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Effect of exercise training and detraining on bone mineral density in postmenopausal women with osteoporosis

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Abstract We examined the effect of exercise training and detraining on bone mineral density (BMD) in postmenopausal women with osteoporosis. Thirty-five postmenopausal women with osteoporosis, aged 53–77 years, were randomly assigned to three groups: a control group (n = 20), a 2-year exercise training group (n = 8), and an 1-year exercise training plus 1-year detraining group (n = 7). Exercise training consisted of daily brisk walking and gymnastic training. Calcium lactate, 2.0 g, and 1α-hydroxyvitamin D_3, 1 μg were supplied daily to all subjects. No significant differences in initial lumbar BMD, measured by dual-energy X-ray absorptiometry (DXA) were found among the three groups. The mean percent change in BMD compared with the baseline was significantly higher at 1 and 2 years in the exercise training group and at 1 year in the detraining group than in the control group, and did not differ significantly at 2 years between the detraining and control groups. These findings indicate that our exercise training program led to a significant increase in lumbar BMD in postmenopausal women with osteoporosis compared with the control, but that the BMD reverted toward a level that was not significantly different from the control with detraining. Continued exercise training is needed to maintain the bone mass gained through exercise training.

Key words Osteoporosis · Postmenopausal women · Exercise training · Detraining · Bone mineral density (BMD)

Introduction

Osteoporosis, which is characterized by low bone mass and an increased risk of fractures, constitutes a major public health problem. In particular, marked bone loss is observed in women after menopause, with accelerated bone remodeling; thus, osteoporosis primarily affects postmenopausal women. When bone mineral density (BMD) decreases below the fracture threshold, osteoporotic fractures, such as vertebral fractures, may occur without evidence of a fall.[5] Accordingly, in osteoporotic patients, it is important not only to prevent falls but to maintain or increase lumbar BMD to a level above the fracture threshold to reduce vertebral fractures. One approach to therapy should focus on preventing loss of lumbar BMD.

Various changes in lifestyle, primarily reduction of physical activity, with inadequate intake of calcium and vitamin D and exposure to sunlight, seem to be some of the major reasons for the increase in the population with osteoporosis.[10,13] Inadequate exposure to sunlight, in particular, results in decreased production of vitamin D_3, and induces vitamin D_3 deficiency with inadequate vitamin D intake. Therefore, increasing the physical activities of daily living, plus calcium and vitamin D_3 supplementation, may be a reasonable therapeutic approach to the treatment of osteoporosis.

Actually, it has been reported that exercise training can prevent loss of lumbar BMD or even increase lumbar BMD in postmenopausal women with an adequate calcium intake.[2,7,20,27] However, it is not known whether BMD gained through exercise is preserved, decreased, or lost when exercise is stopped. The purpose of this study was to examine the effect of exercise training and detraining on lumbar BMD in postmenopausal women with osteoporosis who were receiving calcium and vitamin D_3 supplementation.

Subjects and methods

Subjects

Thirty-five postmenopausal women, 53–77 years of age, participated in a controlled trial for 2 years. All subjects were diagnosed with osteoporosis, based on Japanese criteria.[23] Fifteen women, selected randomly, engaged

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in exercise training, and the remaining 20 served as controls (control group). Preliminary screening included medical history, physical examination, blood biochemical studies, plain X-ray examination of the lumbar spine, and BMD measurement of the lumbar spine. Biochemical studies were performed by standard automated laboratory techniques. Lumbar BMD was measured as described below. None of the subjects had a history of hormone (estrogen) replacement therapy or had ever taken medication that affects bone metabolism prior to the trial. None of the subjects had engaged in sporting activity for the previous 5 years. Plain X-ray examinations of the lumbar spine did not show any evidence of vertebral fractures or marked deformation, and their BMD values were all more than 30% below the young adult mean (YAM). Their serum calcium, phosphorus, and alkaline phosphatase levels were all within normal limits. All 15 women who entered the exercise training program completed it for 1 year. Eight of them continued for another year (exercise training group) and 7 stopped (detraining group). Informed consent was obtained from all participants.

Exercise training program

The women who entered the exercise training program were instructed to measure their daily step count, with a pedometer provided by our hospital, for the first 7 days. The reproducibility of the step count measurements obtained with the pedometer was within 10% when evaluated by five measurements of 1000 steps each. After the individual means of the daily step counts for 7 days had been calculated, the subjects were encouraged to increase the step count by 30% through brisk walking. They were also encouraged to perform two sets a day of gymnastic training, consisting of 15 repetitions of straight leg raising, squatting, and abdominal and back muscle strengthening exercises.[29] The daily step count and gymnastic training program executed were recorded in a notebook every day. All participants received calcium lactate, 2.0 g, and 1α-hydroxyvitamin D_3, 1 μg daily, throughout the study period.

Measurement of lumbar BMD

Lumbar (L2–L4) BMD was measured in the anteroposterior view by dual-energy X-ray absorptiometry (DXA), using a Norland XR-26 instrument (Fort Atkinson, WI, USA). The coefficient of variation (100 × SD/mean) of five measurements each time with repositioning within 72 h was 1.14% in three persons. After serum calcium, phosphorus, and alkaline phosphatase levels were measured each time, BMD was assessed at 0, 1, and 2 years after the trial started.

Statistical analysis

All data values are expressed as means ± SD. Analysis of variance (ANOVA) with Fisher's protected least significant difference (PLSD) test was used to examine differences among the three groups in baseline characteristics, initial BMD, and percent changes in BMD at 1 and 2 years after the trial started. One-way ANOVA with repeated measurements was used to examine the significance of longitudinal changes in BMD and serum calcium, phosphorus, and alkaline phosphatase levels in the control, exercise training, and detraining groups. Two-way ANOVA with repeated measurements was used to examine the effects of exercise training and detraining on BMD and serum calcium, phosphorus, and alkaline phosphatase levels during the study period. A significance level of $P < 0.05$ was used for all comparisons.

Results

Characteristics of subjects

Table 1 shows the characteristics of the study subjects in the control, exercise training, and detraining groups.

Table 1. Characteristics of study subjects

	EX ($n = 8$)	DET ($n = 7$)	CON ($n = 20$)
Age (years)	65.3 ± 4.7	64.3 ± 3.0	64.9 ± 5.7
Height (m)	1.52 ± 7.84	1.50 ± 3.98	1.52 ± 5.66
Body weight (kg)	45.5 ± 6.5	46.1 ± 6.5	45.8 ± 4.0
Body mass index (kg/m^2)	19.7 ± 1.3	20.5 ± 2.6	19.9 ± 2.1
Time since menopause (years)	16.3 ± 5.9	14.7 ± 9.2	14.8 ± 6.4
Serum calcium (mg/dl)	9.4 ± 0.4	9.3 ± 0.4	9.5 ± 0.4
Serum phosphorus (mg/dl)	3.6 ± 0.4	3.5 ± 0.4	3.4 ± 0.3
Serum alkaline phosphatase (IU/l)	214 ± 69	263 ± 17	216 ± 52

No significant differences in any characteristics were found among the three groups [by analysis of variance (ANOVA) with Fisher's protected least significant difference (PLSD)] test
EX, Exercise training group; DET, detraining group; CON, control group

No significant differences in mean age, height, body weight, body mass index, and time since menopause were found among the three groups, nor were any significant differences found in mean serum calcium, phosphorus, or alkaline phosphatase levels among the three groups. Initial lumbar BMD was 0.611 ± 0.045 g/cm^2 in the control group, 0.595 ± 0.067 g/cm^2 in the exercise training group, and 0.618 ± 0.068 g/cm^2 in the detraining group. These corresponding initial BMD values as a percentage of the YAM were 58.2 ± 1.6% in the control group, 56.7 ± 5.7% in the exercise training group, and 58.9 ± 5.7 g/cm^2 in the detraining group. No significant differences in BMD and BMD as a percentage of the YAM were found among the three groups.

Daily step count and gymnastic training

The daily step count in the control group was 5280 ± 1432 at baseline, 5028 ± 1008 at 1 year, and 5384 ± 1248 at 2 years. The initial daily step count in the exercise training group was 5465 ± 1973; after encouragement to increase their daily step count by brisk walking, the count rose to 7909 ± 2445 at 1 year and 8511 ± 2622 at 2 years. The percent increase in the daily step count was 44.4 ± 10.8% at 1 year and 61.3 ± 44.5% at 2 years. In the detraining group, the initial daily step count was 5352 ± 941. After encouragement to increase their daily step count by brisk walking, the count rose to 8027 ± 1408 at 1 year, and the percent increase in the daily step count was 50.4 ± 11.0% at 1 year. After they stopped exercise training, the daily step count decreased to 5028 ± 1876. All subjects in the exercise training and detraining groups performed gymnastic training on at least 5 days per week.

Changes in serum calcium, phosphorus, and alkaline phosphatase levels

Serum calcium, phosphorus, and alkaline phosphatase levels in the control group were 9.4 ± 0.4 mg/dl, 3.5 ± 0.4 mg/dl, and 204 ± 48 IU/l at 1 year, and 9.3 ± 0.4 mg/dl, 3.5 ± 0.3 mg/dl, and 213 ± 48 IU/l, respectively, at 2 years. The corresponding levels in the exercise training group were 9.4 ± 0.4 mg/dl, 3.5 ± 0.4 mg/dl, and 245 ± 48 IU/l at 1 year, and 9.3 ± 0.4 mg/dl, 3.5 ± 0.3 mg/dl, and 258 ± 52 IU/l respectively, at 2 years. The corresponding levels in the detraining group were 9.3 ± 0.4 mg/dl, 3.4 ± 0.3 mg/dl, and 246 ± 43 IU/l at 1 year, and 9.4 ± 0.3 mg/dl, 3.6 ± 0.4 mg/dl, and 244 ± 49 IU/l respectively, at 2 years. These longitudinal changes in serum calcium, phosphorus, and alkaline phosphatase levels in the control, exercise training, and detraining groups were not significant (one-way ANOVA). In addition, these changes in the exercise training and detraining groups were not significant compared with the control group values (two-way ANOVA).

Changes in lumbar BMD

Table 2 shows changes in lumbar BMD in the control, exercise training, and detraining groups. In the control group, the percent changes in BMD compared with the baseline were +1.01 ± 3.16% at 1 year and +0.96 ± 3.39% at 2 years, and these longitudinal changes were not significant (one-way ANOVA). In the exercise training group, the percent changes in BMD compared with the baseline were +4.33 ± 1.60% at 1 year and +4.29 ± 2.34% at 2 years, and both 1 and 2 years of exercise training significantly increased BMD compared with the control group values (both $P < 0.05$; ANOVA with Fisher's PLSD). These longitudinal changes were significant compared with the control group values ($P < 0.05$, two-way ANOVA). In the detraining group, on the other hand, the percent changes in BMD compared with the baseline were +4.50 ± 1.55% at 1 year and +2.19 ± 1.98% at 2 years, and, while 1 year of exercise training significantly increased BMD compared with the control group value ($P < 0.05$; ANOVA with Fisher's PLSD), the following year of detraining decreased it to a level that was not significantly different from the control group value (ANOVA with Fisher's PLSD). These longitudinal changes were not significant compared with the control group values (two-way ANOVA).

Table 2. Changes in lumbar BMD

					ANOVA	
		Baseline	1 Year	2 Years	One-way	Two-way
EX	BMD (g/cm^2)	0.595 ± 0.067	0.621 ± 0.074	0.620 ± 0.087	$P < 0.05$	$P < 0.05$
	% Change (%)		+4.33 ± 1.60*	+4.29 ± 2.34**		
DET	BMD (g/cm^2)	0.618 ± 0.068	0.646 ± 0.072	0.632 ± 0.073	NS	NS
	% Change (%)		+4.50 ± 1.55*	+2.19 ± 1.98		
CON	BMD (g/cm^2)	0.611 ± 0.045	0.617 ± 0.043	0.616 ± 0.044	NS	—
	% Change (%)		+1.01 ± 3.16	+0.96 ± 3.39		

* $P < 0.05$ vs CON group at 1 year by ANOVA with Fisher's PLSD; ** $P < 0.05$ vs CON group at 2 years by ANOVA with Fisher's PLSD
NS, Not significant; BMD, bone mineral density; EX, exercise training group; DET, detraining group; CON, control group

Discussion

The efficacy of vitamin D_3 (1α-hydroxyvitamin D_3 or 1,25-dihydroxyvitamin D_3) treatment on reducing lumbar spinal bone loss has been established.[1,9,11,12,22,28] Vitamin D_3 supplementation not only reduces bone loss in the lumbar spine, and maintains or even increases bone mass in the lumbar spine in postmenopausal women,[1,9,11] but it prevents the development of additional vertebral fractures.[9,12,22,28] The positive effect of vitamin D_3 on bone mass in postmenopausal women has been attributed to decreased bone remodeling (turnover).[3] On the other hand, the effects of calcium supplementation on bone mass of the lumbar spine in postmenopausal women have not always been consistent.[4,6] Cumming[4] reviewed published trials by the meta-analysis technique and reported that calcium supplementation had a consistently positive effect in postmenopausal women at all sites, except for the vertebrae, and that its effect was greatest in the studies in which the baseline calcium was low, the mean age of the subjects was high, and/or the subjects had clinical evidence of osteoporosis. Dawson-Hughes,[6] on the other hand, reported that, while the spine in early postmenopausal women was unresponsive to calcium supplementation even at higher doses, bone loss from the spine could be retarded by increasing calcium intake in late postmenopausal women with low-calcium diets. Thus, the findings of these review studies remain a matter of controversy in regard to the effects of calcium supplementation on the bone mass of the lumbar spine. In the present study, combined administration of vitamin D_3 and calcium seemed to prevent loss of lumbar BMD in late postmenopausal women with osteoporosis. This result was similar to the established effect of vitamin D_3 on bone mass of the lumbar spine in postmenopausal women.

In postmenopausal women, exercise training of moderate to high intensity, with an adequate calcium intake, has been reported to prevent loss of lumbar BMD, or even to increase lumbar BMD.[2,7,20,27] In addition, it has also been reported to take at least 22 months until the response to exercise training becomes positive.[5] These lines of evidence suggests that exercise training of adequate intensity and duration maintains lumbar BMD in postmenopausal women when adequate calcium is supplied. It has been reported that the increase in lumbar BMD in postmenopausal women achieved through walking exercise is modest,[14,16,18] while the increase achieved through resistance exercise is greater.[21,24] In the present study, 1 and 2 years of exercise training, consisting of brisk walking and gymnastic training, successfully increased lumbar BMD compared with the control value.

A combination of aerobic and anaerobic exercise training has been suggested to be more effective than either aerobic or anaerobic exercise training alone.[26] One possible explanation of our results is that our exercise training program, consisting of a combination of brisk walking and gymnastic exercise training, had a positive effect on lumbar BMD. Frost[8] proposed the "mechanostat" theory to explain the mechanism of skeletal adaptation to mechanical usage; i.e., increased mechanical loading stimulates bone modeling and depresses bone remodeling, and thresholds that control bone formation and resorption can be influenced by hormones and nutrition. On the basis of this theory, another possibility in the present study is that calcium and vitamin D_3 probably modified the threshold of the intensity of exercise at which bone formation exceeded bone resorption and bone mass increased, and made bone more sensitive to physical activity or mechanical loading.

With regard to the mechanism by which exercise training increased lumbar BMD in postmenopausal women, Dalsky et al.[5] showed, in a clinical study, that short-term exercise training decreased bone Gla-protein (osteocalcin) levels. In an experimental study, on the other hand, Yeh et al.[32] demonstrated that, in ovariectomized rats, the positive effect of treadmill exercise on cancellous bone mass was primarily caused by depression of bone resorption. The findings in these two studies suggest that exercise training depressed the bone remodeling (turnover) accelerated by estrogen deficiency, and resulted in positive effects on the skeleton. This supports the mechanostat theory proposed by Frost.[8]

Decreased physical activity or mechanical loading, i.e., prolonged bed rest, immobilization because of hemiplegia, or weightlessness during space flights is known to result in rapid reduction of bone mass through increased bone resorption and/or decreased bone formation.[15,18,19,25] However, only a few well controlled studies on the effect of cessation of exercise training on bone mass have been reported.[5,17,30,31] Dalsky et al.[5] demonstrated that, although high-intensity aerobic exercise done while individuals received calcium supplementation led to significant increases above baseline in lumbar bone mineral content (BMC) in late postmenopausal women, the BMC reverted to baseline levels after detraining. Although the type of exercise and its intensity may differ between our study and the study of Dalsky et al.,[5] we found that the gain in bone mass of the lumbar spine as a result of our exercise training program was also not preserved during detraining, and that continued exercise training was needed to maintain this gain. It may be necessary to add some other therapeutic manipulations during detraining in order to preserve the bone mass gained through exercise training.

With regard to the mechanism by which detraining results in the loss of the bone mass gained through

exercise training, Yeh and Aloia[31] demonstrated, in an animal study on young rats, that bone mass gained through treadmill exercise was lost during deconditioning as a result of a decline in bone formation and an increase in bone resorption toward the levels of the sedentary control. However, in neither clinical nor experimental studies have the changes in bone metabolism induced by detraining been examined in the presence of estrogen deficiency. The mechanostat theory proposed by Frost[8] also states that decreased mechanical loading decreases bone modeling and increases bone remodeling. Based on this theory, we speculate that, while exercise training decreases bone remodeling in postmenopausal women, resulting in an increased bone mass, detraining increases bone remodeling, resulting in a decrease in bone mass to a level not significantly different from that in the sedentary control. Further studies, assessing bone metabolic markers, are needed to clarify the effects of detraining on bone metabolism in postmenopausal women.

In conclusion, the present study showed that, in postmenopausal women with osteoporosis, exercise training, consisting of daily brisk walking and gymnastic training, led to a significant increase in lumbar BMD compared with the control value. The increase was maintained during continued training, but, with detraining, lumbar BMD reverted toward a level that was not significantly different from the control. Continued exercise training is needed to maintain the bone mass gained through exercise training.

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