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Exercise and bone mineral density in men: A meta-analysis of randomized controlled trials

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ABSTRACT

Objective: Use the meta-analytic approach to examine the effects of ground and/or joint reaction force exercise on femoral neck (FN) and lumbar spine (LS) bone mineral density (BMD) in men.
Methods: Randomized controlled exercise trials ≥24 weeks were included. Standardized effect sizes (g) were calculated and pooled using random-effects models, z-score alpha values and 95% confidence intervals (CI). Heterogeneity was examined using Q and I^2. Statistical significance was set at a two-tailed alpha value (p) of ≤0.05 and a trend at >0.05 to ≤0.10.
Results: A moderate and statistically significant improvement was found at the FN (3 g's, 187 participants, $g = 0.583$, 95% CI = 0.031, 1.135, $p = 0.04$, Q = 5.6, $p = 0.06$, $I^2 = 64\%$) while a small trend was observed at the LS (5 g's, 275 participants, $g = 0.190$, 95% CI = −0.036, 0.416, $p = 0.10$, Q = 3.0, $p = 0.55$, $I^2 = 0\%$). Results were sensitive to influence analysis as well as collapsing multiple groups from the same studies so that only one g represented each study.
Conclusions: There is currently insufficient evidence to recommend ground and/or joint reaction force exercise for improving and/or maintaining FN and LS BMD in men. Additional well-designed randomized controlled trials are needed before any final recommendations can be formulated.

Introduction

Low bone mass (osteopenia) and osteoporosis increase the risk for fracture. For example, it has been estimated that the worldwide incidence of osteoporosis-related fractures is 8.9 million per year, about one every 3 s [1]. The two most common sites for osteoporosis-related fracture are the hip and spine [1].

While the prevalence of osteopenia and osteoporosis is more common in women than men [2], the burden of this problem among men is still substantial. For example, recent data from the US National Center for Health Statistics reported that the age-adjusted prevalence of osteopenia among US men 50 years of age and older was 38% while the age-adjusted prevalence for osteoporosis was 4% [2]. Using the 2010 population estimates from the US Census Bureau [3], this means that approximately 16.8 million US men 50 years of age and older currently have osteopenia while more than 1.7 million have osteoporosis. In addition, fracture-related mortality rates are higher in men than women [4]. For example, men with hip fractures have mortality rates that are two to three times higher than women [5–7]. The issue of fracture-related mortality in men is especially important given that the lifetime risk for any osteoporotic fracture has been estimated to be between 13% and 22% in men 50 years of age and older [8] and 42% in osteoporotic men 60 years of age and older [9]. To compound this problem, it is estimated that by the year 2025, the worldwide incidence of hip fractures occurring in men will increase from 0.5 million in 1990 [10] to 1.16 million in 2025 [11].

Maintaining optimal bone mineral density (BMD) levels in men during the adult years is important for reducing the risk of fracture. While men traditionally reach peak spine BMD by the age of 18 years and peak hip BMD several years later [12], bone loss during the adult years occurs as a result of bone resorption exceeding formation, with reported estimates between 0.5% and 1.0% per year starting as early as 30 years of age [13–16]. One potential, low-cost, readily available non-pharmacologic approach for maintaining optimal BMD levels in men is exercise. Unfortunately, while some consider systematic reviews with meta-analysis as the highest level of evidence for reaching decisions regarding the effectiveness of an intervention on an outcome [17], especially when limited to randomized controlled trials [18], the investigative team is aware of only one meta-analysis, conducted more than a decade ago, focused on the effects of exercise on BMD in men [19]. Included in the meta-analysis were 6 controlled trials and

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only 2 randomized controlled trials in which BMD was assessed at any region [19]. While the results were not statistically significant, the overall benefits of exercise were approximately 2%; a 1.6% increase among exercisers and a 0.4% decrease in controls [19]. When partitioned according to age, a statistically significant benefit of 6.7% (4.2% increase in exercisers, 2.5% decrease in controls) was found in men > 31 years of age with no difference in men ≤31 years of age [19]. In addition, a statistically significant benefit of 10.7% (5.8% increase in exercisers, 4.9% decrease in controls) was observed at the lumbar spine (LS) as well as a 5% benefit at the femur (4.0% increase in exercise groups, 1.9% decrease in controls) [19]. While statistically significant benefits were observed, both randomized and nonrandomized controlled trials were included with only two of the eight studies (25%) reported as randomized controlled trials [19]. In addition, results for the femur were pooled across all femur sites assessed, not just the femoral neck (FN) [19]. The inclusion of nonrandomized controlled trials is potentially problematic because randomized controlled trials are the only way to control for confounders that are not known or measured and nonrandomized controlled trials tend to overestimate the effects of healthcare interventions [20,21]. In addition, since the FN is the most common hip fracture site [22], a focus on this location versus all hip sites combined is important. Furthermore, since this study was conducted more than a decade ago and the median time before a meta-analysis should be updated has been estimated at 5.5 years [23], this work is in need of updating. Given the former, the purpose of this study was to use the aggregate data meta-analytic approach to examine the effects of exercise on FN and LS BMD in men.

Methods

Study eligibility criteria

The a priori inclusion criteria for studies were as follows: (1) randomized trials with a comparative control group (non-intervention, usual care, attention control), (2) men 18 years of age and older, (3) participants not taking part in regular exercise prior to study enrollment, (4) ground and/or joint reaction force exercise intervention of at least 24 weeks, (5) published and unpublished (master's theses and dissertations) studies since January 1989, and (6) data available for changes in FN and/or LS BMD as assessed by dual-energy X-ray absorptiometry (DEXA) or dual-photon absorptiometry (DPA). Studies not meeting all of the above criteria were excluded. Based on exercise-induced changes in BMD, studies were limited to those in which the exercise intervention lasted at least 24 weeks [24]. Since the investigative team was interested in the independent effects of exercise on FN and LS BMD, studies with multiple interventions, for example exercise and milk, were included as long as there was an adequate comparison group, for example, milk only [25]. Resistance training studies were limited to those that included lower body exercise. The year 1989 was chosen as the start date for inclusion since it appeared to be the first time that a randomized controlled trial on exercise and BMD in adult humans was conducted [26].

Data sources

Studies were identified from a large, previously developed reference database that included 1055 exclusive citations (Fig. 1). Records for the original reference database were retrieved from six electronic sources (PubMed, Embase, SportDiscus, Cochrane Central Register of Controlled Clinical Trials, CINAHL, Dissertation Abstracts International). In addition, cross-referencing from retrieved studies, including previous reviews was conducted. Furthermore, hand searching of selected journals took place. A list of journals that were hand searched is available upon request from the corresponding author. Keywords relevant to all searches included various forms of the following: “exercise”, “bone” and “randomized”. All searches were conducted by the second author with assistance from a Health Sciences librarian at West Virginia University, The last search was conducted in August of 2011. Based on the recent Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [27], an example of the search strategy used for one of the electronic databases is shown in Supplementary File 1.

Study selection

Potentially eligible studies were selected autonomously by the first two authors. They then met and reviewed all selections for accuracy. Differences were resolved by consensus. If consensus could not be reached, the third author served as a conciliator. In addition, the final list of selected studies was reviewed for thoroughness and comprehensiveness by the third author, an expert on exercise and BMD. A list of included and excluded studies, including the reasons for exclusion, was stored in Reference Manager, version 12.0.1 [28].

Data abstraction

Prior to data abstraction electronic codebooks were developed using Microsoft Excel 2007 [29]. All codebooks were created by the first author with contributions from the second and third authors. Every codebook was then reviewed and tested by all authors. Codebooks were then modified by the first author and reviewed and tested by all authors until final codebooks for data abstraction were available after three iterations. The main categories of variables coded were (1) study characteristics (journal, risk of bias assessment, etc.), (2) group characteristics (age, bodyweight, etc.) and (3) outcome characteristics (changes in FN and LS BMD, secondary outcomes, etc.). All codebooks could retain up to 324 items from each study.

The a priori primary outcomes for this study were changes in FN and LS BMD. Secondary a priori outcomes included changes in other BMD sites (whole body, Ward's triangle, intertrochanter, trochanter, total hip, radius, ulna, calcaneus, os calcis), body weight, body mass index (BMI), lean body mass (LBM), percent body fat, fat mass, muscular strength (upper and/or lower), muscular power, cardiorespiratory fitness, balance (static and dynamic), calcium intake, vitamin D intake and fractures. The exercise load rating for each exercise group from each study was calculated using the product of vertical ground reaction force and rate of force application as described by Weeks and Beck [30].

All data were abstracted by the first two authors, independent of each other. They then met and reviewed every selection for correctness. Differences were resolved by discussion. If agreement could not be reached, the third author served as a conciliator. Missing data from one study that met all inclusion criteria was requested and successfully obtained [25].

Risk of bias assessment

Risk of bias was assessed using the Cochrane risk of bias assessment tool [31]. Briefly, risk of bias is assessed as either low risk, high risk, or unclear risk in five primary areas: (1) sequence generation, (2) allocation concealment, (3) blinding of participants, personnel and outcome assessors, (4) incomplete outcome data, and (5) selective outcome reporting. Given the objective nature of BMD assessment, all studies were considered to be at a low risk of bias with respect to blinding. Risk of bias for selective outcome reporting was coded as “low risk” only if the study reported a study protocol identification number [32]. All risk of bias assessments were conducted by the first two authors, independent of each other. They then met and reviewed every item for agreement. Disagreements were resolved by consensus.