Effect of Exercise on Bone Mineral Density and Lean Mass in Postmenopausal Women

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ABSTRACT

CHUBAK, J., C. M. ULRICH, S. S. TWOROGER, B. SORENSEN, Y. YASUI, M. L. IRWIN, F. Z. STANCZYK, J. D. POTTER, and A. McTIERNAN. Effect of Exercise on Bone Mineral Density and Lean Mass in Postmenopausal Women. *Med. Sci. Sports Exerc.*, Vol. 38, No. 7, pp. 1236–1244, 2006. **Purpose:** To evaluate the effects of physical activity on bone mineral density, bone mineral content, and lean mass in postmenopausal, overweight/obese women. **Methods:** We conducted a 12-month randomized controlled aerobic exercise intervention versus control in 173 sedentary, overweight/obese, postmenopausal women, aged 50–75 yr. The exercise prescription consisted of ≥45 min of moderate-intensity aerobic exercise (60–75% of maximal heart rate), 5 $d \cdot wk^{-1}$ for 12 months. Control participants attended 45-min stretching sessions once a week. Ninety-eight percent ($N = 170$) completed the trial. Exercisers averaged 172 $min \cdot wk^{-1}$ (SD = 89) of exercise and expended 3828 $kJ \cdot wk^{-1}$ (SD = 2053). We assessed body fat, total lean mass, and total body bone mineral density and content using dual-energy x-ray absortiometry (DXA). We compared baseline with 12-month changes in exercisers versus controls. **Results:** Exercisers lost significantly more weight than stretchers (1.3-kg loss vs 0.1-kg gain, $P = 0.01$). However, no differences between exercisers and controls in the change from baseline to 12 months in total bone mineral density, bone mineral content, or lean mass were detected: exercisers' average bone mineral density increased by 0.005 $g \cdot cm^{-2}$ and controls' by 0.003 $g \cdot cm^{-2}$ ($P = 0.61$). Similarly, no significant differences were detected for bone mineral content. Lean mass increased by 0.2 kg in both groups ($P = 0.84$). **Conclusion:** Overall, the results from this randomized controlled study suggest that a yearlong moderate-intensity aerobic exercise intervention does not affect total body bone mineral density, bone mineral content, or lean mass in overweight/obese postmenopausal women. **Key Words:** PHYSICAL ACTIVITY, AGING, BONE HEALTH, FEMALE

Physical activity is a key component of weight loss; however, if exercise programs are to be promoted for weight loss, it is important to understand other health effects such programs might have. One aspect of health that is particularly important to postmenopausal women is bone mineral density. Decreasing estrogen concentrations after menopause can cause a decline in bone mineral density (22,24,26), which can lead to osteoporosis (24). Osteoporosis is a major cause of morbidity and mortality, especially among older adults, leading to more than 1.5 million fractures in the United States annually (http://www.nof.org/osteoporosis/stats.htm).

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Weight-bearing exercise is advocated as a strategy for preventing osteoporosis (http://www.nof.org/osteoporosis/stats.htm). In 2000, a review of 24 randomized controlled exercise trials in postmenopausal women found that both impact and nonimpact exercise prevented bone loss in the lumbar spine and femoral neck (31). However, little is known about the frequency, duration, and intensity necessary to strengthen bones (14).

One mechanism through which physical activity could increase bone strength is by increasing muscle mass. Lean body mass is thought to increase bone mineral density through mechanical loading of the skeleton. Muscle, a component of lean mass, is important because muscle contractions exert a greater force on bones than do other weight-associated gravitational forces (6). Furthermore, recent research in humans and animals has suggested that muscle contractions resulting from applying mechanical vibrations can increase the amount and quality of bone (25,30).

Although physical activity is protective against bone loss, the weight loss associated with it could, hypothetically, counteract the beneficial effect of exercise in overweight/obese women. In postmenopausal women, adipose tissue is the main site of androgen conversion to estrogen by the

enzyme aromatase. As overweight and obese postmenopausal women lose body fat, their serum estrogen concentrations decrease (17). Furthermore, body weight, particularly fat mass, contributes to the skeletal load and is therefore an important factor in increasing bone density and reducing bone turnover (7,23).

Given the relationship between fat mass and bone strength, it is plausible that physical activity accompanied by weight loss could actually have a negative effect on postmenopausal bone health in overweight/obese women. For this reason, we assessed the effect of a 12-month randomized controlled exercise intervention on total bone body mineral density, total body bone mineral content, and lean mass in postmenopausal, overweight/obese women. We also investigated the potentially intermediating role of metabolic and sex hormones. Levels of estradiol, testosterone, leptin, and insulin have been associated with physical activity as well as bone mineral density (23,24,28). Adherence in our study was high (12) and, to our knowledge, the present study had more participants than any other randomized exercise trial that has evaluated total body bone density in postmenopausal women not taking hormonal therapy (3,31).

METHODS

Participants. Participants were studied as part of the Physical Activity for Total Health study, which is described in detail elsewhere (13,18). This randomized controlled trial was designed to investigate the hormonal effects of a yearlong moderate-intensity exercise intervention versus stretching control in 173 postmenopausal women. Stratifying on body mass index (BMI) (above and below 27.5 $kg \cdot m^{-2}$), we randomly assigned women to either the exercise or the stretching arm of the trial (13). Randomization was performed by random number generation, and group assignment was placed in a sealed envelope, which was opened by the study coordinator at the time of randomization, after all baseline measures had been completed and the participant had agreed to enroll. Women were ages 50–75 yr, sedentary (< 60 $min \cdot wk^{-1}$ of moderate- to vigorous-intensity exercise), overweight (BMI 25.0 to < 30.0 $kg \cdot m^{-2}$, or BMI between 24.0 and < 25.0 $kg \cdot m^{-2}$ and percent body fat > 33%) or obese (BMI ≥ 30.0 $kg \cdot m^{-2}$), and resided in the greater Seattle, WA area. We defined postmenopausal as having had no menstrual periods for the previous 12 months and, for women ages 50–54 yr, a serum follicle–stimulating hormone concentration > 30 $mIU \cdot mL^{-1}$. We obtained written informed consent, and the Fred Hutchinson Cancer Research Center institutional review board approved all study procedures.

We identified potentially eligible women primarily via mass mailings and media advertisements (29). Interested women were screened for eligibility by phone interview and clinic visit. Major ineligibility criteria included using hormone therapy in the past 6 months, being too physically active, having medical conditions contraindicating moderate- to vigorous-intensity exercise, having a clinical diagnosis of diabetes, and currently using tobacco.

Exercise intervention. The exercise prescription consisted of at least 45 min of moderate-intensity exercise, 5 $d \cdot wk^{-1}$ for 12 months. Participants were required to attend three supervised sessions per week at a study facility (University of Washington or a commercial gym) during months 1–3 and to exercise 2 $d \cdot wk^{-1}$ at home. For months 4–12, they were required to attend at least one of the three sessions offered weekly at a study facility and to exercise 4 $d \cdot wk^{-1}$ either at home or at the facility. The training program started with participants at 40% of observed maximal heart rate for 16 min per session and gradually increased to 60–75% of maximal heart rate for 45 min per session by week 8 (17). Facility sessions consisted of treadmill walking and stationary bicycling. Strength training, consisting of two sets of 10 repetitions of leg extension, leg curls, leg press, chest press, and seated dumbbell row, was recommended, but not required, to decrease risk of injury and maintain joint stability. Performance of strength-training activities was minimal, with only 0.4% of all recorded facility-based activities falling into this category. A variety of home exercises were suggested and encouraged, including walking, aerobics, and bicycling. Participants wore Polar heart rate monitors (Polar Electro Inc, Woodbury, NY) during facility sessions and were encouraged to wear the monitors when exercising at home as well (13). Walking and bicycling accounted for over 95% of the activity at the facility and over 80% of recorded at-home activities. Strength training accounted for 5.8% of at-home activities. Other activities were performed at a frequency of less than 4% (13). Control participants attended 45-min stretching sessions once a week for the 12 months and were asked not to change other exercise habits. There was no attempt to elicit a calorie deficit in either group; both exercisers and control participants were asked to maintain their usual diet. On average, exercisers lost 1.3 kg overall and over the yearlong intervention, compared with controls, who averaged a gain of 0.1 kg. Body fat decreased by 1.4 kg in exercisers and 0.1 kg in stretchers (13).

We used several measures of adherence. We assessed baseline and 12-month $\dot{V}O_{2max}$ in all participants using a maximal graded treadmill test, with heart rate and oxygen uptake monitored by an automated metabolic cart (Medigraphics, St. Paul, MN). The test was started at 3.0 mph and 0% slope grade. Speed was raised to 3.5 mph at 2 min, and thereafter slope grade was increased by 2% every 2 min until the participant reached volitional fatigue. No treadmill tests were terminated for reasons other than volitional fatigue (13). Exercise intervention participants kept daily activity logs (facility attendance logs and home activity logs) of all sports or recreational activities of at least three metabolic equivalents (MET), where 1 MET is equal to the oxygen cost at rest (1 $kcal \cdot kg^{-1} \cdot h^{-1}$) (1). They recorded the type of exercise, peak heart rate, rating of perceived exertion (5), and duration of exercise. We used these data to measure exercise adherence. We added together the total minutes of aerobic exercise from the facility attendance

logs, plus daily minutes per week of sports and recreational data from home logs, and calculated average number of minutes per week of exercise over the study period. To compute the average weekly expenditure for a participant in the exercise arm, we multiplied the METs of each activity recorded in her daily physical activity log (excluding those of < 3 METs) by the duration of the activity and the participant's baseline weight in kilograms divided by 60. We summed all her activities over the year and then divided by 52 to obtain her weekly average. For the stretchers, we used responses from physical activity interviews administered at baseline and 12 months to estimate the minutes per week of exercise in the preceding 3 months.

Study measures. At baseline, 3 months, and 12 months, we collected demographic information, medical history, health habits, reproductive history, physical activity, and diet (20) over the past 3 months via self-administered questionnaires. Use of supplements was assessed by inventory at clinic visits. Height and weight (to the nearest 0.1 cm and 0.1 kg, respectively) were obtained using a wall-mounted stadiometer and a balance beam scale, respectively. Measurements were taken in duplicate and averaged. BMI was computed based on these measures.

We assessed body fat (kg), lean mass (kg), total body bone mineral density ($g \cdot cm^{-2}$), and total bone mineral content (g) using a dual-energy x-ray absorptiometry (DXA) whole-body scanner (Hologic QDR 1500, Hologic Inc, Waltham, MA). All DXA scans were performed by a technician blinded to the participants' group randomization. Each scan took approximately 30 min and was performed with the participant lying in the supine position. Six women (four exercisers and two controls) did not receive a DXA scan at 12 months.

Hormone assays. A 12-h fasting blood sample, collected prior to randomization, was processed within 1 h of collection, aliquoted into 1.8-mL tubes, and stored at −70°C. Serum testosterone and estradiol assays were performed at the Reproductive Endocrine Research Laboratory (University of Southern California), directed by one of the authors (FZS). Testosterone and estradiol were quantified by sensitive and specific radioimmunoassay, following organic solvent extraction and celite column partition chromatography (10,21). Chromatographic separation of the steroids was achieved using different concentrations of toluene in isooctane and ethyl acetate in isooctane. The Diabetes Endocrinology Research Center Immunoassay Core Laboratory (University of Washington), directed by Dr. Santica Marcovina, quantified insulin by a 48-h, PEG-accelerated, double-antibody radioimmunoassay; the primary antibody was guinea pig antihuman insulin, and the secondary antibody was goat antiguinea pig immunoglobulin. Leptin was measured by Dr. Scott Weigle at the University of Washington using a commercially available radioimmunoassay (Linco Research, St. Charles, MO) with a lower and upper detection limit of 0.5 and 100 $ng \cdot mL^{-1}$, respectively.

Two quality control, pooled samples were placed in each batch. Laboratory personnel were blinded to the identity of study subject and quality control samples. The intra- and interassay coefficients of variation were, respectively: 8.4 and 12.0% for testosterone, 12.4 and 15.8% for estradiol, 6.5 and 9.3% for insulin, and 8.7 and 11.2% for leptin.

Statistical analysis. We compared the two randomization groups at baseline with respect to mean age, body fat, lean mass, percent body fat, total body bone mineral density, total body bone mineral content, serum estradiol, testosterone, leptin, and insulin concentrations, daily intake of vitamin D, calcium, caffeine, and alcohol using the *t*-test and the chi-square test (see Table 1 for additional covariates considered).

We compared the changes from baseline to 12 months in total body bone mineral density in exercisers versus stretchers. We considered total body bone mineral density at baseline and 12 months as repeated measures and assessed the intervention effect using a generalized estimating equation modification of the linear regression model (32). The analysis was performed in accordance with the intention-to-treat principle in that intervention status was based on assignment, regardless of adherence. The total bone mineral content and lean body mass analyses were

TABLE 1. Baseline characteristics of participants by randomization group ($N = 173$)*.

	Stretchers ($N = 86$)	Exercisers ($N = 87$)
	Mean (SD)	Mean (SD)
Age (yr)	60.6 (6.8)	60.7 (6.7)
Weight (kg)	81.7 (12.1)	81.4 (14.1)
BMI ($kg \cdot m^{-2}$)	30.5 (3.7)	30.4 (4.1)
Total fat (kg)	38.4 (8.4)	38.4 (9.6)
Total body fat percent (%)	47.4 (4.6)	47.5 (4.8)
Total lean mass (kg)	39.9 (4.9)	39.6 (5.6)
Total body bone mineral density ($g \cdot cm^{-2}$)	1.04 (0.11)	1.04 (0.11)
Total body bone mineral content (g)	2141 (365)	2129 (328)
$\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	20.5 (3.5)	20.1 (3.6)
Estradiol ($pg \cdot mL^{-1}$)	19.0 (7.4)	19.6 (8.5)
Testosterone ($pg \cdot mL^{-1}$)	243.4 (111.2)	225.7 (84.7)
Leptin ($ng \cdot mL^{-1}$)	27.6 (8.9)	28.4 (7.9)
Insulin ($\mu U \cdot mL^{-1}$)	19.3 (9.0)	20.7 (10.3)
	N (%†)	*N* (%†)
White	75 (87.1)	74 (85.1)
Past hormone use		
None	48 (55.8)	52 (59.8)
< 1 yr	13 (15.1)	11 (12.6)
1–5 yr	11 (12.8)	7 (8.1)
≥ 5 yr	9 (10.5)	10 (11.5)
Unknown duration	5 (5.8)	4 (8.1)
Ever use hormones to prevent bone loss	12 (14.0)	10 (11.2)
Current/past thyroid problem	19 (23.2)	17 (20.0)
Current thyroid/antithyroid medication	14 (16.3)	14 (16.1)
Current use of calcium supplements	50 (63.0)	51 (63.0)
Current use of vitamin D supplements	41 (51.9)	40 (49.4)
Current use of corticosteroids	3 (3.5)	6 (6.9)
Current use of biphosphonates	2 (2.3)	1 (1.2)
Current use of thiazide diuretics	5 (5.8)	7 (8.1)
Ovaries remaining		
Both	77 (90.6)	79 (91.9)
Some (one, part of one, part of two)	2 (2.4)	5 (5.9)
None	6 (7.1)	1 (1.2)
Unknown number remaining	0 (0)	1 (1.2)

* None of the differences between exercisers and stretchers was significant at the $\alpha = 0.05$ level.
† Refers to percent of nonmissing observations with the specified value.

performed in the same manner. We had 80% power to detect differences of 0.01 $g \cdot cm^{-2}$ in total body bone mineral density, 29 g in total body bone mineral content, and 0.5 kg of lean mass.

We performed several exploratory, secondary analyses for total body bone mineral density, bone mineral content, and lean mass. We examined whether the intervention effect differed across strata defined by age (< 60, ≥ 60 yr); calcium supplementation at baseline; BMI at baseline (24 to < 30, 30 to < 35, and ≥ 35 $kg \cdot m^{-2}$); tertiles of body fat at baseline (kg); tertiles of weight at baseline (kg); tertiles of baseline $\dot{V}O_{2max}$ ($mL \cdot kg^{-1} \cdot min^{-1}$); and tertiles of baseline concentrations of estradiol ($pg \cdot mL^{-1}$), testosterone ($pg \cdot mL^{-1}$), leptin ($ng \cdot mL^{-1}$), and insulin ($\mu U \cdot mL^{-1}$). Effect modification was assessed using interaction terms in linear models. For each outcome, we stratified by baseline tertiles of that characteristic. For example, we evaluated the exercise effect stratified by tertiles of total body bone mineral density at baseline. Within each tertile, we had 80% power to detect differences of 0.02 $g \cdot cm^{-2}$ in total body bone mineral density, 50 g in total body bone mineral content, and 0.9 kg of lean mass. For exercisers only, we looked at whether change in total body bone mineral density and content varied by level of adherence (< 130, 130 to < 190, and ≥ 190 $min \cdot wk^{-1}$ of physical activity).

To evaluate whether other physiologic changes modified the exercise intervention effect, we examined whether the intervention effect on bone mineral density differed by tertile of change from baseline to 12 months in body fat, BMI, weight, lean mass, leptin, insulin, estradiol, testosterone, and $\dot{V}O_{2max}$. We adjusted these analyses for age (< 60, ≥ 60 yr) and the baseline tertile of the stratifying factor. For the lean mass analysis, we did not stratify by change in BMI or weight because lean mass is a component of these measures. Because adjustment did not change our results, we have presented the unadjusted results.

We repeated the analyses described above assuming no change from baseline among women who were missing 12-month follow-up values of the outcomes (six women) or hormone concentrations (three women). We have noted where the results from this analysis differed from our main analysis.

RESULTS

Baseline associations. Exercisers and stretchers were similar with respect to demographic characteristics and known predictors of bone mineral density and other subject characteristics (Table 1). On average, participants were 61 yr old at baseline and had a BMI of 30 $kg \cdot m^{-2}$ and a total body bone mineral density of 1.04 $g \cdot cm^{-2}$. Though none of the women were current smokers, nearly half of women in each group had smoked in the past. Exercisers and stretchers consumed a comparable amount of alcohol daily, averaging less than 5 g. Both exercisers and stretchers consumed a daily average of 5 μg of vitamin D, 0.8 g of calcium, and 0.2 g of caffeine. Only one person in each arm of the trial had ever had a hip fracture. None of the women reported current or past osteoporosis, though about one quarter of women in each group reported a family history of osteoporosis.

Adherence and the exercise effect on body fat and mass. Six exercisers discontinued exercise after 3 months, and all but three returned for the 12-month clinic visit. Exercisers engaged in 172 $min \cdot wk^{-1}$ (SD = 89) of moderate-intensity exercise, primarily by walking and bicycling. On average, exercisers expended 3828 $kJ \cdot wk^{-1}$ (SD = 2056). Among exercisers, change in $\dot{V}O_{2max}$ was positively correlated with both average minutes per week of exercise (correlation = 0.36, $P = 0.002$) and average weekly energy expenditure (correlation = 0.30, $P = 0.01$). Controls did not significantly increase their physical activity between the beginning and end of the study. At 12 months, they exercised 45 $min \cdot wk^{-1}$ more than baseline (MET ≥ 3); however, the increase was not significant ($P = 0.13$), and their $\dot{V}O_{2max}$ did not change significantly, either (13). Overall, comparable numbers of exercisers and stretchers initiated and discontinued use of drugs and supplements that can affect bone density, including calcium, vitamin D, thiazide diuretics, biphosphonates, and corticosteroids (results not shown). For each drug/supplement that can affect bone density, no more than six exercisers and six stretchers initiated or discontinued use during the yearlong intervention. The number discontinuing was approximately equal to the number initiating use. For instance, three exercisers and three stretchers discontinued corticosteroid use, and three exercisers and two stretchers initiated corticosteroid use. No women were taking estrogen, other sex hormones, selective estrogen receptor modulators, or parathyroid hormone.

We previously reported that the exercise intervention led to decreases in body fat and weight (13). On average, exercisers lost 1.3 kg over the yearlong intervention, compared with controls who averaged a gain of 0.1 kg ($P = 0.01$) (13). Body fat decreased by 1.4 kg in exercisers and 0.1 kg in stretchers ($P = 0.001$) (13). Intraabdominal fat decreased by 8.5 $g \cdot cm^{-2}$ in exercisers and increased by 0.1 $g \cdot cm^{-2}$ in stretchers ($P = 0.045$) (13). Subcutaneous fat decreased by 21.2 $g \cdot cm^{-2}$ in exercisers and increased by 7.6 $g \cdot cm^{-2}$ in stretchers ($P = 0.003$) (13). Maximal oxygen consumption increased by 11.7% in stretchers compared with 0.7% in controls ($P < 0.001$) (13).

Exercise effect on total body bone mineral density, bone mineral content, and lean mass overall. The exercise intervention was not associated with significant changes in total body bone mineral density, bone mineral content, or lean body mass over the 12-month intervention compared with controls. Exercisers gained 0.002 $g \cdot cm^{-2}$ (95% CI: −0.007, 0.011) more of bone mineral density than stretchers (Figure 1, Table 2). Both exercisers and stretchers experienced a very small, statistically nonsignificant change in bone mineral content over the 12-month study: −9.4 g (95% CI: −23.0, 4.3) in stretchers and −4.6 g (95% CI: −38.6, 29.4) in exercisers (results not shown). The difference between the groups was not statistically significant (4.8 g; 95% CI: −31.9, 41.3).

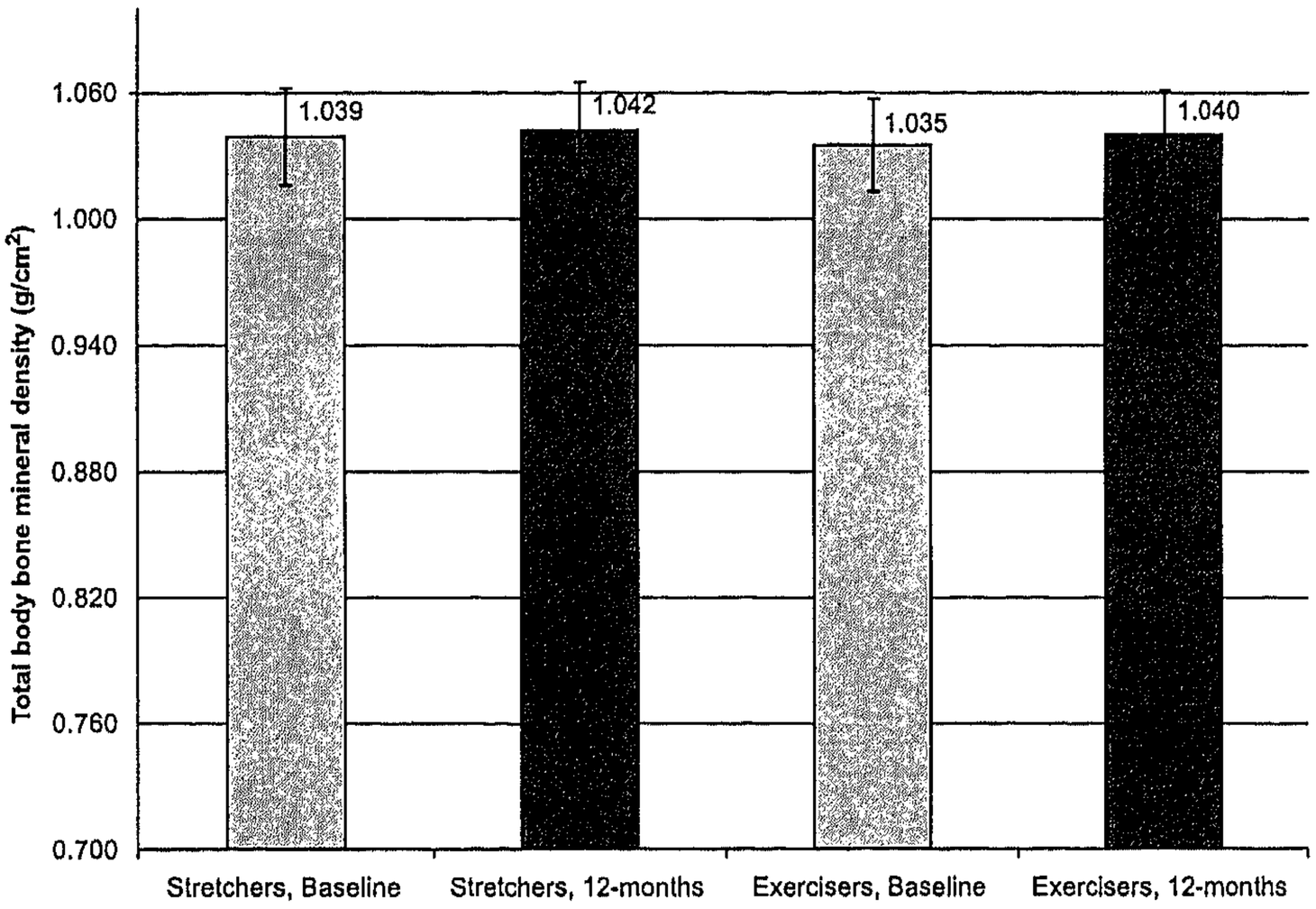

FIGURE 1—Effect of exercise on total body bone mineral density in a randomized controlled trial of postmenopausal, overweight/obese women.

There was no difference in the change in lean mass over the 12-month period between exercisers and stretchers (0.0 kg; 95% CI: −0.3, 0.4) (Figure 2, Table 3). The 0.2-kg increase in lean mass in both groups was not statistically significant.

Exercise effect on total body bone mineral density, bone mineral content, and lean mass in subgroups. In exploratory analyses, we examined whether intervention effects on total body bone mineral density, total body bone mineral content, and lean mass were present in subgroups defined by baseline characteristics or other intervention outcomes. The exercise effect on total body bone mineral density did not vary significantly according to baseline levels of or changes in BMI, body fat, or weight, or concentrations of estradiol, testosterone, leptin, and insulin. (Results for selected subgroups are shown in Table 2.) Additionally, the effect of the intervention did not vary significantly by baseline total body bone mineral density or calcium supplementation. However, the exercise effect did vary by age at baseline (Table 2) and by tertiles of $\dot{V}O_{2max}$ change over the year (not shown). Among women < 60 yr old, exercisers lost −0.007 g·cm^{-2} of total body bone mineral density compared with controls (P = 0.12). In contrast, ≥60-yr-old women who exercised gained 0.013 g·cm^{-2} of total body mineral density compared with stretchers of the same age (P = 0.10). Although the exercise effect was not statistically significant in either group, the difference in the exercise effect between the two groups was (P = 0.03). Among women whose $\dot{V}O_{2max}$ decreased, exercisers lost a small amount of total body bone mineral density (0.003 g·cm^{-2}), whereas stretchers gained a small amount (0.008 g·cm^{-2}). The exercise effect in this stratum differed with borderline significance (P = 0.04) from the null result in women whose $\dot{V}O_{2max}$ decreased.

We observed that exercise appeared to have a more positive effect on lean mass among women whose body fat and estradiol concentrations decreased compared with those whose increased. Results stratified by body fat are shown in

TABLE 2. Exercise effect on total body bone mineral density, overall and by subgroup.

	Total Body Bone Mineral Density (g·cm^{-2}) (95% confidence interval)					
	Stretchers		Exercisers			
	Baseline	12 Months	Baseline	12 Months	Effect[a] (g·cm^{-2})	Difference in Effect[b] (g·cm^{-2})
Overall	1.039 (1.016, 1.062)	1.042 (1.018, 1.065)	1.035 (1.013, 1.057)	1.040 (1.019, 1.061)	0.002 (−0.007, 0.011)	—
Stratified by age (yr) at baseline						
< 60	1.060 (1.027, 1.093)	1.064 (1.031, 1.097)	1.074 (1.046, 1.102)	1.071 (1.043, 1.099)	−0.007 (−0.016, 0.002)	Reference
≥ 60	1.016 (0.987, 1.046)	1.017 (0.986, 1.048)	0.990 (0.961, 1.019)	1.003 (0.974, 1.032)	0.013 (−0.003, 0.028)	0.020† (0.002, 0.037)
Stratified by tertiles of body fat (kg) at baseline						
21.5–33.2	1.017 (0.980, 1.054)	1.015 (0.978, 1.053)	1.011 (0.976, 1.046)	1.020 (0.989, 1.051)	0.010 (−0.010, 0.030)	Reference
33.5–41.0	1.027 (0.986, 1.068)	1.029 (0.986, 1.072)	1.029 (0.989, 1.070)	1.030 (0.991, 1.070)	−0.001 (−0.012, 0.010)	−0.011 (−0.034, 0.012)
41.3–69.0	1.070 (1.033, 1.107)	1.076 (1.039, 1.114)	1.069 (1.033, 1.105)	1.073 (1.038, 1.108)	−0.002 (−0.014, 0.010)	−0.012 (−0.036, 0.011)

[a] Difference between change over time in exercisers vs stretchers.
[b] Difference in exercise effect across tertiles.
† P = 0.05 for difference in exercise effect, (b). P values are from interaction terms in linear models.

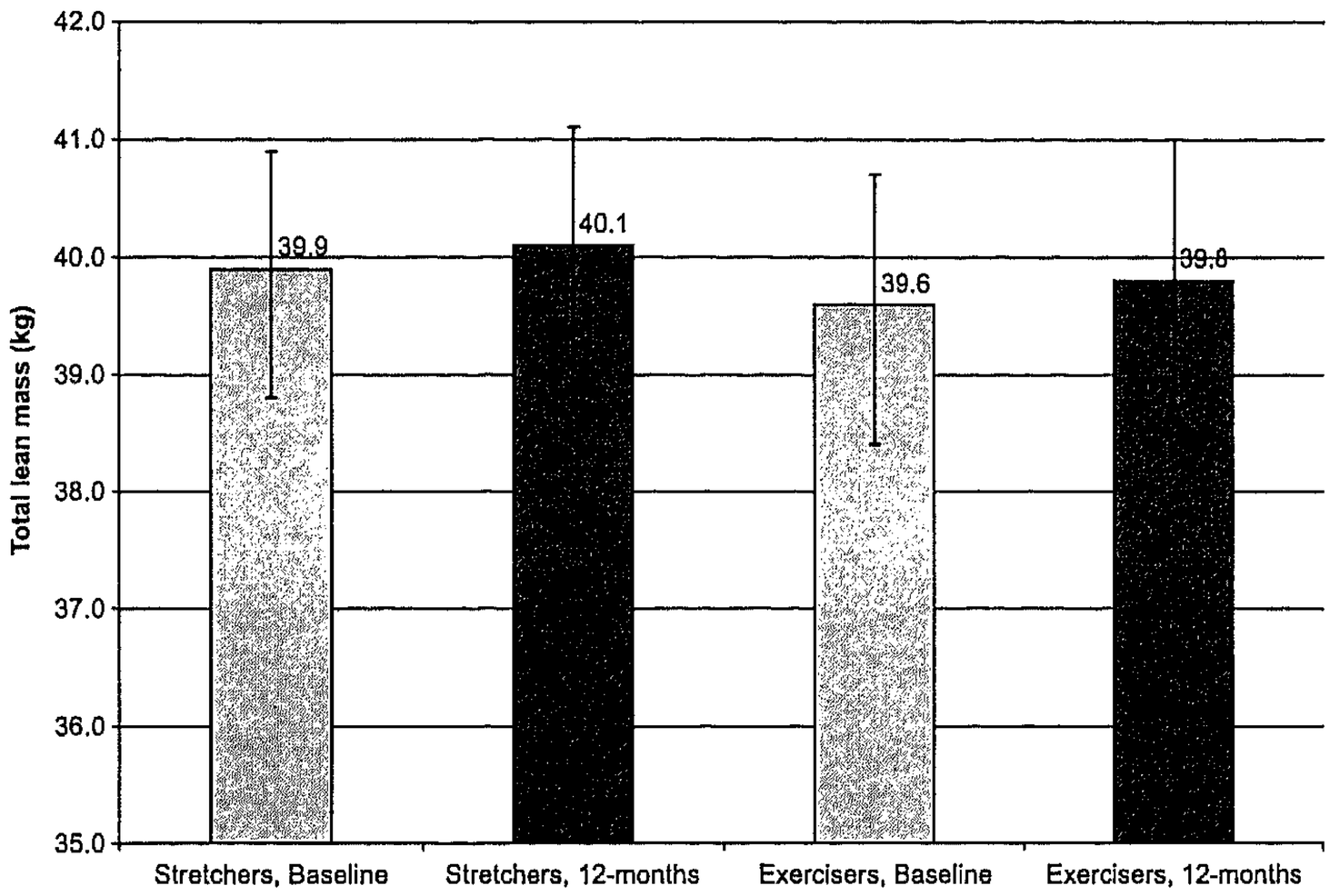

FIGURE 2—Effect of exercise on total lean mass in a randomized controlled trial of postmenopausal, overweight/obese women.

Table 3. In women whose estradiol levels increased, stretchers gained more lean mass than exercisers (0.6 kg vs 0.1 kg). In women whose estradiol levels decreased, exercisers gained 0.4 kg of lean mass, whereas stretchers lost an average of 0.1 kg of lean mass. The *P* value for the difference in the exercise effect across strata was 0.03. The effect of exercise appeared to differ in strata defined by change in leptin concentrations (results not shown); however, this difference was no longer significant when we assumed no change from baseline in the six participants missing leptin or lean mass measurements at 12 months.

The only subgroup in which we noted an effect of exercise on bone mineral content was women who gained body fat (results not shown). Among women who gained body fat, the bone mineral content of stretchers decreased by 8 g, whereas that of exercisers increased by 30 g. The difference between the groups was statistically significant (39, with 95% CI: 3–74). However, this exercise effect was not significantly different from what was observed in women who lost total body fat.

Changes in total body bone mineral density and bone mineral content by intervention adherence. One of the secondary questions we sought to explore was whether the exercise effect was limited to women with high adherence. Because the number of minutes exercised per week was not available for control subjects, we restricted this analysis to the exercisers. We did not observe significant differences in the 12-month change in total body bone mineral density or content according to the average minutes per week of exercise among those assigned to the exercise arm of the trial (results not shown).

DISCUSSION

The main finding from this analysis of data from a randomized controlled trial is that a 1-yr moderate-intensity aerobic exercise program in overweight/obese, postmenopausal women without known osteoporosis or osteopenia does not substantially affect total body bone mineral

TABLE 3. Exercise effect on lean mass, overall and by subgroup.

	Lean Mass (kg) (95% Confidence Interval)					
	Stretchers		Exercisers			
	Baseline	12 Months	Baseline	12 Months	Effect[a] (kg)	Difference in Effect[b] (kg)
Overall	39.9 (38.8, 40.9)	40.1 (39.1, 41.1)	39.6 (38.4, 40.7)	39.8 (38.7, 41.0)	0.0 (−0.3, 0.4)	—
Stratified by age (yr) at baseline						
< 60	40.6 (39.2, 42.0)	40.7 (39.2, 42.2)	41.1 (39.6, 42.6)	41.4 (39.9, 42.9)	0.2 (−0.3, 0.7)	Reference
≥ 60	39.1 (37.7, 40.5)	39.4 (38.0, 40.7)	37.8 (36.1, 39.4)	37.9 (36.3, 39.6)	−0.1 (−0.6, 0.3)	−0.4 (−1.0, 0.3)
Stratified by tertiles of body fat (kg) at baseline						
21.5–33.2	37.8 (36.4, 39.3)	37.8 (36.5, 39.2)	36.8 (35.3, 38.4)	37.4 (35.8, 38.9)	0.6* (0.1, 1.1)	Reference
33.5–41.0	38.8 (37.3, 40.2)	38.9 (37.5, 40.4)	38.4 (37.1, 39.7)	38.5 (37.1, 40.0)	0.0 (−0.6, 0.5)	−0.6 (−1.3, 0.1)
41.3–69.0	42.7 (40.9, 44.4)	43.1 (41.4, 44.8)	43.9 (41.6, 46.1)	43.9 (41.6, 46.2)	−0.4 (−1.1, 0.3)	−0.9† (−1.8, −0.1)

[a] Difference between change over time in exercisers vs stretchers.
[b] Difference in effect across tertiles.
* *P* = 0.05 for effect (a).
† *P* = 0.05 for difference in effect (b). *P* values are from interaction terms in linear models.

density, bone mineral content, or lean mass. The observation that aerobic exercise, even exercise accompanied by weight loss, is not associated with loss of total body bone mineral density or content is important. It is vital to confirm that activities (e.g., exercise) recommended to improve certain aspects of health (e.g., cancer risk) are not detrimental to other components of health (e.g., bone health). At baseline, the women in this study had a mean of total body bone mineral density of 1.04 $g \cdot cm^{-2}$, which is similar to what has previously been reported for healthy, mostly white, postmenopausal women. Reported means from previous studies have generally ranged between 0.9 and 1.1 $g \cdot cm^{-2}$ (2,8,9,16,27).

The reason that the exercise program did not affect lean mass is probably that women were engaged primarily in activities such as walking and bicycling. In general, weight loss in the exercisers resulted from a loss in fat mass.

Several randomized controlled trials on the effect of exercise trials on bone health have been conducted in postmenopausal women not taking hormone therapy (3,29). Although many of these trials have examined site-specific bone mineral density, several have examined total body bone mineral density (4,15,19,27). In two of these studies, the exercise intervention consisted entirely of strength/resistance training (4,19). In one of these reports, there were two exercise groups, one that engaged in strength training and another that engaged in fitness training (15). These studies documented positive, but not statistically significant, increases in total body bone mineral density associated with strength training in postmenopausal women (3).

In contrast to strength training, interventions that consisted largely of fitness training (e.g., bicycling and walking) did not appear to affect total body bone mineral density in postmenopausal women not taking hormone therapy (15,27). Svendsen et al. compared the effects on body composition of an energy-restrictive diet and diet plus exercise versus no intervention in overweight postmenopausal women not taking hormones ($N = 121$) (27). They observed a statistically nonsignificant decrease in total body bone mineral density associated with both intervention groups (diet and diet plus exercise) compared with controls; however, the decreases in the intervention groups were of equal magnitude, which suggests that diet, not exercise, was responsible for the slight decrease. A larger trial ($N = 320$) that included women who used hormonal therapy observed a statistically nonsignificant increase in total body bone mineral density with a yearlong exercise program that consisted of both strength and fitness training (11).

Because few studies have looked at the effect of exercise on total body bone mineral density or content in postmenopausal women, and findings have been inconsistent, results from our randomized study with relatively high compliance are important in establishing the absence of effect in this population.

To our knowledge, the other randomized studies of the exercise effect in postmenopausal women did not look at whether the intervention effect varied by changes in body composition. We decided *a priori* to perform exploratory analyses of the intervention effect by subgroups because we wanted to investigate whether any potential benefits of exercise were restricted to women who did not lose BMI, fat mass, lean mass, or maintain hormone concentrations. Overall, our findings do not suggest an exercise effect on total body bone mineral density or bone mineral content in subgroups defined by body composition or changes in body composition. However, the exercise intervention was associated with an increased total body bone mineral density in older women postmenopausal women ($\geq$ 60 yr) compared with younger postmenopausal women ($<$ 60 yr). The observation that the exercise effect was stronger in women whose $\dot{V}O_{2max}$ did not change relative to those whose $\dot{V}O_{2max}$ decreased is likely due to chance because: 1) no statistically significant difference in the exercise effect was observed in those whose $\dot{V}O_{2max}$ increased relative to those whose decreased (i.e, there was no trend); 2) multiple comparisons were undertaken in this study; and 3) we did not detect a similar effect for bone mineral content.

Although it is encouraging that total body bone mineral density and content of women who lost fat and whose hormone profile changed favorably was not compromised, it should be noted that changes in body composition (e.g., weight loss) could be associated with negative total body bone mineral density outcomes in women who start with a lower total body bone mineral density. Because all women in this study were overweight or obese, we were unable to address this question, and therefore our results should not be generalized to populations that differ considerably in body composition.

One important limitation of this study is that because bone health was not the primary endpoint of the trial, regional scans were not performed. Thus, we were unable to evaluate the effect of the intervention on bone mineral density at the lumbar spine or hip, which are known to be of clinical importance.

Overall, we did not observe an exercise effect on lean mass. However, the exercise effect on lean mass did appear to differ by baseline BMI and body fat and changes in estradiol concentrations over the year. Women with higher baseline BMI and body fat tended to lose lean mass with the exercise intervention. Women whose estradiol concentrations increased tended to lose lean mass with exercise. Because we performed a number of exploratory analyses, statistically significant findings should be interpreted with caution.

CONCLUSIONS

Our randomized exercise trial was relatively large compared with previous trials that have looked at total body bone mineral density, and our adherence was excellent. These two factors increase confidence in the results that the exercise program did not, in fact, change total body bone mineral density in overweight and obese women without known osteoporosis or osteopenia. The population under study here was highly select; however, this does not detract from the importance of the results because this is a group

of individuals who will likely be urged to lose weight by exercise. Like the majority of postmenopausal women in the United States, our study participants were overweight or obese. That moderate-intensity exercise does not affect total body bone mineral density in overweight and obese women may be useful in planning interventions to increase bone mineral density and in ensuring that exercise programs for other purposes do not have harmful side effects on bone health. It should be noted, however, that these results may not extend to the women at greatest risk for osteoporosis (i.e., lighter weight, osteopenic, and very elderly women). We also note that this study was unable to evaluate the exercise effect on regional measures of bone mineral density; it will therefore be important for future studies to address this question.

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