Original Article

Quantitative Ultrasound of the Calcaneus in Brazilian Caucasian Women: Normative Data Are Similar to the Manufacturer’s Normal Range

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Abstract. Quantitative ultrasound (QUS) can be a helpful alternative to identify osteoporotic patients. In this study we establish the QUS Brazilian normal range (BNR) and compare its values (means and standard deviations) with the manufacturer’s normal range (MNR). We measured three QUS parameters (broadband ultrasound attenuation, BUA; speed of sound, SOS; stiffness index, SI) at the right calcaneus in 352 healthy Caucasian Brazilian women, aged 20–84 years. We studied the age-dependent changes in QUS values and correlation with body size and years since menopause (YSM). A comparison of fracture risk classification using the BNR and MNR is also presented. Age was the most significant predictor for all QUS parameters (r = −0.49 for BUA, r = −0.66 for SOS, r = −0.64 for SI). Weight was accepted as the second determinant for BUA (final regression model: $\text{BUA} = 101.3 - 0.282 \times \text{Age} + 0.373 \times \text{Weight}; p<0.001; \text{adjusted } R^2 = 0.33$). Body mass index (BMI) was accepted as the second predictor for SI ($\text{SI} = 94.8 - 0.595 \times \text{Age} + 0.851 \times \text{BMI}; p<0.001; \text{adjusted } R^2 = 0.44$). Height and YSM were accepted as second and third determinants for SOS values ($\text{SOS} = 1718.7 - 1.147 \times \text{Age} - 69.863 \times \text{Height} - 0.521 \times \text{YSM}; p<0.001; \text{adjusted } R^2 = 0.45$). There was a decline in SI of about 41% from the values in young adulthood to those of women in their eighties, about 76.4% of which occurred from age 45–49 years onward. Variation of mean SI with age from the BNR was consistent with the MNR in all but two 5-year age groups. In these two groups (50–54 years, p<0.01; 65–69 years, p<0.05), values derived from the BNR were 5.08% and 5.45% higher than the MNR values, respectively. Comparison of standard deviations in SI with age between the two populations did not show statistically significant differences. Using the fracture risk criteria proposed by the manufacturer, we observed that the MNR was appropriate for skeletal fragility evaluation in Brazilian women.

Keywords: Broadband ultrasound attenuation; Osteoporosis; Quantitative ultrasound; Reference data; Speed of sound

Introduction

Osteoporosis is a common disease which causes significant morbidity and mortality and whose incidence has increased in recent decades [1]. In the absence of osteoporotic fractures the process of identifying patients at high risk is based on bone mineral density (BMD) measurements using mainly dual-energy X-ray absorptiometry (DXA) techniques [2]. Recently, quantitative ultrasound (QUS) has been proposed as a reliable alternative for evaluating skeletal status and fracture risk. It may be a useful measure of both quality and quantity of bone and many studies have demonstrated its ability to prospectively determine fracture risk, independently of age and BMD [3].

The technology has evolved from the observation that sound waves through porous materials such as bone are absorbed, scattered and travel in a manner that reflects the elasticity, structure and density of the material [4–7]. Two basic parameters are measured with QUS: speed of sound (SOS) and broadband ultrasound attenuation

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In vitro studies have demonstrated that both BUA and SOS seem to give structural information and are correlated with axial BMD to about the same degree as peripheral BMD [7]. The validity of using QUS as a method to estimate the risk of osteoporotic fractures is based on prospective studies using calcaneal ultrasound systems in the prediction of vertebral and hip fracture [7–9]. These studies confirmed that the diagnostic sensitivity of QUS is similar to that of hip BMD measured by DXA and is superior to spine BMD in the prediction of hip fracture.

However, before QUS may be routinely applied in the clinical environment, the establishment of accurate normative data for specific ethnic populations must be addressed. QUS experts have emphasized the need for regional reference data in order to improve QUS accuracy and avoid misclassification in individual fracture risk assessment [10]. As has been demonstrated for BMD measurements [11,12], the lack of ethnoscismic data for QUS may lead to misdiagnosis of skeletal fragility. In this study we present a QUS Brazilian normal range and determine the impact of using different reference data on skeletal fragility diagnosis.

**Subjects and Methods**

**Subjects**

A total of 589 Caucasian Brazilian women from the greater São Paulo area were recruited into this study from July 1997 to February 1998. Women were recruited by use of paid advertisements, staff talks to community groups and word of mouth. The study protocol was approved by the UNIFESP Ethics Committee and informed consent was obtained from each participant.

A QUS Brazilian normal range was collected from 589 consecutively evaluated women by applying the following modified exclusion criteria as previously described by Ryan et al. [13]: (1) non-Caucasian, (2) fractures after the age of 25 years, (3) natural menopause or oophorectomy before the age of 40 years, (4) history of non-pregnant secondary amenorrhea of more than 6 months’ duration, (5) history of medical conditions known to affect bone resistance including anorexia nervosa, thyrotoxicosis, obesity (body mass index >30 kg/m²), rheumatoid arthritis, systemic lupus erythematosus, malignant neoplasm, immobilization for a period longer than 2 months, as well as previous diagnosis of osteoporosis, (6) use of systemic corticosteroids, (7) use of tamoxifen or (8) use of hormone replacement therapy for 12 months or more. Three hundred and fifty-two women met the criteria and were included in the study.

Body weight was measured (after removal of shoes and heavy outer clothing) using a balance beam scale. Height was measured (after removal of shoes) using a Filizola stadiometer. Height and weight were used to calculate the body mass index (BMI; kg/m²).

**QUS**

The Achilles Ultrasound (Lunar, Madison, WI) was used to measure speed of sound (SOS), broadband ultrasound attenuation (BUA) and Stiffness index (SI) through the right calcaneus. The SI is a combination of normalized speed of sound and BUA (SI = 0.67 × BUA + 0.28 × SOS − 240) and is claimed to improve the coefficient of variation of SOS and BUA alone [14,15]. The Achilles system consists of two transducers: the transmitter and the receiver. Acoustic coupling is achieved by submerging the transducer pair and the heel in a water bath that is maintained at 35°C. The heel is positioned between the transducers, so that the ultrasound beam propagates through the center of the calcaneus. After five successive measurements in 10 women on the same occasion with calcaneus repositioning, Achilles precision expressed as the root mean square of the coefficients of variation (CV) was 1.01% for BUA, 0.23% for SOS and 1.25% for SI.

**Statistical Methods**

Pearson’s correlation coefficients were calculated between QUS parameters and age, body measures and years since menopause (YSM). Based on the results of Pearson’s correlation coefficient, stepwise forward multiple regression analysis was performed to determine the best predictors of QUS parameters. Since BMI is correlated with weight and height as well as YSM is correlated with age, regression models showing the highest adjusted $R^2$ were chosen. This analysis was done for all women as a group, and separately for premenopausal and postmenopausal women.

Mean BUA, SOS and SI, as well as standard deviations, were derived for 5-year age bands between 20 and 84 years of age and these values were defined as the Brazilian normal range (BNR). QUS values in the BNR were compared with a Gaussian distribution as a whole and for each 5-year age band using the Kolmogorov–Smirnov test.

The values of SI derived from the BNR were compared with the reference data provided by the manufacturer (MNR), which are extracted from a sample of 1933 American white women. A two-tailed one-sample Student’s $t$-test was used to compare mean SI in the BNR and the MNR. A two-tailed chi-squared test with 95% confident intervals was used to compare standard deviations between the two populations.

A subset of young women aged 20–29 years was extracted from the BNR ($n = 75$, mean age 26.4 years). Following the manufacturer’s young normal definition, this subset of young women was taken to represent Brazilian young normal (BYN). Values of mean SI and standard deviations were derived from the BYN and used for $T$-score calculation. The percentage of women identified as normal, at intermediate risk of fractures and at high risk of fractures by applying the manufacturer’s criteria (normal, $T$-score higher than $-1.0$; intermediate...