The osteogenic effect of impact-loading and resistance exercise on bone mineral density in middle-aged and older men: A pilot study

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ABSTRACT

Background: Regular exercise has been recommended as a potential strategy to counteract the age-related bone loss experienced by men, however the optimal exercise prescription is not known.

Objective: To perform a pilot study to examine the osteogenic effect, safety and feasibility of a combined program of upper body resistance exercise and two doses of impact-loading exercise on bone mineral density (BMD) of middle-aged and older men.

Methods: Forty-two community-dwelling men aged 50-74 years were randomly assigned to either an exercise program of combined upper body resistance exercise and either high dose impact-loading (HI, 80 jumps per session) or moderate dose impact-loading (MOD, 40 jumps per session) or a control (CON) group. The nine-month intervention involved four sessions each week: two supervised clinic-based and two home-based. BMD of the lumbar spine, femoral neck, total hip, trochanter and whole body as well as lean and fat mass were assessed at baseline and nine months by dual-energy x-ray absorptiometry. Bone turnover markers, hormone levels, physical function and muscle strength were also assessed.

Results: Following nine months of training, significant differences in BMD among groups were found at the total hip (p=0.010) and trochanter (p=0.047) with BMD in the MOD group decreasing relative to the HI group. Although not significant, the HI group consistently preserved BMD, whereas BMD of MOD and CON groups declined at the hip sites. Mean change for all groups at all skeletal sites was approximately within ± 1%. There was no change in bone turnover markers. There were no adverse events as a result of the intervention, however, overall attendance for the HI and MOD groups was 53% (clinic: 68%, home: 38%) and 65% (clinic: 74%, home: 55%), respectively.

Conclusions: This study indicates that while impact-loading exercise can be safely undertaken in middle-aged and older men, the current combined program did not elicit significant improvements in BMD.

Keywords: jumping, bone-loading, osteoporosis, aging, exercise

Introduction

Approximately one in five men over the age of 50 years will have an osteoporotic fracture in their remaining lifetime [1]. While not all individuals who sustain a fracture have low bone mass, osteoporosis accounts for approximately half of all hip fractures [2]. While regular exercise has been recommended to attenuate the age-related bone loss that is experienced by men and women existing exercise trials to date have generally involved women [3-10]. Results from these trials [3-10] suggest that weight-bearing impact-loading activities, such as jumping, appear to be particularly osteogenic. Meta-analyses of impact-loading trials have shown this type of exercise to be beneficial to hip bone mineral density (BMD) in pre-menopausal women [7] yet only a limited number of impact-loading studies have been trialled in men.

A recent review of trials examining the effect of exercise on the BMD of middle-aged and older men found that those programs involving resistance training alone or in combination with impact-loading exercise appear to be most beneficial for skeletal health [11]. The effect of impact-loading activities in isolation on BMD has only been trialled once in middle-aged or older men [12]. In this recently published 12-month unilateral exercise intervention [12], daily impact-loading (50 multi-directional hops) in 35 older men resulted in a significant difference in femoral neck (FN) BMD between the exercise and control leg with BMD increasing by 0.7% in the exercise leg and decreasing by 0.9% (p=0.003) in the control leg.

Whilst the aforementioned study found impact-loading exercise, as a single modality, to be effective for improving BMD in older men, the optimal exercise prescription of impact-loading exercise is unclear. Dose-response studies in animal models have found that exposure to impact-loading need only be brief [13,14], yet no trial in men or women has addressed the effect of differing doses of impact-loading regimens on BMD.

The present study examined the effect of a combined program of upper body resistance training and two different doses of impact-loading exercise on the primary endpoints of hip and lumbar spine BMD in middle-aged and older men. The pilot study was undertaken to examine not only the osteogenic effect, but also to determine the safety and feasibility of impact-loading training in middle-aged and older men. It was hypothesized that the BMD of men in the exercise groups would increase or at least be preserved, whereas the BMD of those in the control group would decline. Furthermore, it was hypothesized that improvements in BMD would be greater in the high dose than the moderate dose exercise group. Finally it was hypothesized that the training regimen would be safe and feasible.

METHODOLOGY

Study Design and Randomization

In this nine-month pilot randomized controlled dose-response trial, 42 participants were randomized into: 1) upper body resistance exercise and high-dose impact-loading (HI); 2) upper body resistance exercise and moderate-dose impact-loading (MOD); or 3) a control (CON) group. Group allocation was concealed from the tester and participants until after the initial testing session was completed.

Participants

Men aged 50 years and older were recruited from Brisbane (Queensland, Australia). Participants were excluded during pre-screening if they had cardiovascular, neurological, metabolic or musculoskeletal disorders (including osteoporosis or vertebral crush fractures) that may have prevented their safe participation in the testing or exercise sessions or were taking medications known to affect bone metabolism. Further, individuals were excluded if they had

been involved in regular resistance training (two or more times per week), regular jumping activities (two or more bouts of at least 10 minutes per week) or sports involving jumping activities (e.g. volleyball or basketball) for the 12 months prior to recruitment. Medical consent from participants' general practitioner was sought prior to the initial testing session. The study was approved by The University of Queensland Medical Research Ethics Committee and written informed consent was obtained from all participants.

Exercise Program

The main component of the exercise intervention was the impact-loading activities; however, upper body resistance training exercises were included to increase the appeal of the clinic exercise sessions for the participants. For both the HI and MOD groups, the nine-month exercise intervention involved exercising four days per week; two supervised sessions of combined impact-loading and upper body resistance exercise on non-consecutive days in an exercise clinic and two sessions of impact-loading alone on days alternate to the clinic sessions at the participant's home. The only difference between the HI and MOD exercise regimens was the number of impacts (jumps) performed during each session. Each clinic session was approximately 60 minutes in duration and consisted of: 1) a 5-min warm-up and cool-down on a stationary cycle ergometer as well as static muscle stretching activities, 2) impact-loading exercises, and 3) upper body resistance exercises. The sessions were conducted in small groups (≤ eight participants) and supervised by an exercise physiologist.

The clinic impact-loading protocols for the HI and MOD groups are shown in Table 1. Activities included multi-directional jumping (cross jumping), drop jumping from steps and bounding over soft foam hurdles of varying heights (detailed in Table 1). The initial two months of the supervised sessions were used as a conditioning period and thereafter the HI and MOD

groups were asked to complete 80 and 40 jumps per session, respectively. Participants were instructed to land on their heels with approximately 5° knee flexion on impact. Rest periods of 1 min were inserted between each set of jumps. The peak ground reaction forces (GRF) were measured in a subgroup of five individuals. The mean ± SD and ranges of GRFs were 4.6 ± 0.9 (range, 3.0-5.9) times body weight (BW) for multi-directional jumping, 5.6 ± 1.2 (4.7-6.9) and 5.7 ± 1.6 (4.7-7.3) times BW for the 10 and 20 cm hurdles, respectively, and 5.1 ± 0.7 (4.4-6.1) and 5.8 ± 0.8 (5.0-6.9) for the 10 and 20 cm drop jumps, respectively.

The resistance training regimen completed during the clinic sessions consisted of biceps curl, triceps extension, latissimus pull down and chest press. Machine resistance training equipment (Selection MED, Technogym, Cesena, Italy) was used for all exercises with the exception of the biceps curls, where free weight dumbbells were used. Participants completed two sets of 12 repetitions at 60% of their 1-repetition maximum (1-RM) strength. In addition to the sessions conducted at the exercise clinic, participants were asked to complete twice weekly home-based impact-loading sessions. Home sessions for the HI and MOD groups consisted of a total of 80 and 40 impacts, respectively (HI: 40 multi-directional and 40 vertical jumps, MOD: 20 multi-directional and 20 vertical jumps). Exercise attendance at the clinic and home sessions were recorded by the participants and monitored by the exercise physiologists. A minimum attendance was not defined.

Measures

Before and immediately following the nine-month intervention period, participants completed a series of tests conducted by the same investigator using the same equipment.

Primary Endpoints

Total hip, FN, trochanter and lumbar spine BMD (g/cm²) were derived by dual-energy x-ray absorptiometry (DXA, Hologic Discovery W, Waltham, MA). Scans were analysed using software (APEX Version 3.3) provided by the manufacturer (Hologic, Bedford, USA) and according to the manufacturer's instructions. The coefficient of variation (CV) in our laboratory (Brisbane, Australia) for total hip, FN, trochanter and lumbar spine BMD are <1.0%.

Secondary Endpoints

Markers of bone formation and resorption, bone-specific alkaline phosphatase (BAP) and C-terminal telopeptides of type 1 collagen (CTX-1), respectively, were assessed from venous blood (6 mL) collected by a qualified phlebotomist. Serum samples were allowed to clot in 6 mL tubes for 30 min and then centrifuged at 5500 x g at 4˚C for 10 min. CTX-1 (β-CrossLaps/serum assay) was analyzed using a Roche Cobas e411 electrochemilumescence immunoassay autoanalyzer (Roche Diagnostics, Switzerland) whilst BAP was measured using the Ostase BAP immunoenzymatric assay. The CVs in our laboratory (Brisbane, Australia) CTX-1 and BAP are 2.3% and 6.6%, respectively.

Additional Measures

Height and body mass were measured using a stadiometer (Seca, Birmingham, United Kingdom) and electronic scales (A & D Mercury, Pty Ltd, Thebarton, Australia), respectively. Whole body BMD, fat mass (FM), percentage body fat and whole body, arm and leg lean mass (LM) were derived from the whole body DXA scan. In addition, appendicular LM was calculated from the sum of arm and leg LM. The CVs in our laboratory (Brisbane, Australia) for whole body BMD, LM, FM, and % body fat are <1.0%. Dynamic lower body maximal muscle strength (leg press) was measured using the 1-RM method. The 1-RM is the maximal

weight an individual can move through a full range of motion with correct technique [15]. Functional performance tests included the repeated chair rise [15], stair climb [16], 6 m backward tandem walk [15], 6 m usual and fast walk [17], and the 400 m walk [18].

Repeated chair rise: Participants sat in a hard-backed chair with a seat height of 43 cm. They were instructed to rise into a full standing position then return to a full-sitting position as quickly as safely possible five times.

Stair climb: Participants were instructed to ascend a flight of stairs (11-stair flight, with a 16 cm rise) as quickly as safely possible, avoiding the use of the handrail unless necessary.

6 m backwards tandem walk: Participants were instructed to walk a 6 m distance along a line using a backward heel-to-toe protocol as quickly as safely possible.

Usual pace and fast 6 m walk: Two measures of gait speed were undertaken; (i) usual pace, in which participants were instructed to walk at a pace they commonly would during daily activities, and (ii) a fast pace in which participants were instructed to walk as quickly as safely possible.

400 m walk: Participants were asked to walk out and back along a 20 m course, 10 times in succession, and to complete this 400 m course as quickly as safely possible.

The CVs in our laboratory (Brisbane, Australia) for the 1-RM strength tests and physical function tasks are 2.0-7.5%. All participants in the study were asked to maintain customary physical activity patterns over the duration of the intervention period and this was assessed by the Godin Leisure-Time Exercise Questionnaire [19].

Testosterone, estradiol, SHBG and vitamin D (Elecsys assays) were analyzed using a Roche Cobas e411 electrochemilumescence immunoassay autoanalyzer (Roche Diagnostics, Switzerland). Calcium (Calcium Arsenazo III Reagent) was analyzed using a Roche Cobas Mira electrochemilumescence immunoassay autoanalyzer. The CVs in our laboratory

(Brisbane, Australia) for testosterone, estradiol, SHBG, vitamin D, and calcium are 2.3%, 7.7%, 3.9%, 4.8%, and 1.4%, respectively.

Statistical Analysis

To achieve 80% power at an alpha level of 0.05 (two-tailed), 15 participants per group were required to demonstrate a 1 standard deviation (SD) pairwise difference between groups at each bone site at the end of the nine-month intervention. Data were analyzed using the IBM SPSS (Statistical Package for the Social Sciences) 20 statistical package for Windows (SPSS, Chicago, IL, USA). Normality of the distribution for outcome measures was assessed using the Kolmogorov-Smirnov test. Analyses included standard descriptive statistics, one-way ANOVA, paired t-tests, and Pearson correlation coefficients or their non-parametric equivalents as appropriate. ANCOVA adjusted for baseline values and body mass was used for the primary endpoints and ANCOVA adjusted for baseline values for the secondary endpoints. Whole body BMD, 1-RM leg press, 6-m usual walk, sit-to-stand, testosterone, SHBG and vitamin D were log transformed prior to ANCOVA analyses. All tests were 2-tailed and statistical significance set at $p \leq 0.05$. An intention-to-treat approach was used for the analyses with missing values replaced using the expectation-maximization method [20]. Results are provided as mean±SD unless stated otherwise.

RESULTS

Participant Characteristics

A total of 140 men were pre-screened, 95 men were excluded and 45 men were invited to participate in baseline testing (Figure 1). Three participants were excluded following baseline testing because their BMD T-score was ≤ -2.5 SD resulting in 42 participants. Participant characteristics are presented in Table 2. There were no significant differences among groups

for age, height, body mass, body composition, BMD, physical performance, blood markers or physical activity level. Participants in the HI, MOD and CON groups had a mean T-score of -0.4, -0.6 and -0.5 at the total hip, -0.9, -1.3 and -1.0 at the FN, -0.4, -0.4 and -0.2 at the trochanter and -0.3, -0.2 and -0.9 at the lumbar spine, respectively, with no significant difference among groups at any site.

Attendance and Dropout

Overall average attendance rates and ranges for the HI and MOD groups was 53% (5-94.5%) (clinic: 68% (10-100%), home: 38% (0-90%)) and 65% (15-98.5%) (clinic: 74% (31-99%), home: 55% (0-100%)), respectively. There were no between-group differences for total (p=0.334), clinic (p=0.576) or home program attendance (p=0.345). Six of the 42 men withdrew from the study over the nine-month period (HI n=3, MOD n=2, CON n=1). The reason for withdrawal included time constraints (n=3), pre-existing injury (n=1), family illness (n=1) and one participant in the CON group could not be contacted at nine months (Figure 1).

Bone Mineral Density

Absolute values and adjusted mean changes between groups are shown in Table 3. Significant differences among groups were found at the total hip (p=0.010) and trochanter (p=0.047) with BMD in the MOD group decreasing relative to the HI and CON group at the total hip and the MOD group decreasing relative to the HI group at the trochanter. There were no significant between-group changes for whole body (p=0.801), FN (p=0.147) or lumbar spine (p=0.348) BMD; mean change for all groups at all skeletal sites was within ± 1% (Figure 2). Within the exercisers, baseline BMD was not associated with change in BMD (r=-0.313 – 0.076, p=0.105 – 0.869) nor was there a difference between those classified as osteopenic at the hip (n=8) versus those with normal bone density (n=20) for any measurement site (p=0.324 – 0.835).

In addition, there were no significant relationships between total attendance, testosterone, estradiol, calcium nor vitamin D and change in BMD in the HI or MOD group as shown in Table 4. The two exceptions were the inverse relationships between testosterone and lumbar spine BMD in the MOD group (r= -0.60, p=0.04) and vitamin D and whole body BMD in the HI group (r=-0.66, p=0.04). Moreover, there were no significant differences in BMD at any measurement site between participants who attended at least 70% of the exercise sessions and those who did not. Likewise, there were no significant differences in BMD at any measurement site between participants <60 years of age and those 60 years and older.

Bone Turnover Marker

There were no significant differences among the groups at nine months for BAP (p=0.982) or CTX-1 (p=0.866)

Additional Measures

There were no significant between group changes for whole body LM, fat mass, percentage body fat or 1-RM leg press, however, there was a significant difference between groups for arm LM with the HI group's LM increasing relative to the CON group at nine months (p=0.005) with an adjusted difference of 0.3 kg (95% CI, 0.1 to 0.6). In addition, there were no significant differences among groups at nine months for the 6 m usual walk, backwards tandem walk, stair climb or sit-to-stand test, although there was a significant difference among groups for the 6 m fast walk (p=0.002) with the MOD group's performance improving relative to both the HI and CON groups with an adjusted difference of -0.21 sec (95% CI, -0.36 to -0.06) and -0.19 sec (95% CI, -0.34 to -0.04), respectively. There were no significant differences among the groups at nine months for physical activity using the Godin Leisure-Time Exercise Questionnaire

(p=0.431). There was no change in testosterone, estradiol, vitamin D or blood calcium levels over the course of the study among the groups (p>0.05)

Adverse Events

There were no adverse events as a result of the testing or exercise sessions. One participant in the HI dose group was diagnosed with an inguinal hernia during the study period, however after 3 weeks rest his physician permitted him to return to the study.

DISCUSSION

This was the first trial to compare the effect of two differing doses of impact-loading exercise on the BMD of middle-aged and older men. The main finding from this study was that although the program was well tolerated, there were no significant improvements in BMD in either exercise group, with total hip BMD declining in the MOD group relative to the HI and CON groups and trochanter BMD declining in the MOD group relative to the HI group at nine months.

A unique component of the current study was examination of the effect of two differing doses of impact-loading exercise on BMD. While neither of the two exercise regimens in the current trial significantly improved BMD and a consistent dose-response effect was not found, it is a promising finding that although not statistically significant, the HI exercise group did preserve BMD, while the MOD group generally lost BMD. Trials in women have included jumping regimes ranging from 10-100 impacts, two to six sessions per week and training periods of six to twenty-four months [7]. While Kato et al. [21] reported that 10 jumps three times each week was sufficient to illicit significant changes in FN and lumbar spine BMD of college-aged women, the majority of trials that reported a positive effect in women have generally included

50 or more jumps per session [22-25]. One explanation for the success of the relatively brief jumping protocol in the trial by Kato et al. [21] may be that the vertical jumps (GRF of 4.8 BW) were performed barefoot. Consequently, although the GRF reported in the trial by Kato et al. [21] are comparable to those in the current trial, the use of footwear worn during the jumping exercises in our study may have dampened the osteogenic effect of the activity. The role of footwear and the material shock absorption characteristics of differing types of footwear should be investigated in future studies.

Unexpectedly, the MOD group experienced a modest decrease in BMD at the hip. This pattern cannot be described by attendance differences between the exercise groups, or by outliers in the MOD group. Moreover, there was no change in testosterone, estradiol, vitamin D or blood calcium levels over the course of the study among the groups. While participants were asked to maintain customary diet and physical activity patterns over the course of the study, these were not monitored. Consequently, this unexpected reduction, albeit modest, in hip BMD may have been the result of alterations in weight-bearing physical activity during the course of the study.

Neither of the two exercise regimens in the current trial significantly improved BMD. A recent randomized controlled trial of hopping (50 jumps each session) for six months in pre-menopausal women examined the effect of differing session frequencies on BMD [22]. The authors concluded that while the change in BMD for the control group was -0.3%, those jumping two days per week maintained FN BMD (0.0%) and increases were only seen in the groups that jumped four (0.9%) and seven (1.8%) days per week. While the effect was more modest than seen in the study by Bailey and Brooke-Wavell [22], the trial in older men by Allison and colleagues [12] found that daily hopping for 12 months could significantly increase

FN BMD. While there were no significant differences between the groups for total, clinic or home-based attendance in the current study, it should be noted that the attendance of both groups was poor, particularly for the home-based exercises. Higher attendance rates would have allowed for a more accurate understanding of the effects of the regiment on BMD. Therefore, the session frequency in the current trial, due to the poor attendance, may partially explain why BMD did not significantly increase in either exercise group. Future trials should examine the effect of daily impact-loading on BMD of middle-aged and older men and include motivational strategies to optimize attendance rates.

Reviews of exercise and bone health in adults generally suggest that interventions should include resistance and impact-loading exercise and be at least 12 months in duration to detect changes in BMD [3]. However a number of impact-loading studies in women have reported improvements in BMD after only six or nine months of impact-loading. For instance, an early study in premenopausal women by Bassey & Ramsdale [25] showed a significant change in BMD of 3.4% at the trochanter after six months training. Whether differences among groups in the present study may have been observed with a longer duration intervention (for example 12 or 18 months) remains to be elucidated.

Impact-loading studies that examine the effect of rest intervals have not yet been conducted in human trials. However, results from the trials that have investigated the effect of rest breaks in animal trials have shown that the approximate time required for bone cells to re-sensitize to mechanical stimuli is 10-15 sec [26,27]. Trials that specifically examine the effect of rest breaks on the osteogenic potential of impact-loading in humans are required before definitive conclusions can be made on whether one minute was sufficient in the current trial.

Similar to the effects on BMD, no consistent significant changes in bone turnover markers were found between the exercising groups and the control group following the intervention. Although studies of other modalities of exercise have reported changes in bone turnover markers in older men and in response to sports [28,29], the current study is one of only two combined impact-loading and resistance exercise studies in men to measure bone turnover markers. The other study by Kukuljan et al. [30] found a significant increase in ALP, however bone-specific ALP was measured in the current study, making comparisons between the two difficult. While studies (five to eight weeks in duration) have reported differences in bone turnover markers [29], longer duration impact-loading studies similar to the current study, but conducted in women, found no differences in bone turnover markers following a 12-month RCT [31].

This was the first trial to measure the effect of impact-loading activities on lower body muscle strength and physical function. While the upper body resistance training exercise increased upper body LM of the HI exercise group in comparison to the CON group, the 9-month exercise program did not significantly improve lower body muscle strength or any of the measures of physical function, with the exception of the 6 m fast walk time, which improved in the MOD group. Although these changes in LM and walking speed are of interest it should firstly be noted that the magnitude of change was modest between groups and were not the result of outliers. Nevertheless, the difference in lean mass between the MOD group and the HI and CON groups may have been due to a number of factors. Although participants were asked to maintain customary physical activity and dietary patterns, differing dietary intake (specifically protein) or physical activity participation (external to that in the intervention) over the nine months may explain this small but unexpected difference in lean mass between the groups. Anabolic hormone levels may also contribute to differences in LM accretion, however, we

measured testosterone at baseline and following the intervention and found no difference. Nevertheless, we can't discount that there may have been differences in the acute testosterone response which could account for LM differences between training groups. Furthermore, the differences in walking speed between the groups were approximately 0.2 of a second (<1%) and changes in factors not assessed in this study such as lower limb muscle mechanics may partially explain this unexpected difference. These results suggest that impact-loading exercise, at least in the training doses undertaken in this trial, is not an effective modality to improve lower body lean mass, strength or physical function of middle-aged and older men.

In the current trial, the impact-loading activities were well tolerated and did not cause any adverse events. Impact-loading with heel landings have been safely performed in a similar trial in older women [23]. Although impact-loading has shown to be beneficial and well tolerated, high-impact activities with a heel landing may not be suitable for individuals with injuries, particularly of the lower extremities or with certain medical conditions, such as incontinence. In addition, high impact-loading exercise is currently not recommended for individuals with osteoporosis because of the potential increased risk for fracture.

Although changes in sex hormones, nutrition and bone loading contribute to bone loss across the lifespan in men and women, sex-specific differences exist [32,33]. The decline in BMD in men up to the age of 50 years and in pre-menopausal women is approximately 0.3% to 1.1% each year [34], with an increased rate of bone loss in women for four to eight years following menopause [35] due to estrogen withdrawal. During this period, women will lose approximately 15% in BMD leading to a 1.5- to 3-fold increase in fracture risk [36,37]. In contrast, the decline in bone mass for men is more gradual with a loss of ~ 0.7% per year after age 50 [34]. Nonetheless, approximately one third of all osteoporotic fractures are accounted

for by middle-aged and older men [38] and so better understanding the role exercise may have in attenuating bone loss of men in this age group is of great importance.

This study has several limitations worthy of comment. Although BMD derived by DXA is the accepted clinical measure of skeletal health, there are inherent inaccuracies in this method of measurement and it does not provide information regarding changes in bone geometry. The home program component of this trial was not well adhered to; future studies should consider that unsupervised sessions may not be suitable for this type of exercise or should investigate strategies to improve adherence to this type of exercise in the home setting. This study was powered to detect large differences, while the effect sizes found were small to moderate. As such, a substantially larger sample size would have been required to detect these small effects. The men in this trial were screened for medical conditions that may have prevented their safe participation in testing or training and were volunteers in an exercise study, and this should be considered when drawing conclusions based on the results from this study. In a similar fashion, the training exclusion criterion for the current trial prevented resistance trained individuals or those who were performing regular impact-loading activities from participating in the trial; future trials should investigate the effect of impact-loading activities on the BMD of men with differing training status to those in the current trial. Furthermore, in general, the men in the present study had normal bone density; whether the exercise protocol may be more effective for those with poorer skeletal health (e.g. men with osteopenia) remains to be elucidated. To standardize jump height within and between groups, the 40 and 80 impacts were performed in bouts of 10 impacts with 1 min rest periods between bouts; identical instructions were provided by the supervisors. Despite this, it may have been the case that the greater number of jumps performed by the HI group may have resulted in progressively smaller jumps in this group. Future trials should aim to develop methods to better standardize the height of the jumps

performed. Habitual diet and physical activity patterns of the participants were not recorded during this nine-month trial, and alterations, if they occurred, may help explain the changes in lean mass in the current study. Finally, the participants were not required to empty their bladders or be in a fasted state during the DXA scans. While this protocol would not have affected the precision of the bone mineral density measurements, it is possible that it may have affected, albeit minimally, the measurement of lean mass in the current study.

The results of this study indicate that while impact-loading exercise can be safely undertaken in middle-aged and older men, the current combined exercise program did not illicit significant improvements in BMD. Additional exercise trials are needed to establish the optimal exercise prescription to improve bone density in middle-aged and older men.

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Disclosures and competing interests

The authors do not have any conflicts of interest nor any competing financial interests in relation to the work described.

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Table 1 Clinic impact-loading protocol

	HI			MOD		
Month	**Exercise**	**Sets & repetitions**	**Total number**	**Exercise**	**Sets & repetitions**	**Total number**
1 Conditioning	Cross jumping	2 x 8	40	Cross jumping	1 x 8	20
	Drop jumping (10 cm)	2 x 12		Drop jumping (10 cm)	1 x 12	
2 Conditioning	Cross jumping	4 x 8	60	Cross jumping	2 x 8	30
	Drop jumping (10 cm)	2 x 14		Drop jumping (10 cm)	1 x 14	
3-5	Cross jumping	4 x 8	80	Cross jumping	2 x 8	40
	Drop jumping (10 cm)	2 x 14		Drop jumping (10 cm)	1 x 14	
	Bounding (7 cm)	4 x 5		Bounding (7 cm)	2 x 5	
6-7	Cross jumping	4 x 8	80	Cross jumping	2 x 8	40
	Drop jumping (15 cm)	2 x 14		Drop jumping (15 cm)	1 x 14	
	Bounding (7 cm)	4 x 5		Bounding (7 cm)	2 x 5	
8-9	Cross jumping	4 x 8	80	Cross jumping	2 x 8	40
	Drop jumping (15 cm)	2 x 14		Drop jumping (15 cm)	1 x 14	
	Bounding (15 cm)	4 x 5		Bounding (15 cm)	2 x 5	

HI, high dose exercise group; MOD, moderate dose exercise group.

Table 2 Participant characteristics at baseline (values are mean±SD)

	HI (n=13)	MOD (n=15)	CON (n=14)	*p* value
Age (yr)	62.1±6.9	59.3±5.7	58.6±7.4	0.365
Height (cm)	174.1±4.0	177.6±4.0	175.8±6.1	0.162
Body mass (kg)	77.9±8.1	86.5±15.5	84.3±11.6	0.180
BMI (kg/m^2)	25.8±2.8	27.4±4.4	26.6±3.4	0.516
Whole body lean mass (kg)	52.1±4.5	55.9±8.0	54.4±7.2	0.346
Appendicular lean mass (kg)	23.3±2.7	24.6±3.6	24.4±3.5	0.550
Arm lean mass (kg)	6.3±0.8	6.4±0.9	6.4±1.0	0.911
Leg lean mass (kg)	17.0±1.9	18.2±2.8	18.0±2.6	0.422
Fat mass (kg)	23.0±4.6	28.2±8.5	24.9±5.6	0.116
Body fat %	29.3±3.7	31.8±4.6	30.2±3.3	0.242
BMD (g/cm^2)				
Total hip	0.976±0.139	0.944±0.080	0.957±0.157	0.805
FN	0.807±0.140	0.750±0.115	0.789±0.150	0.519
Trochanter	0.733±0.127	0.732±0.077	0.730±0.136	0.998
Lumbar spine (L_{2-4})[a]	1.060±0.113	1.093±0.125	1.001±0.111	0.199
Whole body	1.209±0.097	1.166±0.060	1.164±0.112	0.572[c]
Muscle strength (kg)				
Leg press	172.7±35.9	171.7±34.3	176.4±40.9	0.794[c]
Physical function (sec)				
6 m usual walk	4.3±0.5	4.0±0.7	4.1±0.5	0.306
6 m backwards walk	16.4±3.7	16.1±3.2	17.3±5.1	0.709
6 m fast walk	2.7±0.5	2.8±0.5	2.7±0.3	0.815
Stair climb	3.2±0.5	3.3±0.5	3.1±0.5	0.406
Sit-to-stand	8.8±1.2	9.8±1.5	9.1±1.2	0.167[c]
400 m walk	226.8±20.3	234.9±27.4	228.3±27.9	0.672
Blood markers[b]				
Testosterone (nmol/l)	15.8±5.3	19.2±5.0	18.0±4.9	0.346
Estradiol (nmol/l)	25.2±7.3	36.1±9.8	30.7±6.4	0.311
Vitamin D (nmol/l)	34.3±6.8	31.4±7.8	25.4±10.6	0.367[c]
Calcium (mmol/l)	2.3±0.1	2.4±0.1	2.3±0.1	0.387
SHBG (nmol/l)	51.6±27.0	50.0±15.7	51.4±16.3	0.895[c]
Physical activity-moderate and strenuous (min)	213.2±170.0	225.8±218.6	216.5±257.5	0.989

HI, high dose exercise group; MOD, moderate dose exercise group; CON, control group; SD, standard deviation; BMI, body mass index; BMD, bone mineral density; FN, femoral neck; SHBG, sex hormone-binding globulin; [a], HI n=12, MOD n=15, CON n=12; [b], HI n=10, MOD n=11, CON n=12; [c], denotes the use of the Kruskal-Wallis Test.

Table 3 Absolute BMD values and change over 9 months

	Baseline			9 months			Mean change adjusted group difference at 9 months			
	HI	**MOD**	**CON**	**HI**	**MOD**	**CON**	**HI v CON**	**MOD v CON**	**HI v MOD**	
	Mean±SD	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	***p* value**
BMD (g/cm^2)										
Total hip	0.976±0.139	0.944±0.080	0.957±0.157	0.976±0.146	0.933±0.075	0.955±0.152	0.007 (-0.080-0.022)	-0.012 (-0.026-0.002)	0.019 (0.004-0.034)	0.010
FN	0.807±0.140	0.750±0.115	0.789±0.150	0.807±0.150	0.740±0.096	0.783±0.137	0.013 (-0.013-0.039)	-0.008 (-0.033-0.016)	0.021 (-0.005-0.048)	0.147
Trochanter	0.733±0.127	0.732±0.077	0.730±0.136	0.733±0.136	0.725±0.071	0.725±0.125	0.010 (-0.005-0.026)	-0.005 (-0.020-0.010)	0.016 (0.000-0.031)	0.047
Lumbar spine (L_{2-4})	1.060±0.113	1.093±0.125	1.001±0.111	1.070±0.113	1.089±0.131	1.012±0.099	0.016 (-0.018-0.049)	-0.001 (-0.032-0.030)	0.017 (-0.014-0.048)	0.348
Whole body	1.209±0.097	1.166±0.060	1.164±0.112	1.209±0.098	1.170±0.049	1.165±0.107	0.002 (-0.016-0.021)	0.004 (-0.013-0.021)	-0.002 (-0.020-0.017)	0.801

HI, high dose exercise group; MOD, moderate dose exercise group; CON, control group; SD, standard deviation; CI, confidence intervals; BMD, bone mineral density; FN, femoral neck, p-values are for the interaction (ANCOVA adjusted for baseline values and body mass).

Table 4 Relationships between attendance, blood markers, age and change in BMD

	Attendance		Testosterone		Estradiol		Calcium		Vitamin D	
	HI	**MOD**	**HI**	**MOD**	**HI**	**MOD**	**HI**	**MOD**	**HI**	**MOD**
Total hip	-0.18	0.22	0.09	-0.06	0.01	0.16	0.34	0.56	0.20	0.56
	p=0.56	p=0.42	p=0.82	p=0.86	p=0.99	p=0.64	p=0.34	p=0.07	p=0.58	p=0.07
FN	0.15	0.14	0.07	-0.16	0.48	-0.07	-0.29	0.44	-0.08	0.44
	p=0.62	p=0.63	p=0.84	p=0.62	p=0.16	p=0.85	p=0.41	p=0.18	p=0.83	p=0.18
Trochanter	-0.18	0.12	0.22	-0.37	0.17	0.11	0.26	0.48	0.21	0.48
	p=0.56	p=0.67	p=0.54	p=0.24	p=0.65	p=0.76	p=0.48	p=0.13	p=0.56	p=0.13
Lumbar	-0.31	0.18	0.41	-0.60	-0.26	0.53	0.00	0.06	-0.37	0.06
spine ($_{L2-4}$)	p=0.33	p=0.53	p=0.28	p=0.04	p=0.51	p=0.10	p=0.99	p=0.87	p=0.32	p=0.87
Whole body	-0.05	0.26	0.23	0.49	0.47	0.00	0.09	-0.06	-0.66	0.09
	p=0.88	p=0.35	p=0.53	p=0.11	p=0.17	p=0.99	p=0.80	p=0.86	p=0.04	p=0.79

HI, high dose exercise group; MOD, moderate dose exercise group; BMD, bone mineral density; FN, femoral neck.

Figure legends

Figure 1. CONSORT diagram

DXA, dual-energy x-ray absorptiometry; ITT, intention-to-treat.

Figure 2. Percent change (±SE) in regional and whole body BMD following the 9-month exercise and control period.

*, $p \leq 0.05$ and denotes significant between-group differences, †, $p \leq 0.05$ and denotes significant within-group differences.