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Review Article

The Impact of Exercise during Radiation Therapy for Prostate Cancer on Fatigue and Quality of Life: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Radiation therapy (RT) is clinically proven to improve survival in men with prostate cancer. Despite these advantages, it is known to cause adverse effects such as fatigue. This review proposes to summarize the totality of evidence from randomized controlled trials regarding the effectiveness of exercise on fatigue in men with prostate cancer as a primary outcome. Quality of life was a secondary outcome.

Methods: RCTs that explored the effect of exercise during RT on fatigue for men with prostate cancer were searched using MEDLINE, Embase, CINAHL, Cochrane Library, AMED, ClinicalTrials.gov, and ISRTCN registry. Reference lists of included studies and reviews were also examined. Trials were excluded if they included a mixed cohort of patients where data could not be extracted for prostate cancer patients alone or if the intervention took place after RT had finished. Preferred Reporting Items for Systematic Reviews and Meta-Analyses standardized reporting guidelines were followed to ensure the standardised conduct and reporting of the research.

Results: The search strategy yielded a total of 278 studies, of which five met the inclusion criteria. A meta-analysis pooled data of 392 participants using the Cochrane Review Manager 5.3 random-effects model (DerSimonian-Laird approach) with the post-test means of the control and intervention groups and associated standard deviations. Exercise was significant at alleviating fatigue when compared to the control group (standardized mean differences, −1.03; 95% confidence interval, −1.82 to −0.24).

Conclusion: Exercise during RT is an effective approach to alleviate fatigue in men with prostate cancer. The effect on quality of life was not significant, possibly because of considerable heterogeneity across studies.

RÉSUMÉ

Introduction/contexte : Il a été cliniquement démontré que la radiothérapie augmente le taux de survie chez les hommes ayant un cancer de la prostate. Malgré ces avantages, on sait aussi qu'elle a des effets secondaires, comme la fatigue. Cette étude propose de résumer l'ensemble des données probantes provenant des essais randomisés contrôlés (ERC) concernant l'efficacité de l'exercice sur la fatigue chez les hommes ayant un cancer de la prostate comme premier résultat. La qualité de vie était un résultat secondaire.

Méthodologie : les ERC qui explorent les effets de l'exercice durant un traitement de radiothérapie ont fait l'objet d'une recherche dans MEDLINE, EMBASE, CINAHL, Cochrane Library, AMED, ClinicalTrials.gov et le registre de l'ISRTCN. Les listes référencées d'études et d'examen ont également été examinées. Les essais étaient exclus s'ils comprenaient une cohorte mixte de patients dont il n'était pas possible d'extraire les données pour les seuls patients atteints d'un cancer de la prostate ou si l'intervention a eu lieu après la fin des traitements de radiothérapie. Les lignes directrices normalisées de PRISMA pour l'établissement de rapports ont été suivies pour assurer que la conduite de la recherche et l'établissement du rapport soient faits de façon normalisée.

Résultats : La stratégie de recherche a produit 278 résultats, dont cinq études répondant aux critères d'inclusion. Une méta-analyse a permis de regrouper les données de 392 patients à l'aide du modèle d'effets aléatoires de Cochrane Review Manager 5.3 (approche de DerSimonian-Laird) avec un contrôle postérieur de la moyenne du groupe de contrôle et du groupe d'intervention, avec les écarts-types connexes. L'exercice a eu un effet marqué sur l'atténuation de la fatigue en comparaison du groupe de contrôle (SMD −1,03, 95% IC −1,82, −0,24).

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Conclusion : L'exercice durant un traitement de radiothérapie constitue une approche efficace pour atténuer la fatigue chez les hommes atteints d'un cancer de la prostate. L'effet sur la qualité de vie n'était pas significatif, possiblement en raison d'une forte hétérogénéité entre les études.

Keywords: Exercise; prostate cancer; radiotherapy; fatigue; quality of life

Introduction

Prostate cancer is the second most common cancer diagnosed in men worldwide [1]. In 2012, there were an estimated 307,500 mortalities related to prostate cancer, making it the fifth most common cause of death from cancer in men globally [1]. Active treatment strategies vary depending on the extent of the disease, but radiation therapy with or without androgen deprivation therapy (ADT) is widely used across all risk groups as per National Comprehensive Cancer Network guidelines.

Despite the benefits of radiation therapy (RT), it is associated with various adverse effects for patients, including gastrointestinal and genitourinary problems as well as fatigue. Some studies report fatigue as the most common side effect of RT [2,3]. It is general consensus that cancer-related fatigue (CRF) increases in severity in the proportion of 78%–89% of patients during RT [2,4]. CRF is described as the "subjective sensation of lacking energy or being exhausted because of cancer or cancer treatment that is not proportional to recent activity and interferes with daily activities" [5]. Adverse effects such as fatigue are also commonly reported with ADT [5] and can therefore worsen fatigue experienced by patients undergoing combined RT and ADT [6].

Presently, the causes for CRF are not fully understood. Investigations have found correlations of fatigue with hemoglobin [7] and albumin [8] levels as well as psychological conditions such as depression [9]. Though biological conditions such anaemia are predictors for CRF [10], they do not completely explain the occurrence of CRF in the cancer population [11]. One hypothesis of the cause of CRF during RT is the activation of the proinflammatory cytokine network and subsequent increases in biomarkers of proinflammatory cytokine activity caused by RT [11].

In the past, cancer patients who experienced fatigue as a treatment side effect were often advised to avoid strenuous activities and take rest by health care professionals [10]. Dimeo et al. [12] reported that rest is likely to be counterproductive at alleviating fatigue as inactivity leads to muscle wasting and reduced cardiorespiratory fitness, both of which increase fatigue. To this end, several studies have explored the benefits of exercise on CRF. Recent reviews, the majority of which were conducted on breast cancer, have shown benefits of physical activity on fatigue [13–15].

A Cochrane review [16] of 4,068 participants across 56 trials examining breast, prostate, hematological, colorectal, and head and neck cancers found that aerobic exercise significantly reduced fatigue, but resistance training and other forms of exercise did not have a statistically significant effect. A possible reason for this was the smaller sample of participants that underwent resistance training. This review was not specific to RT nor prostate cancer patients. In addition, it included RCTs where the exercise intervention was carried out after treatment was completed. The authors recommended further research to be carried out to establish the optimum type, intensity, and timing of an exercise intervention.

The primary aim of this review was to systematically search, select, appraise, and synthesise the evidence from RCTs focusing on the effects of exercise on fatigue during RT among men with prostate cancer, using meta-analysis. The results of this review may determine the optimal exercise prescription parameters for these men during RT.

Methods

Search Strategy for Identification of Studies

See Appendix A for detailed search strategy.

The following databases were searched for relevant RCTs, from the initiation of each individual database:

- MEDLINE (1966 to 03/10/16)
- EMBASE (1980 to 03/10/16)
- CINAHL (1982 to 03/10/16)
- AMED (1985 to 03/10/16)
- Cochrane Library (1993 to 03/10/16)
- ClinicalTrials.gov
- ISRTCN Registry

A manual search of reference lists of the included trials and review articles relating to exercise and prostate cancer radiotherapy was also carried out.

Type of Studies

Only randomized controlled trials (RCT's) including cluster and quasi trials were included. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses [17] standardised reporting guidelines were followed to ensure the standardised conduct and reporting of the research.

Type of Participants

Eligible trials included participants above 18 years of age, with histologically confirmed stage I–IV prostate cancer, actively receiving RT with or without adjuvant hormone therapy. Trials were deemed unsuitable if participants had already completed RT.

Trials with a mixed cohort of cancer patients where data could not be extracted for prostate cancer alone were excluded.