Physical Exercise Increases Bone Mineral Density in Postmenopausal Women

SATOSHI SHIMEGI, MASAHIKO YANAGITA, HIROYA OKANO*, MEGUMI YAMADA**, HIROKO FUKUI**, YUKIHITO FUKUMURA***, YOSHITO IBUKI*, AND ITARU KOJIMA

Institute of Endocrinology, Gunma University, *Department of Obstetrics and Gynecology, Faculty of Medicine, Gunma University, **Department of Health and Physical Education, Faculty of Education, Gunma University, and ***Clinical Laboratory Center, Gunma University, Maebashi 371, Japan

Abstract. To examine whether physical exercise is beneficial in preventing postmenopausal osteoporosis, we measured bone mineral density (BMD) in three distinct groups of healthy postmenopausal Japanese women aged 49–61 yrs: 11 volleyball players (V) and 5 joggers (J), and 9 controls (C) who had not been participating in regular physical activity. BMD was measured at the lumbar spine (L2-L4) and proximal femur using dual energy X-ray absorptiometry, and at the radius using single X-ray photon absorptiometry. Serum levels of estradiol (E2), parathyroid hormone (PTH) and calcitonin were also measured by radioimmunoassay. Osteocalcin was determined by enzyme immunoassay. BMD in the lumbar spine was greater in the V and J groups than in the C group (P<0.01). The J group had a significantly lower PTH level than the C group. In contrast to weight-bearing bones, we found no significant differences in BMD at the radius among the three groups. BMD at the distal radius was negatively correlated with years after menopause in both the V group and the J group significantly. These results indicate that regular physical exercise has a positive effect on the maintenance of bone mineral in postmenopausal women and that the protective action is localized in skeletal sites used predominantly for the sport without opposing the negative regulation caused by estrogen deficiency in systemic bones.

Key words: Physical activity, Postmenopausal osteoporosis, Bone mineral density, Dual energy X-ray absorptiometry, Single X-ray photon absorptiometry.

PROFOUND loss of bone mass is frequently observed in elderly subjects. In women, a rapid diminution of bone occurs with high probability after menopause [1] and leads to postmenopausal osteoporosis. Recently, it has been recognized that estrogen has many actions on bone, including stimulation of bone formation by osteoblasts [2, 3], inhibition of PTH action to facilitate bone resorption [4, 5]. Reduction of plasma estrogen after menopause leads to excessive bone loss in postmenopausal women. Although various medications have been tried to prevent osteoporosis, their efficacy has been inconclusive so far, except for the estrogen therapy [6]. Physical activity has been thought to be one of the important factors in preventing osteoporosis since the level of physical activity in daily life determines bone mass [7]. For example, prolonged bed rest or immobilization markedly decrease bone mass even in healthy individuals [8–10]. Also, individuals who exercised regularly have higher bone mineral content than those who do not [11, 12]. It is, however, reported that exercise does not always have a positive effect on bone mineral content but, rather, it is negative when exercise is
too intense [13–16] or mechanical stress exceeds the adaptability of the bone itself. Furthermore, there is some disagreement in the literature as to whether exercise has a general [11, 17–19] or a localized effect on bone mineral density. Thus, the role of physical activity in the prevention of osteoporosis has not been fully identified. This points out that exercise should be defined precisely for preventive use. The contradictory effects of exercise described mainly in animals result from different exercise conditions including the type, intensity, duration and frequency of exercise [20, 21]. Furthermore, only a little information on the condition of exercise to prevent bone loss in man is yet available [22]. It is therefore not clear which types of exercise are most valuable for preventing osteoporosis, or whether appropriate exercise might reduce the need for estrogen therapy in postmenopausal women.

The present study was therefore designed to investigate (1) whether an increase in physical activity prevents osteoporosis after menopause and (2) whether physical activity has a systemic effect in maintaining bone mass.

**Methods**

**Subjects**

Twenty-six healthy, postmenopausal Japanese females, aged 49–61, were studied in this study. Written informed consent was obtained before the study and a medical questionnaire was administered to identify conditions and medications that might influence the results. All subjects were on a normal diet and had not received therapeutic doses of calcium, vitamin D or estrogen. They had no history of metabolic bone disease, cancer, gastrectomy, alcoholism, malabsorption, or renal or hepatic disease. The volleyball players and the joggers were members of local sports clubs. Age matched controls who had no habit of physical exercise were also studied (see Table 1). Joggers ran 40–260 km/month. Exercise history (years of exercise) was 10–35 years and 2–15 years in volleyball players and joggers, respectively.

**Measurement of bone mineral density of radius, femur, lumbar vertebrae**

Bone mineral density (BMD) in the lumbar vertebrae (L2–L4) and proximal femur (neck, Ward’s triangle, greater trochanter) was estimated by Dual Energy X-ray absorptiometry (DXA), using a QDR 1000 (Hologic Corp.) according to a previous study [23]. Radial bone mineral density was measured at two sites (distal site; the distal metaphysis near the styloid apophysis, and proximal site; the diaphysis) by a single photon densitometer (Osteon, Inc.) employing an osteoanalyzer system II. The density values for all bones were expressed as g/cm². All scans were acquired and analyzed by the same individual.

**Biochemical analysis**

A single nonfasting blood sample was obtained by venipuncture between 1100 h and 1600 h. Although one of the joggers ran about 2 km 6 h before the blood test, the other subjects did not do any exercise on the measurement day. The serum samples were stored at −20°C until they were ana-

<table>
<thead>
<tr>
<th>Groups</th>
<th>Controls</th>
<th>Volleyball players</th>
<th>Joggers</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>9</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Age (yr.)</td>
<td>54.2 ± 2.9</td>
<td>53.9 ± 2.9</td>
<td>56.8 ± 2.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>154.6 ± 2.3</td>
<td>154.8 ± 2.9</td>
<td>155.5 ± 2.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>55.4 ± 2.7</td>
<td>56.8 ± 6.9</td>
<td>54.8 ± 6.8</td>
</tr>
<tr>
<td>BMI1 (kg/m²)</td>
<td>23.2 ± 1.1</td>
<td>23.7 ± 3.1</td>
<td>22.6 ± 2.6</td>
</tr>
<tr>
<td>Age at menopause (yr.)</td>
<td>47.7 ± 4.9</td>
<td>50.3 ± 3.1</td>
<td>51.6 ± 3.2</td>
</tr>
<tr>
<td>Years after menopause (yr.)</td>
<td>6.6 ± 5.1</td>
<td>3.7 ± 3.4</td>
<td>5.2 ± 3.1</td>
</tr>
<tr>
<td>Exercise history (yr.)</td>
<td>18.0 ± 6.0</td>
<td>18.0 ± 6.0</td>
<td>8.0 ± 5.3</td>
</tr>
<tr>
<td>Jogging distance (km/month)</td>
<td>110.0 ± 87.2</td>
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</tbody>
</table>

Values are the mean±SD. 1BMI, Body mass index.
alyzed. Serum hormone levels such as intact PTH, calcitonin, estradiol (E2) were determined at Teijin Ltd. (Tokyo) by Allegro Intact Assay (Nihon Medi-Physics Co., Ltd., Takarazuka), Calcitonin Kit "Daiichi" (Daiichi Radioisotope Labs., Ltd., Tokyo), and DPC Estradiol Kit (Nippon DPC Corporation, Tokyo), respectively. Serum levels of intact and N-terminal fragment bone Gla-protein (osteocalcin) were measured at Teijin Limited (Tokyo) with a Sandwich Enzyme immunoassay kit "Osteocalcin (Intact)" and "Osteocalcin (N-region)" (Teijin Ltd., Tokyo), respectively [24]. Alkaline phosphatase (ALP) activity (normal range; 80-260 mU/ml) was determined by the p-nitrophenyl phosphate substrate method.

Statistical analysis

The results are expressed as the mean±SD. All statistical tests were two-sided. One-way analysis of variance of Kruskal-Wallis test and modified t-test were used for statistical evaluation of significant (P<0.05) mean differences among all groups. Pearson correlation coefficients were also calculated for all pairs of variables for each of the subgroups separately.

### Results

The physical data and training characteristics of the 26 subjects in the three groups are presented in Table 1. There were no significant differences in physical and gynecological parameters among the groups. Results of the biochemical analysis of serum are summarized in Tables 2 and 3. Serum calcium, phosphate, total protein, and albumin levels did not differ among the three groups. Estradiol (E2) concentrations in all subjects ranged from 10 to 37 pg/ml and were in an expected low range for postmenopausal women. The average PTH concentration for joggers was significantly lower than that of both controls and volleyball players (P<0.05), although all values were in the normal range (10-65 pg/ml). The basal calcitonin concentration was similar in all three groups and normal (<184 pg/ml). The bone metabolic markers for bone formation, serum ALP activity and osteocalcin (Intact) level, did not differ among the groups. The osteocalcin (fragment) concentration, which is thought to be related to bone resorption [25], was higher in volleyball players than in joggers (P<0.05). Recently, Shiraki et al. proposed the availability of the ratio of N-fragment-osteocalcin.

### Table 2. Biochemical analysis of serum in three groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Controls</th>
<th>Volleyball players</th>
<th>Joggers</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>9</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>9.54±0.37</td>
<td>9.55±0.42</td>
<td>9.64±0.38</td>
</tr>
<tr>
<td>P1 (mg/dl)</td>
<td>3.38±0.37</td>
<td>3.64±0.50</td>
<td>3.68±0.59</td>
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<tr>
<td>Total protein (g/dl)</td>
<td>7.04±0.30</td>
<td>7.31±0.87</td>
<td>7.36±0.31</td>
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<tr>
<td>Albumin (mg/dl)</td>
<td>4.60±0.17</td>
<td>4.53±0.28</td>
<td>4.66±0.17</td>
</tr>
<tr>
<td>ALP (mU/ml)</td>
<td>139.22±36.12</td>
<td>154.36±41.69</td>
<td>145.6±15.79</td>
</tr>
</tbody>
</table>

Values are the mean±SD.

### Table 3. Hormonal and biochemical analysis of serum in three groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Controls</th>
<th>Volleyball players</th>
<th>Joggers</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>9</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>E2 (pg/ml)</td>
<td>10.89±2.67</td>
<td>12.45±8.14</td>
<td>13.75±7.50</td>
</tr>
<tr>
<td>PTH-intact (pg/ml)</td>
<td>26.33±7.40*</td>
<td>35.27±15.05*</td>
<td>15.25±2.75</td>
</tr>
<tr>
<td>Calcitonin (pg/ml)</td>
<td>41.49±25.82</td>
<td>47.10±17.52</td>
<td>43.15±13.87</td>
</tr>
<tr>
<td>Osteocalcin-intact (ng/ml)</td>
<td>2.71±2.01</td>
<td>4.20±2.16</td>
<td>2.28±1.89</td>
</tr>
<tr>
<td>Osteocalcin-fragment (ng/ml)</td>
<td>10.37±2.05</td>
<td>12.14±3.03*</td>
<td>8.38±1.24</td>
</tr>
<tr>
<td>Osteocalcin ratio (fragment/intact)</td>
<td>6.05±4.15</td>
<td>3.83±2.68</td>
<td>5.69±3.59</td>
</tr>
</tbody>
</table>

Values are the mean±SD. *, P<0.05 vs. Joggers.
to intact-osteocalcin as a new biochemical parameter for bone metabolism reflecting relative bone resorption to bone formation [26]. Although this estimation is not established, we adopted it to get preliminary information on bone turnover. There was no difference in the parameter among the three groups.

The BMDs in the lumbar vertebrae (L₂-L₄), proximal femur, and two radius sites are shown in Figs. 1 to 3. The average bone mineral densities of the controls in this study agreed quite well with the BMD reported in our previous studies of a similar group (ages 55-59). The BMD (lumbar vertebrae, L₂-L₄: 0.82±0.09 g/cm², femoral neck: 0.67±0.06 g/cm²) of controls in this study, for example, was similar to the BMD (lumbar vertebrae, L₂-L₄: 0.85±
0.15 g/cm², femoral neck: 0.66±0.10 g/cm²) of the postmenopausal women (N=49, ages 55-59) in the previous study [23].

Vertebral bone mineral density of volleyball players and joggers was significantly greater than that of controls at all sites measured (L2-L4). The volleyball players, but not the joggers, had higher bone density at all sites measured in the proximal femur than control. Unlike weight-loaded bones such as the lumbar vertebrae and femur, there were no significant differences among the three groups in bone mineral density at the proximal and distal radius (non-weight-loaded bone).

Correlation coefficients reflecting the relationships among BMD and physical, gynecological characteristics and exercise career are given in Table 4. Bone mineral density at the distal radius site was significantly correlated in a negative direction with years after menopause in both volleyball players and joggers. While the coefficient of correlation between distal radius mineral density and years after menopause for controls was −0.43 and not significant, mineral density tended to decrease after menopause as in active groups.

Discussion

The present results clearly demonstrate that regular physical activity may prevent involutional bone loss in postmenopausal women, while the protective action is not observed equally among systemic bones. For example, bone mineral densities in lumbar vertebrae (L2-L4) are greater in both volleyball players and joggers than in controls, whereas there is no significant difference among groups in bone mineral density in the radius.

Although the mechanism by which physical activity affects bone mass is not fully understood, hormonal and mechanical factors have been considered to play a role. Dalen & Olsson [11] showed that habitual cross-country runners had higher bone mass than control subject not only in mechanically loaded bones but also in nonloaded upper body bones such as the humerus, radius, and ulna. The results suggest the systemic effect of exercise on bone mineral content and the involvement of hormonal factors. In contrast, the localized effect of physical activity in our study indicates...
that mechanical stress placed locally on the bone, rather than humoral factors acting on systemic bones, is involved in higher lumbar vertebrae mineral density in our active subjects. In fact, lumbar vertebrae appear to receive both the weight-load and the muscular contraction-generated force as mechanical stress. The significance of mechanical stress is also supported by significant hypertrophy of the dominant radius and humerus compared with the nondominant arm in professional tennis players, or baseball pitchers [27-29]. These imply that specific sports appears to have selective effects on the skeletal sites used predominantly in those sports.

It seems, however, to be inconsistent with the above idea that there was no significant difference in radial bone mineral density in volleyball players who receive the impact of the volleyball. This appears to be explained by the results of Lanyon's study [30] in which the long bone of the leghorn was functionally isolated and subjected to mechanical stress. The bone loss due to the isolation could be prevented by 1000 microstrain stress and the bone hypertrophy was observed only when the mechanical stress applied was more than a 1000 microstrain stress. This suggests that bone hypertrophy needs greater mechanical stress than a certain threshold. According to this idea, the stress applied to the arms of volleyball players appears to be less than a threshold to induce bone hypertrophy. In fact, Simkin et al. [31] reported that the distal radius mineral density of postmenopausal osteoporotic women was increased against bone loss due to aging by applying several types of loads to their forearm, in such as tension, compression, torsion, and bending. Therefore, a special exercise program to load the arm must be designed for preventing involutional bone loss in the radius. In an analogy to the condition of the radius, it might be explained that the proximal femur mineral density of joggers was not significantly higher than in controls, although the possibility that the amount of physical activity of the joggers is not enough to increase bone mineral density cannot be ruled out.

It was noted in the present study that a typical decline in bone mineral density after menopause can be seen in the distal radius but not in other sites such as the lumbar vertebrae or proximal femur. The bone mineral deficits after menopause are greater in trabecular bone than compact bone. This appears to be due to the loss of the protective effect on bone mass of humoral factors, especially estrogen, and the high susceptibility of trabecular bones to such humoral factors because of the greater surface-to-volume ratio [17]. Our subjects are therefore all suffering from the hormonal changes due to menopause, reducing bone mineral in systemic bone tissues regardless of their physical activity. This suggests that physical exercise does not directly affect the events regulated by hormones deteriorated after menopause.

In this study, all of the volleyball players and three of the five joggers had started the sport before their menopause. It is therefore possible that physical exercise increases bone mass before menopause start, resulting in higher peak bone mass [32], but does not have any effect on bone loss induced by estrogen deficiency. Although we cannot provide data to deny this possibility in our cross-sectional study, it does not seem to be the case because several studies have indicated that physical exercise sustained for five or ten months increased BMD in postmenopausal women [33]. It therefore appeared likely that an increase in bone mass as well as the prevention of bone loss by physical exercise in both premenopausal and postmenopausal states contributes to the higher BMD observed in our active groups compared with the controls.

On the cellular level, there are three possible reasons why physical activity increases BMD (1) an increase in bone formation by osteoblasts, (2) a decrease in bone resorption by osteoclasts, or (3) both. To examine the effect of physical exercise on these cellular functions and bone turnover, we measured the serum biochemical marker for bone metabolism (See Tables 2 and 3). The parameters reflecting bone formation, serum ALP activity and osteocalcin (intact) show a tendency for volleyball players to have higher values than controls but the differences are not statistically significant. The same tendency was observed in osteocalcin (N-fragment), which is thought to reflect bone resorption, implying that volleyball players have high bone turnover. Moreover, in the ratio of N-fragment osteocalcin to intact osteocalcin, volleyball players have the lowest value among the groups, indicating the lowest relative bone resorption to bone formation in accordance with the highest
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BMD. With regard to the serum concentration of PTH and osteocalcin (N-fragment), joggers have lower mean values than controls and volleyball players. However, the reason for this remains to be determined since the number of jogger subjects was not enough for a definite assessment.

In conclusion, regular physical activities such as volleyball or jogging appear to have a positive effect on the maintenance of bone mineral in postmenopausal women, and the protective action is confined to those skeletal sites used predominantly for that sport without opposing the negative regulation caused by estrogen deficiency in systemic bones. A longitudinal study should be done to determine the relationship between postmenopausal bone loss and physical activity.

Acknowledgments

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achilles tendons and long bones. *Growth* 41: 123–137.


