Osteoporos Int (1999) 9:230–235

Osteoporosis International

Original Article

Quantitative Ultrasound Measurements of the Tibia and Calcaneus in Comparison with DXA Measurements at Various Skeletal Sites

A. M. Tromp[1], J. H. Smit[2], D. J. H. Deeg[1,3] and P. Lips[1,4]

[1]Institute for Research in Extramural Medicine (EMGO Institute), [2]Department of Sociology and Social Gerontology, [3]Department of Psychiatry, and [4]Department of Endocrinology, Vrije Universiteit, Amsterdam, The Netherlands

Abstract. The performance of quantitative ultrasound (QUS) measurements of the tibia and calcaneus was studied in 109 elderly people (age range 65–87 years). Broadband ultrasound attenuation (BUA) and speed of sound (SOS) were measured at the calcaneus and SOS was assessed at the tibia. Short-term precision of tibial QUS was studied in 16 volunteers. The coefficient of variation (CV) was 0.4% and the standardized CV (sCV) was 4.4%. We compared the calcaneal and tibial QUS measurements with bone mineral density (BMD) measurements of the lumbar spine, femoral neck, trochanter and total body assessed by dual-energy X-ray absorptiometry (DXA). Calcaneal QUS correlated better with BMD at various skeletal sites than tibial QUS. Calcaneal BUA showed higher correlations with BMD values of the lumbar spine, femoral neck, trochanter and total body than calcaneal and tibial SOS (r = 0.48–0.64, r = 0.30–0.47, r = 0.35–0.47, respectively; $p < 0.001$). Body weight modified the relationships between calcaneal and tibial QUS and BMD measurements of the hip. Higher body weight was associated with higher BMD values at the femoral neck and trochanter for the same calcaneal and tibial QUS values. After adjustments for body weight correlations of tibial and calcaneal QUS with BMD improved and were very similar. This suggests that correction for body weight is important and could add to the predictive value of QUS measurements.

Keywords: Anthropometry; Calcaneus; Dual-energy X-ray absorptiometry; Quantitative ultrasound; Tibia

Correspondence and offprint requests to: Dr P. Lips, Department of Endocrinology, Academic Hospital Vrije Universiteit, PO Box 7057, 1007 MB Amsterdam, The Netherlands.

Introduction

One of the most important risk factors for osteoporotic fractures is low bone density. Several measurement techniques have been developed to assess bone mineral density (BMD). The most commonly used method is dual-energy X-ray absorptiometry (DXA). With this technique BMD can be measured at specific fracture-related skeletal sites, such as the hip, lumbar spine and radius [1].

Recently, quantitative ultrasound (QUS) has generated widespread interest. This method has some advantages over DXA: it does not use ionizing radiation, it is less costly, it is simple to use, the equipment is portable and it provides information about quality of bone. The great variety of different QUS devices available makes it possible to perform QUS measurements at several peripheral skeletal sites such as the calcaneus, ulna, patella, phalanges and tibia [2–5]. QUS measures the speed at which sound propagates through or along bone (SOS) or the pattern of attenuation of a wide range of ultrasonic frequencies in bone (BUA). It has been postulated that QUS may reflect more than bone density. Qualitative aspects of bone, such as elasticity and microarchitectural characteristics, could also be assessed by QUS [6]. Additional qualitative information regarding bone may improve the ability of QUS measurements to identify subjects most at risk for fractures. This assumption is confirmed by three prospective studies that have shown calcaneal QUS performs similarly to BMD measurements in predicting the risk of fractures in elderly women and may therefore be a useful test for fracture risk assessment [7–9]. Diagnosis of osteoporosis and monitoring of skeletal changes are two other areas for clinical use of QUS.

However, due to precision and accuracy errors of QUS and the moderate correlation between densitometric and ultrasound measurements, QUS cannot yet be recommended for this purpose [10].

Accuracy as well as precision of QUS measurements is decreased by anatomically inconsistent placement and by variability in bone width, soft tissue thickness and marrow composition of the measurement region [10]. Furthermore, several studies found that anthropometric factors such as body weight, body height and soft tissue have a significant influence on QUS measurements [11,12].

QUS has mostly been confined to measurements of the calcaneus, which mainly contains trabecular bone. Calcaneal BUA shows a high correlation (r = 0.8) with BMD at the same site [13–15] but a moderate correlation (r = 0.4–0.6) with BMD of the spine or the proximal femur [16–18]. Tibial QUS measures predominantly cortical bone of the tibia. The latter might better reflect the skeletal status of the whole body, since 80% of the skeleton consists of cortical bone.

The first aim of this study was to compare the QUS measurements in calcaneus and tibia with BMD in the lumbar spine, femoral neck, trochanter and total body. The second aim was to determine the short-term precision of the tibial QUS in comparison with calcaneal QUS. In addition, we examined the influence of anthropometric factors on the relationship between QUS and BMD measurements.

Subjects and Methods

Subjects

Ultrasound measurements were performed in an epidemiologic study on risk factors for osteoporotic fractures in elderly people. This study is part of the Longitudinal Aging Study Amsterdam (LASA), a survey on predictors and consequences of changes in physical, cognitive, emotional and social functioning in aging subjects in three regions of The Netherlands [19]. The additional study on calcaneal and tibial QUS measurements in the elderly was done in a sex-stratified subsample of the urban and rural population in the west of The Netherlands (Amsterdam and vicinity). Subjects were 127 elderly people, 65 years and older, who came to the hospital for DXA measurements. Eighteen of these had to be excluded from the analysis due to edematous limbs (6 participants) and imprecise tibial QUS measurements (12 participants). All participants gave informed consent and the protocol was approved by the Ethical Review Board of the hospital. The results presented in this paper are from 109 participants (57 men and 52 women). Mean age was 75.0 $\pm$ 6.4 years (range 65–87 years).

Measurements

BUA and SOS were measured at the calcaneus with the CUBA Clinical instrument (McCue Ultrasonics, Winchester, UK). Two transducers (receiving and emitting) faced with silicone rubber coupling pads were placed in direct contact on either side of the calcaneus, using a coupling gel. The participants underwent a double measurement at the right calcaneus. The foot was repositioned after the first measurement.

QUS measurements were also performed at the right tibia using the SoundScan 2000 instrument (Myriad Ultrasound System, Rehovot, Israel). Subjects were supine with the lower leg at the right side exposed. The midpoint of the tibia was marked, which is halfway between the distal apex of the patella and the medial malleolus, and a probe placed on the skin at this point. Ultrasonic coupling gel was used to facilitate the propagation of sound between the probe and the skin. The speed of sound through the tibia was calculated from the propagation time and distance between a sound-emitting sensor at one side of the probe and a receiving sensor at the other side. By moving the probe back and forth across the tibial plane, a minimum of 150–200 velocity readings were obtained. The average of the five highest readings was calculated to render the cortical tibial ultrasound velocity [20]. When the variation of these five readings was too high ($>$10 m/s) the measurement was considered imprecise and had to be excluded (12 participants: see above). Duplicate QUS measurements of the right tibia were performed on the same day in 16 volunteers by one trained person. The group consisted of 15 women and 1 man with a mean age and standard deviation of 48.3 $\pm$ 22.6 years.

The BMD and bone mineral content (BMC) were measured at various skeletal sites, using DXA (Hologic QDR 2000). Measurements were performed at the lumbar spine (L2–4), right hip (femoral neck and trochanter) and total body. The precision of total-body measurements was reported as coefficients of variation of 0.6% for total body BMD, 0.5% for lean body mass and 4.2% for total fat mass [21].

Body weight was measured to the nearest 0.001 m using a stadiometer and body weight was measured to the nearest 0.1 kg using a calibrated scale. Body mass index (BMI) was calculated as body weight (kg) divided by the square of body weight (m).

Statistics

The coefficient of variation (CV%), and the standardized CV% (sCV%) for duplicate QUS measurements of the tibia were estimated. CV was calculated as the ratio between the pooled standard deviation (SD) of repeated measurements and the overall mean ($=[\Sigma^n d^2/(2n)]^{0.5}$, where d is the difference between a pair of measurements and n is the number of paired observations) [22]. The sCV was estimated as the pooled SD of repeated measurements divided by the 5–95% range of the study sample [23]. In this study we have determined the precision of the tibial QUS only. In a previous study in our institute [7] we examined the short-term precision of the calcaneal QUS in a comparable group of 20 subjects. Differences between gender in BMD measurements of the lumbar spine, femoral neck, trochanter and total body were checked by Student's *t*-test. The relationship between anthropometric parameters, QUS and BMD measurements was studied calculating Pearson's correlation coefficients. Multiple regression analysis was used for the evaluation of the relation between QUS parameters, BMD or BMC of the lumbar spine, femoral neck, trochanter and total body. Body weight and body height were entered in the regression model to test for modification of the relationship between QUS measurements and BMD at several skeletal sites. The variables gender, body weight and body height were checked for interaction. The effect of body weight on the relation between calcaneal and tibial QUS and BMD of the trochanter and femoral neck was assessed by adding body weight to the regression model separately for men and women. Body weight was transformed into a dichotomous variable, categorizing the participants above or below the median (for women, 69 kg; for men, 78 kg). The sensitivity and specificity were calculated for the lowest tertile of QUS measurements (calcaneal BUA, 52 dB/MHz and 71dB/MHz; calcaneal SOS, 1574 m/s and 1595 m/s; tibial SOS, 3822 m/s and 3874 m/s; for women and men, respectively) to determine BMD values at the femoral neck lower than 2.5 SD below the *T*-value (<0.65 g/cm^2 for women and <0.70 g/cm^2 for men). In all analyses, the mean value of the two QUS measurements of the right calcaneus was used. All results are presented using two-tailed *p* values.

Results

Details of the subjects' characteristics are listed in Table 1. All BMD measurements were significantly higher in men than in women ($p<0.001$). The results of the QUS measurements and coefficients of variation are shown in Table 2. Since the CV is highly dependent on the level and the range of values, the effective precision, as sCV, was also calculated. Values of sCV for various QUS measurements were more similar than CV values.

Body height, body weight and lean body mass, assessed by total-body DXA, were significantly correlated with calcaneal BUA, and with tibial SOS and BMD measurements (Table 3). BMI showed only low correlations with BMD. A negative association was found between fat mass, assessed by total-body DXA, and calcaneal BUA and BMD of the total body. The correlations of QUS and BMD measurements with body

Table 1. Characteristics of the subjects by gender

	Women (*n* = 52)		Men (*n* = 57)	
Age (years)	74.4	(6.4)	75.6	(6.4)
Body height (cm)	162.1	(6.6)	173.2	(6.9)
Body weight (kg)	68.4	(11.3)	78.6	(10.7)
BMI (kg/m^2)	26.1	(4.6)	26.2	(3.1)
Age at menopause (years)	49.3	(5.4)	NA	
BMD femoral neck (g/cm^2)	0.67	(0.11)	0.75	(0.11)
BMD trochanter (g/cm^2)	0.61	(0.10)	0.72	(0.11)
BMD lumbar spine (g/cm^2)	0.91	(0.17)	1.05	(0.17)
BMD total body (g/cm^2)	0.93	(0.09)	1.07	(0.11)
DXA fat mass (%)	39.6	(8.0)	26.4	(5.4)
DXA lean body mass (kg)	39.9	(5.1)	55.5	(5.4)

Values are mean (SD).
NA, not applicable.

Table 2. Results of quantitative ultrasound (QUS) measurements in calcaneus and tibia, coefficients of variation (CV) and standardized CV (sCV)

	Women (*n* = 52) Mean (SD)	Men (*n* = 57) Mean (SD)	CV (%)	sCV (%)
Calcaneus BUA (dB/MHz)	57.7 (17.7)	78.4 (18.0)	3.3[a]	3.3[a]
Calcaneus SOS (m/s)	1588.2 (33.7)	1611.3 (36.3)	1.3[a]	12.8[a]
Tibia SOS (m/s)	3861.4 (140.4)	3921.3 (113.6)	0.4[b]	4.4[b]

BUA, broadband ultrasound attenuation; SOS; speed of sound.
[a]Values from 20 volunteers in our institute [7].
[b]This study.

Table 3. Pearson's correlation coefficients of BUA/SOS calcaneus, SOS tibia, BMD in the lumbar spine, femoral neck, trochanter and total body with body height, body weight, BMI, fat mass (DXA) and lean body mass (DXA) (*n* = 109)

	Measurements of bone fragility						
	BUA calcaneus	SOS calcaneus	SOS tibia	BMD lumbar spine	BMD femoral neck	BMD trochanter	BMD total body
Body height (m)	0.43**	0.24	0.37**	0.40**	0.39**	0.46**	0.66**
Body weight (kg)	0.42**	0.18	0.37**	0.50**	0.46**	0.52**	0.53**
BMI (kg/m^2)	0.19	0.05	0.18	0.28*	0.27*	0.27*	0.13
DXA fat mass (%)	−0.25*	−0.21	−0.08	−0.13	−0.18	−0.19	−0.35**
DXA lean body mass (kg)	0.46**	0.25	0.34**	0.48**	0.44**	0.56**	0.70**

*$p<0.01$; **$p<0.001$.

Table 4. Correlation coefficients of BUA/SOS calcaneus, SOS tibia with BMD in the lumbar spine, femoral neck, trochanter and total body. Adjustment for body weight was made if it significantly altered the relationship (n = 109)

QUS measurement	BMD at different skeletal sites			
	Lumbar spine	Femoral neck	Trochanter	Total body
BUA calcaneus	0.48**	0.54**	0.55**	0.64**
Adjusted for weight	0.59**	0.60**	0.65**	0.71**
SOS calcaneus	0.30**	0.40**	0.41**	0.47**
Adjusted for weight	0.53**	0.51**	0.56**	0.58**
BUA calcaneus	0.41**	0.35**	0.45**	0.47**
Adjusted for weight	0.54**	0.49**	0.56**	0.58**

**$p < 0.001$.

weight and BMI were lower when measured at appendicular sites (calcaneus, tibia) than at axial sites. Therefore, in a later analysis step, it was tested whether body weight significantly altered the association between calcaneal and tibial QUS and BMD measurements.

The association between QUS measurements and BMD measurements at various skeletal sites are shown in Table 4. All correlations were significant at the level of $p < 0.001$. The results were very similar when QUS measurements were correlated with BMC of lumbar spine, femoral neck, trochanter and total body (r = 0.32–0.65; $p < 0.001$). Of the different QUS measurements, calcaneal BUA showed the best correlation with the BMD measurements, especially total-body BMD. Body weight influenced all relationships and body height did not have an additional effect, except for the relationship between QUS measurements and BMD of total body in which body weight as well as body height were significant modifiers.

To examine the direction of the modification by body weight for the relationship between QUS and BMD of the hip, body weight was added as a dichotomous variable to the regression model. The model showed that with a similar QUS value, the BMD at the hip was higher in heavier subjects. Subsequently, an attempt was made to incorporate a correction for body weight into the relationship between QUS and BMD measurement. A simple correction that could easily be used without a computer program in practical settings was preferred. After several exploratory steps, it was found that when summing body weight and calcaneal BUA, the correlations between adjusted calcaneal BUA and BMD of the lumbar spine, femoral neck, trochanter and total body improved from r = 0.48–0.64 to r = 0.57–0.71. To attain similar body weight adjustments for the SOS values body weight was multiplied by a factor of 20 and summed with calcaneal SOS, and by a factor of 50 and summed with tibial SOS, respectively. The correlations of adjusted calcaneal and tibial SOS with BMD improved from r = 0.30–0.47 to r = 0.51–0.58 and from r = 0.35–0.47 to r = 0.49–0.58, respectively. When adjusted for body weight, correlations of QUS calcaneus and tibia with BMD measurements were very similar (Table 4) and not very different from partial correlations between BMD and QUS measurements adjusted for body weight (r = 0.50–0.71). Unadjusted correlations were slightly higher in women (r = 0.27–0.61) than in men (r = 0.12–0.45) (data not shown). However, the relationships between QUS measurements and BMD did not significantly interact with gender.

Table 5. Sensitivity and specificity of the lowest tertile of QUS in predicting BMD of the femoral neck lower than 2.5 SD below the T value (< 0.65 g/cm^2 for women and < 0.70 g/cm^2 for men), osteoporosis according to WHO standards

Lowest tertile of:	Women (n = 52) BMD < 0.65 g/cm^2		Men (n = 57) < 0.70 g/cm^2	
	Sensitivity	Specificity	Sensitivity	Specificity
Calcaneus BUA	48%	88%	52%	78%
Calcaneus SOS	44%	80%	38%	69%
Tibia SOS	37%	72%	48%	75%

Sensitivity and specificity of determining subjects who were more than 2.5 SD below the T value of femoral neck BMD (osteoporosis according to WHO standards) by QUS measurements are shown in Table 5. Femoral neck BMD values of less than 0.65 g/cm^2 (2.5 SD below the T value for women) were observed in 27 women and of less than 0.70 g/cm^2 (2.5 SD below T value for men) in 21 men. In comparison with the lowest tertile of calcaneal or tibial SOS, the lowest tertile of calcaneal BUA measurements showed the highest sensitivity and specificity for women as well as men. When adjusted for body weight (see above) the sensitivity and specificity did not improve (sensitivity ranged from 44% to 41% for women and 52% to 43% for men; specificity ranged from 80% to 76% for women and 78% to 72% for men).

Discussion

The present study compares two different QUS methods with DXA, which may be considered as the gold standard for bone densitometry. The unadjusted data suggest that calcaneal QUS performs slightly better than tibial QUS as a method for assessing bone mass and detecting osteoporosis. The sensitivity and specificity of predicting the BMD of the femoral neck were better using calcaneal BUA than using tibial SOS. Moreover, correlations with the four BMD measurements were lower for tibial QUS than for calcaneal BUA. It was expected that tibial QUS would correlate better with BMD measurements at sites that mainly contain cortical bone, but higher correlations were observed between BMD measurements and calcaneal BUA. These findings are in line with the results of Rosenthal et al. [24]. They found in 220 patients that the tibial SOS correlated worse with BMD of the lumbar spine and femoral neck than did the calcaneal parameters.

The second aim of the present study was to determine the short-term precision of the tibial QUS. The short-term precision was determined as sCV since this expresses the effective clinical precision better than the CV. The sCV of tibial SOS, 4.4% in this study and 1.4%–2.9% observed in other studies [20,22,24], was slightly better than sCV for calcaneal BUA (3.3–6.2%) reported in other studies [13,25]. The short-term precision of QUS measurements is acceptable when compared with the reproducibility of the BMD measurements (sCV = 2.2% estimated for BMD lumbar spine) [23].

Our results show that the correlations of QUS and BMD measurements with body weight and BMI were lower when measured at appendicular (calcaneus, tibia) than at axial sites. The modifying effect of body weight on the relation between BMD of the hip and QUS of the calcaneus and tibia went in a similar direction. These results are consistent with the findings of another study [20] and are surprising since walking and running should have a higher impact on the distal weight-bearing bones such as the calcaneus than on the hip, as was observed by Leblanc et al. [26]. They found a significant loss in BMD of total body, lumbar spine, femoral neck, trochanter, tibia and calcaneus of 1.4%, 3.9%, 3.6%, 4.6%, 2.2% and 10.4%, respectively, after 17 weeks of continuous bed rest, showing a gradually increasing bone loss from the lumbar spine to the calcaneus. The higher impact of body weight and physical activity on the hip than on the calcaneus may be explained by the fact that running and other loading exercises give more stress to the anterior foot than to the calcaneus.

After adjustment for body weight the correlations of tibial and calcaneal QUS with BMD improved considerably, especially regarding the SOS measurements. The adjusted data suggest that increase in body weight underestimates calcaneal and tibial QUS values in comparison with BMD values of the hip. Our findings are in agreement with several other studies [11,12,27] suggesting that small variations in bone width, overlying soft tissue and body weight have a significant effect on QUS measurements. Higher weight may influence bone and soft tissue properties and this may have a greater effect on SOS than on BUA.

This study has several limitations. First, although the manufacturers of the tibial QUS system claim that it is completely independent of soft tissue, we had problems measuring subjects with edematous limbs. Young subjects are usually measured for the manufacturer's reference values whereas we studied a population of frail elderly subjects. Edema is a common problem in the elderly and from another study [28] it is known that ankle edema may cause a considerable reduction in the BUA and SOS values of the calcaneus. Second, we did not have available measurements of BMD of the tibia and calcaneus that might have provided us with a deeper knowledge about the relationship between QUS and BMD measurements and the influence of anthropometric factors.

In conclusion, calcaneal QUS correlated better with BMD at various skeletal sites than did tibial QUS. The findings in this study indicate that body weight adjustments are important. After adjustment for body weight, the correlations of calcaneal and tibial QUS measurements with BMD measurements were very similar. Correlations between QUS and BMD measurements may also be influenced by physical activity. Both body weight and physical activity may have a higher impact on the hip than on the calcaneus and tibia. Further studies are required to investigate the precise role of these variables on appendicular and axial skeletal sites.

Acknowledgements. We thank Dr J. C. Roos, Gaby Reinemuth and colleagues from the department of Nuclear Medicine for the BMD measurements. We also thank Wilco Graafmans, Nel van de Kreeke and Els Lommerse for their contribution to the measurements and administrative work.

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Received for publication 16 July 1997
Accepted in revised form 8 July 1998