DISCORDANCE IN THE DIAGNOSIS OF OSTEOPOROSIS DUE TO PEAK BONE MINERAL DENSITY FROM DIFFERENT REFERENCES: JAPANESE AND NORTHEASTERN THAI WOMEN

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ABSTRACT

According to the WHO guideline in the diagnosis of osteoporosis, use of inappropriate reference can result in the inappropriate bone mineral classification. This study aimed to explore the difference between the prevalence of abnormally low bone mass diagnosed by using the Japanese and the northeastern Thai reference. The subjects were retrospectively recruited from women, aged 20-90 years, residing in the northeast Thailand who underwent bone mineral density (BMD) measurement at the lumbar spines and proximal femur from May 1998 to August 2000 at Srinagarind Hospital. Concordant and discordant rate in the interpretation between both criteria were reported. There were 653 subjects with 779 studies included. Higher prevalence of osteopenia and osteoporosis was observed by using T-score of the northeastern Thai population, compared with that diagnosed by the Japanese reference at almost all sites except Ward's triangle. Concordant diagnoses were found in 73.6% of all sites. Significant diagnostic agreement between both criteria was noted at all sites (Kappa = 0.18-0.80, $p < 0.001$). Although resulting in some discordant classification, using the northeastern Thai reference classified the same BMD status in almost three-fourths of all sites. This study stressed the limitation of the WHO diagnostic guideline regarding the effect of different reference range used.

INTRODUCTION

It has been widely recognized that a low peak bone mass in adults is a significant risk factor for osteoporotic fractures later in life.[1-3] Various factors influence the level of peak bone mass including genetic and environmental factors such as calcium intake, exercise and smoking.[4-7]

The World Health Organization (WHO) proposed diagnostic categories to define normal, osteopenic and osteoporotic individuals accord-

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This study was presented at the 39th Annual Scientific Meeting of the Royal College of Radiologists of Thailand and the Radiological Society of Thailand, 27-29 March 2002.

ing to the standard deviation (SD) in bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DEXA) below the average value in the normal young adults as the reference, or T-score.[8] Although the BMD is peak at the young adult age, the age at which peak bone mass is attained has continued to be debated and estimates range widely in cross-sectional investigations from late adolescence [9-10] and the third decade,[11] into the fourth decade of life [12] and beyond.[13] These certainly affect the reference T-score and also have an impact on the diagnosis of low bone mass or osteoporosis.[14-15] Accordingly, to obtain an appropriate T-score for BMD interpretation, the local reference BMD database should be carried out to provide the appropriate BMD cut-off level for the diagnosis of osteopenia or osteoporosis in that specific group of population. Our group had studied the BMD at the lumbar spines and proximal femur in the normal northeastern Thai women and reported the BMD cut-off value for the diagnosis of osteopenia and osteoporosis for this group of population.[16] However, in the routine service, we have used the T-score from the Japanese reference database, an Asian ethnicity close to Thai, provided by manufacturer's software of our bone densitometer. This can give different diagnostic results from using the northeastern Thai reference database.

We therefore conducted this study to explore the difference between the prevalence of osteopenia and osteoporosis diagnosed by using the Japanese and the northeastern Thai reference range applied to the northeastern Thai women. This study was approved by the Ethics Committee, Faculty of Medicine, Khon Kaen University.

MATERIALS AND METHODS

SUBJECTS

Retrospective review of the medical records and results of BMD measurement of subjects performed at the Division of Nuclear Medicine, Department of Radiology, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from May 1998 to August 2000 was conducted. The inclusion criteria were women, aged 20-90 years, undertaking the BMD study both at the lumbar spines and proximal femur at the same time. The exclusion criteria were those who had the history of fracture and who did not reside in the northeast Thailand.

BMD MEASUREMENT

BMD values (g/cm^2) at the lumbar spines (L_{2-4}) and non-dominant proximal femur including femoral neck, Ward's triangle, trochanteric region and total proximal part were measured using DEXA technique of EXPERT-XL bone densitometer of Lunar Corp., USA, by the standardized well-trained technician. Quality control of the instrument was undertaken daily, using the standard phantom with automatic software program by technicians under the supervision of an experienced nuclear medicine physician. The precision error of BMD measurement at all sites was less than 1.5% measured on phantom.

BMD INTERPRETATION

Both the Japanese and northeastern Thai criteria were used in the interpretation of a measured BMD in each subject. A T-score acquired from the normal Japanese reference was calculated by the manufacturer's software on the process of data analysis of each measurement and was then interpreted as normal bone mineral status, osteopenia or osteoporosis according to the WHO guideline.

In the interpretation of BMD by using the northeastern Thai reference, the BMD cut-off values previously reported by our group were used.[16] From that study, we prospectively recruited

350 subjects aged 20-70 years from the Obstetrics and Gynecology Out-patient Clinic, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from May 1998 to August 2000. The inclusion criteria were healthy women residing in the provinces of northeastern part of Thailand who had body mass index (BMI) in the range of 19-25 kg/m^2. The exclusion criteria were pregnancy, smoking, alcohol drinking, chronic back pain or other skeletal diseases, having prior ovarian surgery, having concurrent diseases such as hyperthyroidism, chronic illnesses, history of hospitalization for more than 2 weeks, taking medications affecting BMD such as corticosteroid, hormonal contraception, calcium, vitamin D, diuretics, anti-convulsant, and having prior radioisotope or radiocontrast study within a week before the BMD study. All subjects were measured for BMD at the antero-posterior lumbar spines and non-dominant proximal femur by the same machine used in the present study. The group of peak bone mass of each skeletal site was identified and the mean BMD with SD of this group were used to define the BMD cut-off level for determining the bone mineral status of that site. According to the WHO criteria, the individuals were classified into three categories with respect to their BMD status as follows: normal (T-score $\geq$ -1), osteopenic (-2.5 < T-score < -1), osteoporotic (T-score $\leq$ -2.5). Accordingly, it was found that osteopenia of the L_{2-4} spines, femoral neck, Ward's triangle, trochanteric region and total proximal femur was diagnosed when the BMD was lower than 1.091, 0.854, 0.734, 0.728 and 0.935 g/cm^2 respectively, whereas BMD of equal or lower than 0.889, 0.678, 0.483, 0.594 and 0.785 g/cm^2 was used for the diagnosis of osteoporosis of these sites respectively. These BMD thresholds were used for the diagnostic classification by the northeastern Thai reference range in the present study.

STATISTICAL ANALYSIS

The recorded data included age, weight, height, BMI, BMD of the antero-posterior lumbar spines (L_{2-4}), femoral neck, Ward's triangle, trochanteric region, total proximal part of the non-dominant femur and its interpretation by the criteria of both reference ranges.

The continuous data were expressed as mean $\pm$ SD. Concordance and discordance in the diagnosis of normal bone mineral status, osteopenia or osteoporosis using the two criteria were presented as the percentage. Statistical test for agreement of the classification was performed by Kappa analysis. P-value less than 0.05 was considered significant.

RESULTS

Of all subjects referred for BMD measurement during the study period, 653 cases meeting our criteria were studied. From all 653 cases, most subjects were studied once, whereas 88 were studied for 2 times and 19 were studied for 3 times resulting in total 779 studies enrolled for analysis. Four hundred and sixty-nine studies (60.2%) were performed in women who were sent from the Menopause Clinic, Srinagarind Hospital, for baseline BMD measurement, to find evidence of low bone mass or osteoporosis, or to follow up BMD after a period of hormone replacement therapy, whereas 310 studies (39.8%) were performed in those sent from various other units in order to find the evidence of osteopenia or osteoporosis.

Baseline characteristics and BMD values of the subjects were shown in Table 1. By using T-score criteria from the two references, the prevalence of osteopenia and osteoporosis in each skeletal site was demonstrated (Table 2). Higher prevalence of both osteopenia and osteoporosis was observed by using T-score reference range of the northeastern Thai population, compared with those diagnosed by the Japanese reference range at almost all sites of the skeleton measured except lower prevalence of osteoporosis at the Ward's triangle diagnosed by the northeastern Thai reference.

Concordant diagnoses-normal, osteopenic or osteoporotic-between criteria from the two references were observed in about three-fourths of all skeletal sites (73.6%), while the diagnoses of the remaining about one-fourth (26.4%) were found to be discordant (Table 3). Ward's triangle was the skeletal site that had the highest percentage of concordant diagnoses (88.1%). Significant agreement in the diagnosis between the two reference criteria was noted at all skeletal sites with the Kappa values ranging from 0.18 to 0.80 (p-value < 0.001).

Regarding the discordant diagnoses, it was noted that of all 1,030 discordant interpretations, mostly at the total proximal femoral part, shown in Table 3, only 4 out of 937 skeletal sites at the non-Ward's region-L_{2-4}, femoral neck, trochanteric region and total proximal femur-were more severe when diagnosed by the northeastern Thai criterion compared with those diagnosed by the Japanese criterion. On the contrary, all 93 discordant interpretations at the Ward's region were found to be more severe when diagnosed by the Japanese criterion compared with those diagnosed by the northeastern Thai criterion.

Table 1. Baseline characteristics and BMD values of the subjects.

Characteristic	Value
Age (year)	
mean $\pm$ SD	51.9 $\pm$ 8.7
range	21 - 88
Weight (kg)	
mean $\pm$ SD	57.1 $\pm$ 8.4
range	33 - 85
Height (cm)	
mean $\pm$ SD	154.9 $\pm$ 5.6
range	133 - 175
BMI (kg/m^2)	
mean $\pm$ SD	23.8 $\pm$ 3.3
range	15.4 - 38.3
BMI (g/cm^2)	
mean $\pm$ SD	
L_{2-4}	1.062 $\pm$ 0.169
Femoral neck	0.874 $\pm$ 0.135
Ward's triangle	0.721 $\pm$ 0.153
Trochanter	0.750 $\pm$ 0.122
Total proximal femur	0.946 $\pm$ 0.133

Table 2. Comparison between the prevalence of osteopenia and osteoporosis in each skeletal site diagnosed by using criteria from the Japanese and the northeast Thai database (N=779 studies).

Skeletal site	Prevalence			
	Osteopenia		Osteoporosis	
	Japanese	Northeastern Thai	Japanese	Northeastern Thai
L_{2-4}	220 (28.2%)	310 (39.8%)	61 (7.8%)	117 (15.0%)
Femoral neck	174 (22.3%)	269 (34.5%)	24 (3.1%)	59 (7.6%)
Ward's triangle	340 (43.6%)	383 (49.2%)	109 (14.0%)	41 (5.3%)
Trochanter	112 (14.4%)	255 (32.7%)	16 (2.1%)	68 (8.7%)
Total proximal femur	101 (13.0%)	279 (35.8%)	15 (1.9%)	84 (10.8%)

Table 3. Comparison of the BMD interpretation classified as concordant or discordant diagnosis between the two reference criteria at each skeletal site.

Skeletal site	Concordance		Discordance
	Number (%)	Kappa[a]	Number (%)
L_{2-4}	575 (73.8%)	0.55	204 (26.2%)
Femoral neck	610 (78.3%)	0.56	169 (21.7%)
Ward's triangle	686 (88.1%)	0.80	93 (11.9%)
Trochanter	532 (68.3%)	0.31	247 (31.7%)
Total proximal femur	462 (59.3%)	0.18	317 (40.7%)
Total	2,865 (73.6%)	-	1,030 (26.4%)

DISCUSSION

According to the WHO diagnostic guideline, T-score values of < -1 and ≤ -2.5 are used to classify a subject's skeletal status at each site as osteopenia or osteoporosis respectively. Although has been widely accepted, this guideline remains have several problems regarding the optimal site for assessment, thresholds for diagnosis in men and the diagnostic inaccuracies at different sites.[17] Several studies from USA,[18] European[19-22] and Asian countries[23] have been conducted to establish the reference BMD values at different skeletal sites for their own population to aid correct diagnosis of osteoporosis, to screen individuals at the higher risk of fractures and to make international or interracial comparisons of bone mass.

Although the local Thai BMD reference ranges are now available, many institutes in Thailand still use their manufacturer's reference criteria, especially from Japanese or Korean population, in the interpretation of BMD results since they are recognized as the database from the Asian races close to that of Thai. This may, in part, be due to some limitations such as different bone densitometer instruments used among the institutes. The mean absolute difference in L_1-L_3 BMD between Hologic and Lunar devices might be up to 18.5%.[24] If this is the case, a cross-calibration for BMD values from one instrument to another is crucial and has to be performed before applying reference database from one instrument to another.[25-26]

Applying T-score from the two reference criteria studied by Lunar bone densitometer to our study population yielded higher prevalence of osteopenia and osteoporosis diagnosed by the northeastern Thai reference criterion at L_{2-4}, femoral neck, trochanteric region and total proximal femur. This could be attributable to the difference in the BMD cut-off levels between the two reference ranges. Although the BMD cut-off values from the Japanese reference range in our study could not be exactly defined, we could calculate them approximately by determining the average BMD values that corresponded to the T-score of -1 for the cut-off level of osteopenia and -2.5 for the cut-off level of osteoporosis in our study population. By this method, it was found that the BMD cut-off levels of the Japanese reference range for osteopenia at L_{2-4}, femoral neck, trochanteric region and total proximal femur were 1.012, 0.799, 0.642 and 0.825 g/cm^2 respectively whereas those for osteoporosis were 0.831, 0.626, 0.516 and 0.625 g/cm^2 respectively. These cut-off levels were clearly lower than those of the northeastern Thai reference range. On the contrary, we found by the same way that the higher prevalence of osteoporosis at Ward's triangle diagnosed by the Japanese reference criteria was due to the higher BMD cut-off level than that of the northeastern Thai (0.561 versus 0.483 g/cm^2).

In choosing a cut-off value of -2.5 SD, the intention of the WHO group was to make osteoporosis a rarity in healthy women before menopause. Assuming a normal distribution of BMD, about 0.7% of the young adult population would be characterized as having osteoporosis.[17] Some problems have been found in applying these concepts in practice. The normal young adults used to calculate mean BMD and SD values may or may not include population that are randomly selected, giving bias results. Moreover, the reference data may exclude individuals with risk factors for osteoporosis and, therefore, artificially increase the mean BMD value and reduce the SD used to compute the cut-off values. Therefore, the choice of a reference range is important for an accurate bone mineral categorization of subjects. This is clearly supported by the study of Chen et al., which showed a reduction of about 40% prevalence of osteoporosis at the spines and/or the total hip when the old Hologic normal reference was replaced by the new Hologic hip normal reference.[27]

In determining the agreement in the diagnosis between the two reference criteria of our study, concordant diagnoses were found in about three-fourths of the subjects with the high strength of agreement at Ward's triangle (Kappa 0.80), moderate strength at L_{2-4} (Kappa 0.55) and femoral neck (Kappa 0.56), fair strength at the trochanteric region (Kappa 0.31) and poor strength at the total proximal femoral part (Kappa 0.18). However, discordant diagnoses were found in about one-fourth of our BMD studies especially at the total proximal femur and, therefore, could have an influence on the decision in giving management of patients. This was evident by the recent study of Pressman et al., which showed that the result of BMD test showing evidence of osteoporosis had a higher influence on the initiation of osteoporosis treatment than other factors including age or gender of the patients, history of recent fracture, history of corticosteroid exposure, or even the specialty of health care practitioners taking care of patients.[28]

To our knowledge, this is the first study reporting the magnitude of difference in the diagnostic classification between using the manufacturer's and local references applied in the northeastern Thai women so far.

The study, however, had some limitations. The northeastern Thai reference range applied in this study was derived from the peak bone mass of 5-year age band of 35 normal northeastern Thai women. This number of sample size in determining the average peak bone mass and also the SD might be too small to represent the actual peak bone mass in the general population. Moreover, the exclusion criteria used to extract our normal database were selected because they are widely quoted as risk factors for osteoporotic fracture rather than because of their inherent validity, and may have led to a bias in our northeastern Thai reference population. Applying this reference, even being the same race and ethnicity of the observed population, to the northeastern women might over-diagnose abnormally low bone mass and, therefore, cause over-treatment in these subjects. Furthermore, it should also be stressed that the data presented in our study dealt with the hospital-based subjects. Extrapolation of these findings to the community-based subjects must be viewed with caution.

In conclusion, this study reported the discordance in the diagnosis of low bone mass in the northeastern Thai women between using the peak BMD range from the Japanese reference and the northeastern Thai reference and stressed the limitation of the WHO diagnostic guideline regarding potentially varying diagnostic classifications of the BMD status in the same individual.

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