Usefulness of quantitative heel ultrasound compared with dual-energy X-ray absorptiometry in determining bone mineral density in chronic haemodialysis patients

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Abstract

Background. Reduced bone mineral density (BMD) is associated with renal osteodystrophy and osteoporosis in end-stage renal failure patients. Dual-energy X-ray absorptiometry (DXA) is the standard non-invasive method to assess BMD, but is not always widely available. Quantitative heel ultrasound (QUS) is a mobile, relatively inexpensive, easy to perform and radiation-free method which can predict fractures to the same extent as DXA. This study assessed the usefulness of QUS vs DXA in determining BMD in chronic haemodialysis patients.

Methods. Patients had their BMD at the hip and spine measured by DXA (Lunar Expert). QUS of the left heel (McCue Cuba Clinical II machine) measured broadband ultrasound attenuation (BUA) and velocity of sound (VOS). Correlations between DXA and QUS parameters were calculated. Receiver operator characteristic (ROC) curves were plotted for BUA and VOS and used to define cut-off points for calculating sensitivities and specificities for BUA and VOS. Femoral neck BMD was applied as the standard for diagnosing osteoporosis (T ≤ −2.5) and osteopaenia (T > −2.5 and ≤ −1) by WHO criteria.

Results. Eighty eight patients (45.5% women), mean age 58 ± 17 years, were studied. A total of 19% and 49% had femoral neck BMDs in the ‘osteoporosis’ and ‘osteopaenia’ ranges, respectively. There were good correlations between hip BMD and QUS parameters (r = 0.68–0.79, P < 0.001). Areas under the ROC curves for BUA and VOS in diagnosing ‘osteoporosis’ were 0.86 and 0.80, respectively. BUA and VOS had sensitivities of 76% and 71% and specificities of 80% and 69%, respectively, for diagnosing ‘osteoporosis’. The positive predictive values for BUA and VOS were 48% and 35%, respectively, and the negative predictive values were 93% and 91% respectively.

Conclusions. DXA and QUS parameters were significantly correlated. However, sensitivities and specificities of QUS parameters were not sufficiently high for QUS to be used simply as an alternative to DXA. The relatively high negative predictive values suggest that QUS may reliably screen out patients unlikely to have a BMD in the osteoporotic range. The relatively low positive predictive values, however, mean that subjects classified as osteoporotic using QUS require further investigations such as DXA to confirm the diagnosis.

Key words: bone mineral density; dual-energy X-ray absorptiometry; haemodialysis; osteoporosis; quantitative heel ultrasound; renal osteodystrophy

Introduction

Renal osteodystrophy and osteoporosis result in considerable morbidity, and occasionally mortality, in patients with end-stage renal disease. The diagnosis of renal bone disease currently relies on clinical suspicion combined with assessment of blood levels of divalent ions, alkaline phosphatase and immunoreactive parathyroid hormone, and bone radiology. More accurate methods of determining bone disease involve bone biopsy, which is invasive, and bone densitometry, which can measure bone mineral density (BMD) non-invasively, but is expensive and not widely available in many countries.

BMD measurements are important in the investigation of bone disease because they have been shown to predict fracture risk and currently are used to define osteoporosis [1]. Several densitometry methods have been used to demonstrate reduced BMD in patients with end-stage chronic renal failure [2–7]. Dual-energy X-ray absorptiometry (DXA) is the currently preferred method due to its high precision, short scanning time and low radiation dose [8].

Quantitative ultrasound (QUS) is a relatively new method of bone assessment which measures the two parameters of velocity of sound (VOS), which is...
related to BMD and 'elasticity', and broadband ultrasound attenuation (BUA), which is related to BMD and 'structure' [9,10]. Studies in subjects without renal failure have shown moderate correlations between QUS parameters and BMD ($r=0.4–0.7$), and fracture subjects can be distinguished from controls by using QUS [11]. Two large independent prospective French and American studies have shown that QUS at the heel can be used to predict future fracture risk in older women, with gradient of risk similar to DXA, and also predict hip fractures independently of BMD [12,13]. Few data are available on the use of QUS in chronic renal failure patients. One study in haemodialysis patients showed a marked reduction in VOS at the tibial site but no comparison was made with any measurement of BMD [14]. Tibial VOS has also been shown to correlate with intact parathyroid hormone (iPTH) levels in chronic haemodialysis patients [15]. These findings suggest that this technique may be a useful method of detecting PTH-related bone disease in such patients.

QUS at the heel site is a mobile, quick, easy to perform, relatively inexpensive and radiation-free method of bone measurement which has the potential to be used whilst patients are undergoing haemodialysis. The aim of this study was to assess the usefulness of QUS in comparison with DXA in determining BMD in an unselected cohort of chronic haemodialysis patients.

Subjects and methods

Patients

Patients were recruited from the dialysis unit at City Hospital, Nottingham and a satellite unit at King’s Mill Centre, Mansfield, UK. All patients with end-stage chronic renal failure who had been on haemodialysis for longer than 1 month and who were able to complete an interview were considered eligible. The study was approved by the Nottingham City Hospital Research Ethics Committee. Of the 106 patients who gave their consent, four died, two moved to another city for technical reasons. One study in haemodialysis patients showed a marked reduction in VOS at the tibial site but no comparison was made with any measurement of BMD [14]. Tibial VOS has also been shown to correlate with intact parathyroid hormone (iPTH) levels in chronic haemodialysis patients [15]. These findings suggest that this technique may be a useful method of detecting PTH-related bone disease in such patients.

QUS was performed using the Cubaclinical ultrasound bone densitometer (McCue Ultrasonics Ltd) which measured VOS and BUA at the left calcaneum (except one patient with a left below-knee amputation in whom the right heel was measured). All measurements were performed by the same operator. DXA measurements of the lumbar spine (L2–L4) and left hip (or right hip if this was not possible for technical reasons) were performed by the Radiology Department at the Nottingham City Hospital using a ‘Lunar Expert-XL’

densitometer (Lunar Corp.). The femoral neck and total hip regions were analysed separately.

Analysis

Actual DXA BMD values and $T$-scores (standard deviation of BMD above or below the mean of a young normal population) were used in the analysis. Osteoporosis and osteopaenia were defined using the WHO definitions ($T$-score $-2.5$ or below, and $T$-score between $-1$ and $-2.5$, respectively) [1]. Statistical Package SPSS for Windows was used for analysis. Correlations between different bone measurements were assessed using Pearson’s correlation coefficients ($r$). Using WHO definitions for osteoporosis and osteopaenia as the standard (DXA-measured BMD), receiver operator characteristic (ROC) curves were plotted for VOS and BUA. From these curves, the optimal cut-offs for VOS and BUA were calculated (the point on the curve closest to the top left corner). These cut-offs were used to calculate the sensitivities, specificities, false positives and negatives, and positive and negative predictive values of VOS and BUA in diagnosing firstly osteoporosis and secondly a combined endpoint of ‘osteoporosis or osteopaenia’.

Results

Eighty eight patients (72 white, nine Asian and seven black) completed the study, of whom 40 (45.5%) were female. The age range was 18–87 years, with a mean age of $58 \pm 17$ years.

The results of the mean bone densitometry measurements, mean $T$-scores, mean $Z$-scores (standard deviation of BMD above or below the age-related mean) and prevalence of osteopaenia and osteoporosis (using WHO definitions) are shown in Table 1.

Table 2 shows the Pearson’s correlation coefficients between the DXA and QUS measurements. The QUS parameters were significantly correlated with each other and with the femoral neck and total hip BMDs. Correlations between the QUS parameters and lumbar spine BMD were lower although still statistically significant. A scatterplot of BUA vs femoral neck and total hip BMDs is shown in Figure 1.

The ROC curves plotted for BUA and VOS using the femoral neck BMD as the standard method to diagnose ‘osteoporosis’ and a combined endpoint of ‘osteoporosis or osteopaenia’ are shown in Figures 2 and 3, respectively. The areas under the curves for BUA and VOS in diagnosing ‘osteoporosis’ were $0.864 \pm 0.026$ and $0.802 \pm 0.031$, respectively, and for diagnosing ‘osteopaenia or osteoporosis’ were $0.821 \pm 0.030$ and $0.784 \pm 0.032$, respectively. The ROC curve optimal cut-offs for BUA and VOS were 55 dB/MHz and 1572 m/s respectively for diagnosing ‘osteoporosis’, and 72 dB/MHz and 1600 m/s respectively for diagnosing ‘osteopaenia or osteoporosis’. The sensitivities, specificities, false positives, false negatives, and positive and negative predictive values for BUA and VOS are shown in Table 3.
Table 1. Results of DEXA and QUS in 88 chronic haemodialysis patients

<table>
<thead>
<tr>
<th>Measurement</th>
<th>T-score mean ± SD</th>
<th>Z-score mean ± SD</th>
<th>Osteoporosisa prevalence (%)</th>
<th>Osteopeniab prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXA femoral neck density (g/cm²)</td>
<td>0.850 ± 0.170</td>
<td>−1.51 ± 1.38</td>
<td>−0.40 ± 1.22</td>
<td>19.3</td>
</tr>
<tr>
<td>DEXA total hip density (g/cm²)</td>
<td>0.890 ± 0.190</td>
<td>−1.25 ± 1.37</td>
<td>−0.48 ± 1.21</td>
<td>13.6</td>
</tr>
<tr>
<td>DEXA lumbar (L2–L4) density (g/cm²)</td>
<td>1.180 ± 0.280</td>
<td>−0.31 ± 2.25</td>
<td>0.56 ± 2.22</td>
<td>15.9</td>
</tr>
<tr>
<td>BUA calcaneus (dB/MHz)</td>
<td>67.94 ± 23.76</td>
<td>−2.16 ± 1.26</td>
<td>−0.70 ± 1.20</td>
<td></td>
</tr>
<tr>
<td>VOS calcaneus (m/s)</td>
<td>1589.6 ± 44.7</td>
<td>−0.51 ± 0.68</td>
<td>0.40 ± 0.52</td>
<td></td>
</tr>
</tbody>
</table>

T-score ≤ −2.5; †T-score < −1.0 but > −2.5.

Table 2. Pearson correlation coefficients between DEXA and QUS measurements

<table>
<thead>
<tr>
<th></th>
<th>DEXA femoral neck</th>
<th>DEXA total hip</th>
<th>DEXA lumbar (L2–L4)</th>
<th>BUA calcaneus</th>
<th>VOS calcaneus</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXA femoral neck</td>
<td>—</td>
<td>0.92*</td>
<td>0.53*</td>
<td>0.72*</td>
<td>0.68*</td>
</tr>
<tr>
<td>DEXA total hip</td>
<td>0.92*</td>
<td>—</td>
<td>0.60*</td>
<td>0.79*</td>
<td>0.72*</td>
</tr>
<tr>
<td>DEXA lumbar (L2–L4)</td>
<td>0.53*</td>
<td>0.60*</td>
<td>—</td>
<td>0.45*</td>
<td>0.31**</td>
</tr>
<tr>
<td>BUA calcaneus</td>
<td>0.72*</td>
<td>0.79*</td>
<td>0.45*</td>
<td>—</td>
<td>0.86*</td>
</tr>
<tr>
<td>VOS calcaneus</td>
<td>0.68*</td>
<td>0.72*</td>
<td>0.31**</td>
<td>0.86*</td>
<td>—</td>
</tr>
</tbody>
</table>

*P < 0.001; **P = 0.003.

Fig. 1. Scatter plots of femoral neck and total hip BMD vs BUA of the calcaneus.

Discussion

This study shows that 19 and 49% of chronic haemodialysis patients had femoral neck BMDs in the ‘osteoporotic’ and ‘osteopaenic range’, respectively. Strictly speaking, the WHO definitions of osteoporosis (T ≤ −2.5) and osteopenia (T ≤ −1) are based in terms of BMD in women. For the purpose of this study, however, we have applied these definitions for both male and female patients. A low BMD can also be caused by bone pathologies, other than osteoporosis, that collectively are called renal osteodystrophy (namely osteomalacia, secondary hyperparathyroidism and adynamic bone disease). DXA cannot distinguish
between these pathologies, but can identify non-invasively low BMD patients who then may require further evaluation. QUS currently is being evaluated as an alternative method of bone measurement which has the advantage of being radiation-free, inexpensive, mobile and easy to perform.

These data in a heterogeneous group of chronic haemodialysis patients show a good correlation between two different measures of hip BMD and both VOS and BUA measurements obtained by QUS of the calcaneus ($r=0.68–0.79$). However, the correlations between lumbar spine DXA measurement and the QUS parameters were not as good ($r=0.45$ and $0.31$). In addition, the correlations between the lumbar spine and the two hip DXA measurements were only moderate ($r=0.60$ and $0.53$). The poor correlations with lumbar spine BMD are probably related to the effects of spinal osteophytes and aortic calcification which spuriously can elevate lumbar BMD measurements [16–18]. Most studies in patients without renal failure have found only moderate correlations of $r=0.40–0.70$ when comparing QUS with a variety of DXA BMD measurements [11]. Nevertheless, longitudinal studies in non-renal subjects have shown that QUS measurements are as good as DXA for predicting fracture risk [12,13].

In terms of diagnosing osteoporosis, the BUA and VOS sensitivities (71 and 76%) and specificities (80 and 69%) were not sufficiently high for QUS to be used simply as a substitute method for DXA. The relatively high negative predictive values (93 and 91%), however, suggest that QUS (especially BUA) shows potential in being able reliably to screen out those individuals who are unlikely to have a BMD below the 'osteoporotic' cut-off. The relatively low positive predictive values (48 and 35%), however, mean that those subjects classified as osteoporotic using QUS should have further investigations such as DXA to confirm the diagnosis. When we consider the combined endpoint of 'osteopaenia or osteoporosis', the positive predictive values are higher (83 and 82%) but the negative predictive values are no longer useful (47 and 48%).

Prospective studies in older women showing that QUS can predict fracture risk independently of BMD suggest that QUS may give us additional information such as the quality of bone [12,13]. This may be because QUS reflects microarchitectural or other mechanical properties of bone [19,20]. Whether the same is true in patients with renal failure is unclear, and further research is required comparing bone biopsies with QUS and DXA parameters in order to answer this question.

In summary, this study suggests that QUS shows potential in chronic haemodialysis patients to screen out those subjects who are unlikely to have a BMD in the osteoporotic range, and to identify a group of patients who require further bone assessment with DXA and/or bone biopsy.
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