Modifications of T-Scores by Quantitative Ultrasonography for the Diagnosis of Osteoporosis in Koreans

To identify a proper T-score threshold for the diagnosis of osteoporosis in Koreans using quantitative ultrasonography (QUS), normative data from 240 females and 238 males (ages 20-29 yr) were newly generated. Then, the osteoporosis prevalence estimate for men and women over 50 yr of age was analyzed using previous World Health Organization (WHO) methods and heel QUS. T-scores were calculated from the normative data. There were definite negative correlations between age and all of the QUS parameters, such as speed of sound (SOS), broadband ultrasound attenuation (BUA), and estimated heel bone mineral density (BMD) (p<0.0001). After applying the recently determined prevalence of incident vertebral fracture in Koreans over 50 yr of age (11.6% and 9.1%, female vs male, respectively) to the diagnosis of osteoporosis by T-scores from heel BMD as measured by QUS, it was revealed that applicable T-scores for women and men were -2.25 and -1.85, respectively. These data suggest that simply using a T-score of -2.5, the classical WHO threshold for osteoporosis, underestimates the true prevalence when using peripheral QUS. Further prospective study of the power of QUS in predicting the absolute risk of fracture is needed.

Key Words : *Osteoporosis; Ultrasonography; Diagnosis; Demography*

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INTRODUCTION

As life expectancy continues to increase, detecting low bone mass has become an important health issue worldwide. This is based on the fact that individuals with low bone mass show a high risk of fracture, which can decrease their quality of life.

Efforts to find the most appropriate T-score range for predicting fracture risk have always been controversial. Several years ago, the World Health Organization (WHO) made the decision to use a T-score value of less than -2.5 to define osteoporosis (1). However, there are several easily accessible peripheral bone densitometry measures other than the classical central dual-energy radiography absorptiometry (DXA). As all densitometry measures just adopted the threshold of T-score only the number itself made by the WHO's decision as the criteria classifying bone mass, discordance in the proper description of bone mass naturally occurred. Additional problems arose from different reference groups and from variations in each company's machines.

In addition, there are several points to consider concerning the sole use of central DXA and the T-score. First, bone size affects the real value of 2-dimensional spinal densitometry; this is responsible for much of difference between sexes and ethnic groups of a relatively small frame. Second, although precise, bone mineral density (BMD) only gives quantitative information; it does not give any data regarding the microstructures and the elasticity of the bone (the recently emphasized measure of bone quality) (2). Third, only a certain proportion of institutions offer this expensive densitometry measure.

Several pieces of evidence suggest that quantitative ultrasonography (QUS) may provide information about both bone mass and the microarchitectural and elastic properties of the bone (3-5). Moreover, recent results from the National Osteoporosis Risk Assessment (NORA) on peripheral densitometry, including QUS, revealed that peripheral BMD results were highly predictive of fracture risk (6). In addition, inexpensive, small, portable QUS equipment will broaden the range of low bone mass detection while improving accessibility to testing. The correlation between calcaneal BMD and the axial skeleton was reasonably acceptable (r=0.6) (7). Therefore,

QUS would be a useful tool for mass screening and in primary care settings.

However, application of the -2.5 T-score criteria to QUS does not seem suitable. This is even more difficult in men. In addition, a problem such as T-score discordance exists; and this appears even in central DXA, the gold standard for densitometry measures. Therefore, by employng the similar approach as was used to develop the WHO definition for Caucasian women, prevalence estimates for osteoporosis in Korean women and men were determined using QUS (1, 8).

MATERIALS AND METHODS

Subjects

For this study, 535 men and 1,089 women (with ages ranging from 20-80 yr old) were recruited voluntarily. Among these subjects, 240 females and 238 males in their third decade were examined to represent a young reference group (9). All subjects gave written informed consent. Subjects with known chronic illnesses (including a history of low trauma fracture) and subjects on chronic medications that could affect bone metabolism were excluded. Women with a history of menopause earlier than the age of 40 and a history of amenorrhea of more than 6 months were also excluded.

Basic anthropometric data and medical history for each subject were completed by the individual questionnaire. The questionnaire on each person's birth weight, milk consumption per week, and the exercise frequency were done in the youngster reference group. The age distribution was as follows: 20-29 yr, n=478; 30-39 yr, n=360, 40-49 yr, n=435; 50-59 yr, n=215; 60-80 yr, n=136.

Bone densitometry

A Sahara QUS (Hologic, Bedford, U.S.A.) was used to measure the broadband ultrasound attenuation (BUA) and speed of sound (SOS). The estimated heel BMD was calculated using the equation $0.002592 \times (BUA+SOS)-3.687$ (10). The measurements were taken at a fixed region of the mid-calcaneus. Instrumental quality control scans of the manufacturer-provided phantoms were done daily.

Data analysis

A subgroup of healthy young subjects (age 20-29 yr) was selected to estimate the young normal mean and SD for QUS measurement parameters in order to calculate T-scores (9):

T-score=[Measurement value-Young adult mean]/
Young adult population SD

To evaluate age-related differences in T-scores, all patients were placed into five-year age groups. To determine the optimal T-score which would represent an approximately similar percentage of men or women with osteoporosis, survey results from the Ansung cohort regarding the prevalence of incident vertebral fracture examined by lateral radiography in Koreans over age 50 (524 females and 441 males, respectively) were used (11).

Statistics

SPSS 11.5 software (Chicago, IL, U.S.A.) was used for sta-

Table 1. Clinical characteristics and normative data for the reference population

	Female	Male
Age (yr)	22. 4±1.5	20.4±2.2
Body weight (kg)	51.6±4.6	66.3±8.1
Height (cm)	162.1±4.0	173.9±5.1
BMI (kg/m²)	19.6±1.6	21.9±2.6
Estimated heel BMD	0.556±0.104	0.567±0.113
BUA	79.4±15.0	80.8±16.5
SOS	1557.2±27.5	1560.1±28.7

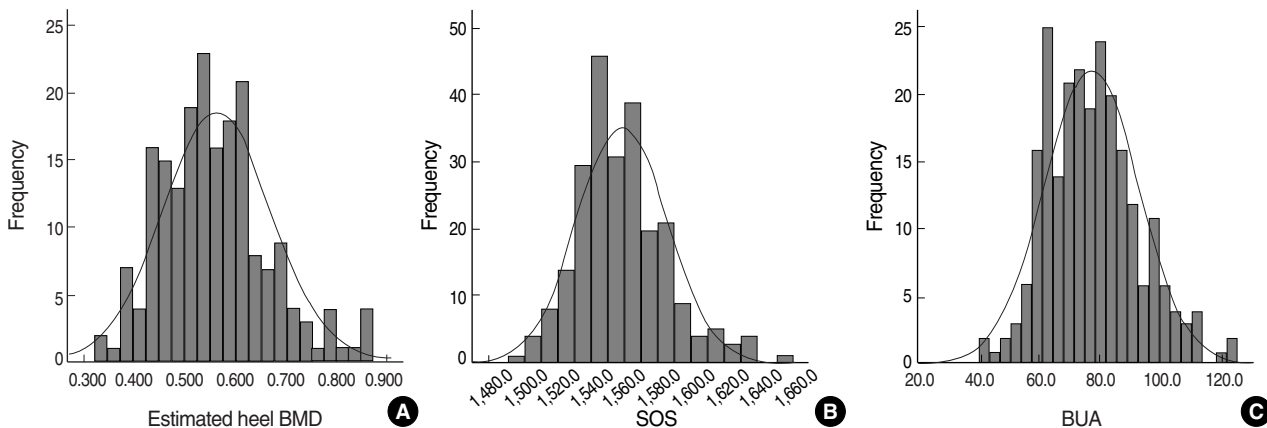BMI, body mass index; BMD, bone mineral density; BUA, broadband ultrasound attenuation; SOS, speed of sound.

Fig. 1. Normal distribution curve of the QUS parameters in the female reference group. **(A)** Estimated heel BMD, **(B)** Speed of sound, **(C)** Broadband ultrasound attenuation.

tistical analysis. Bivariate correlation analysis was performed between age and QUS parameters. A two-sided *p* of less than 0.05 was considered significant.

RESULTS

The clinical characteristics and normative data for Korean men and women (ages 20-29 yr) are shown in Table 1. All of the QUS parameters were included. With these normal data, the mean T-scores for men and women were determined at five-year intervals based on the number of standard deviations from the young reference normal mean. The normal distribution curves of the QUS parameters for these groups are shown in Fig. 1 and 2, respectively.

The age-related decline in T-scores for all QUS parameters is shown in Fig. 3. In the data from females, the rates of BMD loss seem to accelerate at the average age of menopause, where-
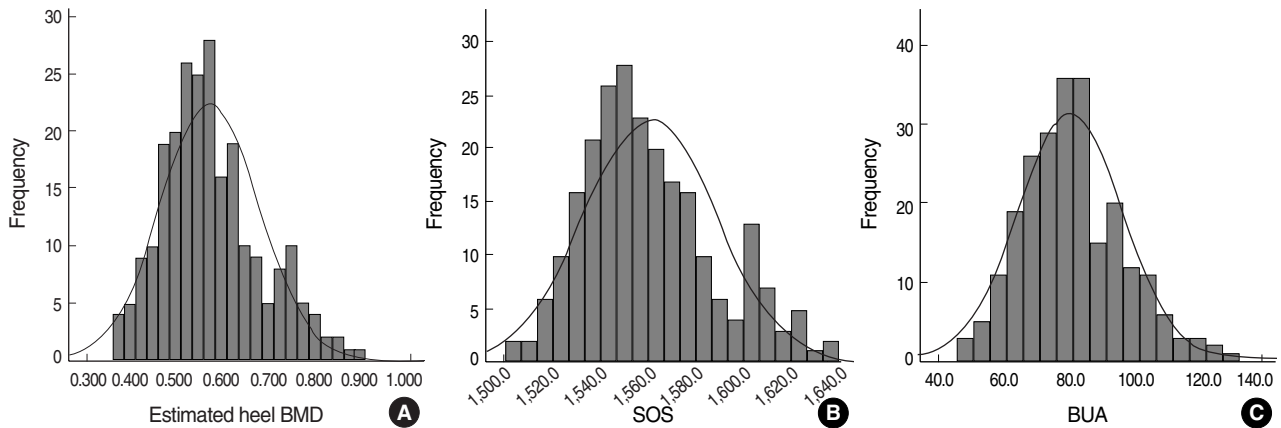
Fig. 2. Normal distribution curve of the QUS parameters in the male reference group. (A) Estimated heel BMD, (B) Speed of sound, (C) Broadband ultrasound attenuation.
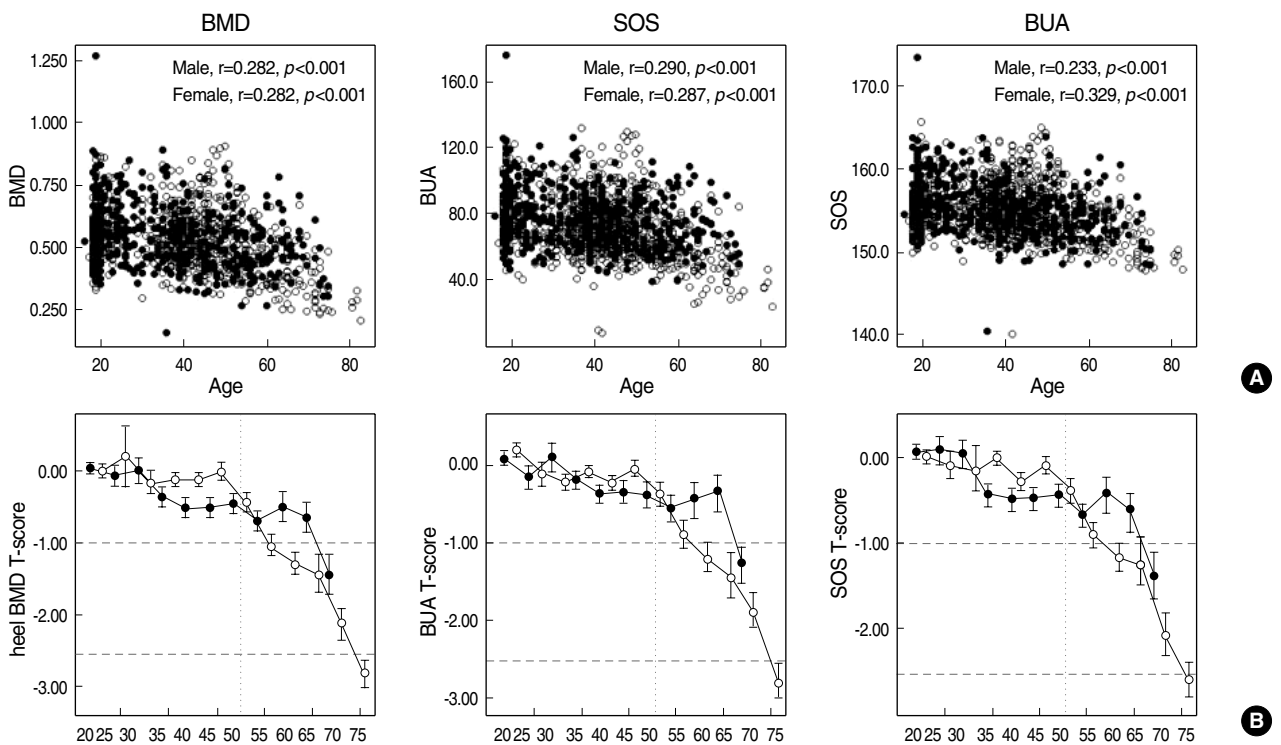
Fig. 3. Age-related changes in QUS data. (A) Actual raw data of QUS parameters with respective correlation values. (B) T-score of QUS parameters. Filled circle, male; void circle, female.
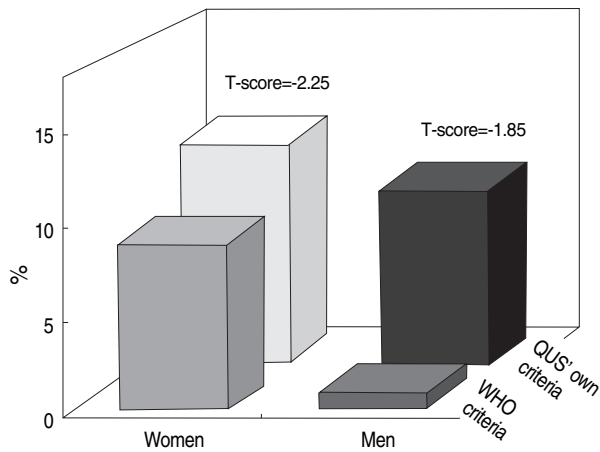
Fig. 4. Comparisons of the prevalence of osteoporosis in Korean women and men, according to either the classical WHO T-score of under -2.5 or the newly- derived heel BMD T-score from QUS adapted from the actual reported occurrence of hip fracture (noted above the each bar).

as BMD starts to decline significantly at approximately 65 yr of age in males. However, there was no increase in BMD after the age 70, which is common in DXA because of degenerative changes.

In addition, analysis of correlated factors in the young-aged reference group showed a positive correlation between body mass index and heel BMD in males (p=0.001, data not shown). There was also a negative correlation between the age of menarche and BMD in females (p=0.002, data not shown).

To detect the actual prevalence of vertebral fracture for those over 50 yr of age using WHO's method, we applied the percentages of 11.6% and 9.1%, which were obtained from the national report (11). The most appropriate T-score cut-points from the heel BMD (measured by QUS) were -2.25 and -1.85. However, using the classical WHO T-score of -2.5 revealed the prevalence of osteoporosis as 8.7% in females and 0.8% in males, both of which are drastic underestimations (Fig. 4).

DISCUSSION

To determine whether a patient has low bone mass, T-scores from central DXA using classical WHO guidelines are used worldwide (1). However, the use of peripheral QUS has been increased in the clinics of primary physicians recently because this method does not subject the patients to radiation and it is relatively easy to use. Therefore, a need for guidelines on how to interpret the results obtained with these devices has also arisen. The aim of this study was to determine a specific threshold that corresponds to the prevalence of osteoporosis by employing the present criterion used in the diagnosis osteoporosis.

The T-scores using the average and the standard deviation of the young normative data were newly calculated. There were definite negative correlations with age and all QUS parameters,

such as SOS, BUA, and estimated heel BMD (p<0.0001). This is comparable to the results of DXA. However, there was no increase in BMD after the age of 70, a common pitfall with central DXA, especially in the lumbar spine due to degenerative changes. An interesting finding was that there was a specific point of accelerated bone loss at the age of menopause in women contrary to previous QUS report showing gradual loss even in women.

There was a positive correlation between body mass index and heel BMD in males (p=0.001). The existence of a positive association between body size and bone mass is well established (12, 13) However, there was a negative correlation between the age of menarche and BMD in females (p=0.002). There is a body of evidence that suggests that late menarche imposes a negative influence on BMD in the early post-menopausal period (14).

The current T-score thresholds used to detect osteoporosis were defined as a T-score under -2.5 for 50-yr-old women and men, which corresponded to a lifetime risk of hip fracture for 50-yr-old Caucasian women and men as high as 16% and 13%, respectively (15). The T-score thresholds for women above the age of 50 that best correspond to the incident vertebral fracture from our Korean report (i.e. 11.6%) are T-scores of -2.25 for heel BMD, -2.16 for BUA, and -2.14 for SOS. The most suitable T-score thresholds for men above the age of 50 are T-scores of -1.85 for heel BMD, -1.69 for BUA and -1.92 for SOS. The T-score thresholds for QUS are all higher than those used in central DXA. A previous report from the United Kingdom using the same QUS as was used in this study suggested that best T-score threshold was -1.8 when using heel BMD (10). One possible explanation of this finding is that QUS has a higher population standard deviation than DXA because of phase cancellation (10). Thus, it is clear that different T-score thresholds should be used when using QUS.

There are a few limitations to this study. The T-score thresholds arising from this study might not reflect the true fracture risk as a clinically significant end-point. Another limitation is the availability of many different QUS devices; our study assessed, only one of these devices. Therefore, it may not be presently possible to recommend a single T-score threshold which would be appropriate for all QUS measurement parameters to identify individuals at risk for osteoporosis (10). Lastly, as the raw data of QUS were taken quite a several years ago and the current IRB approval was not done, only informed consents were taken. This was inevitable since there were no clear data on the prevalence of osteoporotic fracture until the recent survey on Ansung cohort.

In conclusion, this study indicates that simply using a T-score of -2.5 as the criteria for osteoporosis vastly underestimates the true prevalence when using peripheral QUS. Further prospective studies on the power of the peripheral QUS to predict the absolute risk of the fracture are needed.

ACKNOWLEDGEMENT

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