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Response of bone mineral density, inflammatory cytokines, and biochemical bone markers to a 32-week combined loading exercise programme in older men and women

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A B S T R A C T

This study examines the effects of 32 weeks of exercise training on balance, lower-extremity muscle strength, bone mineral density (BMD) and serum levels of bone metabolism and inflammatory markers in older adults. Forty-seven healthy older adults (women = 24, men = 23; mean age 68.2 years) participated in a exercise intervention (60 min/session) that included resistance exercise training (2 days/week) at 75–80% of maximum plus a multicomponent weight-bearing impact exercise training (1 day/week). Outcome measures included lumbar spine and proximal femoral BMD, dynamic balance, muscle strength, serum levels of bone metabolism markers [osteocalcin (OC), C-terminal telopeptide of Type I collagen (CTX), osteoprotegerin (OPG) and receptor activator of nuclear factor kappa B ligand (RANKL)] and serum levels of inflammatory markers [high sensitive (hs)-C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ]. Potential confounding variables included body composition, dietary intake (using 4-day diet records), and accelerometer-based physical activity. After 32 weeks, both men and women increased dynamic balance (6.4%), muscle strength (11.0%) and trochanter (0.7%), intertrochanter (0.7%), total hip (0.6%), and lumbar spine BMD (1.7%), while OC, CTX, OPG and RANKL levels remained unchanged. In addition, hs-CRP and IFN-γ levels were decreased, while TNF-α levels were unchanged, and a decrease in IL-6 levels was only observed in men. These findings suggest that our combined impact protocol reduces inflammation and increases BMD, balance, and lower-extremity muscle strength, despite having little effect on bone metabolism markers. This reinforces the role of exercise to counteract the age-related inflammation, and the muscle strength, balance and BMD reduction.

1. Introduction

Aging is linked to a reduced amount of bone tissue, which consequently motivates bones to become weaker, commonly leading to osteoporosis (Kostenuik & Shalhoub, 2001). This is a common, serious, and disabling condition due to the inherent association with low-energy trauma or fragility fractures, and with also severe economic consequences (Cummings & Melton, 2002). Increasing evidence has suggested a central role for falls as the strongest single risk factor for a fracture (Peeters, van Schoor, & Lips, 2009). Accordingly, strategies targeting the prevention of bone fractures in the elderly should focus on reducing the risk of

Abbreviations: ANOVA, analysis of variance; B-ALP, bone alkaline phosphatase; BMD, bone mineral density; OC, osteocalcin; CTX, C-terminal telopeptide of Type I collagen; OPG, osteoprotegerin; RANKL, receptor activator of nuclear factor kappa B ligand; hs-CRP, high sensitive C-reactive protein; IL-6, interleukin-6; TNF-α, tumor necrosis factor-alpha; IFN-γ, interferon-gamma; PA, physical activity; BMI, body mass index; MVPA, moderate to vigorous physical activity; ES, effect size; RCT, randomized controlled trial; 1RM, one-repetition maximum.

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falls and maintaining or improving bone health. Mixed loading exercise programs combining impact activity with high-magnitude exercise as resistance training and odd-impact protocols appear effective against aging-induced bone weakness (Marques, Mota, & Carvalho, 2012; Martyn-St James & Carroll, 2009). Despite the importance of bone density in the elderly and their attenuated bone response to physical forces (exercise) (Lanyon & Skerry, 2001), most studies have focused on postmenopausal women.

In addition, experimental animal studies have recently implicated inflammation in the pathogenesis of osteoporosis (Nanes, 2003). The effect is primarily driven on the differentiation and activity of the bone-resorbing cell, the osteoclast; and it is established that pro-inflammatory cytokines suppress osteoprotegerin (OPG) expression while simultaneously enhancing receptor activator of nuclear factor kappa B ligand (RANKL) expression (Schett, 2011). Evidence exists to support a relationship between regular exercise and improvements in systemic low-grade inflammation (Gleeson et al., 2011), even in old age (Ogawa, Sanada, Machida, Okutsu, & Suzuki, 2011), along with in vitro and in vivo experiments (Saunders et al., 2006) suggesting that mechanical stimulation can inhibit osteoclast formation and activity by increasing OPG/RANKL ratio. Nevertheless, to date there are no reports documenting whether changes in bone-related inflammatory cytokines are associated with alterations in BMD in both older men and women after long-term exercise training.

Basic and clinical studies have established the relevance of biochemical markers of bone metabolism, showing an early response following treatment compared with BMD; and was proved to be useful for monitoring therapeutic response and efficacy on individual patients (Garnero, 2008). A combination of markers has been used to evaluate the rate of bone remodeling, including measuring predominantly osteoblastic or osteoclastic enzyme activities or assaying bone matrix components in blood and/or urine (Garnero, 2008). Currently, there are very limited data that have addressed the influence of long-term exercise (>12 weeks) on those biomarkers on older adults (Bemben, Palmer, Bemben, & Knehans (2010); Vincent & Braith, 2002).

Therefore, the aim of the this study was to analyze several bone turnover and inflammatory biomarkers that may be associated with increased BMD after combined loading training in older adults. In addition, the alterations in balance and lower-extremity muscle strength as key factors associated with fall risk were also evaluated. We hypothesized that exercise would improve the bone-related inflammatory cytokines and bone turnover markers. Favorable alterations on BMD, muscle strength and balance were also expected.

2. Materials and methods

2.1. Subjects and experimental design

Subjects were recruited through advertisements in Porto area newspapers for participation in this university-based study. A total of 55 Caucasian older adults (29 women and 26 men) volunteered to participate in the study. The eligible subject pool was restricted to older adults with the following characteristics: aged 60–85 years, community-dwelling status, not engaged in regular exercise training in the preceding year, lack of use of bone-acting drugs and nutritional supplements known to affect bone metabolism (such as vitamin D and calcium) within the previous year, and lack of and significant sensory/cognitive impairment or medical conditions that contraindicated exercise participation. On the initial screening visit, all participants received a complete explanation of the purpose, risks, and procedures of the investigation and, after signing a written consent form, medical history and current medications of the subjects were documented. Participants were instructed to continue their daily routines and to refrain from changing their physical activity levels during the course of the experiment.

Table 1
Baseline characteristics of the sample.

Variable	Women (n = 24)	Men (n = 23)	p value
Age (years)	68.2 ± 5.7	68.2 ± 5.2	0.876
Education (years)	7.9 ± 4.5	8.4 ± 3.6	0.373
Number of routine medications	1.9 ± 1.8	2.2 ± 1.6	0.459
History of cigarette smoking (n/%)	1/4.2	2/8.3	0.525
Anthropometry and body composition			
Weight (kg)	64.2 ± 10.2	83.0 ± 11.7	<0.001
BMI (kg/m^2)	28.6 ± 4.1	29.2 ± 3.4	0.134
Lean mass (kg)	38.4 ± 4.8	54.9 ± 5.9	<0.001
Fat mass (%)	37.8 ± 5.8	27.6 ± 27.2	<0.001
Diet			
Energy intake (kcal/day)	1444.6 ± 345.4	1618.3 ± 496.5	0.169
Protein intake (g/day)	68.7 ± 14.6	71.5 ± 19.4	0.578
Calcium intake (mg/d)	643.7 ± 337.9	658.3 ± 253.3	0.868
Phosphorus intake (mg/day)	988.7 ± 299.6	1049.1 ± 319.2	0.507
Vitamin D intake (μg/day)	1.7 ± 1.9	1.5 ± 1.2	0.619
Coffee intake (mL/day)	62.4 ± 57.0	98.2 ± 48.5	0.025
Daily physical activity			
MVPA (min/day)	80.4 ± 30.6	91.9 ± 31.5	0.294
Daily counts per minute	377.6 ± 123.6	418.1 ± 139.1	0.383
Daily step count	9255.7 ± 3195.2	10,629.1 ± 9668.4	0.614
Bone mineral density			
Lumbar spine (g/cm^2)	0.848 ± 0.121	1.039 ± 0.173	<0.001
Femoral neck (g/cm^2)	0.687 ± 0.108	0.817 ± 0.099	0.001
Lumbar spine (T-score)	−1.8 ± 1.2	−0.4 ± 1.6	0.011
Femoral neck (T-score)	−1.5 ± 1.0	−0.7 ± 0.9	0.014

BMI, body mass index; MVPA, moderate to vigorous physical activity.

The baseline characteristics of the participants are given in Table 1. The study was carried out in full compliance with the Helsinki Declaration, and all methods and procedures were approved by the institutional review board.

2.2. Exercise protocol

The 32-week combined loading training involved odd-impact loading training performed once a week (Wednesdays) and high-magnitude joint reaction force loading through resistance training performed twice a week on separate days (Mondays and Fridays). Each session lasted approximately 60 min, and three physical education instructors specialized in PA for older adults, and supervised by the researchers led all sessions at the University of Porto – Faculty of Sport facilities.

The odd-impact training was designed to load bones with intermittent and multidirectional compressive forces, introducing atypical and novel stress on the bone, and to improve neuromuscular function. Each training session included six different components:

I) A 10-min light stretching and warm-up exercise;
II) 15 min of weight-bearing activities, consisting of stepping exercise at a speed of 120–125 beats per minute using a 15-cm-high bench, bounding exercises, and heel-drops performed on a hard surface – a heel-drop consists of raising the body weight onto the toes and then letting it drop to the floor, keeping the knees locked and hips extended;

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