Accelerated Decrease in Bone Mineral Density in Women Aged 52-57 Years

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NOHARA, T., KAMEI, T. and OHTA, A. Accelerated Decrease in Bone Mineral Density in Women Aged 52-57 Years. Tohoku J. Exp. Med., 2006, 210 (4), 341-347 —— Bone mineral density (BMD) has been known to decline in middle-aged and elderly individuals, but when this decline begins and the rate at which it occurs remain unclear. We thus undertook this study to examine the association between BMD and age by their mean values in women visiting the Shimane Institute of Health Science for medical examination. We performed dual energy X-ray absorptiometry measurement of lumbar vertebrae in 1,167 women, and of the entire skeleton in 1,038 women. The ages of subjects ranged from 30 to 70 years. We found that the mean value of whole-body and lumbar BMD changed little in the age range of 30-51 years, and any change after 58 years was a gradual decrease, unlike the sharp decrease found between 52 and 57 years of age. The effects of endocrine kinetics may be reflected in women by the decrease of bone density relative to age. In conclusion, BMD declines more rapidly in women within the age range of 52-57 years than in those 58 years and over. This regression line is considered useful in predicting BMD of whole-body skeleton and lumbar vertebrae relative to age for the prevention of osteoporosis in women. —— age; bone mineral density; climacteric disturbance; menopausal time; osteoporosis

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It is a well established fact that aged people are prone to suffer from osteoporosis, a degenerative change in bone that easily leads to fractures at certain sites (e.g. trabecular bone, femoral neck, etc.). In case the trabecular bone is substantially affected, compression fractures of the thoracic and lumbar vertebrae are common (Kanesaki 2004); should the cortical bone be affected, fractures of the femoral neck are likely to occur especially in postmenopausal women (Horikoshi et al. 1999). Such fractures usually induce acute lumbar or thoracic pain, and vertebral deformities subsequently developing after vertebral fractures cause chronic low back pain (O’Neill et al. 2004).

To prevent osteoporosis, early detection of a decrease in bone mineral content (BMC) is
important. In clinical settings, measurement of bone content or density is frequently employed using dual energy x-ray absorptiometry (DXA) chiefly on the whole-body skeleton or lumbar vertebra (Cater et al. 1992; Revilla et al. 1995).

Bone mineral content and density of the entire skeleton are expressed by the actual measured values, but those for the lumbar vertebrae are done by the average measurement of three lumbar vertebrae (the second to the fourth vertebra: L2-L4). A decrease in bone mineral density (BMD) can be evaluated according to the following World Health Organization (WHO) criteria: BMD of subjects, 2.5 s.d. (T-score < or = −2.5) lower than the young adult mean (YAM) of the whole body skeleton or lumbar vertebra (Wu et al. 2004).

In estimating DXA, a form of T-score values is the most popular presentation of results. The T-score is a numerical value of BMD in s.d. below a peak bone mass (= YAM) and a Z-score is a result in SD below the values of healthy individuals’ BMD of the same age and sex. The Z-score has less value in the diagnosis of osteoporosis, due to the natural degradation of BMD in the elderly. However, Z-scores may also be of practical value as suggestive results for 40-60-year-old women for prevention of osteoporosis.

Bone mineral content and density are related to aging as well as to daily food intake and physical exercise (Heinonen et al. 1996; Larijani et al. 2004), and are greatly influenced by endocrine dynamism, especially estrogen in pre- and post-menopausal women (Ettinger et al. 1998; Recker et al. 1999; Liu and Muse 2005). Aside from BMD as the absolute reference value used for diagnosis of osteoporosis, we think it would be useful to formulate a suggestive value in relation to age, and the age at which BMD begins to decline.

METHODS

Subjects

Our study protocol was approved by the institutional review board of Shimane Institute of Health Science. Following the approval, informed consent was obtained from women visiting the Shimane Institute of Health Science for general medical examination to participate in our study. Our institution regularly performs health check-ups for lifestyle-related diseases for adults living in and around Izumo City. We performed DXA measurement of the lumbar vertebrae in 1,271 women, and of the full skeleton in 1,116 women in the course of the health check-ups. Of the first group, we excluded 104 women, due to their osteoporotic condition, thus the remaining 1,167 women were included in the group. Of the second group (full skeleton), we excluded 78 women due to osteoporosis, thus the remaining 1,038 women were included in the group. Therefore, a total of 1,167 adult women, ranging from 30 to 70 years, who consulted us for a regular health check-up between 2000 and 2002 were subjects of the present study including those with a medical history of bone fracture or receiving medications for symptoms other than osteoporosis. However, the subjects were not questioned on the number of the pregnancies or whether they were receiving any form of hormone replacement therapy.

Measurement of bone mineral content and density

For the entire skeleton. DXA was conducted on the head, both clavicles, both scapulae, both arms, the ribs, spine, pelvis and both legs. Total area and total BMC of the entire skeleton were measured. The whole-body BMD was then calculated by dividing the BMC by the total area of entire skeleton.

For the lumbar vertebrae. DXA was conducted in the region from the first to the fifth lumbar vertebra (L1-L5). Bone area and BMC of each vertebra were measured. BMD was calculated by dividing the BMC by the bone area. The average bone area and average BMC of three vertebrae (L2-L4) were calculated.

DXA was performed using a bone density measurement device (QDR 2000, Hologic, Bedford, MA, USA). When data were obtained twice at different times for the same person, we used only the initial data for our analysis. When foreign substances such as metal were detected, the relevant data were discarded. Consequently, the number of data utilized for the statistical study was slightly less than that of all the data obtained with DXA measurement.

Statistical analyses

For the purpose of investigating an association between age and BMD, a scatter diagram was made using a software (Microsoft Excel), plotting subject’s age along the x-axis and bone mineral density of whole-body
skeleton or lumbar vertebrae measured with DXA along the y-axis. To find the correlation, subjects were classified into age-related groups and analysis of variance was performed on each group. We used SPSS software program for Windows (Ver. 11.0.1) to analyze by one-way ANOVA and pair-wise comparison (Student-Newman-Keuls) (Winer et al. 1991), in which correlation between BMD and age was investigated by means of linear regression analysis.

RESULTS

Fig. 1 shows changes of whole-body BMD relative to age. Whole-body BMD changed significantly depending on age ($F = 29.778$, $df_1 = 40$, $df_2 = 1,074$, $p < 0.01$), and we noted three age phases (cf. Fig. 2): 30-51-years-old (Phase 1), 52-57-years-old (Phase 2) and 58-70-years-old (Phase 3). The linear regression ($y = a + bx$) applied to each phase was as follows ($x$: age, $y$: mean of whole-body BMD): $y = 1.051 - 0.000146x$ in Phase 1, $y = 1.535 - 0.01081x$ in Phase 2, $y = 1.173 - 0.004869x$ in Phase 3 (cf. Fig. 1). A coefficient of $x$, that is $b$, was not significantly different from zero in Phase 1 ($t = -0.274$, $df = 544$, $p > 0.05$), but was significantly different from zero in Phase 2 ($t = -3.072$, $df = 180$, $p < 0.01$), and in Phase 3 ($t = -4.481$, $df = 385$, $p < 0.01$). Pearson’s correlation coefficients between whole-body BMD and age were $-0.012$ ($p > 0.05$) in Phase 1, $-0.223$ ($p < 0.05$) in Phase 2, and $-0.223$ ($p < 0.05$) in Phase 3.

Correlations of whole-body BMD with either height, weight or body mass index (BMI) were analyzed based on age. Pearson’s correlation coefficient with height was $0.381$ ($p < 0.05$) and with BMI was $0.086$ ($p < 0.05$). As the correlation with height was the greatest, the correlation in each phase was analyzed. Pearson’s correlation coefficients between BMD and height were $0.175$ ($p < 0.05$) in Phase 1, $0.116$ ($p > 0.05$) in Phase 2 and $0.253$ ($p < 0.05$) in Phase 3.

Fig. 3 shows changes of L2-L4 BMD with age. The L2-L4 BMD changed significantly ($F = 20.384$, $df_1 = 40$, $df_2 = 1230$, $p < 0.01$), and we divided subject’s age into three phases as in the case for whole-body BMD (cf. Fig. 4). The linear regression applied to each phase was as follows ($x$: age, $y$: mean L2-L4 BMD): $y = 1.014 + 0.0007241x$ in Phase 1, $y = 1.784 - 0.01612x$ in Phase 2, $y = 1.155 - 0.005341x$ in Phase 3 (cf. Fig. 3). A coefficient of $x$: that is $b$, was not significantly different from zero in Phase 1 ($t = -0.966$, $p > 0.05$), but was significantly different from zero in Phase 2 ($t = -3.108$, $p < 0.05$) and Phase 3 ($t = -2.874$, $p < 0.015$). Pearson’s correlation coefficients between L2-L4 and age were $0.039$ ($p > 0.05$) in Phase 1, $-0.212$ ($p < 0.05$) in Phase 2 and $-0.135$ ($p < 0.05$) in Phase 3.

Correlations of L2-L4 BMD with either height, weight or BMI were analyzed based on age. Pearson’s correlation coefficient with height was $0.360$ ($p < 0.05$), with weight it was $0.260$ ($p < 0.05$) and with BMI was $0.064$ ($p < 0.05$). As the correlation with height was the greatest, the correlation in each phase was analyzed. Pearson’s correlation coefficients between BMD and height were $0.172$ ($p < 0.05$) in Phase 1, $0.183$ ($p < 0.05$) in Phase 2 and $0.163$ ($p < 0.05$) in Phase 3.

DISCUSSION

The diagnostic criterion of osteoporosis has been established by the WHO definition as $-2.5$ SD (T-score $< -2.5$) of peak bone mass in the whole-body skeleton or lumbar vertebrae (Siris et al. 2001). Based on this diagnostic criterion, most people over 80 years of age will encounter osteoporosis. On the other hand, young women who experience puberty with low body weight due to forced dieting prone to experience osteoporosis also (Grinspoon et al. 2000; Van Loan and Keim 2000). The standard value based on T-score is very important in the treatment and diagnosis of osteoporosis, but from a preventative standpoint, it seems that relative evaluation within same-age groups as used for Z-score, should be supplemented.

The onset of menopause in woman is usually around 50 years of age (Amigoni et al. 2000; Ozkan et al. 2005). In our previous study, we found the average menopause age to be 50.7 years for 95 women attending a “guidance for lifestyle improvement” lecture at the Shimane Institute of
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Fig. 1. Correlation of age and whole-body BMD (1). Figure shows changes of whole-body BMD relative to age. Whole-body BMD changed significantly, and we noted three age phases (cf. Fig. 2). Scatter diagram is plotted where subject age is x-axis and BMD of whole-body skeleton measured with dual energy x-ray absorptiometry is y-axis. Closed squares indicate mean of whole-body BMD, and error bars indicate standard error of mean. Whole-body BMD changes depending on age. Lines are fitted by linear regression. The linear regression applied to each phase was as follows ($x$: age, $y$: mean whole-body BMD): $y = 1.051 - 0.000146 x$ in Phase 1, $y = 1.535 - 0.01081 x$ in Phase 2, $y = 1.173 - 0.004869 x$ in Phase 3.

Fig. 2. Correlation of age and whole-body BMD (2). Whole-body BMD changed significantly, and we noted three age phases: 30-51-years-old (Phase 1), 52-57-years-old (Phase 2) and 58-70-years-old (Phase 3). Pair-wise comparisons were conducted by Student-Newman-Keuls. Matrix shows significant difference indicated by asterisk between corresponding row and columnar ages. Age can be divided into three phases: 30-51 (Red zone = Phase 1), 52-57 (Yellow zone = Phase 2) and 58-70 (Blue zone = Phase 3).
Fig. 3. Correlation of age and lumbar BMD (1).
Figure shows changes of L2-L4 BMD with age. The L2-L4 BMD changed significantly, and we divided age into three phases (cf. Fig. 4). Scatter diagram is plotted where subject age is x-axis and BMD of lumbar vertebrae measured with dual energy x-ray absorptiometry is y-axis. Closed squares indicate mean of second to the fourth lumbar vertebra (L₂-L₄) BMD, and error bars indicate standard error of mean. L₂-L₄ BMD changes depending on age. Lines are fitted by linear regression. The linear regression applied to each phase was as follows (x: age, y: mean L2-L4 BMD): \( y = 1.014 + 0.0007241x \) in Phase 1, \( y = 1.784 - 0.01612x \) in Phase 2, \( y = 1.155 - 0.005341x \) in Phase 3.

Fig. 4. Correlation of age and lumbar BMD (2).
The L2-L4 BMD changed significantly, and we divided age into three phases as in the case for whole-body BMD. Pair-wise comparisons were conducted by Student-Newman-Keuls. Matrix shows significant difference indicated by asterisk between corresponding row and columnar ages. Age can be divided into three phases: 30-51 (Red zone = Phase 1), 52-57 (Yellow zone = Phase 2) and 58-70 (Blue zone = Phase 3).
Health Science (Nohara et al. 2000). That group also included women who had experienced premature menopause due to surgery or gynecological problems, which probably affected the average. The time after onset of menopause (climacteric) is accompanied by various indefinite complaints resulting from the changes of endocrine kinetics (climacteric disturbances). Climacteric disturbances continue for approximately 10 years (Berg et al. 1988), generally stabilizing at around age 60. Interestingly, in our findings, the first turning point in the relative change of bone density by age coincided with the average age (51 years) of menopause onset. The second age-related turning point (58 years) closely corresponded to the age at which climacteric disturbances stabilize, so it appears that these two identifiable points coincide with changes in endocrine kinetics. From an endocrine kinetic standpoint, while menarche or pregnancy may also affects on the BMD (Ozdemir et al. 2005), we focused on the time of the menopause and climacteric in the present study.

BMC and BMD have been reported to be lower in Asian than Caucasian adults (Tobias et al. 1979; Walker et al. 2006). These racial differences may be the result of differences in life style, such as food intake and physical exercise. However, as the decline in BMC is influenced by gynecological endocrine changes, it is hard to conceive that the timing of the decline in BMC would vary much between races or nationalities in so far as the 52 to 57-year-olds age group is concerned. A report describing no observable significant racial differences in apparent density and BMD in young Asian and Caucasian Americans supports this view (Bhudhikanok et al. 1996).

In the 51 years and under age group, we inferred that the application of the regression coefficient was not statistically significant from the dispersed measured value of each age group. The reason for the dispersion of measured value was individual variation which was greatly reflected by the physical activities of the younger age group. However, it was possible to lump together various age groups, and as a result of ANOVA, we found there were no significant differences between the 51 years and under age groups. There were fluctuations of data in the 30-year-olds age bracket, thus further study on a greater number of subjects will be required in the future. Between the age range of 52-57 years and that of 58 years and over, there was a statistically significant difference ($p < 0.01$) based on the regression coefficient. The BMD of the whole-body skeleton and lumbar vertebrae seem to fluctuate similarly in the age range of 30 to 67 years while the lumbar BMD surpassed the whole-body BMD in the age of 68 years and over. The accretion of the lumbar BMD is presumably caused by the contamination of lumbar compression fractures in the age of 68 years and over. Consequently, we interpreted the difference in the gradient of the regression line between the age range of 52-57 years and over 58 years to be significant.

References