

# Does Quantitative Tibial Ultrasound Predict Low Bone Mineral Density Defined by Dual Energy X-Ray Absorptiometry?

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**Purpose:** Efforts for the early detection of bone loss and subsequent fracture risk by quantitative ultrasound (QUS), which is a non-invasive, radiation free, and cheaper method, seem rational to reduce the management costs. We aimed in this study to assess the probable correlation of speed of sound (SOS) values obtained by QUS with bone mineral density (BMD) as measured by the gold standard method, dual energy X-ray absorptiometry (DEXA), and to investigate the diagnostic value of QUS to define low BMD. **Materials and Methods:** One hundred twenty-two postmenopausal women having prior standard DEXA measurements were included in the study. Spine and proximal femur (neck, trochanter and Ward's triangle) BMD were assessed in a standard protocol by DEXA. The middle point of the right tibia was chosen for SOS measurement by tibial QUS. **Results:** The SOS values were observed to be significantly higher in the normal BMD (t score > -1) group at all measurement sites except for the lumbar region, when compared with the low BMD group (t score < -1). SOS was negatively correlated with age ( $r = -0.66$ ) and month since menopause ( $r = -0.57$ ). The sensitivity, specificity, and positive and negative predictive values for QUS t score to diagnose low BMD did not seem to be satisfactory at either of the measurement sites. **Conclusion:** Tibial SOS was correlated weakly with BMD values of femur and lumbar spine as measured by DEXA and its diagnostic value did not seem to be high for discriminating between normal and low BMD, at these sites.

**Key Words:** Quantitative tibial ultrasound, low bone mineral density

## INTRODUCTION

The diagnosis and management of osteoporosis and especially related fractures cause a great economic burden on society.<sup>1</sup> Thus efforts for early detection of bone loss seem rational to predict future fractures and thereby reduce the management costs.<sup>2</sup> Despite recent advances on the effect of bone quality to predict fractures, the routine simple practice to assess bone quality seems not as established and the bone mineral density (BMD) measurement still preserves its leading popularity among factors predicting the risk of fracture.<sup>3</sup> Dual energy X-ray absorptiometry (DEXA) has been accepted to be the gold standard method of BMD measurement, discriminating the osteopenic and osteoporotic patients from patients with normal BMD and it has also been demonstrated to predict osteoporotic fractures in postmenopausal women.<sup>4</sup> However the expense of the method makes it difficult to apply DEXA to a wide range of subjects within the postmenopausal population.<sup>5</sup> There is a growing interest in the use of quantitative ultrasound (QUS) measurement which is portable, non-invasive, cheaper and which allows radiation free assessment of bone status and fracture risk.<sup>6,7</sup> Ultrasound consists of acoustic waves above the audible frequency range. It provides information about bone mass and micro-architecture according to the ultrasound broadband attenuation (BUA) and speed of sound (SOS) by showing the velocity of transmission of sound waves through soft tissues and bones. It has been reported that BUA and SOS, which can be determined at various measurement sites like distal radius, os calcis,

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tibia and phalanges, have the potential to predict future osteoporotic fractures.<sup>8</sup> However the correlation between QUS and BMD as measured by DEXA has been observed to vary considerably in previous studies.<sup>9,10</sup> This correlation seemed to be lower when QUS was applied at the tibia region.<sup>8,11</sup>

We aimed in this study firstly to assess the correlation of SOS values obtained from tibia bones with spine and femur BMD values as measured by DEXA. Our second purpose was to determine the diagnostic value of QUS and to find a cut-off point for SOS to define low BMD (osteopenia and osteoporosis). These will help us define the potential role of tibial QUS in diagnosing regional low BMD as a screening method.

## MATERIALS AND METHODS

### Patient selection

Two hundred postmenopausal women having prior standard DEXA measurements within the previous 3 months in the Nuclear Medicine Department were invited by phone call to undergo a tibial QUS investigation. The following exclusion criteria were applied to the subjects: 1) Prior DEXA evaluation performed more than 3 preceding months, 2) secondary osteoporosis, 3) lumbar vertebra osteoarthritis with prominent osteophytes, and 4) presence of calf pathologies especially around the tibia region such as oedema, acute traumatic conditions, osteomyelitis, Paget's disease and any painful skin problem. Age, height, weight, body mass index (BMI) and month since menopause (MSM) of all patients were recorded.

### Bone mineral density measurement

Areal BMD was measured using a DEXA device (Norland XR36, Norland Medical Systems Inc., Fort Atkinson, WI, USA). Lumbar spine (anteroposterior, L2-L4) and right proximal femur (neck, trochanter, Ward's triangle) scans were performed according to the manufacturer's procedures. All scans were reviewed by experienced physicians to ensure that analyses

were correct and that measurements did not include areas of vessel calcification, degenerative arthritis, or overlap with the iliac crest or ribs. To obtain t scores, BMD values were compared with normative data for lumbar spine and proximal femur. Patients with t scores lower than -1 formed the osteopenic-osteoporotic group (low BMD group) while the ones with t scores higher than -1 constituted the normal BMD group according to the osteoporosis definition regarding t score for DEXA measurements.<sup>12</sup>

### Tibial QUS measurement

The middle point of the right tibia was chosen as the application area for site matched scans because this region consists of a small amount of soft tissue. SOS values were measured by tibial QUS (Soundscan 2000, Myriad Ultrasound System) at the inner anterior site of the horizontally extended tibia. This device measures SOS along a 5 cm fixed longitudinal distance with pulse transmission at a frequency of 250 kHz.

### Statistical analysis

Statistical analysis was performed by using MINITAB version 13.1. First, the demographic factors, DEXA and QUS parameters of all patients were summarised. Then the number of patients with normal and low BMD at every skeleton region was identified. Independent samples t test was used to compare the means of demographic parameters, such as age, BMI and MSM (month), and QUS parameters, such as t score and SOS, between the patients with normal and low BMD at lumbar and femoral regions, taking a t score of -1 as the cut off point of discrimination. Afterwards, the probable correlation of demographic properties and QUS parameters was assessed with DEXA parameters by using Spearman rank correlation analysis, at lumbar and femoral regions. The diagnostic value of QUS t score, which also was determined as normal if its t value was above -1 and low if it was under -1, in assessing the existence of DEXA-defined low BMD at the same skeletal regions was evaluated by identifying the sensitivity, specificity, and positive and negative predictive values. Receiver operating character-

istic (ROC) analysis was performed to assess the ability of SOS in identifying patients with low BMD. Any probable contributions of certain variables, such as age, weight, BMI, MSM and SOS, to BMD estimation was evaluated by linear regression analysis.

## RESULTS

Of 200 postmenopausal women with prior DEXA investigations who were invited by phone call, 138 applied to our clinic for quantitative tibial ultrasound investigation. Sixteen patients could not be included in the study either because they did not accept the tibial QUS investigation or they fell within the exclusion criteria. The demographic findings of all the patients are summarised in Table 1, together with average BMD and t score values measured at 4 sites in lumbar and femur regions by DEXA. The tibial QUS parameters, average t score and SOS values of all patients can also be seen in the same table.

According to the osteoporosis definition regarding t score, 55 patients had normal BMD status

with t scores higher than -1, 45 were osteopenic with t scores between -1 and -2.5, while 22 were osteoporotic with t scores less than -2.5 for the lumbar spine region. The patient numbers in the same groups were 68, 49, and 5 for the femur neck region, 65, 49, and 8 for the femur trochanter, and 33, 60, and 29 for the femur Ward's triangle, respectively. The numbers of normal, osteopenic and osteoporotic patients were 33, 59, and 30, respectively, according to tibial QUS t score findings.

The patients with t scores lower than -1 (the sum of osteopenic and osteoporotic patients) formed the low BMD group while the ones with t scores higher than -1 constituted the normal BMD group. On this basis, the tibial QUS t score and SOS values were significantly higher in the normal BMD group at all measurement sites except for the lumbar region (Table 2).

A negative correlation was found between SOS and age ( $r = -0.66$ ), and between SOS and MSM ( $r = -0.57$ ). However no correlation was found between SOS and BMI. QUS t score and SOS parameters were observed to be correlated positively with all BMD parameters at all sites (Table 3).

**Table 1.** The Demographic, Dual Energy X-Ray Absorptiometry and Tibial Quantitative Ultrasound Findings of All Patients

Parameters	Patients (n = 122)
Age (yrs)	56.3 ± 8.7
Month since menopause (months)	136.4 ± 121.6
Body mass index (kg/m <sup>2</sup> )	27.8 ± 4.1
L2-4 BMD (gr/cm <sup>2</sup> )	0.971 ± 0.194
L2-4 t score	-1.0 ± 1.7
Femur neck BMD (gr/cm <sup>2</sup> )	0.811 ± 0.145
Femur neck t score	-0.7 ± 1.2
Femur trochanter trokanter BMD (gr/cm <sup>2</sup> )	0.637 ± 0.345
Femur trochanter trokanter t score	-0.9 ± 1.1
F. Ward's triangle BMD (gr/cm <sup>2</sup> )	0.597 ± 0.154
F. Ward's triangle t score	-1.7 ± 1.1
QUS t score	-1.7 ± 1.1
QUS SOS (m/sn)	3787.8 ± 123.4

BMD, bone mineral density; F. Ward's triangle, Femur Ward's triangle; SOS, speed of sound.  
Data presented are mean ± SD.

**Table 2.** The Demographic and Quantitative Ultrasound Values Between Patients with Normal and Low Bone Mineral Density, According to All Measurement Sites

	Age (yrs)	Body mass index (kg/m <sup>2</sup> )	Month since menopause (months)	QUS T score	SOS (m/s)
<b>Lumbar (L2 - 4)</b>					
Normal BMD group (n = 55)	54.8 ± 9.2	29.3 ± 4.2	118.3 ± 105.8	-1.5 ± 1.2	3809.5 ± 135.6
Low BMD group (n = 67)	57.3 ± 7.9	26.6 ± 3.7	148.5 ± 131.7	-1.9 ± 0.9	3773.7 ± 109.5
<i>p</i> value	0.091	< 0.001	0.157	0.065	0.093
<b>Femur neck</b>					
Normal BMD group (n = 68)	53.5 ± 7.8	28.3 ± 4.5	112.9 ± 123.6	-1.5 ± 1.2	3815.9 ± 127.7
Low BMD group (n = 54)	59.8 ± 8.6	27.2 ± 3.6	163.1 ± 113.5	-2.1 ± 1.0	3756.6 ± 108.1
<i>p</i> value	< 0.001	0.185	0.020	0.006	0.006
<b>Femur trochanter</b>					
Normal BMD group (n = 65)	54.4 ± 8.4	28.7 ± 4.0	121.8 ± 113.9	-1.5 ± 1.2	3811.1 ± 128.4
Low BMD group (n = 57)	58.2 ± 8.6	26.8 ± 3.9	149.7 ± 128.4	-1.9 ± 1.0	3766.1 ± 112.2
<i>p</i> value	0.014	0.010	0.179	0.020	0.035
<b>Femur Ward's triangle</b>					
Normal BMD group (n = 33)	50.3 ± 7.9	28.7 ± 3.3	75.5 ± 76.6	-1.2 ± 1.1	3843.7 ± 122.9
Low BMD group (n = 89)	57.8 ± 8.2	27.6 ± 4.3	152.3 ± 126.4	-1.8 ± 1.1	3773.2 ± 120.0
<i>p</i> value	< 0.001	0.263	0.005	0.009	0.012

BMD, bone mineral density; QUS, quantitative ultrasound; SOS, speed of sound.  
Data presented are mean ± SD

**Table 3.** Correlation Coefficients Between Demographic-Quantitative Ultrasound and Dual Energy X-Ray Absorptiometry Parameters

	L2-4 BMD	L2-4 t score	F neck BMD	F neck t score	F troch BMD	F troch t score	F Ward BMD	F Ward t score
Age (yrs)	0.30	0.30	0.38	0.36	0.37	0.34	0.42	0.41
BMI (kg/m <sup>2</sup> )	0.30	0.30	NS	NS	0.25	0.24	NS	NS
Month since menopause (months)	-0.20	-0.20	-0.34	-0.34	-0.25	-0.25	-0.42	-0.41
QUS t score	0.30	0.30	0.37	0.36	0.35	0.34	0.36	0.42
SOS (m/s)	0.29	0.29	0.36	0.36	0.34	0.33	0.41	0.40

BMI, body mass index; QUS, quantitative ultrasound; SOS, speed of sound; BMD, bone mineral density; F, femur; NS, not significant.

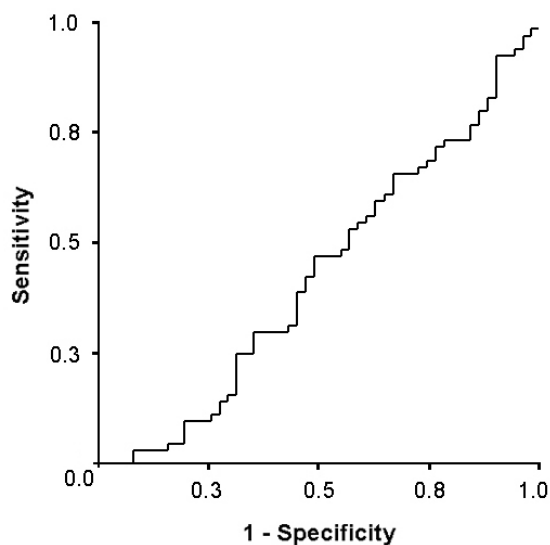
The number of patients with normal BMD according to QUS of tibia was 33, while the number with low BMD was 89. The sensitivity, specificity, and positive and negative predictive values for QUS t score to diagnose low BMD were not observed to be satisfactory at either of the measurement sites (Table 4).

The ROC curves plotted for SOS, using the DEXA t scores as the standard method to diagnose low BMD, were not satisfactory and the areas under the curve for the lumbar spine, femur neck, femur trochanter and femur ward's triangle were 0.43, 0.36, 0.39, and 0.32, respectively. The curve for the lumbar region can be seen in Fig. 1.

**Table 4.** The Diagnostic Value of Quantitative Ultrasound t Score to Diagnose Low Bone Mineral Density at All Measurement Sites

	L2 - 4	Femur neck	Femur trochanter	F. Ward's triangle
Sensitivity	0.50	0.60	0.83	0.52
Specificity	0.81	0.65	0.38	0.73
+ predictive value	0.91	0.87	0.83	0.88
- predictive value	0.30	0.31	0.38	0.29

F. Ward's triangle, Femur Ward's triangle.



**Fig. 1.** ROC curves for SOS in diagnosing low BMD using L 2 - 4 DEXA t scores as the standard. ROC, receiver operating characteristic; SOS, speed of sound; BMD, bone mineral density; DEXA, dual energy x-ray absorptiometry.

The equation below was obtained after linear regression analysis performance demonstrating the contribution of an independent variable that is BMI to SOS in estimating BMD at the lumbar region. The most convenient regression equation was found at the lumbar region at the end of regression trials:

$$\text{L2 - 4 BMD} = -1.329 + (5.05 \times 10^{-4} \times \text{SOS}) + (1.40 \times 10^{-2} \times \text{BMI}).$$

This significant contribution was not obtained for other skeletal regions.

## DISCUSSION

Cortical bone has attracted less attention in

BMD research due to a common belief that trabecular bone is likely to be more sensitive to disease-induced changes as it is metabolically more active.<sup>13,14</sup> Thus QUS assessment of tibia has not been a focus of research. Although there are several QUS devices used routinely in clinical practice, no criteria for diagnostic decisions have yet been established.<sup>6</sup> In this study we selected tibia bone to assess the capability of a cortical bone QUS to a reveal threshold value for discriminating between normal and low BMD in different skeletal sites, such as the femur and spine, that consist prominently of trabecular bone and that are more prone to osteoporotic future fractures.

In general it has been observed that QUS parameters, such as BUA and SOS, of a local bone correlated well with the BMD of the same local areas investigated with DEXA.<sup>15</sup> A study by Prevrhal et al. demonstrated that SOS of tibia was significantly correlated with BMD of tibia.<sup>14</sup> However the more important aspect of the question is whether these QUS parameters are able to predict the BMD of the skeletal sites which are classically prone to fractures. The correlation between QUS parameters and BMD at various sites has been determined to vary considerably with r values between 0.29 and 0.89.<sup>9,10</sup> According to a review of the parallel studies on this point, the weakest correlation, in the range of 0.31 and 0.47, was between femur neck BMD and tibial SOS.<sup>8</sup> The correlation coefficients that we found, ranging between 0.29 and 0.41 for tibial SOS and BMD detected in various regions of femur and lumbar regions, were similar to this data. Many questions arise from the considerably variable differences of predictive ability of QUS between the studies and

from the low predictive value for tibial region QUS. The variability of results may be due to methodological and technological differences and perhaps errors.<sup>16</sup> The calibration of the QUS and DEXA devices also seems to be very important. On the other hand QUS has been introduced not only for detecting the bone density of the related region but also for the structural quality that may conflict with the correlation values with BMD.<sup>15,17</sup> Perhaps this additional beneficial effect of QUS may explain the reason why QUS predicted fracture risk partially independently of BMD, as shown in a recent large study.<sup>18</sup> The favourable correlation found between QUS parameters of the calcaneus, and spinal or femur BMD, rather than the tibial region, seems to be related with the structural content of the assessed bones.<sup>8,15</sup> The calcaneus may have the advantage as it is a trabecular bone like the lumbar spine and femur, contrary to the tibial bone which is mainly a cortical bone. However data exists on the importance of the detection of cortical bone status in predicting the future trabecular bone fractures because 80% of the whole skeleton is cortical bone.<sup>19</sup> Our major aim in this study was not to find out the predictive ability of tibial QUS evaluation for future fractures, but rather the indirect relation of its ability to predict BMD, along with its ability to detect structural properties that may provide useful information. Although some studies have reported the ability of calcaneal QUS to predict osteoporotic fractures,<sup>2,20,21</sup> not much data exist about the tibial region and future studies are needed.

A study reported that the SOS value declined with age after 40 years of age, with a rate of decrease of 9.68 ms per year.<sup>22</sup> Our finding of a negative correlation between age, MSM and SOS of tibia is not surprising as it is known that bone resorption accelerates during menopause and ageing.

Although some researchers did not accept using the WHO definition of osteoporosis regarding DEXA, for QUS t scores,<sup>6</sup> many of them applied this definition to QUS.<sup>23</sup> In this study, we also used t scores obtained from QUS evaluation for discriminating normal BMD from osteopenic and osteoporotic to determine the diagnostic value of QUS for BMD detection of various skeletal

regions. We not only found that the diagnostic sensitivity and specificity of QUS for discriminating between normal and low BMD was unsatisfactory, we also could not find a cut-off value for SOS, independent from t score arguments. Similarly, Cetin et al. reported a very low sensitivity and specificity of QUS for predicting BMD-defined osteoporosis.<sup>23</sup> Furthermore, we investigated the potential contributions of independent variables, such as demographic factors, using linear regression analysis and showed that BMI can give additional benefit in predicting low BMD in the lumbar region.

In conclusion, tibial SOS was correlated weakly with BMD values of the femur and lumbar spine as measured by DEXA and its diagnostic value did not seem to be high for discriminating between normal and low BMD at these sites. However the integration of independent risk factors such as BMI can contribute to this analysis. Perhaps future studies using both calcaneal and tibial QUS will have the advantage of investigating both trabecular and cortical bone simultaneously and this will provide more accurate information about the BMD and structural quality of bone. This will help identify the place of QUS, as a cheaper and more practical method, in predicting fracture risk.

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