Published in final edited form as:

Calcif Tissue Int. 2009 April ; 84(4): 257–265. doi:10.1007/s00223-009-9232-z.

Addition of Aerobic Exercise to a Weight Loss Program Increases BMD, with an Associated Reduction in Inflammation in Overweight Postmenopausal Women

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Abstract

Increased inflammation and weight loss are associated with a reduction in bone mineral density (BMD). Aerobic exercise may minimize the loss of bone and weight loss may contribute to a decrease in cytokines. We tested the hypothesis that aerobic exercise in combination with a weight loss program would decrease circulating concentrations of inflammatory markers, thus mediating changes in BMD. This was a nonrandomized controlled trial. Eighty-six overweight and obese postmenopausal women (50–70 years of age; BMI, 25–40 kg/m²) participated in a weight loss (WL; $n = 40$) or weight loss plus walking (WL + AEX; $n = 46$) program. Outcome measures included BMD and bone mineral content of the femoral neck and lumbar spine measured by dual energy X-ray absorptiometry, interleukin-6, tumor necrosis factor- α , soluble receptors of IL-6, and TNF- α (sTNFR1 and sTNFR2; receptors in a subset of the population), VO₂ max, fat mass, and lean mass. Weight decreased in the WL ($p < 0.001$) and WL + AEX ($p < 0.001$) groups. VO₂ max increased ($p < 0.001$) after WL + AEX. There was a 2% increase in femoral neck BMD in the WL + AEX group ($p = 0.001$), which was significantly different from the WL group. The change in sTNFR1 was significantly associated with the change in femoral neck BMD ($p < 0.05$). The change in VO₂ max was an independent predictor of the change in femoral neck BMD. Our findings suggest that the addition of aerobic exercise is recommended to decrease inflammation and increase BMD during weight loss in overweight postmenopausal women.

Keywords

Aging; Cytokines; Inflammation; Exercise; Weight loss

Obesity is a risk factor for many chronic diseases such as diabetes, hypertension, hypercholesterolemia, stroke, and heart disease. However, obese women are thought to have a reduced risk for osteoporosis [1], potentially due to increased skeletal loading and increased concentrations of certain hormones, such as estradiol [2,3]. The prevalence of obesity among postmenopausal women has risen dramatically over the past 30 years [4] and weight loss is recommended to reduce fat mass. While weight loss is beneficial in reducing many risk factors associated with obesity, it also often results in an increase in bone resorption and subsequent loss of bone mineral density (BMD) in postmenopausal women [5–7]. Studies investigating obese and overweight postmenopausal women demonstrate that BMD of the total body, spine, and trochanter decrease during weight loss compared with a weight maintenance group [5,7]. In contrast, we and others have shown that bone loss can be prevented when weight loss is combined with exercise training in postmenopausal women [6,8,9].

In addition to the relationship with bone, obesity is associated with low-grade systemic inflammation which is related to an increased risk of type 2 diabetes and cardiovascular disease [10]. Research has demonstrated an association between increased inflammation and decreased BMD [11–13]. Increased production of cytokines is a possible mechanism that contributes to postmenopausal bone loss [14]. Cytokines play both a direct and an indirect role in the regulation of osteoclast and osteoblast activity [15]; therefore, a decrease in cytokine production may be beneficial to BMD. We and others report that tumor necrosis factor (TNF)- α and interleukin (IL)-6 are reduced through weight loss, by either caloric restriction alone or a combination of caloric restriction and exercise [16–19]. Therefore, we hypothesized that an exercise training program combined with a hypocaloric diet would prevent a loss of BMD in overweight, postmenopausal women compared to those undergoing a hypocaloric diet alone and that the changes in BMD would be associated with changes in circulating inflammatory markers. Thus, the purpose of this study was to determine if changes in inflammation mediate changes in BMD in postmenopausal women undergoing weight loss alone and combined with aerobic exercise training.

Materials and Methods

Subjects

Healthy, nonsmoking, overweight and obese (BMI, 25–40 kg/m²), postmenopausal (>1 year since last menstrual cycle) women aged 50–70 years were recruited from the Baltimore metropolitan area. All women were sedentary (<20 min of aerobic exercise, two times/week) and weight stable (<2.0-kg weight change in the past year). Initial evaluations included a medical history, physical examination, fasting blood profile, 2-h oral glucose tolerance test to exclude those with diabetes, and 12-lead resting electrocardiogram. Subjects with evidence of hypertension (blood pressure > 160/90 mmHg), hypertriglyceridemia (triglyceride > 400 mg/dl), heart disease, cancer, liver disease, renal or hematological disease, other medical disorders, or orthopedic limitations were excluded from the study. We conducted a post hoc analysis of a total of 158 women who were enrolled in a weight loss (WL) or a weight loss plus walking (WL + AEX) intervention. Subjects in the WL + AEX group were compliant with exercise (75% attendance) and/or had a 7% or greater improvement in VO₂ max. The WL group did not exercise (<5% improvement in VO₂ max). Eighty-six women completed the intervention. Forty women (78% Caucasian, 22% African American) were in the WL group and 46 (80% Caucasian, 20% African American) were in the WL + AEX group. Five women in the WL and two women in the WL + AEX were taking a form of hormone replacement therapy, which did not change for the duration of the study. Removal of the women on hormone replacement therapy from the data set and statistical analyses did not change the reported results. All women provided written

informed consent to participate in the study. All procedures and methods for the study were approved by the Institutional Review Board of the University of Maryland.

Study Design

Measurements of body composition, BMD, bone mineral content (BMC), and maximal aerobic capacity (VO_2 max) were performed before and after the 6-month interventions. During the 6-month period, all subjects met weekly with a registered dietitian for instruction in the principles of a hypocaloric diet (250–350 kcal/day deficit). The program focused on nutrition education, eating behavior, stress management, control of portion sizes, modification of binge eating and other adverse habits, and promotion of walking. Women were asked to record their daily food intake, and the dietitian reviewed their food logs. In addition, the WL + AEX group walked 3 days per week. Subjects walked at a target heart rate of 50–75% of heart rate reserve (HRR) for 45–60 min. An exercise physiologist supervised at least one exercise session per week at our exercise facility. Compliance was 80% for the WL group for their meetings with the dietitian and 78% for the WL + AEX group for each of their meetings with the dietitian and exercise sessions.

Maximal Aerobic Capacity

VO_2 max was measured on a motor-driven treadmill (Quinton Instruments, Seattle, WA) during a progressive exercise test to voluntary exhaustion as previously described [20]. A valid VO_2 max was obtained when at least two of these three criteria were met: (1) maximal heart rate $>90\%$ of age-predicted maximal heart rate (220 bpm–age), (2) respiratory exchange ratio of at least 1.10, and (3) plateau in VO_2 (<200 ml/min change) with increasing work rate. Ten of the 86 VO_2 max tests (12%) at the 6-month timepoint were missing from analysis due to failure to reach VO_2 max criteria or medical conditions that prohibited testing.

Body Composition and Bone Mineral Density and Content

Using a stadiometer and electronic scale, height (cm) and weight (kg) were measured to calculate BMI as weight (kg)/height (m^2). A total body scan was performed with dual energy X-ray absorptiometry (DXA; GE Lunar DPXIQ; Madison, WI) to determine lean mass and fat mass. The same DXA scanner was used to scan the total body, femoral neck, and lumbar spine (L_2 – L_4) to obtain total and regional BMD (g/cm^2) and BMC (g). Five repeat scans of the lumbar spine and femoral neck were obtained in two healthy volunteers who were repositioned for each scan. The coefficients of variation (CVs) for these regions are 0.8% and 1.3%, respectively. All scans were performed and analyzed by a radiology technician who was blinded to the treatment groups. Five bone scans ($<1\%$ of total) were missing from analysis (one femoral neck and one lumbar spine scan at baseline and one femoral neck, one lumbar spine, and one total body scan at 6 months). All measurements were done at baseline and after the 6-month intervention.

Inflammatory Markers

Blood samples were collected via venipuncture in the early morning (0700–0900 h) after a 12-h fast both at baseline and after the 6-month intervention. Plasma samples for assays were collected in EDTA-treated collection tubes and separated after centrifugation for 20 min at 4°C . Samples were stored at -70°C until analysis. All samples were run in duplicate. Values that did not have a coefficient of variance $<15\%$ were reanalyzed, and all values were averaged for analysis. Cytokines ($n = 86$ pre- and post-intervention) and cytokine soluble receptors (due to insufficient plasma volume, receptors were run in a subset of the entire group; $n = 27$ pre and post [WL + AEX, $n = 17$; WL, $n = 10$] and were partially previously published [17]) were measured using Quantikine ELISA kits (R&D Systems,

Minneapolis, MN). The inter- and intra-assay coefficients of variance for IL-6 were 5.4% and 3.5%, respectively. The CVs for TNF- α were 11.8% and 6.2%, respectively. CVs for soluble receptors of IL-6 (sIL-6R) and TNF- α (sTNFR1 and sTNFR2) were <5%.

Statistics

Statistical analyses were performed using SPSS for Windows version 12 (SPSS, Inc., Chicago, IL). The IL-6 and TNF- α data were not normally distributed, therefore the logarithm of each value was used for analysis. Analysis of variance (ANOVA) was used to determine differences in baseline values for weight, BMI, fat and lean mass, VO₂ max, BMD, and BMC of the femoral neck, lumbar spine, and total body, and IL-6, TNF- α , sIL-6R, sTNFR1, and sTNFR2. Analysis of covariance (ANCOVA) to control for baseline values was used to determine differences in the change (6 months–baseline) for the above-mentioned variables. A paired *t*-test was used to determine differences between baseline and 6 months for the above variables within groups when the change between groups was significantly different.

Pearson's correlations coefficients were used to calculate relationships among BMD and BMC of the femoral neck, lumbar spine, and total body, as well as body composition, VO₂ max, and inflammatory markers. Correlation analyses were also used to determine relationships among the change (6 months–baseline) of the above variables. Linear regression analysis was used to determine if changes in those independent variables with significant correlations with bone measurements were significant predictors of changes in BMD or BMC. The level of significance was set at $p < 0.05$ for all analyses.

Results

Baseline Characteristics

At baseline, groups were well matched with respect to physical characteristics. Age, weight, BMI, total body fat, lean mass, and VO₂ max did not differ between the two groups (Table 1). In addition, femoral neck and lumbar spine BMD and BMC as well as inflammatory markers, IL-6, TNF- α , sTNFR1, and sTNFR2 (Table 2) were not significantly different between groups at baseline. Only sIL-6R was significantly greater ($p < 0.05$) in the WL + AEX group compared to the WL group at baseline (Table 2).

Bone Mineral Density, Bone Mineral Content, and Body Composition

There was a significant decrease in weight (−7.6% and −7.7% in the WL and WL + AEX groups, respectively; $p < 0.001$) and BMI (−7.6% in the WL and WL + AEX groups; $p < 0.001$) after the 6-month intervention. Fat mass decreased after 6 months in both groups (−15.4% in the WL group, $p < 0.05$; and −12.5% in the WL + AEX group, $p < 0.001$).

There was a significant treatment effect for BMD shown by the 2.01% increase in femoral neck BMD ($p = 0.001$) in the WL + AEX group with no change in femoral neck BMD after WL. The change (6 months–baseline) in femoral neck BMD in the WL + AEX (0.02 ± 0.04 g/cm³) group was significantly greater than in the WL (-0.01 ± 0.05 g/cm³) group (Fig. 1; $p < 0.05$). There was no treatment effect on either femoral neck or lumbar spine BMC.

According to the definitions of osteoporosis and osteopenia set by the World Health Organization [21], 26% of the women were osteopenic and 6% were osteoporotic at the lumbar spine at baseline. Thirty-six percent were osteopenic and 4% were osteoporotic at the femoral neck at baseline. After the 6-month intervention, 11% of the WL + AEX group had an improvement in WHO osteoporosis classification (either from osteoporotic to osteopenic or from osteopenic to normal), compared to 6% of the WL group. In addition,

9% of the WL group saw a worsening in classification status, compared to 2% in the WL + AEX group.

Inflammatory Markers

The WL + AEX group experienced a significant decrease in sIL-6R (-2.14 ± 3.25 pg/ml; $p < 0.05$) and sTNFR1 (-125.06 ± 122.89 µg/ml, $p < 0.001$; Table 2; data were partially previously published [17]). The WL group experienced a significant increase in sIL-6R ($p < 0.05$; Table 2).

Predictors of Change in Bone Mineral Density

At baseline, age was negatively correlated with femoral neck and lumbar spine BMD and BMC (Table 3). Weight, BMI, and fat and lean mass were positively correlated with femoral neck and lumbar spine BMD and BMC, and VO₂ max was positively associated with femoral neck BMD and BMC and lumbar spine BMC. There were no significant correlations between inflammatory markers and baseline BMD or BMC at any bone site.

The change (6 months–baseline) in VO₂ max correlated significantly with the change in femoral neck BMD ($r = 0.32$, $p < 0.001$; Fig. 2). The change in IL-6, TNF-α, fat and lean mass, weight, and BMI did not correlate significantly with change in BMD at any site (Table 4). The change in lumbar spine BMC correlated significantly with the change in lean mass ($r = 0.320$, $p < 0.001$). The change in femoral neck BMD was negatively correlated with change in sTNFR1 ($r = -0.39$, $p < 0.05$; Fig. 3), and the correlation with change in sIL-6R approached significance ($r = -0.36$, $p = 0.09$). The change in VO₂ max was negatively associated with change in sIL-6R ($r = -0.51$, $p < 0.05$).

Linear regression models were run to determine the independent predictors of the change in BMD. Changes in weight, fat and lean mass, and VO₂ max were entered into the first model. Results of the regression analysis indicated that the change in VO₂ max was a significant predictor of the change in femoral neck BMD ($r^2 = 0.11$, $p < 0.05$). Changes in VO₂ max, sIL-6R, and sTNFR1 were included in the second model ($n = 27$) and the change in VO₂ max approached significance as the single independent predictor of the change in femoral neck BMD ($r^2 = 0.29$, $p = 0.06$).

Discussion

While weight loss was achieved in both the WL and the WL + AEX groups after a 6-month intervention, the treatment effect on bone outcomes and cytokines was very different. Our results show that women in the WL + AEX group experienced a 2% increase in femoral neck BMD without a significant change in femoral neck BMC or lumbar spine BMD or BMC. Cytokine concentrations decreased only with WL + AEX, and not with WL alone. Further, our results suggest that the increase in BMD experienced during WL + AEX is associated with a decrease in sTNFR1 and an increase in aerobic fitness.

Previous studies report that aerobic training is associated with either maintenance or improvement of BMD in postmenopausal women [22,23], whereas weight loss diets are often associated with a decrease in BMD [5,6]. Moreover, weight loss that occurs during an exercise treatment is associated with either the prevention of loss or an improvement in BMD [6,8,9,24]. Our previous work demonstrates the benefits of weight loss plus aerobic exercise on BMD [8,17]. The results of the current study confirm these results in a larger sample and also show associations among the changes in VO₂ max and inflammation and BMD after an exercise training intervention. Various studies report an association among VO₂ max and femoral neck BMD [25], total body BMD [26], and BMD of the legs [27]. However, our study additionally demonstrates a relationship between an increase in VO₂

max and the subsequent increase in femoral neck BMD after a 6-month WL + AEX intervention. The corresponding decrease in inflammatory markers in the WL + AEX group suggests a possible mechanistic relationship among exercise intensity, inflammatory response, and bone metabolism.

The association between menopause and reduced BMD is well established. However, the relationship between inflammation and bone metabolism is less clear. Human studies investigating the relationship between inflammation and BMD are inconsistent, in part due to the variation in subject characteristics including wide variations in age, years since menopause, and physical activity levels. In addition, since cytokines function primarily at a local level and the use of bone biopsies is uncommon, researchers employ a variety of methods to study levels of inflammation including circulating cytokines, stimulated whole blood production of cytokines, and peripheral blood mononuclear cells [28]. It is believed that estrogen deficiency leads to increased activity and maturation of osteoclasts [29], thus contributing to high rates of bone resorption and eventually to osteoporosis. The rate of osteoclast development depends on, among other factors, the number of osteoclast progenitors and the production of cytokines that are involved in osteoclast differentiation [30]. Cytokines are produced in the bone microenvironment by osteoblasts [31], bone marrow stromal cells, and peripheral blood monocytes as well as by adipose tissue [32–34]. Thus, a decrease in inflammation through weight loss plus aerobic exercise could contribute to a resulting increase in BMD.

The relationship of IL-6 and bone metabolism in pre-and postmenopausal women is inconsistent [13,35–37]. However, sIL-6R may be more important than IL-6 with regards to the rate of bone turnover [38], as the activity of IL-6 is increased in the presence of sIL-6R [39]. Giuliani et al. [36] found that the concentration of sIL-6R is significantly higher in osteoporotic vs. healthy women, while Abrahamsen et al. determined that a reduction in the concentration of sIL-6R was negatively associated with bone loss at the femoral neck [38]. Similar to previous findings [17,40,41], we found that WL alone did not lead to a decrease in cytokines or cytokine receptors. Although unexpected, the increase in sIL-6R by the WL group could potentially lead to increased activity of IL-6, which would, in turn, negatively effect BMD. However, due to the small sample size of sIL-6R in the WL group, these results should be interpreted with caution. The amount of weight loss (without the addition of aerobic exercise) may have been insufficient to decrease inflammation. In the current study, the increase in VO₂ max was negatively associated with the change in production of sIL-6R and positively associated with femoral neck BMD, again highlighting the importance of adding an aerobic exercise program to weight loss to reduce inflammation.

TNF- α signals through two receptors, TNFR1 and TNFR2, both of which are released by adipose tissue [42]. Tumor necrosis factor-R1 is required for TNF-mediated inhibition of osteoblast differentiation [43] and also for osteoclast activity [44]. Our results indicate that the change in femoral neck BMD was significantly associated with the change in sTNFR1. A reduction in adipose tissue via weight loss combined with aerobic exercise may result in a decrease in TNF- α activity and subsequent attenuation of bone loss. Therefore, the decrease in sTNFR1 seen in the WL + AEX group may have contributed to increased osteoblast formation and decreased osteoclast formation, with the resultant effect of improving BMD.

While we did not conduct a randomized control trial, the improvement in femoral neck BMD demonstrated in this study is consistent with other controlled trials [45–48]. It should be noted that controlled trials may overestimate treatment effects compared to randomized controlled trials [24]. In addition, the ability of DXA to accurately report BMD during the course of a weight loss study is limited due to changes in fat mass and distribution and has been discussed by various researchers [49–53]. However, DXA is currently the standard

method of assessing BMD and the changes in weight and fat mass were not significantly different between the WL and the WL + AEX groups. Finally, while we did see a significant change in femoral neck BMD, a longer exercise training and/or weight loss period may have allowed for the detection of other significant changes in BMD in both the WL and the WL + AEX groups.

In summary, we report that aerobic exercise during weight loss is necessary to decrease inflammation and increase BMD. To our knowledge, this study is the first to simultaneously and longitudinally investigate the effect of weight loss and aerobic exercise on inflammation and BMD and their association. This study indicates that the reduction in inflammation that accompanies weight loss plus aerobic exercise may partially explain the resulting improvement in BMD. Inclusion of aerobic exercise to improve VO₂ max may be critical for overweight and obese postmenopausal women undergoing weight loss programs, with respect to reduction of inflammation and the resulting effect on BMD. Since the change in VO₂ max was predictive of the change in both femoral neck BMD and lumbar spine BMD, it is possible that a greater increase in VO₂ max (>12% as reported here) may be needed to improve BMD at additional bone sites other than the femoral neck.

The relationship among exercise intensity and changes in BMD as well as inflammatory response needs to be explored further. In addition, the optimal training intensity and duration to elicit both the greatest reduction of cytokine production and subsequent improvements in BMD would be an important area of investigation. Future research is also needed to determine the independent effects of aerobic exercise programs on BMD and inflammatory response without weight loss.

Acknowledgments

This work received funding from the Baltimore Veterans Medical Research Service; the Baltimore Veterans Affairs Geriatric Research, Education, and Clinical Center; National Institutes on Aging Grants T32 AG-00219, R01-AG-18408, R01-AG-019310, R29-AG-14066, and K01-AG-00747; National Institutes of Health Grant P01-DK-072488; and National Institute of Nursing Research Grant R01 NR-03514. We thank the women who participated in the study, Karin Murphy for her technical assistance, and Dr. Andrew Goldberg for his support.

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Fig. 1. Percentage change of femoral neck bone mineral density in weight loss and weight loss plus walking groups after 6-month intervention ($n = 96$)

Fig. 2. Relationship between change in femoral neck BMD and change in VO₂ max after 6-month intervention ($n = 86$). (●) Weight loss; (□) weight loss + walking

Fig. 3. Relationship between change in femoral neck BMD and change in plasma sTNF-α1R concentrations after 6-month intervention ($n = 86$). (●) Weight loss; (□) weight loss + walking

Table 1

Physical characteristics of the weight loss (WL) and weight loss plus walking (WL + AEX) groups before and after intervention

	WL (<i>n</i> = 40)		WL + AEX (<i>n</i> = 46)	
	Baseline	6 months	Baseline	6 months
Age (yr)	58 ± 5 ^a		60 ± 5	
Years since menopause	10.6 ± 7.4		12.2 ± 8.4	
Weight (kg)	87.4 ± 14.4	81.0 ± 15.2	84.6 ± 11.3	78.2 ± 10.6
BMI (kg/m ²)	32.6 ± 4.6	30.2 ± 5.1	32.1 ± 4.2	29.7 ± 3.8
Fat mass (kg)	41.5 ± 10.0	36.1 ± 11.4	38.9 ± 8.3	33.8 ± 8.0
Lean mass (kg)	41.8 ± 5.0	41.2 ± 4.4	41.2 ± 5.2	41.0 ± 4.5
VO ₂ max (L/min)	1.70 ± 0.28	1.66 ± 0.28	1.62 ± 0.27	1.80 ± 0.30 ^{b,c}

Note: Data were analyzed using ANOVA and ANCOVA. There were no significant differences among the groups at baseline

^aMean ± SD (all such values)

^bSignificantly different from baseline (*p* < 0.001)

^cChange from baseline significantly different from WL group (*p* < 0.001)

Table 2

Bone mineral density (BMD) and content of femoral neck and lumbar spine and plasma inflammatory markers of the weight loss (WL) and weight loss plus walking (WL + AEX) groups before and after intervention

	WL (<i>n</i> = 40)		WL + AEX (<i>n</i> = 46)	
	Baseline	6 months	Baseline	6 months
Femoral neck BMD (g/cm ²)	0.919 ± 0.149 ^a	0.911 ± 0.131	0.914 ± 0.143	0.931 ± 0.148 ^{b,c}
L ₂ –L ₄ BMD (g/cm ²)	1.118 ± 0.162	1.120 ± 0.165	1.195 ± 0.190	1.200 ± 0.191
Femoral neck BMC (g)	4.377 ± 0.877	4.427 ± 0.816	4.234 ± 0.914	4.306 ± 0.839
L ₂ –L ₄ BMC (g)	47.089 ± 10.133	47.361 ± 9.438	49.466 ± 9.995	50.196 ± 11.194
IL-6 (pg/ml) ^d	2.04 ± 0.90	2.03 ± 1.24	2.42 ± 1.71	2.40 ± 2.85
TNF-α (pg/ml) ^d	2.12 ± 3.49	3.02 ± 7.90	1.74 ± 2.34	1.64 ± 2.51
sIL-6R (pg/ml) ^{e,f}	19.2 ± 5.7	20.8 ± 4.6 ^b	24.5 ± 5.2 ^g	22.4 ± 5.1 ^{b,h}
sTNFR1 (μg/ml) ^{e,f}	730.3 ± 236.1	736.9 ± 208.9	836.9 ± 185.1	711.8 ± 191.8 ^{c,i}
sTNFR2 (pg/ml) ^{e,f}	1648.8 ± 497.9	1834.1 ± 556.1	1859.5 ± 386.1	1749.0 ± 382.5

Note: Data were analyzed using ANOVA and ANCOVA

^a Mean ± SD (all such values)

^b Significantly different from baseline (*p* < 0.05)

^c Change from baseline significantly different from WL group (*p* < 0.05)

^d Log-transformed values of IL-6 and TNF-α were used for analysis

^e Soluble receptors were run in a subset of the population (WL = 10, WL + AEX = 17)

^f Previously reported data [17]

^g Significantly different from WL group at baseline (*p* < 0.05)

^h Change from baseline: WL vs. WL + AEX (*p* = 0.08)

ⁱ Significantly different from baseline (*p* < 0.001)

Table 3Correlations among baseline BMD, BMC, body composition, and cytokine production in all subjects ($n = 86$)

	Femoral neck BMD (g/cm²)	L₂-L₄ BMD (g/cm²)	Femoral neck BMC (g)	L₂-L₄ BMC (g)
Age (yr)	-0.309 ^a	-0.151	-0.250 ^a	-0.100
Weight (kg)	0.498 ^a	0.429 ^a	0.590 ^a	0.489 ^a
BMI (kg/m ²)	0.468 ^a	0.413 ^a	0.496 ^a	0.325 ^a
Fat mass (kg)	0.384 ^a	0.309 ^a	0.455 ^a	0.292 ^a
Lean mass (kg)	0.503 ^a	0.465 ^a	0.604 ^a	0.620 ^a
VO ₂ max (L/min)	0.401 ^a	0.146	0.418 ^a	0.275 ^b
IL-6 (pg/ml) ^c	0.177	0.111	0.206	0.068
TNF- α (pg/ml) ^c	0.061	-0.030	0.149	0.141

Note: Pearson correlation coefficients^a
 $p < 0.001$ ^b
 $p < 0.05$ ^c Log-transformed values of IL-6 and TNF- α were used for analysis

Table 4

Correlations among change in production of inflammatory cytokine-soluble receptors, BMD, BMC, and body composition ($n = 27$)

	Δ Femoral neck BMD (g/cm ²)	Δ L ₂ –L ₄ BMD (g/cm ²)	Δ Femoral neck BMC (g)	Δ L ₂ –L ₄ BMC (g)
Δ sTNFR1 (μg/ml)	−0.385 ^a	0.135	0.154	0.110
Δ sTNFR2 (pg/ml)	−0.306	−0.098	0.220	0.375
Δ sIL-6R (pg/ml)	−0.335	0.208	0.347	0.127
Δ Weight (kg)	−0.039	−0.065	0.019	−0.020
Δ Fat mass (kg)	−0.048	−0.062	0.075	−0.203
Δ Lean mass (kg)	0.087	−0.067	−0.053	0.320 ^b
Δ VO ₂ max (L/min)	0.323 ^c	−0.061	−0.131	0.153

Note: Pearson correlation coefficients

^a
 $p < 0.05$

^b
 $p < 0.001$