

Metabolic Characteristics and Prevalence of Osteoporosis among Women in Tae-An Area

Understanding the metabolic changes in women is one of the important ways to prevent and treat osteoporosis. To reveal the metabolic characteristics of 289 healthy women aged between 35-65 yr in Tae-An, Korea we evaluated the association between bone mass assessed by broadband ultrasound attenuation (BUA) using quantitative ultrasound 2 (QUS2) and various parameters such as age, body mass index, serum levels of alkaline phosphatase, calcium, phosphorus, parathyroid hormone, 25(OH)D, and urinary ratios of calcium/creatinine and deoxypyridinoline (Dpyd)/creatinine. Among the subjects, 3.0% were osteoporotic, and 40.9% were osteopenic. When the subjects were classified according to their years since menopause (YSM) and age, the prevalence of osteoporosis increased along with an increase of YSM and age. Bone turnover markers such as serum alkaline phosphatase and fasting urinary Dpyd/creatinine were significantly higher in the group with low bone mass than in the normal group. In summary, this study shows, by use of biochemical markers of bone turnover and QUS2, the prevalence of osteoporosis in women aged between 35-65 in Tae-An was 3.0% and the risk of low bone mass increased with the bone turnover markers.

Key Words : Menopause; Metabolism; Osteoporosis; Quantitative Ultrasound

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Received : 20 October 2000

Accepted : 14 March 2001

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INTRODUCTION

Osteoporosis is the most frequently encountered metabolic bone disease which is characterized by low bone mass and microarchitectural deterioration of the bone tissues with an increased susceptibility of fracture. It is a complex and chronic disease that can progress without any symptoms for decades until a fracture develops. The prevention and treatment of osteoporosis is of particular importance in the field of medicine owing to the increase of its prevalence along with an increase of life expectancy. Early detection of low bone mineral density and recognition of metabolic characteristics in women are very important to prevent osteoporosis, since it takes much time and effort to treat the disease once diagnosed. Although there are several reports on the prevalence of osteoporosis in Korea (1-3), no study has been performed attempting to reveal the metabolic characteristics in addition to the prevalence of osteoporosis among their subjects.

In this regard, this study was designed to demonstrate

the prevalence of osteoporosis and the metabolic characteristics of the subjects by measuring the calcaneal bone mass with quantitative ultrasound 2 (QUS2) along with bone markers and by employing questionnaires in women between the ages of 35 to 66 yr in Tae-An, Korea.

MATERIALS AND METHODS

Subjects

The study was designed as a cross-sectional survey. A total of 298 healthy women (40.8%), out of eligible 731 who are all women aged between 35-65 yr, volunteered to take part in this study. Distribution of subjects number was 13, 116, 128, 41 for age 35-40, 41-50, 51-60, >60 yr, respectively. The subjects in this study were community-dwelling Korean women from 4 villages (Mohang-ri, Pado-ri, Joongjang-ri, Hwangdo-ri) of Tae-An, which is located on the west coastal area of Korea with the latitude approximately 37° N.

Methods

Screening survey including questionnaire on life styles (smoking, alcohol consumption, calcium intake, menstruation), blood and urine tests, and quantitative calcaneal ultrasound measurement was carried out from February, 1999 to May, 1999. Physical activity was evaluated as follows: walking for more than 30 min together with exercise was given 1 point, more than 30 min of walking without exercise was 0.5 point, and less than 30 min of walking was given 0 point.

From all the subjects, fasting blood samples were drawn to measure the serum calcium, phosphorus, albumin, alkaline phosphatase, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), follicle stimulating hormone (FSH, Biodata, NY, U.S.A.), intact parathyroid hormone (PTH, Nichols Institute, San Juan Capistrano, CA, U.S.A.), and 25(OH)D (Incstar Corp, Stillwater, MN, U.S.A.), while fasting urine samples were assessed for deoxypyridinoline (Dpyd, ACS: 180, Chiron/Diagnostics, MA, U.S.A.), creatinine, calcium, and phosphorus. The serum and urine measurements except intact PTH, 25(OH)D, and Dpyd were done by automated standard laboratory methods. The menopause was practically defined as the absence of menstruation for 6 months (4) and was confirmed by increased serum values for FSH (>40 mIU/mL) (5).

QUS2 (Metra Biosystems Inc., U.S.A.) was used to measure broadband ultrasound attenuation (BUA) at calcaneus in units of dB/MHz. All ultrasonic measurements were performed on the right calcaneus. To determine the normal values of BUA by QUS2 in Korean women, we previously measured BUA at calcaneus from 423 healthy Korean women aged between 17 to 72 yr, who visited our health-care center (6). The peak BUA of 90.7 ± 17.0 dB/MHz in the 30-34 yr group in this study was used for T-scores. T score was used to determine normal (>-1), osteopenia ($-1 \leq >-2.5$), or osteoporosis (≤ -2.5) based on the World Health Organization (WHO) criteria for osteoporosis (7).

Statistics

Mean and standard deviation (SD) were calculated for BUA, age, body mass index (BMI) and all serum and urinary parameters.

The SPSS statistical software was used to analyze the data. The values of BUA with biochemical values and bone markers were compared by Kruskal-Wallis test, and by General Linear Model based on ranks adjusting years since menopause followed by multiple comparison using Bonferroni's correction. The influence of the smoking status, alcohol intakes, or exercise on BUA was tested

by the chi-square test or Fisher's exact test.

RESULTS

Of the 298 women between the ages of 35-66 yr in Tae-An, the prevalence of osteoporosis and osteopenia were 3.0% and 40.9%, respectively. When the subjects were classified according to their menopausal status, none was osteoporotic and 26.5% were osteopenic in premenopausal women, while 5.0% were osteoporotic and 50.3% were osteopenic in postmenopausal women. After stratifying our subjects according to years since menopause (YSM), the prevalence of osteoporosis increased along with an increase of YSM (0, 0, 3.3, 11.1% for YSM 0, 5, 10, 15 yr, respectively) and that of osteopenia showed the same tendency (26.5, 37.9, 51.7, 60.3% for YSM 0, 5, 10, 15 yr, respectively) (Fig. 1). And also stratifying the subjects according to age, the prevalence of osteoporosis was 1.4, 1.6, 11.9% for age between 50-54, 55-59, 60-65 yr, respectively and that of osteopenia was 34.8, 54.1, 57.6%. None was osteoporotic below age of 50 yr.

Among the normal, the osteopenic and osteoporotic women based on the WHO criteria, the level of serum alkaline phosphatase was significantly higher in the osteopenic and osteoporotic groups than in the normal group, and the level of serum calcium corrected by albumin was higher in the osteoporotic group than the normal group. Fasting urinary Dpyd/creatinine was significantly higher in the osteopenic group than in the normal group. The younger age and higher body weight were noted in the normal group compared to the osteopenic or osteoporotic group (Table 1). There was no significant difference in

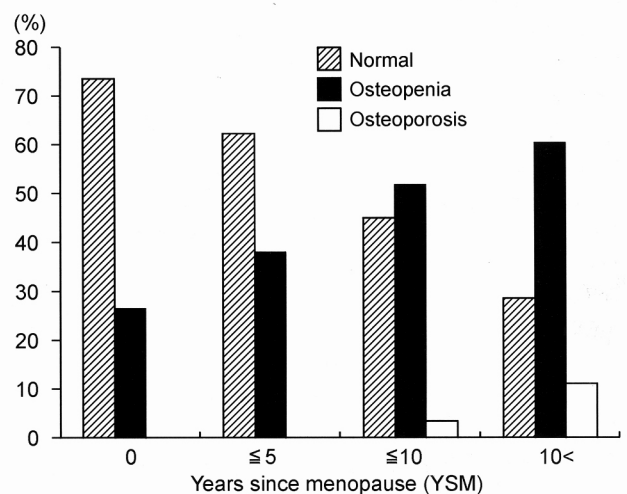


Fig. 1. Distribution of normal, osteopenia, and osteoporosis in the study subjects according to years since menopause.

Table 1. Sociodemographic and habitual characteristics of the study subjects (n=298)

	Normal	Osteopenia	Osteoporosis
Number of the subjects	167	122	9
Age (yr)	50.35±6.29	53.93±7.69*	61.11±4.14*
Body weight (kg)	60.23±7.47	56.47±7.36*	52.89±6.58*
Body mass index (kg/m ²)	25.12±2.84	24.33±3.14	23.28±2.73
Years since menopause	3.43±5.30	7.80±7.29*	16.78±6.04*
Smoking (%)	0.6	0.2	0
Alcohol (%)	13.2	11.5	0
Exercise (=1) (%)	14.4	12.4	22.2
(=0.5) (%)	73.1	81.0	55.6

*The mean difference is significant at the 0.05 level compared to normal group

Exercise: more than 30-min and exercise =1

more than 30-min walking without exercise =0.5

Table 2. Metabolic characteristics of the study subjects (n=298)

	Normal	Osteopenia	Osteoporosis
Serum alkaline phosphatase (IU/L)	72.59±21.18	84.10±24.90*	97.78±33.06*
Serum calcium corrected by albumin (mg/dL)	8.83±0.37	8.89±0.38	9.22±0.44*
Serum phosphorus (mg/dL)	3.65±0.49	3.67±0.48	3.50±0.49
Calcium phosphorus product	32.20±4.52	32.61±4.47	32.27±4.67
Parathyroid hormone (pg/mL)	22.24±22.68	21.53±22.72	18.44±5.08
Serum 25-hydroxy vitamin D (ng/mL)	22.37±8.09	20.45±10.10	20.33±7.23
Fasting urinary calcium/creatinine ratio	0.15±0.08	0.17±0.09	0.19±0.08
Fasting urinary deoxypyridinoline (nM/mM creatinine)	9.88±3.14	10.80±3.17*	10.83±2.28

*The mean difference is significant at the 0.05 level compared to normal group

Table 3. Metabolic characteristics in the study subjects according to YSM

	Pre-menopause (n=116)	YSM ≤5 (n=59)	5<YSM ≤10 (n=60)	10<YSM (n=63)
Serum alkaline phosphatase (IU/L)	64.1±19.9	84.9±17.6*	91.8±23.5*	84.3±24.0* [†]
Serum calcium corrected by albumin (mg/dL)	8.7±0.4	8.9±0.4*	9.0±0.4*	8.9±0.3*
Serum phosphorus (mg/dL)	3.5±0.5	3.8±0.5*	3.7±0.4*	3.8±0.5*
Calcium phosphorus product	30.5±4.6	33.6±4.0*	33.5±3.6*	33.6±4.4*
Parathyroid hormone (pg/mL)	19.7±13.2	20.7±26.7	24.0±22.8	24.8±29.8
Serum 25-hydroxy vitamin D (ng/mL)	21.4±9.3	22.3±8.5	20.5±8.8	22.0±9.0
Fasting urinary calcium/creatinine ratio	0.13±0.06	0.21±0.09*	0.17±0.09* [†]	0.16±0.09* [†]
Fasting urinary deoxypyridinoline (nM/mM creatinine)	8.9±3.0	11.1±2.7*	11.6±2.7*	10.8±3.0*

YSM, years since menopause

*The mean difference is significant at the 0.05 level compared to premenopause group

[†]The mean difference is significant at the level compared to 5<YSM≤10 group

[‡]The mean difference is significant at the level compared to YSM≤5 group

PTH, 25(OH)D, calcium-phosphorus product or other biochemical data such as AST, ALT, and creatinine among the normal, osteopenic, and osteoporotic groups (Table 2). It was revealed that smoking, alcohol, and physical activity had no influence on the bone markers or bone mass in these groups.

A significant difference was observed in bone markers such as serum alkaline phosphates, calcium, phosphorus,

calcium-phosphorus product, fasting urinary dpyd/creatinine, fasting urinary calcium/creatinine between premenopause and menopause, however no difference was found in markers among different YSM (ysm≤5, 5<ysm≤10, ysm>10 yr) except serum alkaline phosphatase, fasting urinary calcium/creatinine (Table 3).

Analysis of bone markers in normal, osteopenia, and osteoporosis group adjusting YSM after categorizing

YSM into $ysm=0$ (premenopause), $ysm \leq 5$, $5 < ysm \leq 10$, $ysm > 10$ yr showed that the level of serum alkaline phosphatase was significantly higher in the osteopenic group than in the normal group ($p=0.038$) and the level of serum 25(OH)D was significantly higher in the normal group than osteopenic group ($p=0.040$).

DISCUSSION

Although axial densitometers remain as the gold standard for diagnosing osteoporosis, more portable peripheral devices such as ultrasound are increasingly used to diagnose osteoporosis. Several reports have suggested that quantitative ultrasound (QUS) parameters of the calcaneus were significantly correlated with the bone mineral density (BMD) assessed by the dual energy radiography absorptiometry (8, 9) and that mean T-scores derived by comparing BMD and BUA values with those of the young healthy group were similar to each other (10, 11). These and other reports, showing that ultrasound measurements could predict the risk of hip and any fractures (12, 13), collectively support the usefulness of ultrasound devices in detecting osteoporosis. QUS2 is a radiation-free approach that utilizes a pulse of ultrasonic waves passing through the calcaneus for measuring BUA (14). The calcaneus is thought to be an ideal peripheral site for bone mass measurement because it is a weight-bearing and trabecular-rich bone. Since the WHO criteria for the definition of osteoporosis can be applied to the results of QUS2 (10), we stratified our subjects according to the results of QUS2 based on the WHO criteria. There are two important issues for diagnosing osteoporosis based on the WHO criteria. The most important issue is whether or not the -2.5 SD cut-off level should be used to diagnose osteoporosis in men and women of different races, where the relationship between bone density and fracture risk may differ from that in white women (15). Another important issue is determining whether or not WHO definition of osteoporosis can be applied to the ultrasonometer measurement at the calcaneus using QUS2, although multivariable analyses revealed that QUS measurements would predict the risk for hip or other fractures in elderly people (12). Although WHO definition could be applied to QUS2 measurements (10), other study showed that a T score threshold of -1.80 could be applied to diagnose osteoporosis using three QUS devices such as Sahara Clinical Bone Sonometer (SAH, Hologic, Bedford, MA, U.S.A.), Ultrasonic Bone Analyzer 575+ (UBA, Hologic, Bedford, MA, U.S.A.), and DTUone (DTU, Osteometer Meditech, CA, U.S.A.) (17). Further studies are needed in order to determine the appropriate T score thresholds for diagnosing

osteoporosis using QUS devices in Korean women. Until appropriate prospective data on fracture risk in Korean women are available, it seems reasonable to use the 2.5 SD criterion to estimate the prevalence of osteoporosis among Korean women.

This study presents that 3.0% were osteoporotic and 40.9% were osteopenic in 298 women between the ages of 35-66 yr in Tae-An, Chungcheongnam-do. The level of serum alkaline phosphatase was significantly higher in osteopenic and osteoporotic groups than in the normal group, and that of serum calcium corrected by albumin was higher in the osteoporotic group than in the normal group. In addition, fasting urinary Dpyd/creatinine was significantly higher in the osteopenic group than in the normal group. These findings suggest a close relationship between the high bone turnover and low bone mass as is expected. Higher body weight was associated with higher BUA values. However, we could not observe any relationships between PTH, 25(OH)D, or calcium-phosphorus product and bone mass. After stratifying our subjects according to YSM and age, it was shown the prevalence of osteoporosis and osteopenia increased as YSM and age increased. Since the BUA decreased along with an increase of YSM, we analyzed bone markers between premenopausal and menopausal women. The results of analysis showed a significant difference in serum alkaline phosphates, calcium, phosphorus, calcium-phosphorus product, fasting urinary dpyd/creatinine, fasting urinary calcium/creatinine. Comparisons among the different duration of YSM showed no significant difference in bone markers except serum alkaline phosphates, fasting urinary calcium/creatinine in this study subjects. Although a significant difference in the level of serum alkaline phosphates and 25(OH)D was observed in normal and osteopenic group after categorizing YSM, a further study is needed since the subjects in each group were small.

A questionnaire regarding the lifestyle factors such as smoking, alcohol intake, physical activity and calcium intake was used to examine the relationship between these factors and bone mass. As for the smoking history, only 4 women were documented to be smokers in our study, and they reported that they had been smoking only occasionally. In this regard, although smoking harbored no statistically significant effect on the bone mass according to our study, further well-designed studies are needed to evaluate the relationship between smoking and bone mass. With regard to alcohol intake, 36 subjects stated themselves to be alcohol consumers. They reported that they had been drinking 1-2 glasses of beer or 1-2 glasses of Soju occasionally. Alcohol drinking was revealed to have no effect on bone mass in this study. Concerning the physical activity, most women in this study (266/298 women) spent at least 30 min in walking

everyday, and also worked on the seashore picking shells. The remaining subjects were maintaining their physical activity through their chores around the home. Therefore, the relationship between physical activity and bone mass could not be identified. Calcium intake (mg/day) was estimated by two dietitians based on questionnaires on the composition of recent meals. Information about dietary intake of calcium was available in 72 subjects through questionnaires, which showed the variable calcium intake (170 mg-1,281 mg). Since only 72 out of 298 subjects could be assessed for dietary calcium intake, data from a larger number of subjects is needed to elucidate a more reliable relationship between dietary calcium and bone mass even though no relationship was observed in this study.

Taken together, the prevalence of osteoporosis and osteopenia in Tae-An area using QUS2 were 3.0% and 40.9%, respectively and also increased along with the increase of YSM and age. There was a positive correlation between low bone mass and high bone turnover in our study. Considering that much time, efforts, and cost are needed to treat the overt osteoporosis, it is very important to understand the metabolic characteristics in osteoporosis to prevent the development of disease. Further studies are needed to elucidate the metabolic characteristic in osteoporosis.

ACKNOWLEDGEMENT

This study was supported by a 98-Grant from the Korean Academy of Medical Sciences. The authors are grateful to Mr Lee, Seung-Woo, Minister of Planning and Management, Jeollabuk-do and the staffs of Tae-An Healthcenter and County Hospital for their helps. We also thank Ms Lee, Min-Jung for proofreading the manuscript.

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