Age-related variation in quantitative ultrasound at the tibia and prevalence of osteoporosis in native Chinese women

X-P WU, MD, E-Y LIAO, MD, X-H LUO, MD, R-C DAI, MD, H ZHANG, MD and J PENG, MD

Institute of Metabolism and Endocrinology, The Second Xiang-Ya Hospital, Central South University, Changsha, Hunan 410011, P.R. China

Abstract. This study investigated the variations in age-related speed of sound (SOS) at the tibia and prevalence of osteoporosis in native Chinese women, and establishment of a reference database by quantitative ultrasound. SOS at the right midtibia was measured using a quantitative ultrasound device (SoundScan 2000, Myriad Ultrasound Systems, Israel) in 1596 healthy Chinese women ranging from 12 years to 96 years of age. Healthy women were selected on the basis of (1) a detailed questionnaire about their medical history, (2) face to face questioning about their medical history, and (3) a physical examination. Women with a medical condition that required medication that affected bone metabolism or those who had had a pathologic or moderate traumatic fracture were excluded. We followed the diagnostic criteria provided by the instrument’s manufacturer and equivalent to the WHO criteria (using the T-score cut-off that diagnoses 30% of the post-menopausal women aged > 50 years with osteoporosis) as the diagnostic criteria for osteoporosis in this group of women. Data were analyzed in age groups divided by intervals of 5 years. The peak SOS at the tibia of 3991 ± 68 m s⁻¹ (mean ± SD) occurred in the 35–39 year age group and the T-score precision was 0.99 T-score units. The SOS value increased with age up to 34 years of age and then declined with age after 40 years of age with the rate of decrease at 9.68 m s⁻¹ per year. The curve representing the SOS change according to age is best fitted by the regression analysis of cubic model, and the cubic equation for SOS = 3383·39.9 (age) – 0.78 (age)² + 0.0059 (age)³ (R² = 0.905, p = 0.000). The T-score cut-off that diagnoses 30% of the post-menopausal women (n = 559, mean age 63.2 ± 8.97 years) aged ≥ 50 years with osteoporosis was SOS ≤ 3733 m s⁻¹, T-score ≤ −3.8. In the 40–49, 50–59, 60–69 and 70–79 years age groups and the group aged ≥ 80 years, the prevalences of osteoporosis detected using equivalent to the WHO criteria were 0.39%, 9.47%, 50.3%, 58.4% and 69.0%, respectively. The prevalences detected following the manufacturer’s diagnostic criteria (cut-off value: SOS ≤ 3800 m s⁻¹, T-score ≤ −2.0) were 3.14%, 20.5%, 53.2%, 78.8% and 89.7%, respectively. There were significant differences in the prevalence between the diagnostic criteria in the various age groups (p = 0.000–0.002). In 769 women from 40 years to 59 years of age, the mean SOS was significantly higher in pre-menopausal women (n = 500) than in post-menopausal women (n = 269) (3977 ± 89 vs 3881 ± 118 m s⁻¹, p = 0.000). The prevalence of osteoporosis in these women was 0.40% in pre-menopausal women, 8.92% in post-menopausal women, respectively. There were significant differences in prevalence of osteoporosis between the two groups of pre- and post-menopausal women (p = 0.000). In conclusion, SOS at tibia can provide useful information about bone status in the normative population of native Chinese women for determination of osteoporosis. The reference database based on these data will be appropriate for the diagnosis of osteoporosis by tibial quantitative ultrasound in native Chinese women.

Osteoporosis is now recognized as a “silent epidemic disorder” [1] and affects an estimated 75 million people in Europe, the USA and Japan [2]. In the USA it affects more than 25 million people, predisposes to more than 1.3 million fractures annually [3] and costs the nation in excess of US $13.8 billion [4]. In China, there were about 83.9 million patients with osteoporosis in 1997 [5]. It is recognized as a major public health problem in both developed and developing countries.

Osteoporosis can lead to the decline of bone mass and strength and the increase of bone fragility, and subsequently, an increase in risk of fractures [3]. Bone density (BMD) accounts for 60–80% of the variations in bone strength [6, 7]. Non-invasive bone densitometry, such as single photon absorptiometry (SPA), single X-ray absorptiometry (SXA), dual-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) and so on [8], can only provide information on the structural and material properties of bone, whereas quantitative ultrasound (QU S) measurements can reflect bone elasticity, fragility and density closely associated with bone strength and fracture risk [1, 9]. Therefore, QUS assessment of bone is a strong predictor of hip fractures and is currently an United States Food and Drug Administration (FDA)-approved tool to identify women at risk of osteoporosis [10]. It provides a precise, ionizing radiation-free, low-cost, and rapid method for fracture risk assessment in clinical practice [11, 12]; but its role in pre-menopausal women, men and children in fracture prediction is not established. The goal of this study is to investigate variations in tibial speed of sound (SOS) and prevalence of osteoporosis with age in native Chinese women and to establish a tibial SOS reference database useful for the diagnosis of osteoporosis in native Chinese women.

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Subjects and methods

Subjects

1596 healthy Chinese females aged 12–96 years (mean age 46.5±15.4 years) were randomly selected from Changsha and its surrounding area. These healthy volunteers are all residents in Changsha area, recruited by public health organizations (health stations/clinics) at the grassroots level responsible for the health of local residents. They included working personnel from government institutions, department stores, environmental sanitation bureaus and schools, farmers in the suburb of Changsha City, primary and high school students around hospitals, health workers at hospitals and nursing staff. Among these subjects, students account for 9.65% (154 persons); public functionaries, 27.4% (435 persons); workers at environmental sanitation administration bureaus, 26.6% (425 persons); salespersons at department stores, 22.4% (358 persons); medical workers, 4.89% (78 persons); and others 8.96% (143 persons). All subjects were screened using a detailed questionnaire, history and physical examination. Subjects were excluded from the study if they had conditions affecting bone metabolism, such as diseases of the kidney, liver, parathyroid, thyroid, diabetes mellitus, oligomenorrhea or amenorrhea before 40 years old, hyperprolactinaemia, oophorectomy, rheumatoid arthritis, ankylosing spondylitis, malabsorption syndromes, malignant tumours, haematologic diseases, previous pathologic fractures and with low or atraumatic fractures. Subjects were also excluded if they had been receiving glucocorticoids, oestrogens, thyroid hormone, fluoride, biphosphonate, calcitonin, thiazide diuretics, barbiturates, anti-convulsant medication, vitamin D or calcium-containing drugs. All subjects had their body height and weight measured using a stadiometer and standardized balance-beam scale, respectively. Distribution by age of subject weight, height and body mass index (BMI) is shown in Table 1. 984 pre-menopausal and 612 post-menopausal women with a mean age of menopause of 48.6±3.8 (mean±SD) years (range, 41–59 years) and a menopause duration (median) 12.0 years (range, 1–48 years) were involved in this study. For all subjects, informed consent was obtained. This study was approved by the Ethical Committee of Xiang-Ya Medical College, Central South University.

Ultrasound measurement

Ultrasound velocity measurements were obtained at the midshaft tibia using a prototype SoundScan 2000 ultrasound device (Myriad Ultrasound Systems, Rehovot, Israel) by Njeh et al [13] and SoundScan 2000 User’s Guide [14] published methods. The SoundScan calculated the speed of sound propagation (SOS in m s⁻¹) from ultrasound waves through a defined and fixed longitudinal distance of the cortical layer of the tibia parallel to its long axis. Measurements were taken on the non-dominant tibia at the midtibial site (contralateral to the dominant hand). The midtibial site was defined as the midpoint between the distal apex of the patella (identified by palpation with the leg in extension) and the distal apex of the medial malleolus. To facilitate acoustic contact, ultrasound gel was applied to the skin at the measurement sites. SOS of the tibia was assessed by the probe along the longitudinal axis of the tibia in a series of 150–200 single readings aimed at finding the peak of bone velocity. The procedure typically takes less than 5 min. SOS was defined as the average of the five maximum readings.

The in vitro precision experiment was carried out on the control phantom supplied with the instrument. The measurement was repeated three times daily over a continuous observation period of 2 months. Root mean square coefficient of variation (RMSCV) was calculated to express precision according to the method of Gluer et al [15]. The RMSCV was 0.21% (degrees of freedom (df)=143). The coefficient of variation (CV) between the five maximal SOS values measured daily and displayed automatically by the instrument was <0.04%. The in vivo short-term precision was performed in the same individual on the same day. For each individual, the measurement was repeated three or four times. RMSCV was 0.58% (df=67). The in vivo interpatient short-medium term precision was carried out in two individuals over 20 days. The measurement was repeated three times for each individual. RMSCV was 0.89% (df=119). As all measurements were carried out by the same operator the precision estimations are all intraoperator.

Statistical analysis

SPSS v10.0 for Windows statistical software (SPSS Inc., Chicago, IL) was used in this analysis. SOS at tibia in women with age-related changes was evaluated and the model of best fit was determined following comparison of different regression models for linear, logarithmic, quadratic, cubic, compound, power, growth and exponential equations. All subjects were stratified according to 5 year intervals and the results of SOS, body weight, height, and body mass index (BMI) were reported in terms of the mean and standard deviation (mean±SD) for each group (Table 1). The peak SOS was determined from the age group with the highest SOS mean value. The SOS peak occurred in the 35–39 years age group, mean±SD was 3991±68 m s⁻¹, and the T-score precision was 0.99 T-score units. In the 40–59 years age range, the t-test was used to compare the SOS values between pre- and
post-menopausal women. The calculation method for SOS minus T-score in various age groups is $T\text{-score} = (\text{mean of group } \text{SOS} - 3991)/68$. The diagnostic criteria for osteoporosis were based upon the SOS peak (mean $\pm$ SD = 4000 $\pm$ 100 m s$^{-1}$) and cut-off critical value for diagnosis of osteoporosis ($\text{SOS} \leq 3800$ m s$^{-1}$; $T \leq -2.0$) provided by the instrument’s manufacturer [14] and a $T$-score equivalent to the WHO criteria for the diagnosis of osteoporosis was calculated, i.e. use the $T$-score cut-off that diagnoses 30% of the post-menopausal women aged $\geq$ 50 years with osteoporosis. The $T$-score cut-off that diagnoses 30% of the post-menopausal women ($n=559$, mean age 63.2 $\pm$ 8.97 years) aged $\geq$ 50 years with osteoporosis was $\text{SOS} \leq 3733$ m s$^{-1}$ and $T$-score $\leq -3.8$. After the SOS peak, subjects were grouped according to age in 10-year intervals. The unpaired two-tailed $t$-test was used to assess the differences in osteoporosis detection rate between different groups and between the results of the same group obtained using different diagnostic criteria.

Results

1596 subjects were divided into groups at 5-year intervals. The mean and standard deviation (mean $\pm$ SD) of tibial SOS for each age group are displayed in Table 2. The peak SOS at the tibia of 3991 $\pm$ 68 m s$^{-1}$ (mean $\pm$ SD) occurred in the 35–39 year age group. Scattergrams and cubic regression curves (Figure 1) depicting variations of SOS according to age indicates that SOS increases with age before the peak and decreases with age after the peak. By a comparison of various regression models, the model of best fit, describing the association of SOS and age in Chinese women, was found to be the cubic regression (Figure 1), whose $R^2$ value was the highest ($R^2=0.505$, $p=0.000$). No significant differences were demonstrated in the fit between various models in evaluating variations of SOS with age after the peak; each had a very similar $R^2$ ($R^2=0.478–0.493$, $p=0.000$). There was a negative correlation between SOS and age after its peak (Figure 2).

Table 2. Change of age-related speed of sound (SOS) and $T$-score at tibia in Chinese women (mean $\pm$ standard deviation (SD))

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>$n$</th>
<th>SOS (m s$^{-1}$)</th>
<th>$T$-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>12–19</td>
<td>62</td>
<td>3851 $\pm$ 67</td>
<td>$-2.06 \pm 0.99$</td>
</tr>
<tr>
<td>20–24</td>
<td>75</td>
<td>3850 $\pm$ 75</td>
<td>$-2.07 \pm 1.10$</td>
</tr>
<tr>
<td>25–29</td>
<td>84</td>
<td>3961 $\pm$ 72</td>
<td>$-0.44 \pm 1.06$</td>
</tr>
<tr>
<td>30–34</td>
<td>146</td>
<td>3983 $\pm$ 79</td>
<td>$-0.12 \pm 1.16$</td>
</tr>
<tr>
<td>35–39</td>
<td>117</td>
<td>3991 $\pm$ 68*</td>
<td>0</td>
</tr>
<tr>
<td>40–44</td>
<td>290</td>
<td>3981 $\pm$ 86</td>
<td>$-0.15 \pm 1.26$</td>
</tr>
<tr>
<td>45–49</td>
<td>220</td>
<td>3965 $\pm$ 93</td>
<td>$-0.38 \pm 1.37$</td>
</tr>
<tr>
<td>50–54</td>
<td>149</td>
<td>3922 $\pm$ 106</td>
<td>$-1.01 \pm 1.56$</td>
</tr>
<tr>
<td>55–59</td>
<td>110</td>
<td>3831 $\pm$ 122</td>
<td>$-2.35 \pm 1.79$</td>
</tr>
<tr>
<td>60–64</td>
<td>133</td>
<td>3787 $\pm$ 130</td>
<td>$-3.00 \pm 1.91$</td>
</tr>
<tr>
<td>65–69</td>
<td>68</td>
<td>3778 $\pm$ 109</td>
<td>$-3.13 \pm 1.60$</td>
</tr>
<tr>
<td>70–74</td>
<td>68</td>
<td>3727 $\pm$ 146</td>
<td>$-3.88 \pm 2.15$</td>
</tr>
<tr>
<td>75–79</td>
<td>45</td>
<td>3675 $\pm$ 173</td>
<td>$-4.65 \pm 2.54$</td>
</tr>
<tr>
<td>$\geq$ 80</td>
<td>29</td>
<td>3634 $\pm$ 163</td>
<td>$-5.25 \pm 2.40$</td>
</tr>
</tbody>
</table>

*Peak SOS was 3991 $\pm$ 68 m s$^{-1}$ (mean $\pm$ SD) in the 35–39 year of age group.

According to the linear regression equation, the tibial SOS of Chinese women, after 40 years of age, declined at a mean rate of 9.68 m s$^{-1}$ per year.

The diagnostic criteria provided by the manufacturer and equivalent to the WHO criteria were employed to diagnose the variation with age of prevalence of Chinese women with osteoporosis (Table 3). For ages greater than 39 years, i.e. the age of peak SOS, subjects were grouped in 10-year intervals. The result showed that the prevalence of osteoporosis increased remarkably in various groups of women aged less than 80 years. In all age groups, the prevalence from osteoporosis detected with the manufacturer’s diagnostic criteria was significantly higher than the prevalence detected following equivalent to the WHO criteria (Table 3). For post-menopausal women aged $\geq 50$ years ($n=559$, mean age 63.2 $\pm$ 8.97 years), prevalence from osteoporosis detected using the manufacturer’s diagnostic criteria was 48.3%, and prevalence detected using equivalent to the WHO criteria was 30.3%. There were statistically significant differences between the two groups ($p=0.000$). In 769 women from 40 years to 59 years of age, the mean SOS was significantly higher in pre-menopausal women ($n=500$) than in post-menopausal women ($n=269$) ($3977 \pm 89$ vs $3881 \pm 118$ m s$^{-1}$, $p=0.000$). The prevalences of pre- and post-menopausal women with...
osteoporosis detected according to the manufacturer's diagnostic criteria were 3.20% and 19.7%, respectively, whereas the corresponding prevalences determined using equivalent to the WHO criteria were 0.40% and 8.92%, respectively. Post-menopausal women with osteoporosis had a significantly higher prevalence than pre-menopausal women (p<0.000). The prevalence from osteoporosis detected according to the manufacturer's criteria was significantly higher than that detected following equivalent to the WHO criteria (p<0.000).

In the 25–49 years age range (n=857), tibial SOS showed few changes with age (r=−0.026, p=0.447) (Table 2) and remained “stable”. During this period, SOS had a mild positive correlation with the height (r=0.106, p=0.002) and weight (r=0.079, p=0.020) of the subjects and had no correlation with BMI (r=0.032, p=0.353). SOS values after the peak were negatively correlated with age (r=−0.701, p<0.000) or years since menopause (r=−0.547, p=0.000) and positively correlated with height (r=0.397, p=0.000) or weight (r=0.224, p=0.000), while not correlated with menopausal age (r=0.043, p=0.284) or BMI (r=0.037, p=0.212).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>n</th>
<th>Prevalence of osteoporosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>510</td>
<td>3.14 (0.394)</td>
</tr>
<tr>
<td>50–59</td>
<td>259</td>
<td>20.8* (9.27*4)</td>
</tr>
<tr>
<td>60–69</td>
<td>201</td>
<td>52.2* (30.3*4)</td>
</tr>
<tr>
<td>70–79</td>
<td>113</td>
<td>78.8* (58.4*4)</td>
</tr>
<tr>
<td>≥80</td>
<td>29</td>
<td>89.7</td>
</tr>
</tbody>
</table>

Notes: *Osteoporosis cut-off value (speed of sound (SOS)≤3800 m s⁻¹) was used manufactures T-score (mean±SD) of peak SOS=4000±100 m s⁻¹).
*Osteoporosis cut-off value (SOS<3733 m s⁻¹) was used equivalent to the WHO criteria T-score cut-off that diagnoses 30% of the post-menopausal women aged ≥50 years with osteoporosis (mean±SD of peak SOS=3991±68 m s⁻¹).
*Compared with previous age group, p=0.000.
*Compared with Manufacturer’s criteria, p=0.000–0.002.

**Table 3. Prevalences of age-related osteoporosis at tibia in Chinese women**

Discussion

Cortical bone is known to play a pivotal role in fracture resistance. Early research demonstrated that the medullary canal of the tibia gradually expands with age [16]. The cortical area at the tibia in women decreases about 5.6–11.0% every 10 years while only 5.5% at the femoral neck accompanied by cortical wall thinning. Thompson discovered that, during the period from 60 years to 90 years in women, the Haversian canal area in the non-osteoporotic femur increases from 9.6% to 14.6% while the cortical thickness decreases by 30%, resulting in a decline in bone weight loading ability and mechanical competence [17]. Recent studies have confirmed that tibial strength is mainly reflected in the density of the cortex near the surface; the tibial SOS depends not only on cortical density, but also cortical thickness [18]. Myriad data [14] indicate that individuals with osteoporotic hip or vertebral fracture are approximately 3 SD below peak mean. This suggests that women who are below some level (for example, 3889 m s⁻¹, T-score=−1.5), are at increased risk for sustaining an osteoporotic fracture, and that women who are at 3787 m s⁻¹ (T-score=−3.0) or below are at highest risk of fracture.

In this study, we found that the peak value of tibial SOS of Chinese women occurred between 35 years and 39 years (Table 2), similar to American women (35–39 year) [19] but later than Israeli women (20–24 year) [20]; the peak is slightly higher for Chinese women (3991±68 m s⁻¹) compared with that of women in the USA (3975.3±94.1 m s⁻¹) and Israel (3938±118 m s⁻¹) but lower than Myriad data (4000±100 m s⁻¹) [14], while the SD of the peak SOS of Chinese women is lower than that of American, Israeli women and Myriad data. These findings indicate that Chinese women have a relatively low biological variability of tibial SOS. Since tibial SOS measured by QUS mainly reflected the bone density and tibial cortex thickness [18], the coefficient of biological variation indirectly showed very few differences in bone density and tibial cortex thickness between individual Chinese women at the peak SOS value. However, there were significant differences between individual American and Israeli women. The biological variation (expressed in SD) of the SOS peak will directly impact the calculation of the T-score and diagnosis of osteoporosis. The equation is T-score=(x−mean)/SD, where x is the measured value of an individual subject, mean is the mean peak SOS value, and SD is standard deviations (also known as the coefficient of biological variation). The formula shows that SD increases as the T-score absolute value decreases when x and mean remain unchanged, indicating low prevalence for an individual subject with osteoporosis. Conversely, SD decreases as the T-score absolute value increases, indicating a high prevalence for an individual subject with osteoporosis. Assuming that SD is 100 m s⁻¹, then the T-score of the individual subject is −3.93 (T-score=−3991)/100, indicating that this individual subject has a low bone mass. After the peak value, as women were affected by a lack of oestrogen after menopause and increased age, mean SOS of each age group decreased gradually and SD increased (Table 2). This trend demonstrates that the bone density of the tibia was lower and the cortex was thinner. The variation of bone density and tibial cortex thickness caused by ageing and menopause resulted in gradually increased differences between individuals. These changes led to an increased coefficient of biological variation of tibial SOS of elderly women after menopause. The tibial SOS of Chinese women before the peak value increases with age and decreases with age after the peak. The variation curve was fitted with various regression models and it was determined that the cubic regression had the best fit (Figure 1) with the highest R² value (R²=0.505); similarly, the fitting result for calcaneus SOS against age in British women [21] was determined, but with a smaller R² of cubic regression (R²=0.349).
Calculated with the linear regression equation (Figure 2), the mean decreasing rate of tibial SOS of Chinese women was 2.36 times that of American women (9.68 m s⁻¹ per year, and 4.1 m s⁻¹ per year [19], respectively).

When we followed the diagnostic criteria for osteoporosis provided by the instrument’s manufacturer (SOS peak, mean = 4000 ± 100 m s⁻¹, and cut-off value for diagnosis of osteoporosis T-score < -2.0) and equivalent to the WHO criteria, i.e. using the T-score cut-off that diagnoses 30% of the post-menopausal women aged ≥ 50 years with osteoporosis as the cut-off for diagnosis of osteoporosis, T-score < -3.8, we found that in various age groups the prevalence of osteoporosis detected using the manufacturer’s criteria was significantly higher than that detected using equivalent to the WHO criteria (Table 3). Thus, the manufacturer’s diagnostic criteria were not suitable for Chinese women. Using equivalent to the WHO criteria, the prevalences for Chinese women with osteoporosis in the Mainland aged 50–59, 60–69, 70–79 and ≥80 years were 9.30%, 30.0%, 58.4% and 69.0%, respectively. For women living in Taiwan [22] (when the broadband ultrasound attenuation of the heel was measured and the WHO recommended criteria were applied, T-score ≤ -2.5) prevalences were 9.64%, 28.9%, 51.1% and 68.6%, respectively. There was a great similarity between the prevalence of osteoporosis in women in Mainland China and prevalence in women in Taiwan across the various age groups. In the 40–59 years age range, the prevalences of pre- and post-menopausal women with osteoporosis were 0.40% and 8.92%, respectively. There were significant differences between pre- and post-menopausal women (p = 0.001), indicating that QUS measurement could differentiate the variation of tibial SOS of pre- and post-menopausal women. Nairus et al [23] discovered that although the QUS measurement had a very high false-positive rate for the diagnosis of osteoporosis, it was still sensitive enough to diagnose perimenopausal or pre-menopausal women with osteoporosis. The latest reports indicate that QUS measurements and DXA-BMD are comparable in predicting post-menopausal spinal fracture risk and diagnosing osteoporosis [24, 25].

The tibial SOS positively correlated with height and weight, suggesting that these two factors played roles in maintaining or delaying the decline of tibial SOS. Human tibiae are weight bearing bones. If middle-aged and elderly women maintain their appropriate weight and participate in sports activities, the balance between bone absorption and bone formation will be maintained because biological stress stimulates the tibia and ensures that it is strong enough to bear weight. Thus, such activities slow the rate of descent of tibial SOS. In the absence of such activities, the opposite phenomenon will occur. Tromp et al [26] found that, following adjustments for body weight, correlations of tibial and calcaneal QUS with BMD improved and were very similar, suggesting that correction for body weight is important for QUS measurements. No correlation was revealed between SOS and BMI or menopausal age; the tibial SOS did not vary according to BMI or age of menopause. SOS was negatively correlated with years since menopause as well as age; therefore, while ageing and years since menopause increased, the tibial SOS gradually decreased.

The present study offers valuable reference data in order to better understand the relationship between the variations of tibial SOS with age and the prevalence of osteoporosis for Chinese women. The reference database based on these data will be appropriate for the diagnosis of osteoporosis by tibial QUS in native Chinese women.

References


