based on previously published studies [22, 25–27, 32, 36]—were included. An overview of the whole selection process is shown in Fig. 1.

Furthermore, the methodological quality of the included articles was rated by using the validated Downs and Black [43] checklist. This checklist consists of 27 items which help to examine reporting, external validity, bias, confounding, and power [43].

Results

After the described selection process, 13 studies [22, 24–32, 34–36] were considered eligible for elucidating the effects of resistance exercise on PCaPs (Table 1). A total of 876 PCaPs were included in these exercise intervention studies, 441 assigned to RE intervention groups, and 435 assigned to various control groups (Fig. 2).

A short summary of the main results is given subsequently, while the complete display of the characteristics and key findings of all the included studies and the additional articles are summarized in Tables 3 and 4.

Methodological quality

The detailed rating of the quality of included articles is presented in Table 2. The scores of the rated studies ranged from 23 to 30 of a maximum of 32 points. A weakness of all included studies is that the study subjects could not be blinded to the interventions (Table 2, item 14). Furthermore, in 7 of the 13 studies, no attempt was made to blind those measuring the main outcomes of the intervention (Table 2, item 15).

Furthermore, some potentially limiting factors concerning the test results were found in a number of studies [22, 28–30, 32]. Galvao et al. [32]—a multicenter study—performed the strength testing with the participants only in one study center (n=57 of 100). Cormie et al. [30] comprised two potentially limiting factors. On the one hand, contrary to the rest of the included studies, they investigated the effect of RE on PCaPs with established metastases, a condition which was an exclusion criterion in the rest of the included papers. On the other hand, they only tested a very small group of 20 participants. Galvao et al. [22] as well as Bourke et al. [28, 29] assessed only the body mass index (BMI) and therefore are not able to provide qualitative information towards changes in muscle and fat mass [44].

Physical performance

Nine studies assessed cardiovascular fitness and endurance capacity [22, 25, 27–32, 34]. Galvao et al. [22], Santa Mina et al. [25], Segal et al. [27] and Cormie et al. [30] studied the effects of RE on cardiovascular performance, and four of them [22, 25, 27, 30] were able to show a significant increase in cardiorespiratory fitness at least at one time point.

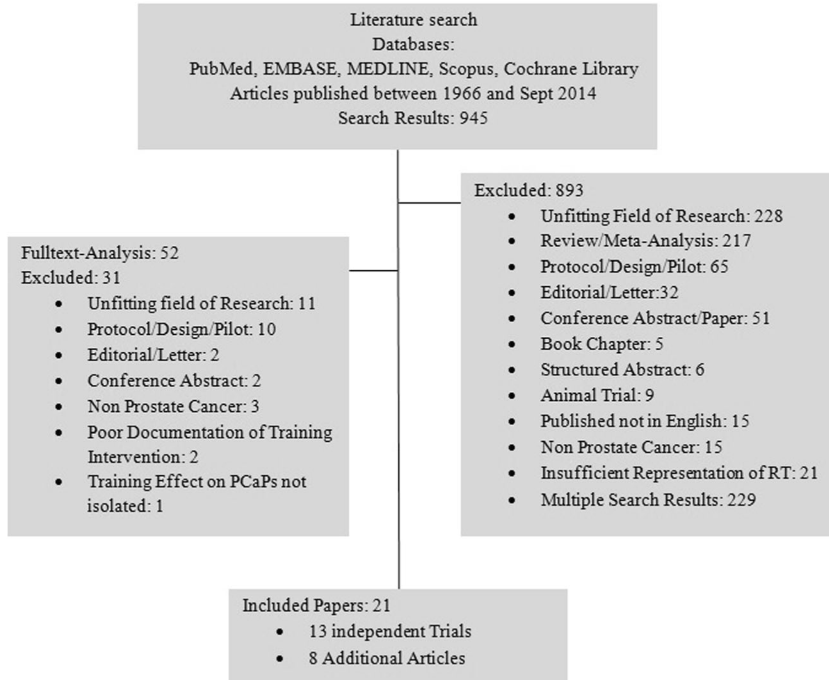

Fig. 1 Flowchart of the systematic literature research and the selection process. *PCaPs* prostate cancer patients, *RE* resistance exercise

Eleven studies assessed muscle strength [22, 24–28, 30–32, 34, 35]. Galvao et al. [22], Hanson et al. [24], Cormie et al. [30], as well as Segal et al. [26, 27] studied the isolated effects of RE on muscle strength and consistently found significant increases in muscle strength and muscular endurance capacity.

Assessment of functional performance by Galvao et al. [22, 32] as well as Hanson et al. [24] showed significant improvements in almost all functional tests after the exercise interventions (Table 3).

Body composition

In most of the studies, a body composition assessment was performed [22, 24, 25, 27–35]. Such a specific assessment

Table 1 Level of evidence, type of exercise, and risk of bias assessment total score

Study	Year	Level of evidence	Type of exercise intervention	Risk of bias assessment total score [4, 43]
Galvao et al. [22]	2006	IIb	RE only	25
Hanson et al. [24]	2013	IIb	RE only	23
Santa Mina et al. [25]	2013	Ib	RE vs. AE	28
Segal et al. [26]	2003	Ib	RE only	30
Segal et al. [27]	2009	Ib	RE vs. AE	30
Bourke et al. [28]	2011	Ib	RE+AE+health education +nutrition advice	30
Bourke et al. [29]	2014	Ib	RE+AE	28
Cormie et al. [30]	2013a	Ib	RE only	30
Cormie et al. [31]	2014	Ib	RE+AE	30
Galvao et al. [32]	2010	Ib	RE+AE+Flex	30
Galvao et al. [34]	2014	Ib	RE+AE	29
Park et al. [35]	2012	Ib	RE+pelvic flex +Kegel exercises	27
Winters-Stone et al. [36]	2014a	Ib	RE+impact exercises	27

RE resistance exercise, *AE* aerobic exercise, *Flex* flexibility training

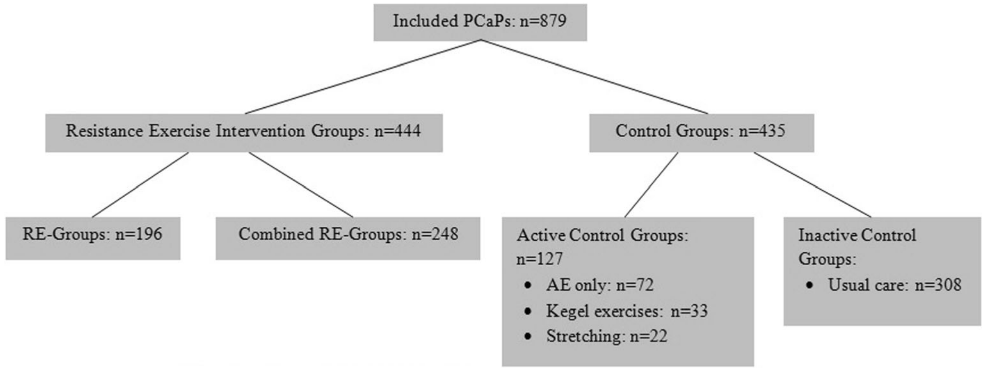

Fig. 2 Summary of the allocation of all included participants. *PCaPs* prostate cancer patients, *RE* resistance exercise, *AE* aerobic exercise

was conducted in seven studies [24, 25, 27, 30–32, 34], where positive effects of exercise on body composition—whether through RE only [24, 25, 27, 30], aerobic exercise (AE) only [25], or combined training [31, 32, 34]—have been shown (Table 3).

Fatigue and quality of life

Eleven studies [24–35] assessed fatigue, QoL, and mental health. Nine [24–32] assessed the development of fatigue either in a RE only [24, 26, 30], a combined RE+AE [28, 29, 31, 32] or a RE versus AE [25, 27] setting. All except Santa Mina et al. [25] and Cormie et al. [30] reported significant improvements in the exercise intervention branch (Table 3).

Cormie et al. [30] showed no effects of a RE intervention on QoL, fatigue, or psychological distress in PCaPs with metastatic bone disease, however, this study had a very small sample size resulting in low power [30].

Prostate-specific antigen

Eight studies [22, 26–29, 31, 32, 34] assessed prostate-specific antigen (PSA) levels either in a setting of RE only [22, 26], RE versus AE [27], or in combination with other exercise methods [28, 29, 31–33]. No one reported any changes in PSA levels (Tables 3 and 4).

Endocrine anabolic indicators

Six studies reported data of testosterone levels and resistance training interventions [22, 24, 26, 28, 32, 33]. In patients receiving ADT, RE only [22, 24, 26] or a combined RE program

Table 2 Extended analyses from risk of bias assessment [4, 43]

Risk of bias assessment of the included original studies

		Checklist items																											
		Reporting										External validity			Internal validity—bias							Internal validity—confounding (selection bias)						Power	
Study	Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Total
Galvao et al. [22]	2006	1	1	1	1	2	1	1	1	1	1	1	1	1	0	0	1	1	1	0	1	1	1	0	0	0	0	5	25
Hanson et al. [24]	2013	1	1	1	1	1	1	1	1	1	0	1	1	0	0	0	1	1	1	1	1	1	1	0	0	0	0	5	23
Santa Mina et al. [25]	2013	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	1	5	28
Segal et al. [26]	2003	1	1	1	1	2	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	5	30
Segal et al. [27]	2009	1	1	1	1	2	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	5	30
Bourke et al. [28]	2011	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	5	30
Bourke et al. [29]	2014	1	1	1	1	2	1	1	1	1	1	0	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	5	28
Cormie et al. [30]	2013	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	5	30
Cormie et al. [31]	2014	1	1	1	1	2	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	5	30
Galvao et al. [32]	2010	1	1	1	1	2	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	5	30
Galvao et al. [34]	2014	1	1	1	1	2	1	1	1	1	1	1	1	1	0	0	1	1	1	0	1	1	1	1	1	1	1	5	29
Park et al. [35]	2012	1	1	1	1	0	1	1	1	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	1	1	1	5	27
Winters-Stone et al. [36]	2014	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	0	1	1	1	1	1	1	1	5	27

Table 3 Study characteristics and main outcomes of the 13 included studies

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
Bourke et al. [28]	2011	Patients n=50: 1. Lifestyle intervention (n=25) 2. Standard care (n=25)	72 years (range 60–87 years)	Sedentary men with PCa, receiving AST for at least 6 months	12	Supervised exercise session: 30-min AE (55–85 % predicted HFmax and/or RPE 11–15 Borg Scale, "fairly light–hard") 2–4 sets RE (body resistance and free weights); large skeletal muscle groups +Health education and encouraging to perform up to 5 exercise sessions per week +Nutrition advice pack	Weeks 1–6: 2× supervised+1 self-directed exercise session (brisk walking, cycling, gym exercise) for 30 min (at least) per week Weeks 7–12: 1× supervised+2× self-directed exercise sessions	Baseline/12 weeks/ 6 months ↑Total exercise behavior (Godin Leisure Score Index, LSI) ↑Dietary behavior (3-day diet diaries: ↓total energy and ↓total/ saturated/ monosaturated fat intake) ↓Fatigue (FACT-F) ↔QoL (FACT-P and FACT-G) ↑Physiologic/functional fitness (aerobic exercise tolerance, sit-to-stand, muscle strength) ↔Anthropometric variables (BMI) ↔Blood samples (baseline, 12 weeks): IGF-1, IGFBP-1, IGFBP-3, plasma insulin, PSA, testosterone, free androgen index, sex hormone-binding globulin
Bourke et al. [29]	2014	Patients n=100: 1. Lifestyle intervention (n=50) 2. Standard care (n=50)	71 years (range 53–87 years)	100 PCaPs on ADT (n=80 locally advanced, n=20 metastatic), receiving ADT for at least 6 months and planned for long-term ADT	12	AE+RE, supervised and self-directed+dietary advice 30-min aerobic exercise (55–75 % predicted HFmax and/or RPE 11–13 Borg Scale; stationary cycles, rowing ergometers, treadmills) RE 2–4 sets, 8–12 reps, beginning at 60 % 1RM, then ↗ Dietary advice: nutrition advice pack+small-group healthy eating seminars (20 min) every 2 weeks	Same as in Bourke et al. [28]	↑(12 weeks), ↔(6 months) disease specific QoL (FACT-P) ↓Patient-reported fatigue (FACT-F) ↑Total exercise behavior (Godin Leisure Score Index, LSI) ↑Aerobic exercise tolerance ↔Blood pressure ↔BMI ↑Dietary behavior (3-day diet diaries: ↓total/ saturated/ monosaturated fat intake)

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
								↔PSA
Cormie et al. [30]	2013a	Patients n=20 Exercise intervention n=10 Control n=10	EI 73.1±7.5 Cont. 71.2±6.9	PCaPs with established bone metastases	12	RE 8 exercises (major upper and lower body muscles); exercise prescription based on the location of the bone lesions (affected regions not targeted); small groups (1–5 PCaPs); supervised Cont.: usual care	2 days per week, ~60 min per session including 5-min warm-up and 10 min cool-down (low level aerobic exercise and stretching), 2–4 sets, 12–8RM, progressive, smooth movements	RE safe and well tolerated ↑Muscle strength (leg extension 1RM) ↑Submaximal aerobic exercise capacity (400-m walk) ↑Ambulation (↑usual and (↑) fast pace 6-m walk) ↔Timed up and go ↔Balance (SOT: Neurocom Smart Balance Master and ABC score) ↑Physical activity level (accelerometer ↑low and (↑) vigorous intensity; ↔GLTEQ) ↑Body composition (whole body and appendicular lean mass) ↔Fatigue (MFSI-SF) ↔QoL (SF-36) ↔Psychological distress
Cormie et al. [31]	2014	Exercise intervention n=32 Control n=31	EI 69.5±6.5 Cont. 67.1±7.5	Initiating treatment with leuprorelin acetate depot (Lucrin®) ≥within 10 days of the first ADT injection	12	AE+RE, supervised Standard warm-up 20- to 30-min AE 8 exercises RE (major upper and lower body muscles) Standard cool-down ≥"Moderate-high intensity aerobic and resistance exercises"	2 days per week ~60 min per session AE 70–85 % of est. HRmax RE 12–6RM (60–85 % 1RM)	↑Cardiorespiratory fitness ↑Body composition ↑Strength ↑ Physical, mental, and sexual function ↓Fatigue (↓)CRP (borderline) ↔BMD ↔PSA ↔Blood biomarkers (triglycerides, insulin, glucose, glycated hemoglobin, vitamin D)
Galvao et al. [22]	2006	RE group n=10	59–82	At least 2 months of ADT received and at least 5 months of ADT to go ADT types:	20	RE only, supervised Weeks 1–10: Hydraulic RE machines, only concentric contractions, 12 exercises (all major muscle groups)	2 days per week 1 h per session 2–4 sets/exercise 12–6RM	↑Cardiorespiratory fitness ↑Muscle strength and endurance ↑Balance

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
				5/10 LHRHa (luteinizing hormone-realizing hormone agonist), 1/10 A (antiandrogen), 4/10 LHRHa+A		Weeks 11–20: Common RE machines, concentric and eccentric contractions, 10 exercises ≥"High intensity progressive resistance training"		↑Some functional tests (StS, 6-m walk, 6-m backward walk, stair climb) ↔6-m fast walk ↔Body composition ↔BMD, BMC ↔Testosterone, PSA, hGH, cortisol, hemoglobin
Galvao et al. [32]	2010	PCaP n=57 1. Resistance and aerobic exercise n=29 2. Usual care n=28	1. EI 69.5±7.3 2. Cont. 70.1±7.3	ADT for >2 months, anticipated to remain hypogonadal for the subsequent 6 months	12	Combined progressive resistance and aerobic training session: 1. General flexibility exercises 2. RE: chest press, seated row, shoulder press, triceps extension, leg press, leg extension, leg curl, abdominal crunches 3. AE: cycling, walking/jogging 4. General flexibility exercises	2 days per week Small supervised groups (1–5 PCaP) RE 12–6RM, 2–4 sets/exercise AE 15–20 min, 65–80 % HFmax and RPE 11–13 Borg Scale (6–20)	↑Whole body and ↑ regional lean mass (upper and lower body, appendicular skeletal muscle) ↑Muscle strength (1RM, muscle endurance) and ↑function ((↑)s-t-s, ↑6-m walk) (↑) Cardiorespiratory capacity (400-m walk) ↔Balance (SOT: Neurocom Smart Balance Master) ↑Dynamic balance (6-m backward walk) (↑)Falls self-efficacy (ABC scale) ↓CRP ↔Testosterone, PSA, insulin, glucose, lipid profile levels, homocysteine ↑General QoL: ↑general health, ↓fatigue (SF-36) ↑Cancer specific QoL (QLQ-C30): ↑role, cognitive, fatigue, nausea, dyspnea; (↑) physical, emotional, pain, insomnia
Galvao et al. [34]	2014	PCS n=100 1. Supervised resistance/aerobic exercise=EI (n=50)	EI 71.9±5.6 PA 71.5±7.2	ADT+radiation therapy (enrolled in RADAR trial)	26 weeks EI+26 weeks to follow-up	1. EI: progressive training, RE+AE: Months 1–6: Supervised session, small group, ~60 min:	1. EI Months 1–6: 2×/week supervised session: RE 12–6RM, 2–4 sets/exercise	Study end points assessed at baseline, 6 and 12 months ↑Cardiovascular fitness (400-m walk)[a]

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
		2. Printed material comprising general physical activity recommendations= PA (n=50)				• RE: 8 exercises (chest press, seated row, shoulder press, triceps extension, leg press, leg extension, leg curl, abdominal crunches) • AE: 20–30 min (walking/ jogging, cycling) Months 7–12: Home-based exercise programme (booklet with detailed info about home exercise), no supervision anymore! 2. PA group: Months 1–12: Pedometer and educational booklet with general recommendation (150 min/ week moderate PA)	AE 70–85 % HFmax and RPE 11–13 (Borg Scale 6–20) 2×/week aerobic exercise session at home Months 7–12: Home-based exercise programme	↑Physical function (repeated chair-rise-test)[a] ↔Blood pressure (SBP, DBP of dominant arm) ↑HDL cholesterol at 12 months[a] ↑Total cholesterol at 12 months[b] Patient-reported outcomes (SF-36)[a]: ↑QoL (role physical, social functioning and mental health at 6 months; role emotional at 12 months) ↔PSA, testosterone Only at Western Australian site (n=57): ↑Dynamic muscle strength (1RM ↑chest press and ↑leg extension)[a] Body composition (DXA): ↑Appendicular skeletal muscle at 6 months[a] ↔Total-body fat mass, trunk fat mass, %fat, est. visceral adipose tissue, total body weight, waist circumference If not mentioned otherwise, the difference occurred both at 6 and 12 months
Hanson et al. [24]	2013	Black PCaP (non-metastatic) receiving ADT n=17	67±2	On ADT since 3.7 years (on average); medication was maintained (93.8 % received LHRHa; 31.3 % bicalutamide)	12	RE only! Keiser machines: Unilateral knee extension, chest press, seated row, seated hamstring curl, abdominal crunch, leg press	3×/week (~60 min each) 1 set per exercise of 15 reps at the 5RM (4–5 reps until exhaustion, weight lowered, next 1–2 reps to exhaustion, weight lowered, etc. until the 15 reps were completed)	↑Body mass, total body muscle mass, upper and lower body muscle mass, appendicular muscle mass ↑Sex hormone-binding globulin (slight increase)

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
								↔Total and free testosterone ↑Thigh muscle volume ↓Body fat ↔Subcutaneous and intermuscular fat ↑Unilateral 1RM strength (knee extensors, chest press, leg press) ↑Muscle endurance (chest press, leg press) ↑Power (absolute and relative) ↑Peak torque ↑Peak velocity ↑Functional tests (5 chair stands, 6-m walk test, TUG, stair climb, 400-m walk) ↓Fatigue ↑Functional Assessment of Cancer Therapy-prostate scores ↑Physical well-being (↑)Functional well-being Relationships: • Improvements in functional performance≡increased muscle strength and power • Improvements in 400 m walk time≡knee extensor 1RM • Increase in 6-m rapid walk≡increase in power • QoL≡fatigue and physical function • Reduction in fatigue (≡) improved muscle endurance
Santa Mina et al. [25]	2013	PCS receiving ADT for study duration (12 months) n=66 AE n=32	AE72.1±8.9 RE 70.6±9.5	Currently receiving ADT for PCa for at least study duration (12 months), non-	24	RE vs. AE (home-based) Exercise+exercise and healthy lifestyle education+supervision (telephone and booster sessions)	3–5×/week (3–60 min each) Individualized training program, moderate to vigorous intensity	Baseline, mid-intervention (3 months), post-intervention (6 months), post-

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
		RE n=34 High attrition rate! (AE n=13, RE n=22 losses until the end of the exercise intervention!)		metastatic, no chemotherapy or radiation		AE: walking/running, swimming, cycling RE: resistance bands, exercise mat, stability ball ≥ball squats, hamstring curls, push-ups, upright rows, triceps extensions, biceps curls, seated row, lateral raises, abdominal crunches on the ball, hip extensions	AE: 60–80 % of HR-reserve ↗ (first volume, then intensity) RE: 2–3×, 8–12 reps, RPE 12–15 (~60–80 % 1RM), 3 levels of intensity: beginner, intermediate, advanced	intervention follow-up (12 months): Effects of AE: From baseline to 3 months: • (↑)Fatigue (FACT-F) • ↓Weight, WC, BMI, chest skinfold thickness • ↑PA volume • (↓)%Body fat From baseline to 6 months: • ↑PA volume • (↓)WC, chest skinfold, %body fat From 6 to 12 months: • (↑) HRQOL (PORPUS) From baseline to 12 months: • ↑PA volume • ↓WC, % body fat • (↑)VO_2peak • (↓)Chest skinfold thickness at 12 months ↔Grip strength Effects of RE: From baseline to 3 months: • ↔ No changes from baseline to 3 months From baseline to 6 months: • ↑ VO_2peak • (↓) Chest skinfold thickness, %body fat From 6–12 months: • ↓ %Body fat ↔Grip strength Between group differences: AE vs. RE at 3 months:[c] • Weight, WC, BMI, PA volume sig. better in AE

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
								AE vs. RE at 6 months:[c] • PA volume sig. better in AE AE vs. RE at 12 months:[c] • PA volume sig. better in AE • HRQOL (PORPUS) sig. better in RE
Park et al. [35]	2012	Elderly PCaPs after radical prostatectomy n=66 EI n=33 (completed n=26) Cont. n=33 (completed n=25)	EI 69.1±5.7 Cont. 69.4±7.2	Exclusion criterion: adjuvant or neoadjuvant therapy	12	EI: resistance, pelvic flexibility and Kegel exercises Cont.: Kegel exercises only Exercise program started at postoperative week 3 PostOP weeks 1–4: adaptation period PostOP weeks 5–8: Ball exercises PostOP weeks 9–12: elastic band exercises	2×/week (60 min each) EI: RE with elastic bands at 50–70 % 1RM; 45–75 % maxHR reserve and/or 9–13 RPE EI and Cont.: Kegel exercises: 3 daily sessions (1 each lying, sitting, standing), 30 reps, –5 s. contraction of the pelvic floor muscles	Primary outcomes: ↑Functional physical fitness (muscle endurance), flexibility, balance ability ↔Grip strength, fat mass, skeletal muscle mass, BMI, waist/hip ratio Secondary outcomes: ↑Continence status ↑QoL (SF-36) physical and mental score EI ↔ QoL (SF-36) physical and mental score Cont. ↓Depression scores EI
Segal et al. [26]	2003	PCS n=155 EI n=82 Cont. n=73	EI 68.2±7.9 Cont. 67.7±7.5	All participants (PCS) receiving ADT for at least 3 months ADT types: EI: Monotherapy n=44 Combined therapy n=38 Cont.: Monotherapy n=30 Combined therapy n=43	12	RE only, supervised, progressive Leg extension, leg curl, calf raises, chest press, latissimus pulldown, overhead press, triceps extension, biceps curls, modified curl-ups Standard warm-up and cool-down exercises	3×/week 2 sets of 8–12 reps at 60–70 % of est. 1RM (starting at 60 %, then ↗) Individual training in fitness center, no training in group	↓Fatigue (13-item fatigue scale: Functional Assessment of Cancer Therapy Fatigue) ↑Health-related QoL (FACT-P) ↑Muscular fitness (standard load test: 20-kg chest press, 40-kg leg press at a cadence of 22 reps/min) ↔Body composition (BMI, waist circumference, skinfolds) ↔Testosterone, PSA
Segal et al. [27]	2009	121 PCaP initiating radiotherapy RE n=40 AE n=40 Cont. (usual care) n=41	Overall 66.3±7.0 RE 66.4±7.6 AE 66.2±6.8 Cont. 65.3±7.6	PCaPs scheduled to receive radiotherapy with or without ADT	24	All training sessions: supervised, warm-up and cool-down: 5 min of light aerobic exercise and stretching RE: leg extension, leg curl, seated chest fly, latissimus pulldown,	RE: 3×/week, 2 sets of 8–12 reps at 60–70 % of est. 1RM, 10 exercises, weight increased when >12 reps AE:	Outcome assessments at baseline, 12 and 24 weeks Fatigue: ↓ RE and AE baseline to 12 weeks vs. Cont.

Table 3 (continued)

Study	Year	Sample	Mean age±SD (years)	Treatment/patient details	Duration of intervention (weeks)	Exercise program details	Frequency, duration and intensity	Key findings/comments
						overhead press, triceps extension, biceps curls, calf raises, low back extension, modified curl-ups AE: cycle ergometer, treadmill, or elliptical trainer	3×/week, starting with 15 min, +5 min every 3 weeks up to 45 min Weeks 1–4 at 50–60 % of VO_2max Weeks 5–24 at 70–75 % of VO_2max	↓ RE baseline to 24 weeks vs. Cont. Sig. positive effects of RE on: QoL, muscular strength, triglycerides, body fat %, VO_2max VO_2max preserved by AE and unexpectedly also by RE! Less reduction in PSA with RE compared to Comp. from baseline to 12 weeks (clinically not important!) No training effect on serum lipid levels
Winters-Stone et al. [36]	2014	51 PCS Training intervention (POWIR) (impact+RE) n=29 Placebo (FLEX) (stretching) n=22	Overall 70.2 POWIR 69.9±9.3 FLEX 70.5±7.8	PCSs on ADT, not currently receiving chemo	52	Progressive, moderate-intensity, RE+impact training (POWIR) vs. control group performing flexibility training only (FLEX) POWIR: (progressive increase in intensity and volume) Impact training (IT): jumps with bodyweight+weighted vest RE lower body: Bodyweight+weighted vest RE upper body: Dumbbells	Baseline, 6 months, 12 months Training 3×/week, 1 h each (2×/week supervised, 1×/ week home-based) IT: 0–10 % of bodyweight in weighted vest, 1–10 sets, 10 reps/jumps each RE lower body: 0-15 % of bodyweight in weighted vest, 1–2 sets, 8–12 reps RE upper body: From 1–2× 12–14 reps at 13–15RM up to 1–2× 8–10 reps at 8–10RM	↔BMD (femoral neck, lumbar spine L1–L4) ↑BMD L4 (preserved in POWIR, loss in FLEX) (↑)BMD L1, L2, L3 ↔Bone turnover (serum osteocalcin, urinary deoxypyrodinoline cross-links)

AE aerobic exercise, *RE* resistance exercise, *PCa* prostate cancer. *PCaP* prostate cancer patient, *QoL* quality of life, *Ca* cancer, *PCS* prostate cancer survivor, *ADT* androgen deprivation therapy, *AST* androgen suppression therapy, *BMD* bone mineral density, *BMC* bone mineral content, *s-t-s* chair sit to stand test, *EI* exercise intervention, *Cont* control; *est.HFmax* estimated maximum heart rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *PA* physical activity, *1RM*, one repetition maximum, *RepMax70 %* maximal numbers of repetitions performed at 70 % of the 1RM; ↗ progressive increase, *SOT* sensory organization test (Neurocom® Smart Balance Master®), ↑ sig. increase, ↓ sig. decrease, ↔ no sig. change/difference, (↑) tendency to increase, (↓) tendency to decrease, ≡ related to

[a] Significant differences between EI and PA in favor of EI

[b] Significant difference between EI and PA in favor of PA

[c] Between-group differences rather underpowered due to high attrition rate!

Table 4 Results of the 8 Additional Articles

Additional article	Year	Expansion	Results
Alberga et al. [39] Additional article of Segal et al. (2009) [27]	2011	Additional differentiation: • Age ≤65 y vs. >65 years • Treatment: ADT vs. no ADT	Age differentiation: Body composition (DXA): • ↑Body fat% in AE and Cont (>65 years); ↔body fat% in RE; RE sig. better than AE/Cont (>65 years) • ↓Lean mass in AE and Cont (>65 years); ↔lean mass in RE; RE sig. better than AE/Cont (>65 years) Aerobic fitness: • ↓VO_2max in Cont (≤65 years); ↔VO_2max in AE and RE; RE borderline better than Cont (≤65 years) Muscular strength (8RM): • ↑Leg extension in AE (≤65 years) and in RE (both age groups); ↔leg extension in Cont (both age groups) and in AE (>65 years); RE sig. better than AE and Cont (both age groups) • ↑Bench press in RE (both age groups); ↓bench press in Cont (>65 years); AE better than Cont (>65 years); RE better than AE and Cont (both age groups) ADT vs. no ADT: No changes in PCaPs without ADT in body composition Changes in PCaPs receiving ADT: Body composition (DXA): • ↑BMI in RE and Cont; ↔BMI in AE; sig. difference AE vs. Cont • ↑Body fat% in AE and Cont; ↔body fat% in RE; RE ↓ Body fat% than Cont; RE (↓) body fat% than AE • ↓Lean mass in AE and Cont; ↔lean mass in RE; RE ↓ loss of lean mass than Cont; RE (↓) loss of lean mass than AE Aerobic fitness: • ↓VO_2max in Cont (ADT); RE ↓ loss of VO_2max than Cont (no ADT) Muscular strength (8RM): • ↑Leg extension in RE (both ADT and No ADT); RE ↑ leg extension than AE and Cont (both ADT and no ADT) • ↑Bench press in RE (both ADT and No ADT); ↓bench press in Cont (ADT); AE ↑ bench press than Cont (ADT); RE ↑ bench press than AE and Cont (both ADT and no ADT)
Buffart et al. [37] Additional article of Galvao et al. (2010) [32]	2014	Mediator analysis	Improvement in physical health was mediated by upper body muscle strength and walking speed Improvement in general health was mediated by walking speed and fatigue
Cormie et al. [40] Additional article of Galvao et al. (2010) [32]	2013a	Additional results Sexual activity and interest	Sexual activity (EORTC QLQ-PR25) EI vs. Cont post intervention: • ↑Sexual activity in EI • ↑Major interest in sex in EI • (↑)Any level of interest in sex in EI Sig. associations: • Change in sexual activity post intervention with change in perceived general health and role-emotional
Courneya et al. [38] Additional article of Segal et al. (2003) [26]	2004	Analysis of predictors for exercise adherence	8 sig. predictors for exercise adherence (weighted) 1. Intention, PBC, subjective norm 2. QoL, fatigue 3. Preprogram overall exercise stage, leg-press test 4. Age Regression equation: Intention+preprogram exercise stage+age explain 20.4 % of the variance in exercise adherence Independent predictors of exercise adherence: • Preprogram overall exercise stage • Age • Intention
Galvao et al. [23] Additional article of Galvao et al. (2006) [22]	2008	Additional results Blood samples	↔PSA, testosterone • ↑hGH (partly: weeks 10–20) • ↑DHEA (dehydro-epiandrosterone) • (↑)IGF-1 (tendency) • ↔Cortisol, CRP • ↑IL-6, IL-8, TNF-α, hemoglobin, monocytes, lymphocytes (partly) • ↑Neutrophils • ↑Alkaline phosphatase, TRACP5b • ↑CK (acute reaction) • ↑Leukocytes (acute reaction) • ↓Leukocytes (chronic reaction)

Table 4 (continued)

Additional article	Year	Expansion	Results
Galvao et al. [33] Additional article of Galvao et al. (2010) [32]	2011	Additional differentiation: • Duration of AST Acute (AST <6 months) vs. chronic (AST ≥6 months) Acute (Ac): n=16 Chronic (Chro): n=34	Age at baseline (Chro sig. older than Ac) Body composition (DXA): • ↔Change in lean mass • ↑Fat mass, ↑%fat (sig. higher increase in Ac than in Chro) • *↔Appendicular skeletal muscle • ↔Waist and hip circumference Blood parameters: • ↑Triglyceride at 12 weeks (sig. higher in Ac) • ↔Testosterone, PSA, insulin, glucose, homocysteine, CRP Performance tests: • *↔Muscle strength and endurance (1RM and RepMax70%) • ↑Chest press 1RM at 12 weeks (sig. higher increase in Chro than Ac) • *↔Physical function (s-t-s, 6 m usual and fast walk) • *↔Cardiorespiratory fitness (400 m) Physical and mental health: • ↔QoL (SF-36) • ↑Physical function, general health, vitality, physical health composite score (sig. higher increase in Chro than Ac)
Mina et al. [41] Additional article of Santa Mina et al. (2013) [25]	2013	Additional results Adipokines and IGF axis	IGF-1, IGFBP-3, and IGF-1/IGFBP-3 ratio: • IGF-1: ↓ in RE at 3 months • IGFBP-3: ↓ in AE at 6 months, ↑ in RE at 6 months • IGF-1/IGFBP-3 ratio: ↑ in AE at 6 months, ↓ in RE at 6 months Correlations at baseline: • Positive between body weight, BMI, WC, body fat % to leptin and leptin/adiponectin ratio • Negative to adiponectin Correlations at 3 months: • Positive between weight changes, BMI, WC to changes in leptin • Between increase in VO_2peak to decrease in leptin • Inversely between IGF-1/IGFBP-3 ratio to changes in weight, BMI and WC and trend to positive corr. to VO_2peak Correlations at 6 months: • Positive between changes in leptin to changes in weight and BMI • Negative to VO_2peak • Positive changes in leptin/adiponectin ratio to changes in weight & BMI • Negative to body fat % • Positive between WC and IGF-1/IGFBP-3 ratio
Winters-Stone et al. [42] Additional article of Winters-Stone et al. (2014a) [36]	2014b	Additional results Physical performance parameters	• ↑1RM leg press • ↑1RM bench press • ↔Objective physical function (PPB) • ↑Self-reported physical function (SF-36 and QLQ-C30) • ↓Self-reported disability (LLFDI) • ↔Fatigue (SCF)

DXA dual energy X-ray absorptiometry, *RE* resistance exercise, *AE* aerobic exercise, *Cont* control group, *VO_2max/VO_2peak* maximal oxygen uptake, *ADT* androgen deprivation therapy, *PCaPs* prostate cancer patients, *BMI* body mass index, *EORTC QLQ-PR25* European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Prostate Module (25 items), *EI* exercise intervention, *PBC* perceived behavioral control, *QoL* quality of life, *PSA* prostate-specific antigen, *hGH* human growth hormone, *DHEA* dehydro-epiandrosterone, *IGF*-1 insulin-like growth factor 1, *CRP* C-reactive protein, *IL* interleukin, *TNF-α* tumor necrosis factor-α, *TRACP5b* tartrate-resistant acid phosphatase 5b, *CK* creatine kinase, *AST* androgen suppression therapy, *Ac* acute, *Chro* chronic, *1RM* one repetition maximum, *SF-36* Short Form-36, *IGFBP-3* insulin-like growth factor binding protein-3, *WC* waist circumference, ↑ sig. increase, ↓ sig. decrease, ↔ no sig., (↑) tendency to increase, (↓) tendency to decrease, * sig. increase in both Ac & Chro, but no group difference

[28, 32, 33] had no impact on testosterone levels in any of the studies (Tables 3 and 4).

Mina et al. [41] found several significant changes in insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) in their additional article of Santa Mina et al. [25] (Table 4).

The effects of RE on human growth hormone (hGH) in PCaPs receiving ADT remain inconclusive [22, 23].

Blood lipids (total cholesterol, LDL and HDL cholesterol, triglycerides)

Cormie et al. [31], Galvao et al. [32, 33, 34], as well as Segal et al. [27] investigated the effects of combined resistance and endurance exercise on blood lipid levels. They showed both none [31, 32], beneficial [27, 34], and detrimental [27, 33] changes (Table 3).

Bone mineral density

Cormie et al. [31], Galvao et al. [22], and Winters-Stone et al. [36] investigated the effects of RE on BMD in PCaPs. Neither combined RE and AE [31], nor RE only [22], nor combined RE and impact training [36] lead to changes in bone mineral density (BMD). Only Winters-Stone et al. [36] reported a significantly better preserved BMD at one measurement site (L4) compared to a stretching exercise routine (Table 3).

Discussion

To our knowledge, this is the first systematic review about the influence of RE on prostate cancer. Previous reviews either focused on general exercise with PCaPs and not specifically on RE [4, 19], or—if RE was the only reviewed training method—the review was not limited to PCaPs [45].

Physical performance is the key outcome in training intervention studies and is a major contributor to health-related QoL in cancer patients [4, 46, 47]. AE is associated with cardiovascular improvements, while RE is associated primarily with an increase in strength and muscle mass in the healthy population. Almost half of the PCaPs receive ADT at some point in their therapy [48–50], either as the single therapy, adjuvant with radical prostatectomy, or adjuvant with radiation therapy [50]. As testosterone levels seem to have a great impact on prevention of the loss of muscle mass [51, 52], the side effects of ADT on body composition—namely a loss of muscle mass and a gain of body fat—are substantial [4, 5, 53]. Therefore, RE obtrudes itself as the most logical type of physical therapy to counteract the negative changes in body composition in PCaPs.

The question to what extend PCaPs are actually trainable seems to be rarely discussed in the literature. Bourke et al. concluded that a supervised exercise program in combination with dietary advice is feasible for men with advanced PCa receiving ADT [28]. However, all studies experienced dropouts in the exercise intervention groups due to individual reasons (Table 5), but not a single dropout was related to the exercise program. Therefore, PCaPs seem to be well trainable with RE stimuli of different intensities and modalities. Nevertheless, for patients suffering from metastatic bone disease, affected bone regions need to be excluded from RE.

Segal et al. [26] were the first to explore the effects of RE only on PCaPs receiving ADT. They found significant improvements in fatigue, QoL, and muscular fitness but no effect on body composition. Segal et al. [27] verified and extended these findings when they performed nearly the same RE protocol a few years later with PCaPs scheduled to receive radiotherapy, and they demonstrated significant improvements not just in fatigue, QoL, and muscular strength but this time also in body fat percentage, triglycerides and unexpectedly even in maximal oxygen uptake (VO_2max).

Segal et al. [22, 27] performed their progressive RE program three times per week with two sets of 8–12 repetitions at 60–70 % of the estimated 1RM. The only difference was the number of exercises and the duration of the training intervention with Segal et al. [22] performing nine exercises in a 12-week training program and Segal et al. [27] ten exercises in a 24-week training intervention. Considering these results, it can be concluded that this kind of training intervention leads to positive adaption in PCaPs and a longer similar training intervention leads to further positive adaptations. These results therefore lead to the question until which duration further improvements could be accomplished with this training regimen?

Santa Mina et al. [25, 41] compared a 24-week long individualized home based AE to a home-based RE program performed with resistance bands, stability ball, and exercise mat. Their main focus was to explore the relationships between training and body composition [25] as well as adipokines and the IGF axis [41]. They concluded that home-based exercise is correlated with positive changes in adipokine levels as well as the IGF axis [41]. Although the exact impact in the prostate cancer environment is still indefinite, positive changes in the IGF axis might be seen as indicators for a lowered prostate cancer risk [41, 54]. RE seemed to be slightly more beneficial on adipokine levels than AE, although they did not detect significant changes in body composition in both groups [41]. They mentioned that, contrary to home based RE, AE in a home-based environment seems to be easier to perform than RE, which in comparison is much more difficult to perform without supervision [25]. They also noted the social importance for cancer patients of being able to share the training experience with a partner, friend, or family member [25].

Galvao et al. [22] performed a supervised high-intensity progressive RE program over 20 weeks. In the initial

Table 5 Dropout analysis

Study	Number of participants	Dropouts	Dropout reasons
Galvao et al. [22]	11	1	Severe respiratory infection (n=1)
Hanson et al. [24]	19	2	Recurring hypotension (n=1), unrelated illness (n=1)
Santa Mina et al. [25]	34	22	Disease progression/death (n=3), too far to travel (n=3), loss of interest (n=3), comorbidities (n=4), no time (n=2), no explanation (n=7)
Segal et al. [26]	82	8	No information
Segal et al. [27]	40	7	No information
Bourke et al. [28]	25	4	Family commitments (n=2), previously undiagnosed cardiac conditions (n=2)
Bourke et al. [29]	50	7	Unrelated medical problems (n=3), accident at home (n=1), developed atrial fibrillation (n=1), family commitments (n=2)
Cormie et al. [30]	10	2	Further treatment (chemotherapy) (n=1), increased bone pain during a 2-week break from intervention over holiday (n=1)
Cormie et al. [31]	32	1	Androgen deprivation therapy side effects (n=1)
Galvao et al. [32]	29	1	No information
Galvao et al. [34]	50	14	Not interested (n=3), health deterioration (n=2), unable to contact (n=1), back pain (n=1), moved away (n=2), working commitment (n=1), surgery (n=1), knee injury (n=1), bone metastases (n=1), deceased (n=1)
Park et al. [35]	33	7	Orthopedic surgery for preexisting ankle problem (n=1), transurethral surgery for a urethral stricture (n=1), long distance from the center/personal affairs (n=4), new employment after surgery (n=1)
Winters-Stone et al. [36]	29	3	Too busy (n=1), disinterested (n=1), deceased (n=1)
Total	444	79	

10 weeks, an introductory resistance exercise program (consisting of 12 concentric exercises) by using hydraulic resistance training machines was performed by the participants. In the following 10 weeks, the exercise program was altered to isotonic RE, which provided concentric and eccentric muscle contractions using similar exercises on different apparatus. After the intervention, a significant increase in muscle strength and endurance, balance, and surprisingly also in cardiorespiratory fitness was reported. The results of some functional tests (sit-to-stand, 6-m walk, 6-m backward walk, stair climb) also significantly improved, whereas further outcomes like body composition, BMD, and 6-m fast walk remained despite ADT stable. Therefore, the authors concluded that progressive RE should be considered to preserve body composition and reduce treatment side effects of ADT.

Beneficial effects on body composition with RE only were reported by Hanson et al. [24]. Seventeen black PCaPs receiving ADT performed a high-intensity strength exercise program consisting of only six exercises (details in Table 3) using Keiser air-powered machines (Keiser Corporation Inc., Fresno, CA). The participants performed exercise three times per week, only a single set per exercise although at a very high intensity. They performed 15 repetitions at their individual five repetition maximum, so they completed the first four to five repetitions until muscular fatigue, then the weight was slightly lowered so that they could complete the next one to two repetitions. This process was repeated until completion of all of the 15 repetitions of the training set. The training weight was progressively altered to reflect the strength gains. The improvements of muscle strength, endurance, and muscle mass indicated that the used exercise program might prevent the loss of muscle mass, strength, and power commonly observed during ADT [24]. Such an exercise program was already shown to improve muscle strength, power, and mass as well as physical performance in healthy sedentary elderly [55]. The fact that these kinds of multiple beneficial responses to high-intensity RE already showed after 12 weeks of supervised training [24] leads to the question if this intervention was superior to the other RE protocols [22, 25–27]. Further investigation into the impact of this kind of exercise intervention is needed.

The importance of muscle strength and its influence on functional performance was shown by Buffart et al. [37] and Holviala et al. [56]. Buffart et al. [37] conducted a study in order to identify mediators of a combined RE and AE program on perceived physical and general health in patients with ADT. The authors concluded that an improvement in physical health was mediated by upper body muscle strength and walking speed while an improvement in general health was mediated by walking speed and fatigue. Holviala et al. [56] stated that both RE and combined strength and aerobic training produce significant improvements in walking speed in aging men, so therefore should be beneficial for both physical and general health. They found out that moderate but significant relationships were observed between muscle strength and walking speed, whereas AE did not show any effect on walking speed [56].

This would explain why the patients of Mina et al. [41] improved their VO2peak in the RE group, while those of the AE group did not. During an aerobic capacity test on an inclined treadmill, PCaPs on ADT might be primarily limited due to their muscular weakness and not because of their limited endurance capacity.

Winters-Stone et al. [36] investigated a combined resistance and impact exercise program with PCaPs. Although they did not report any significant increases in BMD, they found that this exercise program was able to preserve the BMD in the L4 region of the lumbar spine compared to a placebo stretching group [36]. Before, the same exercise program was investigated regarding its effects on BMD in older women and breast cancer survivors [57–59]. Because the lower lumbar spine bears most of the weight when performing RE with free weights or jumping with weighted vests, the question emerges, if resistance and impact exercise with higher loads would have led to preservation of BMD at more skeletal regions. Nevertheless, Winters-Stone et al. [36] showed promising findings, namely that the right mode of RE might lead to positive bone adaptations even in androgen-depleted PCaPs.

When planning exercise and lifestyle interventions for PCaPs, it seems important to notice that education alone does not lead to a healthier behavior [60].

Although, for the moment, a combination of AE and RE seems to be the best treatment modality of ADT side effects in PCaPs, there is still not enough existing knowledge about the effects of different exercise parameters and interventions on some essential parameters like endocrine anabolic indicators (e.g., IGF-1, IGFBP-3, hGH, dehydroepiandrosterone), blood lipids (e.g., triglycerides, cholesterol), markers of the immune system (e.g., C-reactive protein, interleukins, tumor necrosis factor-α), or BMD.

Furthermore, the effects of additional exercise and training interventions like sensorimotor training and/or flexibility exercise on QoL of PCaPs have to be studied.

Therefore, on the one hand, there is great need for further research, namely prospective RCTs, focusing on the effects of various RE parameters and stimuli. Interventions comparing different RE intensities, volumes, frequencies, or durations are needed for being able to identify the most effective and feasible resistance training stimulus for PCaPs fighting their ADT side effects. Because there are not many high-quality RCTs referring to the aim of this systematic review and because of the heterogeneity of the exercise interventions and the outcome measures of the included articles, we did not perform a meta-analysis, which can be seen as a limitation of the present study. Nevertheless, we suggest that a minimum of about 20 high-quality RCTs would be necessary in total for being able to conduct a thorough meta-analysis. After this, a meta-analysis should be performed to support the conclusions of the present study.

Furthermore, on the other hand, at the moment, a combination of various lifestyle interventions [1, 61] seems to be beneficial of attenuating the side effects of ADT, and therefore, a leading role for the so-called clinical comparative research should be considered [62]. This due to the fact that many different lifestyle and treatment factors affect and interfere with outcomes of PCa rehabilitation interventions. Practice-based evidence (PBE) studies designed to collect data as part of the clinical daily routine are able to include and describe the effects of different interventions in a combined rehabilitation plan [62], and to analyze complex rehabilitation interventions "en bloc" and therefore might play an important role in establishing best practice guidelines for PCaPs receiving ADT.

In conclusion, AE seems to be an effective and safe treatment modality to counteract cardiovascular risk factors in PCaPs on ADT, while RE might be the equivalent for the prevention and therapy of weakness, fatigue, loss of muscle mass, and QoL.

For future purposes, an international research group "Exercise interventions in the treatment and rehabilitation of prostate cancer" should be established to increase the number of high quality RCTs in this field, which would be essential for the conduction of a meta-analysis. This future research could increase knowledge and benefit for PCaPs fighting their ADT side effects.

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Ethical Statement This review was written complying the international guidelines of good scientific practice. As this is a review article, no primary data is available but all background information concerning the methodology of the creation of this paper is open for journal review if requested.

References

1. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL (2010) American

College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 42:1409–1426. doi:10.1249/MSS.0b013e3181e0c112
2. Harrison MR, Jones LW (2014) Exercise as treatment for androgen deprivation therapy-associated physical dysfunction: ready for prime time? Eur Urol 65:873–874. doi:10.1016/j.eururo.2013.11.033
3. Cormie P, Newton RU, Taaffe DR, Spry N, Galvão DA (2013) Exercise therapy for sexual dysfunction after prostate cancer. Nat Rev Urol 10:731–736. doi:10.1038/nrurol.2013.206
4. Gardner JR, Livingston PM, Fraser SF (2014) Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: a systematic review. J Clin Oncol 32:335–346. doi:10.1200/JCO.2013.49.5523
5. Ahmadi H, Daneshmand S (2013) Androgen deprivation therapy: evidence-based management of side effects. BJU Int 111:543–548. doi:10.1111/j.1464-410X.2012.11774.x
6. Galvão DA, Spry N, Taaffe DR, Newton RU, Stanley J, Shannon T, Rowling C, Prince R (2008) Changes in muscle, fat and bone mass after 36 weeks of maximal androgen blockade for prostate cancer. BJU Int 102:44–47. doi:10.1111/j.1464-410X.2008.07539.x
7. Galvão DA, Taaffe DR, Spry N, Joseph D, Turner D, Newton RU (2009) Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. Prostate Cancer Prostatic Dis 12:198–203. doi:10.1038/pcan.2008.51
8. Smith MR, Lee H, Fallon MA, Nathan DM (2008) Adipocytokines, obesity, and insulin resistance during combined androgen blockade for prostate cancer. Urology 71:318–322. doi:10.1016/j.urology.2007.08.035
9. Braga-Basaria M, Muller DC, Carducci MA, Dobs AS, Basaria S (2006) Lipoprotein profile in men with prostate cancer undergoing androgen deprivation therapy. Int J Impot Res 18:494–498
10. Dockery F, Bulpitt CJ, Agarwal S, Donaldson M, Rajkumar C (2003) Testosterone suppression in men with prostate cancer leads to an increase in arterial stiffness and hyperinsulinaemia. Clin Sci (Lond) 104:195–201
11. Galvão DA, Taaffe DR, Spry N, Joseph D, Newton RU (2009) Cardiovascular and metabolic complications during androgen deprivation: exercise as a potential countermeasure. Prostate Cancer Prostatic Dis 12:233–240. doi:10.1038/pcan.2009.12
12. Collier A, Gosh S, McGlynn B, Hollins G (2012) Prostate cancer, androgen deprivation therapy, obesity, the metabolic syndrome, type 2 diabetes and cardiovascular disease. Am J Clin Oncol 35:504–509
13. Shahinian VB, Kou YF, Freeman JL, Goodwin JS (2005) Risk of fracture after androgen deprivation for prostate cancer. New Engl J Med 352:154–164
14. Chipperfield K, Fletcher J, Millar J, Brooker J, Smith R, Frydenberg M, Burney S (2013) Predictors of depression, anxiety and quality of life in patients with prostate cancer receiving androgen deprivation therapy. Psychooncology 22:2169–2176. doi:10.1002/pon.3269
15. Benedict C, Traeger L, Dahn JR, Antoni M, Zhou ES, Bustillo N, Penedo FJ (2014) Sexual bother in men with advanced prostate cancer undergoing androgen deprivation therapy. J Sex Med 11:2571–2580. doi:10.1111/jsm.12645
16. Beydoun N, Bucci JA, Chin YS, Spry N, Newton RU, Galvao DA (2014) Prospective study of exercise intervention in prostate cancer patients on androgen deprivation therapy. J Med Imaging Radiat Oncol 58:369–376. doi:10.1111/1754-9485.12115
17. Galvão DA, Taaffe DR, Spry N, Newton RU (2007) Exercise can prevent and even reverse adverse effects of androgen suppression treatment in men with prostate cancer. Prostate Cancer Prostatic Dis 10:340–346
18. Hvid T, Winding K, Rinnov A, Dejgaard T, Thomsen C, Iversen P, Brasso K, Mikines KJ, van Hall G, Lindegaard B, Solomon TPJ, Pedersen BK (2013) Endurance training improves insulin sensitivity and body composition in prostate cancer patients treated with androgen deprivation therapy. Endocr Relat Cancer 20:621–632. doi:10.1530/ERC-12-0393
19. Keogh JWL, MacLeod RD (2012) Body composition, physical fitness, functional performance, quality of life and fatigue benefits of exercise for prostate cancer patients: a systematic review. J Pain Symptom Manag 43:96–110. doi:10.1016/j.jpainsymman.2011.03.006
20. Larkin D, Lopez V, Aromataris E (2013) Managing cancer-related fatigue in men with prostate cancer: a systematic review of non-pharmacological interventions. Int J Nurs Pract NOV. doi:10.1111/ijn.12211
21. Parsons JK (2014) Prostate cancer and the therapeutic benefits of structured exercise. J Clin Oncol 32:271–272. doi:10.1200/JCO.2013.53.4289
22. Galvao DA, Nosaka K, Taaffe DR, Spry N, Kristjanson LJ, McGuigan MR, Suzuki K, Yamaya K, Newton RU (2006) Resistance training and reduction of treatment side effects in prostate cancer patients. Med Sci Sports Exerc 38:2045–2052
23. Galvao DA, Nosaka K, Taaffe DR, Peake J, Spry N, Suzuki K, Yamaya K, McGuigan MR, Kristjanson LJ, Newton RU (2008) Endocrine and immune responses to resistance training in prostate cancer patients. Prostate Cancer Prostatic Dis 11:160–165
24. Hanson ED, Sheaff AK, Sood S, Ma L, Francis JD, Goldberg AP, Hurley BF (2013) Strength training induces muscle hypertrophy and functional gains in black prostate cancer patients despite androgen deprivation therapy. J Gerontol A Biol Sci Med Sci 68:490–498. doi:10.1093/gerona/gls206
25. Santa Mina D, Alibhai SMH, Matthew AG, Guglietti CL, Pirbaglou M, Trachtenberg J, Ritvo P (2013) A randomized trial of aerobic versus resistance exercise in prostate cancer survivors. J Aging Phys Act 21:455–478
26. Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, Venner PM, Quinney HA, Jones LW, Slovinec D'Angelo ME, Wells GA (2003) Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 21:1653–1659
27. Segal RJ, Reid RD, Courneya KS, Sigal RJ, Kenny GP, Prud'Homme DG, Malone SC, Wells GA, Scott CG, Slovinec D'Angelo ME (2009) Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 27:344–351. doi:10.1200/JCO.2007.15.4963
28. Bourke L, Doll H, Crank H, Daley A, Rosario D, Saxton JM (2011) Lifestyle intervention in men with advanced prostate cancer receiving androgen suppression therapy: a feasibility study. Cancer Epidemiol Biomarkers Prev 20:647–657. doi:10.1158/1055-9965.EPI-10-1143
29. Bourke L, Gilbert S, Hooper R, Steed LA, Joshi M, Catto JW, Saxton JM, Rosario DJ (2014) Lifestyle changes for improving disease-specific quality of life in sedentary men on long-term androgen-deprivation therapy for advanced prostate cancer: a randomised controlled trial. Eur Urol 65:865–872. doi:10.1016/j.eururo.2013.09.040
30. Cormie P, Newton RU, Spry N, Joseph D, Taaffe DR, Galvao DA (2013) Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. Prostate Cancer Prostatic Dis 16:328–335. doi:10.1038/pcan.2013.22
31. Cormie P, Galvao DA, Spry N, Joseph D, Chee R, Taaffe DR, Chambers SK, Newton RU (2014) Can supervised exercise prevent treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy: a randomized controlled trial. BJU Int. doi:10.1111/bju.12646

32. Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU (2010) 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. J Clin Oncol 28:340–347. doi:10.1200/JCO.2009.23.2488
33. Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU (2011) Acute versus chronic exposure to androgen suppression for prostate cancer: impact on the exercise response. J Urol 186:1291–1297. doi:10.1016/j.juro.2011.05.055
34. Galvao DA, Spry N, Denham J, Taaffe DR, Cormie P, Joseph D, Lamb DS, Chambers SK, Newton RU (2014) A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 65:856–864. doi:10.1016/j.eururo.2013.09.041
35. Park SW, Kim TN, Nam JK, Ha HK, Shin DG, Lee W, Kim MS, Chung MK (2012) Recovery of overall exercise ability, quality of life, and continence after 12-week combined exercise intervention in elderly patients who underwent radical prostatectomy: a randomized controlled study. Urology 80:299–306. doi:10.1016/j.urology.2011.12.060
36. Winters-Stone KM, Dobek JC, Bennett JA, Maddalozzo JF, Ryan CW, Beer TM (2014) Skeletal response to resistance and impact training in prostate cancer survivors. Med Sci Sports Exerc 46: 1482–1488. doi:10.1249/MSS.0000000000000265
37. Buffart LM, Galvao DA, Chinapaw MJ, Brug J, Taaffe DR, Spry N, Joseph D, Newton RU (2014) Mediators of the resistance and aerobic exercise intervention effect on physical and general health in men undergoing androgen deprivation therapy for prostate cancer. Cancer 120:294–301. doi:10.1002/cncr.28396
38. Courneya KS, Segal RJ, Reid RD, Jones LW, Malone SC, Venner PM, Parliament MB, Scott CG, Quinney HA, Wells GA (2004) Three independent factors predicted adherence in a randomized controlled trial of resistance exercise training among prostate cancer survivors. J Clin Epidemiol 57:571–579
39. Alberga AS, Segal RJ, Reid RD, Scott CG, Sigal RJ, Khandwala F, Jaffey J, Wells GA, Kenny GP (2012) Age and androgen-deprivation therapy on exercise outcomes in men with prostate cancer. Support Care Cancer 20:971–981. doi:10.1007/s00520-011-1169-x
40. Cormie P, Newton RU, Taaffe DR, Spry N, Joseph D, Akhlil Hamid M, Galvao DA (2013) Exercise maintains sexual activity in men undergoing androgen suppression for prostate cancer: a randomized controlled trial. Prostate Cancer Prostatic Dis 16:170–175. doi:10.1038/pcan.2012.52
41. Mina DS, Connor MK, Alibhai SMH, Toren P, Guglietti C, Matthew AG, Trachtenberg J, Ritvo P (2013) Exercise effects on adipokines and the IGF axis in men with prostate cancer treated with androgen deprivation: a randomized study. Can Urol Assoc J 7:E692–698. doi:10.5489/cuaj.235
42. Winters-Stone KM, Dobek JC, Bennett JA, Dieckmann NF, Maddalozzo GF, Ryan CW, Beer TM (2014) Resistance training reduces disability in prostate cancer survivors on androgen deprivation therapy: evidence from a randomized controlled trial. Arch Phys Med Rehabil. doi:10.1016/j.apmr.2014.08.010
43. Downs SH, Black N (1998) The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 52:377–384
44. Prentice AM, Jebb SA (2001) Beyond body mass index. Obes Rev 2:141–147
45. De Backer IC, Schep G, Backx FJ, Vreugdenhil G, Kuipers H (2009) Resistance training in cancer survivors: a systematic review. Int J Sports Med 30:703–712. doi:10.1055/s-0029-1225330
46. Weaver KE, Forsythe LP, Reeve BB, Alfano CM, Rodriguez JL, Sabatino SA, Hawkins NA, Rowland JH (2012) Mental and physical health-related quality of life among U.S. cancer survivors: population estimates from the 2010 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev 21:2108–2117. doi:10.1158/1055-9965.EPI-12-0740
47. Silver JK, Baima J, Mayer RS (2013) Impairment-driven cancer rehabilitation: an essential component of quality care and survivorship. CA Cancer J Clin 63:295–317. doi:10.3322/caac.21186
48. Higano CS (2012) Sexuality and intimacy after definitive treatment and subsequent androgen deprivation therapy for prostate cancer. J Clin Oncol 30:3720–3725. doi:10.1200/JCO.2012.41.8509
49. Harrington JM, Schwenke DC, Epstein DR, Bailey DE Jr (2014) Androgen-deprivation therapy and metabolic syndrome in men with prostate cancer. Oncol Nurs Forum 41:21–29. doi:10.1188/14.ONF.21-29
50. Shahinian VB, Kou YF, Freeman JL, Orihuela E, Goodwin JS (2005) Increasing use of gonadotropin-releasing hormone agonists for the treatment of localized prostate carcinoma. Cancer 103:1615–1624
51. Bhasin S (2003) Testosterone supplementation for aging-associated sarcopenia. J Gerontol A Biol Sci Med Sci 58:1002–1008
52. Yuki A, Otsuka R, Kozakai R, Kitamura I, Okura T, Ando F, Shimokata H (2013) Relationship between low free testosterone levels and loss of muscle mass. Sci Rep 3:1818. doi:10.1038/srep01818
53. Nguyen PL, Alibhai SM, Basaria S, D'Amico AV, Kantoff PW, Keating NL, Penson DF, Rosario DJ, Tombal B, Smith MR (2014) Adverse effects of androgen deprivation therapy and strategies to mitigate them. Eur Urol. doi:10.1016/j.eururo.2014.07.010
54. Rowlands MA, Gunnel D, Harris R, Vatten LJ, Holly JM, Martin RM (2009) Circulating insulin-like growth factor peptides and prostate cancer risk: a systematic review and meta-analysis. Int J Cancer 124:2416–2429. doi:10.1002/ijc.24202
55. Hanson ED, Srivatsan SR, Agraval S, Menon KS, Delmonico MJ, Wang MQ, Hurley BF (2009) Effects of strength training on physical function: influence of power, strength, and body composition. J Strength Cond Res 23:2627–2637. doi:10.1519/JSC.0b013e3181b2297b
56. Holviala J, Kraemer WJ, Sillanpää E, Karppinen H, Avela J, Kauhanen A, Häkkinen A, Häkkinen K (2012) Effects of strength, endurance and combined training on muscle strength, walking speed and dynamic balance in aging men. Eur J Appl Physiol 112:1335–1347. doi:10.1007/s00421-011-2089-7
57. Snow CM, Shaw JM, Winters KM, Witzke KA (2000) Long-term exercise using weighted vests prevents hip bone loss in postmenopausal women. J Gerontol A Biol Sci Med Sci 55:M489–491
58. Winters-Stone KM, Dobek J, Nail LM, Bennet JA, Leo MC, Torgrimson-Ojerio B, Luoh SW, Schwartz A (2013) Impact+resistance training improves bone health and body composition in prematurely menopausal breast cancer survivors: a randomized controlled trial. Osteoporos Int 24:1637–1646. doi:10.1007/s00198-012-2143-2
59. Shaw JM, Snow KM (1998) Weighted vest exercise improves indices of fall risk in older women. J Gerontol A Biol Sci Med Sci 53: M53–58
60. Carmack Taylor CL, Demoor C, Smith MA, Dunn AL, Basen-Enqquist K, Nielsen I, Pettaway C, Sellin R, Massey P, Gritz ER (2006) Active for life after cancer: a randomized trial examining a lifestyle physical activity program for prostate cancer patients. Psychooncology 15:847–862
61. Brown JK, Byers T, Doyle C, Courneya KS, Demark-Wahnefried W, Kushi LH, McTiernan A, Rock CL, Aziz N, Bloch AS, Eldridge B, Hamilton K, Katzin C, Koonce A, Main J, Mobley C, Morra ME, Pierce MS, Sawyer KA (2003) Nutrition and physical activity during and after cancer treatment: an American Cancer Society guide for informed choices. CA Cancer J Clin 53:268–291
62. Horn SD, DeJong G, Deutscher D (2012) Practice-based evidence research in rehabilitation: an alternative to randomized controlled trials and traditional observational studies. Arch Phys Med Rehabil 93(Suppl 2):127–37