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Effects of exercise training on bone mineral density in frail older women and men: a randomised controlled trial

Sir—Prospective studies suggest that bone loss accelerates with advancing age [1, 2], leading to markedly decreased bone mineral density (BMD). Because physical activity provides the mechanical stimulus for bone health [3], low BMD in old age may be due, in part, to disuse atrophy [4]. Some randomised controlled trials (RCT) have found that exercise increases BMD in older adults [5–9], but a limitation is that older physically frail individuals were not included. The aim of this study was to evaluate the effects of a multi-component exercise programme, compared with low intensity home exercise, on BMD in older frail individuals.

Methods

Participants were women and men (aged ≥78 years) recruited from the community. The screening procedures for this study have been described [10, 11]. All participants had mild-to-moderate physical frailty, defined as meeting two out of the following three criteria: peak aerobic power of 11–18 ml/kg/min, physical performance test score of 18–32, and difficulty or need for assistance with two instrumental or one basic activities of daily living. Exclusion criteria included medical conditions that contraindicated vigorous exercise, cancer diagnosis within the previous 5 years, use of bone-acting drugs within the previous year, and significant sensory/cognitive impairment.

Eligible participants were randomly assigned to either an exercise training group (ET), or home exercise group (HOME). The study personnel who maintained the randomisation log were not involved in screening, testing or training procedures.

The ET program included successive phases of physical therapy (Phase 1), resistance (Phase 2), and endurance exercises (Phase 3), as previously described in detail [12, 13]. Phase 1 consisted of exercises designed to improve flexibility, balance and coordination. Phase 2 added progressive resistance training and included leg press, knee extension, knee flexion, seated row, upright row, bench press, biceps curl and triceps extension. Initially, 1–2 sets of 6–8 repetitions of each exercise were completed at 65–75% of one-repetition maximum (1-RM). This progressed to 3 sets of 8–12 repetitions done at 85–100% of 1-RM. Phase 3 added endurance exercises and included walking on a treadmill, cycling, and rowing. The initial goal was to exercise 15 minutes at 65–75% of peak heart rate and progress to 30 minutes. After 4–6 weeks, the goal was to perform four 5-minute intervals at 85–90% of peak heart rate. The HOME program consisted of a subset of the Phase 1 exercises of the ET program.

Participants completed 3-day food records at the beginning and end of the study. Participants were provided supplemental calcium and vitamin D to adjust intake to about 1200 mg/day and about 800 U/day, respectively.

BMD of the whole body, lumbar spine, and proximal femur was measured at 3-mo intervals using dual-energy X-ray absorptiometry (DXA) (DXA; Hologic Inc, Waltham, MA) on a Hologic QDR-1000/W instrument. Coefficients of variation were 0.6 ± 0.2 to 1.1 ± 0.6%.

Baseline characteristics were compared using unpaired t-tests and X² tests except where nonparametric alternatives were used. Longitudinal analyses were performed using mixed model repeated measures ANOVA (SAS: Cary, NC). The focus of the analyses was on the significance of the Group × Time interaction. Statistical contrasts were used in testing hypotheses that changes between two time-points in one group was equal to changes in the other group. Results are reported as mean ± SD.

Results

We prescreened 657 individuals and invited 444 for screening evaluations. Of these, 165 did not meet selection criteria, 67 elected to enroll in a concurrent study of exercise combined with hormone replacement therapy (HRT) and 93 declined participation. One hundred and nineteen individuals were randomised: 69 to ET and 50 to HOME. Of these, 87 completed the study and 32 dropped out. Reasons for drop-out included: death (1 HOME), personal reasons (3 ET, 4 HOME), medical problems (17 ET, 4 HOME), and noncompliance (3 ET). Seven participants were excluded due to incomplete data (4 ET, 3 HOME). Of the
119 participants randomised, 112 (65 ET and 47 HOME) were included in the analyses.

Baseline characteristics were not different between groups (Table 1). Consistent with our selection of individuals with physical frailty, there was a high prevalence of comorbidities. Thirteen HOME and 16 ET participants did not have baseline BMDs. ET participants had slightly higher BMD values than HOME participants due, in part, to the smaller proportion of women in the ET group. These differences were not significant.

At baseline calcium intake averaged 783 ± 223 and 792 ± 282 mg/day in the HOME and ET groups, respectively, and 1254 ± 330 and 1286 ± 322 mg/day at the end of the study period. Vitamin D intake averaged 130 ± 86 and 147 ± 94 U/day at baseline in the HOME and ET groups, respectively, and 610 ± 111 and 613 ± 119 U/day at the end of the study period.

ET participants attended 2.2 ± 0.2 sessions/week. The total weight lifted/session increased by 24 ± 29% between the first eight and last eight sessions during phase 2. For the endurance training during phase 3, the heart rate and exercise duration were 107 ± 11 beats/minute and 21 ± 4 minutes/day during the first eight sessions, and 108 ± 12 beats/minute and 29 ± 4 minutes/day during the last eight sessions. During phases 2 and 3, ET participants lifted 73 ± 9% of their most recent 1-RM. During phase 3, ET participants trained at 80 ± 7% of their peak heart rate. HOME participants reported exercising 2.9 ± 1.5 days/week.

We did not observe a significant GroupXTime effect for the changes in BMD between the 1st DXA assessment and the end of Phase 3 (Table 2). There were trends, however, for significant GroupXTime effects for BMD at the total hip (P = 0.08) and trochanter sites (P = 0.07). Test of contrasts showed that the mean changes in total hip and trochanter BMD from 3 months to 6 months were different between groups (P = 0.02 and P = 0.04) with positive changes in the ET group compared with the HOME group. At the end of the 9-month study, both the ET and the HOME group demonstrated no significant bone loss at the BMD sites examined (P > 0.05). No gender effects for the BMD changes were observed.

Discussion

This is the first RCT to evaluate the effects of exercise on BMD in frail, community-dwelling elderly individuals. We have reported that the ET intervention improves muscle strength and peak aerobic power in this population, thus reducing disability [12]. The current findings suggest that a 9-month multi-component ET program does not significantly increase BMD in comparison to low intensity home exercise in frail older women and men supplemented with calcium and vitamin D.

While some RCTs have found that exercise increases BMD in older adults [5–8], other studies did not find positive results [14–16]. Such mixed findings may be related to
differences in subject characteristics, and the type and quantity of exercises. Our ET protocol included different types of exercises that stimulated major muscles attached to bone. Despite our ET strategies, BMD remained stable for both intervention groups. It is possible that the type and quantity of exercises in ET participants exercised at moderate-to-high intensity, the threshold for exercise-induced bone accretion [17]. Although ET participants exercised at moderate-to-high intensity, the low absolute muscle forces applied to bone. Despite our ET strategies, BMD remained stable for both intervention groups. It is possible that the type and quantity of exercises in ET participants exercised at moderate-to-high intensity, the threshold for exercise-induced bone accretion [17].

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time point</th>
<th>Home exercise $(n=47)$</th>
<th>Exercise training $(n=65)$</th>
<th>Analysis results Group X Time effect</th>
<th>Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total hip BMD (g/cm²)</td>
<td>Baseline</td>
<td>0.79 ± 0.17</td>
<td>0.84 ± 0.18</td>
<td>$P = 0.08$</td>
<td>Baseline to 3-month: $P = 0.41$</td>
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<td></td>
<td>3-months</td>
<td>0.77 ± 0.16</td>
<td>0.83 ± 0.18</td>
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<td>Baseline to 6-month: $P = 0.35$</td>
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<td>6-months</td>
<td>0.77 ± 0.16</td>
<td>0.85 ± 0.18</td>
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<td>Baseline to 9-month: $P = 0.93$</td>
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<td>9-months</td>
<td>0.75 ± 0.15</td>
<td>0.85 ± 0.19</td>
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<td>3- to 6-month: $P = 0.02$</td>
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<td>3- to 9-month: $P = 0.45$</td>
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<td>6- to 9-month: $P = 0.26$</td>
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<tr>
<td>Trochanter BMD (g/cm²)</td>
<td>Baseline</td>
<td>0.59 ± 0.14</td>
<td>0.65 ± 0.17</td>
<td>$P = 0.07$</td>
<td>Baseline to 3-month: $P = 0.68$</td>
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<td>3-months</td>
<td>0.58 ± 0.12</td>
<td>0.64 ± 0.17</td>
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<td>Baseline to 6-month: $P = 0.29$</td>
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<td>6-months</td>
<td>0.58 ± 0.13</td>
<td>0.66 ± 0.17</td>
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<td>Baseline to 9-month: $P = 0.87$</td>
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<td>9-months</td>
<td>0.58 ± 0.12</td>
<td>0.65 ± 0.17</td>
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<td>3- to 6-month: $P = 0.04$</td>
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<td>3- to 9-month: $P = 0.91$</td>
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<td>6- to 9-month: $P = 0.08$</td>
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<td>Femoral neck BMD (g/cm²)</td>
<td>Baseline</td>
<td>0.66 ± 0.13</td>
<td>0.70 ± 0.15</td>
<td>$P = 0.58$</td>
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<td></td>
<td>3-months</td>
<td>0.66 ± 0.13</td>
<td>0.70 ± 0.15</td>
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<td></td>
<td>6-months</td>
<td>0.65 ± 0.13</td>
<td>0.69 ± 0.15</td>
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<td></td>
<td>9-months</td>
<td>0.63 ± 0.11</td>
<td>0.70 ± 0.17</td>
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<td>L2–L4 BMD (g/cm²)</td>
<td>Baseline</td>
<td>1.01 ± 0.24</td>
<td>1.09 ± 0.26</td>
<td>$P = 0.65$</td>
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<td>3-months</td>
<td>0.98 ± 0.21</td>
<td>1.07 ± 0.27</td>
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<tr>
<td></td>
<td>6-months</td>
<td>0.98 ± 0.21</td>
<td>1.08 ± 0.27</td>
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<td></td>
<td>9-months</td>
<td>0.97 ± 0.23</td>
<td>1.08 ± 0.28</td>
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<tr>
<td>Whole body BMD (g/cm²)</td>
<td>Baseline</td>
<td>1.08 ± 0.16</td>
<td>1.09 ± 0.16</td>
<td>$P = 0.61$</td>
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<tr>
<td></td>
<td>3-months</td>
<td>1.04 ± 0.16</td>
<td>1.08 ± 0.17</td>
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<tr>
<td></td>
<td>6-months</td>
<td>1.05 ± 0.16</td>
<td>1.10 ± 0.17</td>
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<tr>
<td></td>
<td>9-months</td>
<td>1.03 ± 0.17</td>
<td>1.09 ± 0.18</td>
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</table>

Means ± standard deviations are reported at each test. $P$-values are based on mixed model repeated measures analysis of variance and indicate the comparisons of change in BMD between specific time points. When a Group X Time interaction was found significant, specific contrasts were used in testing the null hypothesis that changes between two time points in one group were equal to corresponding changes in the other group.

Baseline calcium and vitamin D intakes were low, so supplements were provided to maximize the osteogenic response to exercise and to control for micronutrient intake. We did not collect information on sun exposure but our participants were sedentary. Several studies have shown positive effects of nutritional supplements on BMD [18], so we cannot exclude the possibility that the vitamin and mineral supplementation contributed to maintenance of BMD for both groups. However, previous RCTs that showed positive effects on BMD also provided calcium supplementation [16].

There are other limitations. We did not include a non-exercising arm in this study, which may have limited our ability to detect changes over time in the ET group. Our rate of dropout (26%) was comparable with exercise studies in older persons [6–8]. Some participants did not have baseline DXA assessments. However, to minimize the potential bias introduced by dropouts and missing DXA studies, we used an intention-to-treat analysis. Because we included only individuals with mild-to-moderate physical frailty, our results may not be generalizable to healthy older individuals.
Research letters

In conclusion, in physically frail older women and men taking calcium and vitamin D supplements, relatively vigorous exercise training does not appear to increase BMD compared to low intensity exercise. Further study will be necessary to elucidate the BMD effects of exercise training in frail older individuals.

Acknowledgement

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