Bone Mineral Density Obtained by Peripheral Quantitative Computed Tomography (pQCT) in Middle-Aged and Elderly Japanese

Shigeki Tsuzuku, Naoakira Niino, Fujiko Ando, and Hiroshi Shimokata

To clarify age-related changes in bone mineral density (BMD) by peripheral quantitative computed tomography (pQCT), 1,124 Japanese middle-aged and elderly community-dwelling people were examined. The BMD of the trabecular bone was assessed at the distal part of the radius (D50), and the BMD of the cortical bone was assessed at the diaphysis of the radius (P100). P100 during age 40 to 49 was significantly higher in females (1359.6±10.7 mg/cm³, mean±SE) than in males (1253.5±9.5 mg/cm³), while there was no difference in D50, 245.3±5.1 mg/cm³ in females and 293.0±5.5 mg/cm³ in males. Females and males aged 50 to 59 lost 8.09±2.08 (mean±SE) mg/cm³ and 3.80±1.77 mg/cm³ of D50 every year, respectively. As for P100, females lost 25.1±4.48 mg/cm³, and males lost 6.37±3.89 mg/cm³ every year. Because of these gender differences, both D50 and P100 were significantly higher in males than in females aged 50 and over. Assuming that the average BMD between ages 40 and 44 was the maximum bone mineral density (BMD max), the percentage change from the BMD max with age was examined. Females aged 60 to 69 whose BMD were under 70% of the BMD max made up 73.9% in D50 and 23.2% in P100. Only 21.1% of males aged 60 to 69 showed less than 70% of the BMD max in D50 and only 3.8% in P100. The percentage decrease in BMD by age was larger in D50 than in P100 in both males and females. The individual difference in BMD was larger in D50 than in P100. These results suggest that pQCT may be useful to independently assess aging effects on cortical and trabecular bone density. J Epidemiol, 2000; 10: S39-S45.

INTRODUCTION

One of the most serious public health problems is osteoporosis, characterized by a reduction in the amount of bone mass. Elderly individuals who have had hip fractures show lower bone mineral density (BMD) than those of similar age who have not had fractures. Recently, it has been accepted that not only BMD, but also estimation of bone architecture, is necessary to predict fracture risk precisely. Dual energy x-ray absorptiometry (DXA), which is used worldwide can only measure BMD by cross-sectional area (g/cm²), and it is hard to estimate the bone architecture. In contrast, peripheral quantitative computed tomography (pQCT) has the potential to measure the true volumetric bone density; mass per unit volume (mg/cm³). It allows separation of the bone sections into the trabecular and cortical bones, and can also visualize the bone structure. Thus, it is expected to be a new equipment to estimate bone architecture. Moreover, with its high resolution performance, the precision of pQCT is excellent. The in vivo coefficient of variation (CV) after measuring the same person repeatedly was 0.48%, and the in vitro CV was 0.90% with phantom measurements.

However, there have been few studies concerning pQCT, especially in Japanese people. In the National Institute for Longevity Sciences Longitudinal study of aging (NILS-LSA), the BMD of 1,124 people aged from 40 to 79 years were measured by pQCT. The purpose of this study was to clarify BMD changes with age using pQCT in Japanese middle-aged and elderly people.
MATERIALS AND METHODS

Subjects

The subjects in this study were 1,124 participants in the NILS-LSA, which includes medical, physical, dietary and psychological research. They were community-dwelling males and females aged 40 to 79 years randomly selected from the area neighboring the National Institute for Longevity Sciences (NILS). The subjects were divided into eight groups according to their age and gender; in their 40s, 50s, 60s and 70s, males and females. Table 1 shows the characteristics of the subjects. The study protocol was approved by the ethics committee of the National Chubu Hospital. After being informed of the purpose of this study, all subjects gave their written informed consent.

Peripheral quantitative computed tomography (pQCT)

The BMD of the non-dominant radius was measured with a pQCT DENSISCAN 1000 (Scanco Medical., Zurich, Switzerland). The forearm was positioned in a cast during the measurement. The examination site in the ultradistal radius was scanned with 10 tomograms (slice thickness 1mm, interslice distance 0.5mm) and the average bone density over the core volume (D50, D100) was calculated. D50 corresponded to the trabecular bone density. D100 included both the trabecular and cortical bones. Cortical bone density was measured in the diaphysis from 6 tomograms (P100) (Figure 1). pQCT enabled us to visualize the cross-sectional peripheral bones; radius and tibia. All scanning and analyses were done by the same operator.

Statistical Analysis

All statistical analyses were made with the SAS system release 6.12. Two independent measurements were compared by t-test (PROC TTEST), and two categorical data from the same subjects were compared by McNemar’s test (PROC FREQ with AGREE option). The trend by category was examined using a general linear model (PROC GLM with CONTRAST option). The relationship between age and BMD was estimated with a regression model (PROC REG). The individual difference was compared by F test using the standard deviation of each measurement divided by its mean (PROC TTEST). All comparisons were considered statistically significant at p<0.05.

RESULTS

Anthropometry and pQCT BMD of the subjects by gender and age

Table 1 shows the height, weight, BMI and pQCT BMD by gender and age group. Height and weight significantly decreased with age in both males and females (P trend<0.001). There was no significant change in BMI in females, while BMI decreased slightly with age in males (P trend=0.04). The BMI was 22.8±0.1 (mean±SE) in males and 23.0±0.1 in females. The gender difference in BMI was not significant.

In all groups, the D50, D100 and P100 in males were significantly higher than those in females (p<0.01). The D50, D100 and P100 were also higher in males than in females aged 50 and over (p<0.001), but D100 and P100 were higher in females than in males aged 40 to 49 (D100: p=0.02 and P100: p<0.001).

Age-related changes in BMD

Figures 2A, 2B and 2C show the distribution and 3-year moving average of BMD by age in males and females. BMD D50, D100 and P100 decreased with age in both genders, while the change was greater in females than in males, especially between 50 and 59 years of age.

Slopes of BMD by age were examined by site, age group and gender. The left panel of Figure 3 shows age-related changes in D50 in males and females. In females, D50 decreased 3.15±1.88 mg/cm³/year between the ages of 40 and 49. This decrease was not statistically significant. However, from 50 to 59 years, D50 rapidly decreased (8.09±2.08 mg/cm³/year between the ages of 50 and 49.

Table 1. Height, weight, BMI and pQCT BMD of the subjects by gender and age.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>N</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>BMI</th>
<th>D50 (mg/cm²)</th>
<th>D100 (mg/cm³)</th>
<th>P100 (mg/cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>40-49</td>
<td>153</td>
<td>169.0 (0.5)</td>
<td>66.3 (0.8)</td>
<td>23.2 (0.2)</td>
<td>293.0 (5.5)</td>
<td>581.2 (6.8)</td>
<td>1253.5 (9.5)</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>149</td>
<td>165.7 (0.5)</td>
<td>63.0 (0.7)</td>
<td>22.9 (0.2)</td>
<td>271.4 (5.0)</td>
<td>554.4 (6.7)</td>
<td>1197.9 (10.9)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>134</td>
<td>163.3 (0.4)</td>
<td>61.2 (0.7)</td>
<td>22.9 (0.2)</td>
<td>256.9 (6.0)</td>
<td>537.2 (9.4)</td>
<td>1167.6 (12.0)</td>
</tr>
<tr>
<td></td>
<td>70-79</td>
<td>138</td>
<td>160.5 (0.5)</td>
<td>57.5 (0.7)</td>
<td>22.3 (0.3)</td>
<td>243.1 (5.7)</td>
<td>489.5 (7.0)</td>
<td>1111.0 (14.6)</td>
</tr>
<tr>
<td>Total</td>
<td>574</td>
<td>62.1 (0.4)</td>
<td>22.8 (0.1)</td>
<td>266.9 (2.9)</td>
<td>541.9 (4.0)</td>
<td>1184.7 (6.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>40-49</td>
<td>145</td>
<td>154.5 (0.4)</td>
<td>54.2 (0.7)</td>
<td>22.7 (0.3)</td>
<td>245.3 (5.1)</td>
<td>604.3 (7.1)</td>
<td>1359.6 (10.7)</td>
</tr>
<tr>
<td></td>
<td>50-59</td>
<td>135</td>
<td>153.2 (0.4)</td>
<td>53.8 (0.7)</td>
<td>22.9 (0.3)</td>
<td>203.0 (6.0)</td>
<td>516.5 (8.6)</td>
<td>1219.3 (13.6)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>138</td>
<td>150.0 (0.4)</td>
<td>52.2 (0.7)</td>
<td>23.2 (0.3)</td>
<td>148.1 (4.5)</td>
<td>418.3 (7.1)</td>
<td>1057.3 (11.6)</td>
</tr>
<tr>
<td></td>
<td>70-79</td>
<td>132</td>
<td>147.4 (0.5)</td>
<td>50.0 (0.7)</td>
<td>23.0 (0.3)</td>
<td>140.9 (5.4)</td>
<td>392.5 (7.8)</td>
<td>970.4 (14.0)</td>
</tr>
<tr>
<td>Total</td>
<td>550</td>
<td>52.6 (0.3)</td>
<td>23.0 (0.1)</td>
<td>185.4 (3.2)</td>
<td>485.2 (5.3)</td>
<td>1155.9 (8.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The standard error of the mean is given in parentheses.
Figure 1. Measurements of BMD with pQCT (DENSISCAN 1000).

Figure 2A. Distribution and 3-year moving average of D50 BMD in males and females.
Figure 2B. Distribution and 3-year moving average of D100 BMD in males and females.

Figure 2C. Distribution and 3-year moving average of P100 BMD in males and females.
mg/cm³/year, p<0.001). Then, after age 60 the decrease in D50 became small again (1.02±0.66 mg/cm³/year, NS). In males, D50 did not significantly decrease between the ages of 40 and 49 (0.15±1.86 mg/cm³/year, NS), but D50 decreased between 50 and 59 years of age (3.80±1.77 mg/cm³/year, p=0.03) and between 60 to 79 years of age (1.67±0.76 mg/cm³/year, p=0.03). There was no significant difference in slope between these two age groups in males.

Changes in D100 in males and females are shown in the middle panel of Figure 3. The change in D100 in females between age 40 and 49 was not significant (5.11±2.63 mg/cm³/year), but the decrease between age 50 and 59 was highly significant (16.79±2.80 mg/cm³/year, p<0.001). The decrease from age 60 and over was also significant in females (3.32±0.99 mg/cm³/year, p<0.001). The change in D100 in males between 40 and 49 years of age was small (0.44±2.30 mg/cm³/year, NS), while the change in D100 was significant between the ages of 50 and 59 (5.18±3.28 mg/cm³/year, p=0.03), and 60 and 79 (4.76±1.07 mg/cm³/year, p<0.001).

The right panel of Figure 3 shows the slope of P100 in males and females. The P100 in females decreased between the ages of 40 and 49 (9.15±3.90 mg/cm³/year, p=0.02) and between 60 and 79 (9.49±1.69 mg/cm³/year, p<0.001). However, the decrease between the ages of 50 and 59 was large (25.1±4.48 mg/cm³/year, p<0.001). In males, the decrease in P100 between the ages of 40 to 49 was 2.32±3.23 mg/cm³/year and between 50 and 59 was 6.37±3.89 mg/cm³/year. Neither change was significant. In males aged 60 and over, the change was significant (6.11±1.74 mg/cm³/year, p<0.001). The slope of decrease in P100 was much greater in females than in males between the ages of 50 and 59 (p=0.002). Thus, in subjects aged over 50, the P100 was significantly higher in males than in females (p<0.001), while the P100 in subjects aged 40 to 49 was higher in females than males (p<0.001).

**Percentage change in BMD by age**

Assuming that the average BMD between the ages of 40 and 44 was the max bone mineral density (BMD max), the percentage change in BMD for the BMD max was estimated. There were 70 males and 47 females aged between 40 and 44. The average D50 as the BMD max was 295.5 mg/cm³ in males and 252.7 mg/cm³ in females. The D100 results were 588.8 mg/cm³ and 616.9 mg/cm³, and the P100 results were 1269.1 mg/cm³ and 1374.7 mg/cm³, respectively.

These BMD max were compared with the BMD in the 50s, 60s and 70s age groups in males and females. The percentage and number of subjects whose BMD was under 70%, 70% to 80%, and over 80% of the BMD max were calculated (Table 2). More than half of the females aged 60 and over had less than 70% BMD max in the distal radius. The percentage of females aged 60 to 69 whose BMD were under 70% of the BMD max was 73.9% for D50 and 64.8% for D100. The percentage of the females aged 60 to 69 whose BMD P100 was lower than 70% of the BMD max was small (23.2%). In males, the percentage of subjects whose BMD was under 70% of the BMD max was much smaller. Only 21.1% of males aged 60 to 69 showed less than 70% of the BMD max for D50, 10.5% for D100, and 3.8% for P100. These percentage changes in BMD...
Table 2. Number and percentage of subjects whose BMD was 70% and 80% of the mean in subjects under 45 years old.

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th></th>
<th>Female</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50-59 yr</td>
<td>60-69 yr</td>
<td>70-79 yr</td>
<td>50-59 yr</td>
</tr>
<tr>
<td>D50</td>
<td>under 70%</td>
<td>18 (12.2)</td>
<td>28 (21.1)</td>
<td>40 (29.2)</td>
</tr>
<tr>
<td></td>
<td>70-80%</td>
<td>24 (16.3)</td>
<td>29 (21.8)</td>
<td>28 (20.4)</td>
</tr>
<tr>
<td></td>
<td>over 80%</td>
<td>105 (71.4)</td>
<td>76 (57.1)</td>
<td>69 (50.3)</td>
</tr>
<tr>
<td>D100</td>
<td>under 70%</td>
<td>5 (3.4)</td>
<td>14 (10.5)</td>
<td>23 (16.8)</td>
</tr>
<tr>
<td></td>
<td>70-80%</td>
<td>20 (13.5)</td>
<td>23 (17.3)</td>
<td>33 (24.1)</td>
</tr>
<tr>
<td></td>
<td>over 80%</td>
<td>123 (83.1)</td>
<td>96 (72.2)</td>
<td>81 (59.1)</td>
</tr>
<tr>
<td>P100</td>
<td>under 70%</td>
<td>2 (1.4)</td>
<td>5 (3.8)</td>
<td>11 (8.0)</td>
</tr>
<tr>
<td></td>
<td>70-80%</td>
<td>11 (7.4)</td>
<td>8 (6.0)</td>
<td>24 (17.5)</td>
</tr>
<tr>
<td></td>
<td>over 80%</td>
<td>135 (91.2)</td>
<td>120 (90.2)</td>
<td>102 (74.5)</td>
</tr>
</tbody>
</table>

Percentages are given in parentheses.

Individual difference in BMD

As an index of the individual difference in BMD, the standard deviation of the measurements divided by its mean was compared by F test. The individual difference was greater for D50 than for P100 (F=4.56, p<0.001), and was greater in females than in males (D50: F=2.48, p<0.001; D100: F=2.09, p<0.001; P100: F=2.05, p<0.001). The individual difference in BMD was also greater in elderly subjects aged 70 to 79 years than in middle-aged subjects aged 40 to 49 years (D50: F=2.79, p<0.001; D100: F=2.41, p<0.001; P100: F=2.86, p<0.001).

DISCUSSION

DXA is the most popular bone mass evaluation system in the world. There are many data and studies concerning DXA. However, it is well accepted that not only BMD, but also the estimation of bone architecture is necessary to predict fracture risk precisely. DXA alone may not be adequate because it only evaluates BMD by cross sectional area (g/cm²). In contrast, quantitative computed tomography (QCT) of the spine has been used to measure the true volumetric bone density and skeletal status. However, the high exposure dose and poor reproducibility of the lumbar spine made research impossible.

Recently, the pQCT technique has been developed. It has the potential to provide determination of trabecular and cortical bone density in the radius and tibia, and can perform trabecular imaging. Neff et al. reported that the trabecular elements of the skeleton are primarily affected to a relatively high degree by bone loss in the first few years after menopause. They also reported that pQCT can be used to diagnose postmenopausal osteoporosis before it reaches an irreversible stage.

Elderly individuals sometimes show a high lumbar spine DXA BMD because of lumbar deformity or aortic calcification. It is hard to assess the true BMD with a cross-sectional measurement system like DXA, especially in the elderly people. As calcification and deformity are not so frequently observed in the radius compared with the lumbar spine, the radius is suitable to evaluate the effect of aging on bones.

Our previous research also showed high lumbar spine and whole body BMD in an exercise group. Some researchers also showed that the lumbar spine and femoral neck are affected by exercise, but the radius does not gain BMD with physical exercise. These results also suggest that the pQCT of the radius is useful to evaluate the effects of aging on bones.

There have been few studies concerning pQCT. In this study, we showed a significant decrease in all skeletal sites; D50, D100 and P100, and the pattern of age-related changes in different sites by gender and age. It is interesting that the cortical bone density of the radius (P100) in the middle-aged subjects aged 40 to 49 was significantly higher in females than in males, while there was no difference in the trabecular bone (D50). The slope of decrease in BMD was greater in females than in males between the ages of 50 and 59. The mean age of menopause was 48.8 years in our subjects. A postmenopausal acceleration in bone mass loss was clearly seen. Thus, in subjects aged over 50, the BMD was significantly higher in males than in females. The decrease in BMD with age was greater in the trabecular bone than the cortical bone. The percentage of females whose BMD was less than 70% of the BMD max was 73.9% for the trabecular bone (D50), whereas only 23.2% of females had less than 70% in the cortical bone (P100). A similar pattern of changes was also observed in males, but the changes were smaller. The individual difference was greater in the trabecular bone than the cortical bone. This may indicate that the decreasing pattern of BMD with age differs in various skeletal sites. pQCT has the potential to estimate cortical and trabecular BMD separately.

In conclusion, we showed age-related changes in BMD by pQCT in a large number of community-dwelling males and females aged 40 to 79. We clarified the differences in density...
changes between the cortical and trabecular bones using the pQCT measurements. There was a greater age-related decline in trabecular bone density than in cortical bone density, and individual differences in trabecular bone density were greater than those in cortical bone density. pQCT is a very useful tool to assess cortical and trabecular bone density separately.

ACKNOWLEDGMENTS

This study was supported by a Grant-in-Aid for the Comprehensive Research on Aging and Health from the Ministry of Health and Welfare of Japan.

REFERENCES

15. Dambacher MA, Kranich M, Schacht E, Neff M. Can the fast bone loss in osteoporotic and osteopenic patients be stopped with active vitamin D metabolites? Calcif Tissue Int, 1997; 60: 115-118.