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Collaborative Review – Prostatic Disease

Exercise for Men with Prostate Cancer: A Systematic Review and Meta-analysis

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Abstract

Context: Exercise could be beneficial for prostate cancer survivors. However, no systematic review across cancer stages and treatment types addressing potential benefits and harms exists to date.
Objective: To assess the effects of exercise on cancer-specific quality of life and adverse events in prostate cancer trials.
Evidence acquisition: We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, AMED, CINAHL, PsycINFO, SPORTDiscus, and PEDro. We also searched grey literature databases, including trial registers. Searches were from database inception to March 2015. Standardised mean differences (SMDs) were calculated for meta-analysis.
Evidence synthesis: We included 16 randomised controlled trials (RCTs) involving 1574 men with prostate cancer. Follow-up varied from 8 wk to 12 mo. RCTs involved men with stage I–IV cancers. A high risk of bias was frequently due to problematic intervention adherence. Seven trials involving 912 men measured cancer-specific quality of life. Pooling of the data from these seven trials revealed no significant effect on this outcome (SMD 0.13, 95% confidence interval [CI] –0.08 to 0.34, median follow-up 12 wk). Sensitivity analysis of studies that were judged to be of high quality indicated a moderate positive effect estimate (SMD 0.33, 95% CI 0.08–0.58; median follow-up 12 wk). Similar beneficial effects were seen for cancer-specific fatigue, submaximal fitness, and lower body strength. We found no evidence of benefit for disease progression, cardiovascular health, or sexual function. There were no deaths attributable to exercise interventions. Other serious adverse events (eg, myocardial infarction) were equivalent to those seen in controls.
Conclusions: These results support the hypothesis that exercise interventions improve cancer-specific quality of life, cancer-specific fatigue, submaximal fitness, and lower body strength.
Patient summary: This review shows that exercise/physical activity interventions can improve quality of life, fatigue, fitness, and function for men with prostate cancer.

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1. Introduction

Prostate cancer is the primary cause of years lived with cancer disability in the Americas, Northwest Europe, Australia, New Zealand, and much of sub-Saharan Africa [1]. Management of prostate cancer ranges from no intervention (active surveillance or watchful waiting) to radical local treatment (prostatectomy and radiation therapy) with or without combined androgen deprivation therapy (ADT), ADT alone, to taxane-based chemotherapy for progressive castration-resistant disease [2] and second-line hormone agents [3,4]. First-line radical treatment for prostate cancer can negatively impact quality of life (eg, erectile dysfunction, incontinence, radiation proctitis), as can ADT (eg, loss of muscle mass, fatigue, psychological morbidity, higher risk of cardiovascular disease and bone fracture) [5,6]. Direct symptoms for advanced or metastatic cancer (eg, pain, hypercalcaemia, spinal cord compression, pathological fractures) can also adversely affect health [7,8].

Several recent systematic reviews have examined the effects of exercise in cancer survivors in terms of quality of life [9,10], exercise behaviour [11], and fatigue [12]. These reviews cover an amalgamation of heterogeneous primary cancers. Most evidence comes from trials in breast cancer and thus cannot be generalised to men with prostate cancer. Furthermore, exercise therapy appears to be beneficial in the short term, but little is known about dose, duration, and longer-term effects of such therapy, including adverse effects over extended follow-up. Finally, despite the potential health benefits for men with prostate cancer, few clinicians are aware of the role of exercise, and in many cases it goes unprescribed. The aim of this review was primarily to evaluate the effect of exercise interventions on cancer-specific quality of life after prostate cancer diagnosis and to assess adverse effects.

2. Evidence acquisition

Methods for this systematic review have been described in detail elsewhere [13]. In brief, the primary review outcomes were quality of life and adverse events. Secondary outcomes include effects on fatigue, disease progression, cardiovascular health, physical fitness and function, and sexual function.

We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, AMED, CINAHL, PsycINFO, SPORTDiscus, and PEDro databases from inception to March 31, 2015. We expanded the database search by attempting to identify unpublished studies and references in the grey literature (via the OpenGrey database). We also searched the World Health Organization (WHO) trials page, the ISRCTN meta-register of controlled trials (www.isrctn.com), and ClinicalTrials.gov.

2.1. Inclusion and exclusion criteria

We included only randomised controlled trials (RCTs) involving adults in which trial participants had been diagnosed with prostate cancer. Only interventions that included a component targeted at increasing aerobic exercise and/or resistance exercise behaviour compared with a usual care or waiting-list control group with at least 6 wk of follow-up (from trial baseline assessment) were considered in the review. We excluded trials addressing recovery of continence only. Only studies that reported the frequency, duration, and intensity of aerobic exercise behaviour, or the frequency, intensity, type, sets, and repetitions of resistance exercise behaviour as prescribed in the intervention were included in the review.

2.2. Data extraction

After extraction piloting, three review authors (L.B., D.S., and A.C.) worked independently to screen all titles and abstracts to identify records that met the inclusion criteria or that could not be safely excluded without assessment of the full text (eg, when no abstract was available). Disagreements at this stage were resolved by discussion with another review author (D.J.R.). Full-text articles for these records were retrieved. After training to ensure a consistent approach to study assessment and data abstraction, three review authors (L.B., D.S., and A.C.) worked independently to assess the full-text articles retrieved. The selection process is documented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram (Figure 1) [14].

The review authors did not conduct data extraction for any primary studies for which they were listed as an author. Data were entered into the statistical software of The Cochrane Collaboration Review Manager (RevMan 5) for calculation of meta-analyses. Where appropriate, we contacted study authors to request information that was missing from reports for the studies included.

The risk of bias was assessed using The Cochrane Collaboration tool [15]. Two of three review authors (L.B., D.S., and A.C.) applied the risk-of-bias tool independently to each study. Differences were resolved by discussion or by appeal to a third review author (D.J.R.). Review authors did not assess the risk of bias for any studies for which they were an author. The results are summarised in Figure 2.

2.3. Data synthesis

If the data available were sufficient and if it was appropriate to do so, we performed a meta-analysis using Review Manager software. I^2 calculations were performed in STATA. If statistical heterogeneity was noted, meta-analysis was performed using a random-effects model. Fixed-effect models were used only if no significant statistical heterogeneity was present. We noted the time points at which outcomes were collected and reported. If adverse effects data were insufficient or if meta-analysis was not appropriate, we provide a narrative synthesis.

For continuous outcomes (eg, cancer-specific quality of life), we extracted the point estimate for the measure of central tendency for the final value of the outcome of interest and the number of participants assessed at stated follow-up in each treatment arm to estimate the