

## Clinical Investigations

# The Effects of Walking at the Anaerobic Threshold Level on Vertebral Bone Loss in Postmenopausal Women

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Received June 19, 1992, and in revised form November 23, 1992

**Summary.** The purpose of this study was to determine the optimal intensity of exercise necessary to prevent the postmenopausal bone loss on the basis of anaerobic threshold (AT). Thirty-three postmenopausal women were randomized to control (group C:  $n = 12$ ) or two exercise groups (group H and group M). All women performed a treadmill exercise test, and the AT was measured by expired gas analysis. The exercise regimen consisted mainly of walking at a speed that kept the exercise heart rate above the AT (group H:  $n = 12$ ) or below the AT (group M:  $n = 9$ ). Exercise was performed for 30 minutes, three times a week for 7 months. The bone mineral density (BMD) of the lumbar vertebrae was measured using dual energy X-ray absorptiometry. The BMD level in group C decreased by  $1.7 \pm 2.7\%$ , but there was a significant increase of  $1.1 \pm 2.9\%$  in group H. In group M there was a decrease of  $1.0 \pm 3.1\%$  which did not differ from group C. In group C, serum osteocalcin and urinary hydroxyproline excretion were significantly increased, but no changes were seen in either of the exercise groups. Urinary calcium significantly decreased in the exercise groups. We conclude that short-term (7 months) exercise with intensity above the AT is safe and effective in preventing postmenopausal bone loss.

**Key words:** Menopause – Bone density – Exercise – Anaerobic threshold.

Osteoporosis is a widespread bone disorder that primarily affects postmenopausal women. Bone loss usually begins in the third decade, and accelerates after menopause. The rate of bone loss in postmenopausal women 3–5 years following menopause is 4.5% of spinal trabecular mineral density per year [1]. Exercise has been demonstrated to either retard bone loss or to increase bone mass in postmenopausal women [2–4]. However, it is not yet clear which type and intensity of physical exercise is effective in maintaining bone density and in preventing the development of osteoporosis. We performed walking training, using an exercise regimen

designed on the basis of the anaerobic threshold (AT), to determine the optimal intensity of exercise in maintaining bone mineral density. The AT is defined as the level of exercise oxygen consumption above which aerobic mechanisms are supplemented by anaerobic mechanisms, leading to increased lactate production. Therefore, exercise intensity below the AT is consistent with aerobic exercise with a balanced oxygen supply-demand relationship.

## Materials and Methods

### Subjects

Thirty-five healthy women, aged 45–67 years, participated in a controlled trial for 7 months. Twenty-three women entered the exercise program, and 12 served as controls. All subjects were postmenopausal and had no history of oophorectomy. In addition, they were placed on ordinary diets without supplements of calcium, vitamin D, thiazide diuretics, or estrogen.

### Measurement of Anaerobic Threshold

The subjects performed cardiopulmonary exercise testing to obtain an exercise prescription. A treadmill exercise test was performed using our ramp protocol which has been previously described [5]. A 12-lead electrocardiogram and the heart rate were recorded continuously (STS-7000, Nihon Kohden, Tokyo). Systemic blood pressure was measured every minute with cuff sphygmomanometry. The exercise end points were symptoms of muscle fatigue, hyperpnea, and Borg's indices greater than 17 (very hard) [6]. Ventilatory volumes and gas exchange were measured with an automated breath-by-breath system on a Metabolic Monitor 2L01 (NEC Sanei, Tokyo). The AT was identified as the value of oxygen uptake ( $\dot{V}O_2$ ) at which the linear relationship between minute ventilation ( $\dot{V}_E$ ) and  $\dot{V}O_2$  was lost, whereas the relationship between  $\dot{V}_E$  and carbon dioxide production remained unchanged [7].

### Exercise Prescription

The exercise group was randomly divided into two groups: a moderate intensity group and a high intensity group. The heart rate at the work load of anaerobic threshold was determined by cardiopulmonary exercise testing. Moderate exercise means the work intensity

**Table 1.** Baseline characteristics from control and exercise groups of healthy postmenopausal women

	Control	Exercise intensity	
		Moderate	High
No. of subjects	12	9	12
Age (years)	58 ± 8	58 ± 5	56 ± 4
Years since menopause	8.9 ± 7.6	5.8 ± 4.3	7.5 ± 4.8
Height (cm)	151.1 ± 5.2	151.4 ± 4.9	151.5 ± 3.4
Weight (kg)	53.9 ± 6.0	53.4 ± 6.8	54.0 ± 5.0
BMI (kg/m <sup>2</sup> )	24.6 ± 3.3	23.5 ± 2.4	23.3 ± 2.3
Lumbar spine density (g/cm <sup>2</sup> )	0.83 ± 0.14	0.83 ± 0.18	0.85 ± 0.14
AT (ml/min/kg)	22.2 ± 6.0	18.8 ± 3.0	20.3 ± 5.1

below the AT (about 90% of the heart rate at the AT). High exercise means the work intensity above the AT (about 110% of the heart rate at the AT). The exercise program consisted of stretching of the legs, torso, and arms followed by 30 minutes of walking on flat grass-covered ground, three times a week for 7 months. The walking speed performed was that which maintained the heart rate at each exercise intensity. The women were instructed in techniques of taking their own heart rate at the radial artery. The heart rate was recorded immediately after each walk. Ambulatory electrocardiographic monitoring was performed on a calibrated Kenz recorder (Suzuken Medical Inc., Japan) to confirm whether or not the subjects achieved the target heart rate and to monitor for serious arrhythmia.

#### Measurement of Bone Mineral Density

The bone density of the lumbar spine (L2-L4) was measured by dual-energy X-ray absorptiometry (QDR-1000, Hologic Co. USA), according to instructions. The coefficient of variation of these measurements was 0.4%. All bone mineral values were determined by one author who had no knowledge of the group assignment of the subjects. Data were reported as bone mineral density (BMD) in grams per square centimeter.

#### Biochemical Analysis

Serum ionized calcium, inorganic phosphate, alkaline phosphatase, and serum and urinary creatinine were measured by automated methods. Serum osteocalcin was measured with an OC.I-125 kit obtained from the Midori-juji Institute. Serum calcitonin was measured by radioimmunoassay (calcitonin kit Mitsubishi-yuka). Urinary hydroxyproline was measured by high-pressure liquid chromatography (HPLC) analysis of the phenylisothiocyanate derivative and expressed relative to creatinine levels.

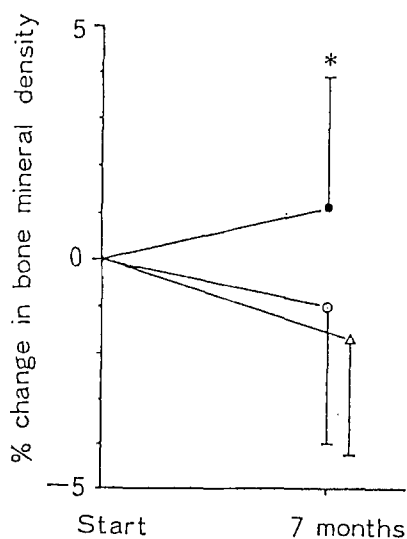
The variables were determined prior to the start of the trial and after 7 months.

#### Statistical Analysis

The comparability of the three groups at baseline was tested by one-way analysis of variance. The unpaired Student's *t*-test was used to test for differences between the control and the exercise groups. Changes from baseline in biochemical variables were compared by paired *t*-tests. The results were expressed as the mean ± SD, and differences were considered significant at the level of *P* < 0.05. The body mass index (BMI) in kg/m<sup>2</sup> was calculated from the height and weight of the patient.

#### Results

Twenty-one women completed the trial without adverse events, and two failed to complete the program because of



**Fig. 1.** Percentage changes of the bone mineral density in the exercise and control group from baseline to 7 months. ●, high intensity group; ○, moderate intensity group; △, control group. Values are given as the mean (SD) from the values before the beginning of the trial. \*Significantly different from the control group (*P* < 0.05).

lack of time. Table 1 gives the details of three groups of women who completed the study. There was no significant difference in mean age, time since menopause, or BMI among the three groups. The AT was 22.2 ± 6.0 ml/minute/kg in the control group, 18.8 ± 3.0 ml/minute/kg in the moderate intensity group, and 20.3 ± 5.1 ml/minute/kg in the high intensity group. There was no significant difference among groups, and all had good exercise capacity for their age. There was no significant difference in BMD among the three groups prior to the study. The mean heart rate during exercise, measured by Holter electrocardiogram, was 126 bpm in the high intensity group and 113 bpm in the moderate intensity group. The walking speed calculated from the record of Holter monitoring was on average 7.2 km/hour in the high intensity group and 6.2 km/hour in the moderate intensity group.

Seven months after exercise, the BMD in the high intensity group showed an increase of 1.1 ± 2.9%, whereas a decrease of 1.7 ± 2.8% was found in the control group. This difference was statistically significant (*P* < 0.05). In the moderate intensity group the BMD decreased by 1.0 ± 3.1% during the 7-month period, but the loss of BMD was less than that of the control group (not significant, Fig. 1). The

**Table 2.** Serum and urinary biochemical indexes before and after 7 months of exercise

	Control		Exercise intensity			
			Moderate		High	
	Before	After	Before	After	Before	After
<b>Serum</b>						
Calcium	9.0 ± 0.2	9.2 ± 0.2 <sup>a</sup>	9.2 ± 0.4	9.0 ± 0.6	9.4 ± 0.5	9.3 ± 0.5
Phosphorus (mg/dl)	3.6 ± 0.3	3.8 ± 0.4	3.5 ± 0.3	3.7 ± 0.2 <sup>a</sup>	3.7 ± 0.5	3.7 ± 0.4
Alkaline phosphatase (U/liter)	167 ± 29	181 ± 36	177 ± 30	205 ± 39 <sup>a</sup>	196 ± 37	212 ± 38
Calcitonin (pg/ml)	30.7 ± 2.3	36.8 ± 7.1	35.4 ± 10.6	39.9 ± 11.5	34.5 ± 14.7	42.6 ± 15.8
Osteocalcin (ng/ml)	11.8 ± 2.6	14.9 ± 2.6 <sup>b</sup>	12.0 ± 2.3	13.3 ± 3.5	11.6 ± 2.4	12.8 ± 1.8
<b>Urine</b>						
Hydroxyproline: Creatinine	19.5 ± 3.1	25.1 ± 6.9 <sup>a</sup>	17.6 ± 6.9	20.4 ± 6.9	17.5 ± 4.1	20.2 ± 5.8
Calcium: Creatinine	0.18 ± 0.11	0.16 ± 0.11	0.20 ± 0.10	0.14 ± 0.10 <sup>a</sup>	0.26 ± 0.07	0.20 ± 0.10 <sup>a</sup>

Values are mean ± SD

Urinary hydroxyproline was measured in mM/liter, and creatinine in μM/liter

<sup>a</sup>  $P < 0.05$ , <sup>b</sup>  $P < 0.01$  for the comparison with the baseline

clinical data before and after the study are shown in Table 2. There were no significant differences among the three groups. After exercise, the control group showed significant increases in serum osteocalcin (from  $11.8 \pm 2.6$  to  $14.9 \pm 2.6$  ng/ml,  $P < 0.01$ ), and in urinary hydroxyproline-creatinine ratio (from  $19.5 \pm 3.1$  to  $25.1 \pm 6.9$ ,  $P < 0.05$ ). On the other hand, there were no significant increases in serum osteocalcin and urinary hydroxyproline-creatinine ratio after exercise in the exercise groups. Urinary output of calcium significantly decreased in the high intensity group from  $0.26 \pm 0.07$  to  $0.20 \pm 0.10$  and in the moderate intensity group from  $0.20 \pm 0.10$  to  $0.14 \pm 0.10$  ( $P < 0.05$ ).

## Discussion

Previous studies have suggested that exercise or physical activity of various types may increase bone mass by increasing the muscular stress placed upon bone [2, 8, 9]. However, the threshold level of exercise required to elicit an increase in bone mass has not been defined with reference to frequency, duration, and intensity.

Several groups have reported that walking programs alone do not prevent bone loss [10–12], but exercise was performed below the AT in these studies. Our study showed walking above the AT was effective in increasing BMD, whereas exercise below the AT was not. Dalsky et al. [13] have shown that weight-bearing exercise at 70 to 90% of maximal oxygen uptake leads to significant increases in bone mineral content [13]. Their exercise intensity is above the AT, as the AT generally corresponds to 60 to 70% of maximal oxygen uptake. Chow et al. [14] have similarly reported an increase in bone mass as a result of aerobic exercise at 80% of the maximum heart rate during treadmill exercise. Beverly et al. [15] found that brief periods of stressful exercise have increased grip strength and BMC in the forearm. Their exercise regimen was the squeezing of a tennis ball as hard as possible for 30 seconds each day for 6 weeks. These results support the concept that high intensity of exercise may result in an increase in bone mass even after short periods of training. In the present study, the difference of effects between the two exercise groups may depend not only on the intensity with which the exercises were carried out but also on the total work. Weltman et al. [16] recently re-

ported that endurance training above the AT amplified the pulsatile release of growth hormone (GH), whereas no changes were observed within the AT. As GH affects bone metabolism through plasma insulin-like growth factor-1, exercise above the AT may have an effect on bone formation.

In postmenopausal women, increased bone turnover leads to increased bone loss. In this phase, the relative or absolute increase in resorption exceeds formation. Bone resorption is reflected by an increased urinary output of hydroxyproline and calcium [17, 18]. Serum osteocalcin has been used as a biochemical marker of osteoblastic activity and an indicator of the rate of bone turnover [19, 20]. The results of our 7-month study showed that serum osteocalcin and the ratio of urinary hydroxyproline to creatinine significantly increased in the control group, whereas there was no significant change in the exercise groups. The excretion of urinary calcium significantly decreased in the exercise groups. These results suggest that both exercise programs relatively suppress the rate of increased turnover against control and improve an uncoupling of bone resorption and bone formation. The duration of our study may be too short to evaluate the effects of moderate intensity exercise. Further, the long-term studies are needed to establish the optimal intensity in preventing bone loss.

In conclusion, our 7-month trial showed that postmenopausal women increased significantly in bone mass by doing exercise with intensity above the AT.

*Acknowledgment.* This study was supported by funds from Esso Sekiyu K.K.

## References

- Ettinger B, Genant HK, Cann CE (1987) Postmenopausal bone loss is prevented by treatment with low-dosage estrogen with calcium. *Ann Intern Med* 106:40–45
- Simkin A, Ayalon J, Leichter I (1987) Increased trabecular bone density due to bone-loading exercises in postmenopausal osteoporotic women. *Calcif Tissue Int* 40:59–63
- Smith EL, Smith PE, Ensign CJ, Shea MM (1984) Bone involution decrease in exercising middle-aged women. *Calcif Tissue Int* 36:s129–s138

4. Krolner B, Toft B, Nielsen SP, Tondevold E (1983) Physical exercise as prophylaxis against involutional vertebral bone loss: a controlled trial. *Clin Sci* 64:541–546
5. Hasegawa A, Hatori M, Imanari T, Fukuda T, Yamaguchi E, Yamauchi Y, Naito S, Amano M, Nakano A, Suzuki T, Murata K (1991) Reproducibility and effectiveness of ramp protocol with treadmill exercise test. *Jpn J Appl Physiol* 21:11–15
6. Borg G (1970) Perceived exercise as an indicator of somatic stress. *Scand J Rehab Med* 2:92–98
7. Caiozzo VJ, Davis JA, Ellis JF, Azus JL, Vandagriff R, Prietto CA, McMaster WC (1982) A comparison of gas exchange indices used to detect the anaerobic threshold. *J Appl Physiol* 53: 1184–1189
8. Smith EL, Reddan W, Smith PE (1981) Physical activity and calcium modalities for bone mineral increase in aged women. *Med Sci Sports Exerc* 13:60–64
9. Margulies JY, Simkin A, Leichter I, Bivas A, Steinberg R, Giladi M, Stein M, Kashtan H, Milgrom C (1986) Effect of intense physical activity on the bone-mineral content in lower limbs of young adults. *J Bone Joint Surg Am* 68:1090–1093
10. Cavanagh DJ, Cann CE (1988) Brisk walking does not stop bone loss in postmenopausal women. *Bone* 9:201–204
11. Sandler RB, Cauley JA, Hom DL, Sashin D, Kriska AM (1987) The effects of walking on the cross-sectional dimensions of the radius in postmenopausal women. *Calcif Tissue Int* 41:65–69
12. White MK, Martin RB, Yeater RA, Butcher RL, Radin EL (1984) The effects of exercise on the bones of postmenopausal women. *Int Orthop* 7:209–214
13. Dalsky GP, Stocke KS, Ehsani AA, Slatopolsky E, Lee WC, Birge SJ (1988) Weight-bearing exercise training and lumbar bone mineral content in postmenopausal women. *Ann Intern Med* 108:824–828
14. Chow R, Harrison JE, Notarius C (1987) Effect of two randomised exercise programmes on bone mass of healthy postmenopausal women. *BMJ* 295:1441–1444
15. Beverly MC, Rider TA, Evans MJ, Smith R (1989) Local bone mineral response to brief exercise that stresses the skeleton. *BMJ* 299:233–235
16. Weltman A, Weltman JY, Schurrer R, Evans WS, Veldhuis JD, Rogol AD (1992) Endurance training amplifies the pulsatile release of growth hormone: effects of training intensity. *J Appl Physiol* 72:2188–2196
17. Epstein S (1988) Serum and urinary markers of bone remodeling: assessment of bone turnover. *Endocrinol Rev* 9:437–449
18. Kelly PJ, Pocock NA, Sambrook PN, Eisman JA (1989) Age and menopause-related changes in indices of bone turnover. *J Clin Endocrinol Metab* 69:1160–1165
19. Delmas PD, Wahner HW, Mann KG, Riggs BL (1983) Assessment of bone turnover in postmenopausal osteoporosis by measurement of serum bone Gla-protein. *J Lab Clin Med* 102:470–476
20. Brown JP, Delmas PD, Malaval L, Edouard C, Chapuy MC, Meunier PJ (1984) Serum bone Gla-protein: a specific marker for bone formation in postmenopausal osteoporosis. *Lancet* 1: 1091–1093