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Review

The importance of dose in land-based supervised exercise for people with hip osteoarthritis. A systematic review and meta-analysis

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SUMMARY

Purpose: To compare effects of land-based exercise programmes with high vs low or uncertain compliance with dose recommendations among people with hip osteoarthritis (OA).

Design: A systematic review with meta-analyses of supervised exercise programmes in people with symptomatic hip OA was conducted. Dose of the exercise interventions was evaluated according to the American College of Sports Medicine's (ACSM) recommendations for developing and maintaining cardiorespiratory fitness, muscular strength and flexibility in healthy adults. Compliance ratios with the recommendations were calculated. Standardized Mean Differences (SMDs) were calculated in meta-analyses for the outcomes pain and self-reported physical function. Outcome effects were compared between the sub-groups of studies with interventions with "high" vs "uncertain" compliance with the ACSM recommendations.

Results: Twelve studies including 1202 participants were included. Seven were categorized with "high" and five with "uncertain" compliance with the ACSM recommendations. Ten studies had an overall low risk of bias. Comparing exercise with no exercise, the pooled SMD for pain was −0.42 (95% CI −0.58, −0.26) in the high compliance group, favouring exercise. In the uncertain compliance group the pooled SMD was 0.04 (95% CI −0.24, 0.31). For physical function the SMD was −0.41 (95% CI −0.58, −0.24) in the high compliance group and −0.23 (95% CI −0.52, 0.06) in the uncertain compliance group.

Conclusions: The results show that land-based, supervised exercise interventions with high compliance to the ACSM recommendations result in significantly larger improvements in pain and non-significantly larger improvement in self-reported physical function compared with land-based, supervised exercise interventions with uncertain compliance.

Introduction

Systematic reviews of randomized controlled trials (RCTs) have been conducted to evaluate the symptom modifying effect of exercise on pain and physical function for people with hip osteoarthritis (OA). Synthesized results show consistent effect sizes favouring exercise over control for reducing pain and improving physical function[1,2]. The evidence for land-based exercise has been graded as high-quality[1]. However, the reported effect sizes are only small to moderate, which leaves a potential for obtaining larger effect sizes. Yet, the optimal exercise dose for people with hip OA is still unknown, and the mechanisms behind the effects of exercise on pain and physical function in people with OA are poorly understood[1,3,4]. In contrast, the mechanisms behind the effect of exercise on lowering systemic chronic inflammation in other rheumatic diseases, such as rheumatoid arthritis, are better understood[5]. Runhaar *et al.* (2015) have reviewed potential working mechanisms behind the effect of exercise on pain and physical function in OA[6]. They found that increased upper leg strength and range of motion were possible mediators of reduced OA symptoms. Beckwée *et al.* (2013) summarized rationales proposed in the literature to explain mechanisms behind the effect of exercise on OA[4], and a common trait of the rationales was that symptom reduction worked through the physiological response imposed by exercise. Although both these reviews mainly included knee OA

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studies, it is likely that similar working mechanisms and rationales also are valid for hip OA. In the study by Hall *et al.* (2016), cross-sectional data showed that greater lower limb strength may be associated with better self-reported physical function for hip OA patients with moderate to severe limitations in physical function[7]. If the positive effects of exercise work through physiological responses imposed by exercise, exercise interventions must be sufficiently dosed in order to obtain such responses.

The American College of Sports Medicine (ACSM) has developed recommendations for prescribing exercise in apparently healthy adults, including detailed descriptions of recommended dose[8]. A systematic review on progressive resistance training in elderly people showed that the intensity of the training was the strongest factor affecting lower limb strength, with higher intensity leading to more favourable outcomes[9]. On the other hand, a Cochrane review investigating high vs low intensity physical activity or exercise in hip or knee OA could not conclude on the effect of different exercise intensities due to insufficient evidence[3]. RCTs investigating land-based exercise for people with hip OA display a large variety of interventions with regard to type, dose, supervision and adherence[10–21]. Currently, it is not known whether exercise interventions prescribed according to the American College of Sports Medicine's (ACSM) recommendations would show larger effects on pain and physical function compared with interventions with low compliance to these recommendations.

The aim of this systematic review was to compare land-based, supervised exercise programmes with high compliance vs low or uncertain compliance with the ACSM dose recommendations on the effect on pain and physical function in people with hip OA.

Materials and methods

The protocol for this systematic review is registered in the PROSPERO: CRD42016037988.

Search strategy

The databases Ovid MEDLINE, Embase, AMED, Cinahl and Cochrane CENTRAL were searched from inception to April 2016. Appendix 1 shows the full search strategy for Ovid MEDLINE. The searches were developed and conducted by an experienced medical librarian with input from the research team. The search strategy was developed based on the search strategies published in the systematic reviews of Uthman *et al.* (2014)[22] and Juhl *et al.* (2014)[23], and modified to target studies including a hip OA population. Appropriate filters were applied to identify RCTs. The search was restricted to English, Swedish, Danish and Norwegian language. The bibliographies of relevant reviews and retrieved articles were hand-searched for additional studies. When needed, study authors were contacted for additional information.

Criteria for selection of studies

Published RCTs conducted among people diagnosed with symptomatic hip OA who had not undergone hip OA related surgery were included. The intervention could be any land-based exercise programmes including muscular strengthening, flexibility and/or cardiorespiratory exercises. The control intervention could be no treatment or any treatment that was not exercise related. Thus, studies comparing different types of exercise programs were excluded if they failed to have a control group that did not exercise. Studies including a mixed sample of people with hip and knee OA were included if the study authors could provide separate data for the hip OA participants.

Two of the review authors (TM, NØ) independently screened titles and abstracts for studies fulfilling the inclusion criteria. If at least one of the authors judged a study to be eligible, a full text of the article was obtained. The two authors then independently assessed the full-texts for eligibility. If they did not reach agreement a third author (HD) was adjudicated and agreement was reached through discussion. The study selection process is summarized in a flow chart (Fig. 1). Excluded articles read in full text are listed in Appendix 2.

Data synthesis and analysis

Two authors (GS, TM) independently extracted data from the included studies. Data on pain and self-reported physical function were considered primary outcomes and entered directly into Review Manager[24]. Information on recruitment strategy; the participants' background (age, sex and BMI); the use of appropriate tests to measure muscle strength, flexibility and/or cardiorespiratory fitness; exercise dose; length of intervention; number of supervised sessions and adherence to the intervention was extracted. When more than one measure of pain or physical function was reported in a study, we chose the highest one in a hierarchy of outcome measures for pain and physical function[1,25,26]. For studies with multiple follow-ups, data from the immediate post-intervention assessment was extracted. For the results from the individual studies to correspond with a previous meta-analysis, the use of unadjusted post-treatment scores and the associated standard deviation were preferred over adjusted scores and change scores[1].

A narrative approach was used to synthesize the exercise intervention contents with regard to dose and adherence. The prescribed exercise dose in the included studies was evaluated according to the ACSM recommendations for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults[8]. Compliance with the recommendation was independently evaluated by two of the authors (TM, NØ) by scoring each study's exercise prescription on the different criteria defined for each aspect (e.g., intensity, sets, frequency, duration and volume). Fulfilment of the minimum dose of each criterion was scored on a 0–2 point scale. Two points: fulfilled criterion; one point: uncertain fulfilment; zero point: not fulfilled. When a criterion was not reported, it was scored as “uncertain fulfilment”. If the two authors did not reach similar conclusions, a third author was adjudicated and consensus was reached through discussion. Based on this scoring system, we calculated the proportion of compliance with the total ACSM recommendations for each study's exercise prescription. Studies with a compliance ratio of $\geq$75%, were classified as “high compliance with ACSM recommendations”, while studies with a compliance ratio of <75% were classified as “uncertain compliance with ACSM recommendations”.

A meta-analysis was conducted to allow comparison of the results of the included studies. Since the studies used different scales to evaluate continuous outcomes, estimation of Standardized Mean Difference (SMD) in a random-effects model was applied to calculate a pooled treatment effect size. The SMDs were interpreted according to the original guidelines proposed by Cohen[27]: 0.2 small, 0.5: moderate, and $a > 0.8$: large. The impact of prescribed exercise dose was investigated in the meta-analysis by stratifying the studies into the two groups representing high and uncertain prescription compliance with ACSM recommendations.

Heterogeneity among the studies of each subgroup was evaluated using Higgins' I^2 statistics, with an interpretation as suggested by the Cochrane Handbook[28]. Whereas, 0–40% might not be important; 30–60% may represent moderate heterogeneity; 50–90% may represent substantial heterogeneity and 75–100% considerable heterogeneity. Treatment effects of the subgroups

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