BONE MINERAL DENSITY AT DISTAL FOREARM CAN IDENTIFY PATIENTS WITH OSTEOPOROSIS AT SPINE OR FEMORAL NECK

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SUMMARY

Forearm bone mineral density (BMD) was investigated in women to identify osteoporosis at the spine or femoral neck (or both) defined by WHO criteria (T score \(-2.5\)) without requirement for fracture. BMD was measured by single-energy X-ray absorptiometry (DTX100) and by dual-energy X-ray absorptiometry (DXA) in the lumbar spine and femoral neck in 422 subjects aged 22–90 yr. A total of 62% of subjects with osteoporosis (at the spine, femoral neck, or both sites) were detected with 89% specificity [receiver operating characteristics (ROC) analysis] and included all subjects below forearm BMD 0.34 g/cm\(^2\). Conversely, above 0.419 g/cm\(^2\), only 10% of patients had osteoporosis. A total of 71.8% of women could be assigned either to those who warranted therapy (<0.34 g/cm\(^2\)) or to those who did not (>0.419 g/cm\(^2\)) with 90% certainty. Subjects with forearm BMD between 0.34 and 0.419 g/cm\(^2\), who constituted 28.2% of the total group and included 31% of subjects with osteoporosis, had a 40% chance of having osteoporosis. This leads to a high identification rate on subsequent DXA scanning, which is thus used efficiently.

KEY WORDS: Bone, Density, Forearm, Spine, Femur, Osteoporosis.

The early identification of women with osteoporosis has acquired greater importance in recent years with accumulating evidence that bone loss may be arrested and the incidence of fractures reduced either by oestrogen replacement therapy or by bisphosphonates [1–6]. The most significant sites for osteoporotic fracture are the spine and femoral neck, and to aid recognition of subjects at risk of fracture, the World Health Organization (WHO) has suggested that osteoporosis should also be defined by bone mineral density (BMD) alone, obviating the requirement for previous fracture [7]. There are data, additionally, which support the concept that as BMD falls, so the risk of fracture increases [8]. BMD is generally measured by static densitometers, although mobile systems measuring the spine and upper femur have been investigated [9]. These tend to be expensive and have a substantial downtime if switched off overnight. It is, therefore, attractive to look at alternative systems that the patient might access easily, and to identify those patients in whom lumbar spine and femoral neck densitometry would lead to a high rate of diagnosis. One site that might act as a surrogate for the spine and upper femur is the distal forearm, BMD at which yields data as good as the lumbar spine for the prediction of hip fracture, although inferior to the use of the upper femur sites themselves [8]. The correlation coefficient between bone density at the distal (or ultra-distal) forearm and the femoral neck or lumbar spine has been reported to be between 0.53 and 0.67 [10–12], but was lower using QCT at the distal forearm [13]. However, 50% of women in the lowest quartile of the spine, trochanter and Ward’s triangle were also in the lowest quartile of peripheral QCT values [13]. Since WHO had introduced a new definition for osteoporosis, we sought to investigate whether distal forearm BMD was valuable in detecting those patients who had osteoporosis as defined by lumbar spine or femoral neck BMD values.

SUBJECTS AND METHODS

Subjects (all female) underwent bone density measurement during attendance for bone densitometry either through referral or through studies of bone metabolism in normal subjects. A total of 422 subjects were investigated and comprised 123 healthy volunteers attending for bone densitometry as part of the Shropshire Osteoporosis Study, 38 patients attending for entry into trials of hormone replacement therapy (HRT) or bisphosphonate, 135 new patients attending the osteoporosis clinic and 126 patients attending the follow-up osteoporosis clinic. Of these women, 94 were taking no medications of any kind, 64 were taking calcium supplements only, 129 were taking drugs believed to have minimal effect on bone metabolism (e.g. aspirin, proton pump inhibitors, digoxin, frusemide, indigestion mixtures) and 135 were receiving drugs known to affect bone metabolism (e.g. HRT, corticosteroids, thiazides, bisphosphonates).

Bone densitometry was undertaken using dual-energy X-ray absorptiometry (DXA; Hologic QDR1000 or QDR1000/W: Hologic Inc., Waltham, MA, USA) to measure BMD at the lumbar spine (L2–4; AP view) and at the left femoral neck. Bone density was measured at the distal forearm site using an Osteometer DTX100 (Osteometer, Rodovre, Denmark). This equipment yields data on both the distal and ultra-distal sites, but only the distal site values are reported. Values at the ultra-distal site were found to be less valuable and are not reported. Values at the distal site were obtained on the non-dominant side in all subjects and on the dominant side additionally in 198 subjects. The value on the non-dominant

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side was used for purposes of comparison with the values obtained from DXA.

The definitions used for osteoporosis were based on the recommendations of the WHO relating to the spine and femoral neck [7]. There is some uncertainty about the value of BMD to choose for the "healthy adult bone density" [14]. Thus, a value for the healthy mean BMD was taken from the peak bone mass in a 5 yr period after 30 yr at L2–4 (lumbar spine) (38–42 yr) and the femoral neck (33–37 yr). The reference data base used for DXA was taken from previously published data for women without a history of fracture [15] and did not include any measurements reported in the present study. Using this definition, the value for the T−2.5 score was 0.6 g/cm² at the femoral neck and 0.78 g/cm² at the lumbar spine. Thus, the existence of osteoporosis depended simply upon the presence of a BMD at either spine or femoral neck (or both) being below the respective threshold values and did not require the existence of a fracture. Forearm BMD was used to define a value of BMD at the distal forearm that would identify the presence or absence of osteoporosis at either the spine or the femoral neck, or both sites.

Data analysis was undertaken using the packages on Microsoft Excel (Microsoft Corp., Seattle, WA, USA). Receiver operating characteristics (ROC) curves were constructed using GraphRoc II software (GraphRoc, Turku, Finland) which calculates the area under the curve (AUC). Other statistical tests were conducted according to standard methods [16–18]. Data are presented as mean ± S.D. unless stated otherwise. Permission was obtained for BMD measurements in subjects attending for experimental studies from the research ethics committee of the Robert Jones and Agnes Hunt Hospital.

RESULTS

BMD was measured at the non-dominant distal forearm and at the lumbar spine and femoral neck sites in 422 women (mean age 60.9 ± 12.3 yr). There were 74 subjects aged 22–49 yr, 113 aged 50–59 yr, 126 aged 60–69 yr, 90 aged 70–79 yr and 19 aged 80–90 yr. The oldest group covered 11 yr and included one subject aged 90 yr, the remainder being aged 80–89 yr. There were 155 subjects whose BMD was >2.5 S.D. below the peak adult mean.

BMD measurement was performed at the distal site in both forearms in 198 subjects. The BMD was 2.07 ± 7.73% (95% confidence limits 0.99–3.16) higher on the dominant side (calculated as: (non-dominant − dominant)/non-dominant) × 100). In 129 subjects, the dominant side had the higher BMD, in two the result was equal and 67 subjects recorded a higher BMD on the non-dominant side (P < 0.001, binomial test). The difference rose slightly from −1.79 ± 3.65% in the <49 yr group, to −3.27 ± 9.07% at 60–69 yr and fell to −0.69 ± 9.98% at 70–79 yr. The differences between age groups were not statistically significant.

The relationship of BMD at the forearm with BMD at the lumbar spine and the femoral neck was examined by correlations between the distal forearm and other sites. Distal forearm BMD was correlated with lumbar spine (LS) BMD (LS = 0.311 + 1.47 × forearm BMD, r = 0.64) and with femoral neck (FN) BMD (FN = 0.221 + 1.163 × forearm BMD, r = 0.70). Lumbar spine also correlated with femoral neck (LS = 0.238 + 0.9615 × FN, r = 0.71).

The value of distal forearm BMD in identifying osteoporosis as defined by low bone density at the spine or femoral neck, or both (see Subjects and methods), at either site was examined using ROC curves (Fig. 1). The AUC was 0.8205 ± 0.0627. Maximum efficiency was at 62% sensitivity with 89% specificity. Calculating the AUC for the age groups (<50, 50–59, 60–69, 70–79, 80–90 yr) did not reveal any significant difference. Comparison of ROC curves in relation to taking of drugs and medications, with the whole population divided into non-drug takers, those taking drugs not thought to affect bone, those taking drugs known to affect bone and those on calcium supplements only, did not show any difference between the groups.

The ROC curve analysis returned a maximum efficiency at a distal forearm BMD of 0.339 g/cm² with a specificity of 89%. The predictive value of the positive test (no. of true positives/no. of positives detected by forearm BMD) for all patients with forearm BMD values <0.34 g/cm² was 0.86. At the right-hand part of the ROC curve, a second "cut-off" point which equated to a sensitivity of 89% was chosen and equated to a forearm BMD of 0.419 g/cm². At forearm BMD values >0.419 g/cm², the predictive value of a forearm BMD not being associated with osteoporosis was 0.92.

The number of false positives (subjects without osteoporosis with a forearm BMD <0.34 g/cm²) and false negatives (subjects with osteoporosis, but with a
forearm BMD >0.419 g/cm²) in each age group varied with age. The proportion of false positives was lowest in the 60–69 yr group, followed by the 70–79 yr group, and increased at ages on either side of this range. However, the number of subjects appearing as positive was maximal in the two groups encompassing 60–79 yr (Table I).

Subjects who were positive were further analysed according to the site (spine or femoral neck) at which they were positive when divided into forearm groups <0.34 g/cm², 0.34–0.419 g/cm² and >0.419 g/cm² (Table II). More subjects were positive at the femoral neck than at the lumbar spine in the lowest band (<0.34 g/cm²) of forearm bone density, whereas those subjects in the highest forearm bone density band (>0.419 g/cm²) were more likely to have low bone density at the spine ($\chi^2$, $P < 0.01$), although the numbers in this group were low. Women who were positive for osteoporosis in the forearm bone density band >0.419 g/cm² were significantly younger (59.6 ± 6.0 yr) compared with those in the lowest (<0.34 g/cm²) forearm band (71.3 ± 8.6 yr; $P < 0.01$).

**DISCUSSION**

The study confirmed the relationship between distal forearm BMD and bone density at the lumbar spine and femoral neck reported previously [11, 12]. By comparing both lumbar spine and femoral neck BMD measurements with the forearm BMD measurements, the present study showed that measurement of forearm BMD can be useful in identifying a large number of the population, with almost 90% certainty, who had a BMD that did, or did not, merit therapy with bisphosphonates or HRT. Thus, if the numbers of subjects with BMD <0.34 g/cm² ($n = 111$) and >0.419 g/cm² ($n = 192$) are combined ($n = 303$), 71.8% of the total group were accounted for. Over 90% of this group were placed in the correct category and these subjects might be treated if forearm BMD is <0.34 g/cm² or not treated if it is >0.419 g/cm². This excludes over two-thirds of the population from the requirement of a DXA scan and leaves DXA scanning to identify the osteoporosis in the 28.2% of patients with forearm BMD 0.34–0.419 g/cm². In this group, a positive result for osteoporosis will be found in 40.3% ([48/121]; see Table I), a value which represents an efficient use of DXA scanning. The true false negatives are those patients whose forearm BMD is >0.419 g/cm² and in whom no further action is taken. Alternatively, if absolute certainty were required, forearm BMD could be used to identify patients with forearm BMD <0.34 g/cm² in whom there is a very high likelihood (predictive value of positive test = 0.86) of finding low values on DXA scanning. Substantial numbers of patients can, however, be measured quickly using the forearm BMD equipment. It is important to note that the present data do not refer to fracture, only to bone density values achieving the WHO criteria.

In this initial study, it was also notable that identification of low bone mass at the spine and femoral neck using distal forearm measurements was not unduly influenced either by age or by the use of drugs known to affect bone. This finding requires more detailed analysis with specific conditions such as corticosteroid ingestion.

**TABLE I**

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>18–49</th>
<th>50–59</th>
<th>60–69</th>
<th>70–79</th>
<th>80–90</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
</tr>
<tr>
<td>BMD (g/cm²)</td>
<td>&lt;0.34</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td>% False positive</td>
<td>0.34–0.419</td>
<td>28.5</td>
<td>9.4</td>
<td>14.3</td>
<td>26.7</td>
<td>15.3</td>
</tr>
<tr>
<td>&gt;0.419</td>
<td>0.34–0.419</td>
<td>161</td>
<td>71</td>
<td>15</td>
<td>75</td>
<td>6</td>
</tr>
<tr>
<td>% False negative</td>
<td>0.34–0.419</td>
<td>6.25</td>
<td>14.0</td>
<td>14.3</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>68</td>
<td>21</td>
<td>92</td>
<td>56</td>
<td>70</td>
</tr>
</tbody>
</table>

*% False positive = (no. positive/total) × 100 in that particular age group.†% False negative = (no. negative/total) × 100 in that particular age group.

**TABLE II**

<table>
<thead>
<tr>
<th>Forearm BMD range</th>
<th>Osteoporosis</th>
<th>No osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.34 g/cm²</td>
<td>Spine</td>
<td>13</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>25</td>
<td>13</td>
</tr>
<tr>
<td>Both sites</td>
<td>56</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>0.34–0.419 g/cm²</td>
<td>Spine</td>
<td>13</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Both sites</td>
<td>20</td>
<td>71</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>&gt;0.419 g/cm²</td>
<td>Spine</td>
<td>9</td>
</tr>
<tr>
<td>Femoral neck</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Both sites</td>
<td>0</td>
<td>192</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>
There was a preponderance of low bone density values at the femoral neck, in the forearm group of <0.34 g/cm², whereas the false negatives (i.e. those positive at the spine and femoral neck with BMD at forearm >0.419 g/cm²) exhibited a disproportionate number of subjects with low BMD at the lumbar spine. Since the patients who were positive for osteoporosis in the range of forearm BMD <0.34 g/cm² were older, the lumbar BMD may have been artificially increased by osteophytes [19] in this group or the subjects with forearm BMD >0.419 g/cm² may have included women who had undergone an early menopause and who had lost bone earlier at the spine. Another possibility is that the femoral neck BMD was proportionately higher than the spinal BMD. Some evidence for this was obtained by solving the regression equations relating forearm BMD to either femoral neck or lumbar spine (see Results). Using a value of 0.339 g/cm² for the forearm BMD suggested that this value was associated with a femoral neck BMD of 0.615 g/cm² and a lumbar spine value of 0.809 g/cm². Solving the lumbar spine relationship with the femoral age of 49 yr, but there is a trend to increase up to the age of 70 yr (Table I). These data suggest that the value of T-2.5 for the lumbar spine is relatively lower than that at the femoral neck and that a higher value for the lumbar spine BMD might be more realistic in diagnosing osteoporosis.

The upper limit of forearm BMD associated with the greatest efficiency (<0.34 g/cm²) did not change with age. The best separation of patients with osteoporosis (from those without osteoporosis) in the range of BMD below 0.34 g/cm² in the forearm occurred in the 60–69 yr group, whereas the best detection rate was in the 70–79 yr group. Previous studies have tended to concentrate on the early post-menopausal age group [11] rather than older women. Should distal forearm BMD be used to review large numbers of potentially osteoporotic subjects, the present data suggest that it would be better used in the 60–69 and 70–79 yr groups since the detection rate was poor in those <60 yr.

This finding may be of immediate practical significance. Subjects aged 60–79 yr are in danger of fracturing either a vertebra or the femoral neck more immediately than the perimenopausal women in whom fracture (other than for those at great risk) will be a distant event. Treatment starting in the sixth decade to prevent osteoporotic fracture occurring 15–20 yr later may be unjustified. The beneficial effect of taking HRT between 50 and 60 yr may no longer be evident in the eighth decade of life [20]. Analysis of data showing fracture prevention by alendronate [21] indicates a maximum effect on fracture prevention at the spine and femoral neck by the end of 2 yr treatment with little additional protection in the third year, whilst BMD increments using alendronate are maximal in the first year [4]. Thus, maximum therapeutic efficiency may require targeting the population most immediately at risk of fracture, and this will exclude most women up to 60 yr (Table I).

It is further probable that the detection rate could be increased if attention were paid additionally to known risk factors such as pre-existing fractures, thyrotoxicosis and corticosteroid usage [22]. In the oldest group of subjects (>79 yr), there was a significant false-positive rate. This may reflect forearm bone density declining faster than the femoral neck or spine BMD in the very elderly, but further work is needed to clarify this point.

Some patients may have experienced injury or other insult to the non-dominant forearm that leads to its being unavailable for measurement. In these cases, it is reasonable to measure the dominant hand in the knowledge that the bone density will be between 0.99 and 3.16% higher on the dominant side (95% confidence limits). This higher density on the dominant side is well recognized. The difference ([dominant − non-dominant bone mineral content]/dominant bone mineral content) = width (one-third of the distance between the wrist and the olecranon) in young women was 1.14 ± 5.38% [23]. These data for young women are similar to our subjects under the age of 49 yr, but there is a trend to increase up to the seventh decade, although differences between total upper limb BMD have been found to be less in older women than in younger women, using DXA [24].

REFERENCES