Broadband ultrasound attenuation in the os calcis: relationship to bone mineral at other skeletal sites

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(Received 5 May/6 October 1989; accepted 26 October 1989)

SUMMARY

1. We have examined the relationship between broadband ultrasound attenuation in the os calcis and measurements of bone mineral in the distal forearm and lumbar spine of normal and postmenopausal osteoporotic women.

2. Values of broadband ultrasound attenuation in postmenopausal women with vertebral osteoporotic fractures were significantly lower (35%) than in normal pre- and peri-menopausal women (55.4 ± 3.8 and 79.6 ± 0.8 dB/MHz, respectively).

3. Broadband ultrasound attenuation correlated significantly with bone mineral content measured in the distal forearm by single-photon absorptiometry \( r=0.77, P<0.0001 \) and with bone mineral content \( r=0.66, P<0.0001 \) and bone mineral density \( r=0.72, P<0.0001 \) measured in the lumbar spine by dual-photon absorptiometry.

4. Although significant, these correlations are not sufficiently close to be predictive. However, the accuracy of broadband ultrasound attenuation in discriminating between normal subjects and patients with vertebral fracture compared very favourably with direct measurements in the spine by dual-photon absorptiometry.

5. Broadband ultrasound attenuation, but not the other measurements, correlated significantly with age in the osteoporotic patients \( r=0.50, P<0.05 \).

6. These findings may reflect the partial dependence of broadband ultrasound attenuation on the intrinsic trabecular architecture of cancellous bone, the disruption of which contributes to an increase in fracture risk.

Key words: broadband ultrasound attenuation, os calcis, osteoporosis, photon absorptiometry.

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; BUA, broadband ultrasound attenuation; DPA, dual-photon absorptiometry; QCT, quantitative computed tomography; SPA, single-photon absorptiometry.

INTRODUCTION

Involuntary osteoporosis is characterized by a reduction in bone density and an increased risk of fracture. Several techniques are presently available for the non-invasive assessment of bone mineral, including radiogrammetry \[1\], neutron activation analysis \[2, 3\], quantitative computed tomography (QCT) \[4\], dual-energy X-ray absorptiometry and single (SPA)- and dual (DPA)-photon absorptiometry. SPA of the distal forearm \[5\] is widely available and at skeletal maturity values for bone mineral content (BMC) correlate significantly with total body calcium or density as assessed by neutron activation analysis or DPA \[3, 6\]. However, due to differences in the rates of bone loss from the axial and appendicular skeleton in postmenopausal osteoporosis \[7\], SPA is a relatively poor discriminant of vertebral osteoporosis \[8, 9\]. DPA or X-ray absorptiometry \[10, 11\] and QCT allow accurate and reproducible measurement of bone mineral at more biologically relevant sites (e.g. vertebrae and femoral neck). None of these techniques, however, can discriminate completely between patients with and without osteoporotic vertebral fracture. In addition, they are relatively more expensive, time consuming and, like SPA, expose patients to radiation.

Langton \[12\] proposed that broadband ultrasound attenuation (BUA) in the os calcis, a peripheral site of predominantly trabecular bone, may provide a measure of BMC at this site \[12\]. We have shown that values for BUA in the os calcis correlate significantly with physical measurements of bone density or QCT at the same site in vitro \[12a\]. In this study we have compared this radiation-free technique with BMC or bone mineral density (BMD) measured at other skeletal sites by SPA and DPA and...
have examined its ability to discriminate between normal control subjects and patients with osteoporotic fracture.

METHODS

Subjects

We studied 21 postmenopausal women (aged 41–79 years) with osteoporosis defined as the presence of one or more atraumatic vertebral fractures on spinal radiographs. None had received specific therapy for osteoporosis before the study, and none had osteoporosis secondary to liver or thyroid disease, myelomatosis or hypercortisolism. Patients with lumbar compression fractures were excluded from study. A second group comprised 24 healthy premenopausal women (aged 22–44 years) with no history or clinical evidence of bone disease. A third group comprised 10 perimenopausal females (aged 45–60), all of whom were either experiencing irregular menses or had undergone the menopause within the previous 5 years. None of these women had sustained any osteoporotic fractures at the time of study.

In addition, we studied six female patients with end-stage renal failure, all of whom had biochemical (elevated immunoreactive parathyroid hormone, serum alkaline phosphatase and serum hydroxyproline) and/or radiographic (subperiosteal erosions) evidence of renal osteodystrophy. BUA alone was measured in a further group of six patients (five males, one female) with clinically and radiographically established Sudeck’s algodystrophy of one foot after a fracture.

This study was undertaken with the approval of the local Ethical Committee. Informed consent was obtained from each subject before study. Measurements were made at three skeletal sites (wrist, spine and os calcis).

Measurements

BMC (BMC/bone width) of the distal forearm was measured by SPA utilizing an $^{125}$I source (Nuclear Data 1100 scanner). The measurement is expressed in arbitrary units of mineral content after correction for absorption by soft tissues. Uniformity of position at the distal radius was ensured by commencing measurement at a separation of 8 mm between the radius and ulna. The precision of this technique in vivo was 1.4% (coefficient of variation of paired scans in healthy control subjects). Measurement of vertebral BMC and BMD was undertaken by DPA of the lumbar spine (L2–L4) utilizing a $^{153}$Gd source (Nuclear Data 2100 scanner). The coefficient of variation in paired scans in vivo was 1.2%.

Measurements of BUA were undertaken with the foot submerged in a temperature-controlled water tank to eliminate attenuation of ultrasound by air. The foot was supported so that the os calcis was carefully positioned between a transmitting and a receiving transducer. Once each foot was positioned, the scan took 7 s to complete. The attenuation of ultrasound is frequency dependent and the BUA was measured over a range of frequencies (200 kHz to 1 MHz in steps of 16 kHz) both with and without the foot in the tank. Subtraction of the ultrasonic spectrum obtained after propagation through the heel from that obtained in water provided the attenuation due to the interposed heel. The slope of the linear relationship between BUA and frequency (dB/MHz) was then calculated and recorded for each heel. Assessment of the reproducibility of BUA in the healthy control subjects showed coefficients of variation of 3.1% for paired measurements of one foot, and 4.0% for paired contralateral measurements.

Statistical analysis

The significance of differences between measurements in each group was examined using analysis of variance and the Student’s t-test. The relationship between the sensitivity and specificity of BUA at various values of BUA was studied using receiver-operating-characteristic analysis [13]. Sensitivity was calculated as the proportion of osteoporotic patients with values of BUA less than the cut-off (true positives) and specificity as the proportion of normals (pre- and peri-menopausal women) with values below the cut-off (false positives).

The ability of the four different measurements to discriminate between control subjects (young and peri-menopausal females) and osteoporotic patients was further examined by determining their accuracy (defined as true positives plus true negatives/total number studied) at varying cut-off points.

The relationships between BUA and measurements at the other skeletal sites in the premenopausal control subjects and the osteoporotic patients were examined by statistical comparison of the various slopes and intercepts (analysis of co-variance).

RESULTS

Premenopausal, perimenopausal and osteoporotic females

The results (mean ± SEM) of the measurements in each group are shown in Table 1. BUA (Fig. 1) was significantly lower in the osteoporotic patients (55.4 ± 3.8 dB/MHz, $P < 0.0001$) than in the premenopausal (79.6 ± 1.1 dB/MHz) and perimenopausal (79.6 ± 1.1 dB/MHz) women, as were the measurements at the other skeletal sites. Values for BUA, vertebral BMD, vertebral BMC and forearm BMC were similar in the premenopausal women and the younger control subjects.

A significant correlation was observed between BUA in the os calcis in all subjects and vertebral BMC ($r = 0.66$, $P < 0.0001$), vertebral BMD ($r = 0.72$, $P < 0.0001$) and distal forearm BMC ($r = 0.77$, $P < 0.0001$; Fig. 2). In addition, forearm BMC correlated with vertebral BMD ($r = 0.59$, $P < 0.0001$) and vertebral BMC ($r = 0.62$, $P < 0.0001$), but the correlation within the osteoporotic patients was poor ($r = 0.08$ and $r = 0.20$, respectively) compared with that between BUA and vertebral BMD ($r = 0.36$) and vertebral BMC ($r = 0.39$).
When the relationships between BUA and the other measurements were examined in the osteoporotic patients and premenopausal control subjects, the slopes were greater and the intercepts consistently lower in the osteoporotic group (Table 2). Analysis of co-variance showed that statistically significant differences were only observed in the relationship between BUA and forearm BMC (measured by SPA), and the slope was significantly greater and the intercept significantly lower in the osteoporotic group than in premenopausal women (Fig. 3).

In the premenopausal women, BUA showed a negative but insignificant correlation with age (r = 0.29, not significant; slope -0.25 dB/MHz), whereas in the osteoporotic group a significant correlation was observed (r = 0.50, P < 0.05; slope -0.75 dB/MHz). Similarly, spinal BMD and BMC showed very slight negative correlations in the premenopausal women (r = 0.12 and r = 0.01, respectively). The correlation coefficients in the osteoporotic group, though higher, were less than that seen with BUA (r = 0.16 and r = 0.14, respectively). The corresponding correlations for forearm BMC (measured by SPA) were r = 0.08 and r = 0.41. Estimated rates of bone loss (per cent per annum) as measured from the regression with age by each of the techniques in the premenopausal, perimenopausal and osteoporotic patients are given in Table 3.

Fig. 4 shows the sensitivity and corresponding specificity of BUA in discriminating between pre- and perimenopausal control subjects and patients with osteoporotic fracture. A value of 70 dB/MHz, which corresponds to 2 so below the mean of the normal population, gives a sensitivity of 81% and a specificity of 94%. This value also corresponds to the maximum accuracy (89%) for BUA (Fig. 5). The other measurements had similar maximum accuracy (83.7–88%), but the values at which this occurred lay within 1–1.5 so from the mean of the normal population (Fig. 5). At 2 so below the normal mean, the sensitivities for spinal BMD, spinal BMC and forearm BMC (measured by SPA) were 70%, 53% and 50%, respectively (data not shown).

**Renal osteodystrophy and Sudeck's algodystrophy**

No significant difference was observed in spinal BMD and spinal BMC between the female pre- and peri-menopausal control subjects and patients with renal osteodystrophy, whereas values for BUA (68.3 ± 2.4 dB/MHz, P < 0.001) and forearm BMC (0.73 ± 0.09, P < 0.01) were significantly lower in osteodystrophy (Table 1). Mean values of BUA and forearm BMC were not statistically different from those in the osteoporotic group, whereas spinal BMD and spinal BMC were significantly higher in the renal patients (0.98 ± 0.09, P < 0.05 and 43.09 ± 3.6, P < 0.05, respectively).

The mean duration of algodystrophy in the six patients was 20.6 months (range 10–26 months). BUA in the affected os calcis was reduced by 50% compared with that in the unaffected foot (Table 4).

**Table 1. BUA, spinal BMD, spinal BMC and forearm BMC in the four groups of subjects**

<table>
<thead>
<tr>
<th></th>
<th>Age (years)</th>
<th>BUA (dB/MHz)</th>
<th>Spine</th>
<th>Forearm BMC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>BMD (g/cm²)</td>
<td>BMC (g)</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>31(22–44)</td>
<td>79.6 ± 1.1</td>
<td>1.20 ± 0.03</td>
<td>48.2 ± 2.0</td>
</tr>
<tr>
<td>(n = 24)</td>
<td></td>
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<td></td>
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<tr>
<td>Perimenopausal</td>
<td>51(45–60)</td>
<td>79.6 ± 1.1</td>
<td>1.20 ± 0.08</td>
<td>44.4 ± 3.0</td>
</tr>
<tr>
<td>(n = 10)</td>
<td></td>
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<tr>
<td>Osteoporotic</td>
<td>65(41–79)</td>
<td>55.4 ± 3.8*††</td>
<td>0.78 ± 0.04*††</td>
<td>29.4 ± 2.7*††</td>
</tr>
<tr>
<td>(n = 21)</td>
<td></td>
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<tr>
<td>Renal failure</td>
<td>52(36–62)</td>
<td>68.3 ± 2.4*††</td>
<td>0.98 ± 0.09</td>
<td>43.09 ± 3.6</td>
</tr>
<tr>
<td>(n = 6)</td>
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</table>
Fig. 2. Correlation between BUA in the os calcis and (a) forearm BMC (measured by SPA) \((r = 0.77, P < 0.0001)\), (b) spine BMC (measured by DPA) \((r = 0.66, P < 0.0001)\) and (c) spine BMD density (measured by DPA) \((r = 0.72, P < 0.0001)\).

**DISCUSSION**

Values for BUA in the os calcis are known to correlate with bone density measurements at the same site [12, 12a]. In this study, we have demonstrated that values for BUA in the os calcis are significantly lower (35%) in patients with osteoporotic vertebral fracture than in normal premenopausal and perimenopausal females. Similar reductions in the other measurements were observed, and although the concordance between skeletal sites is perhaps surprising, it probably reflects the relatively large age difference between the groups. Irrespective of the reasons for this, our results suggest that the reduction in bone density in the os calcis appears to parallel that at other skeletal sites. Baran et al. [14] have

**Table 2.** Values of slopes and intercepts for the relationships between BUA and measurements at other skeletal sites in premenopausal and osteoporotic subjects

<table>
<thead>
<tr>
<th>BUA vs</th>
<th>Premenopausal ((n = 24))</th>
<th>Osteoporotic ((n = 21))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slope</td>
<td>Intercept</td>
</tr>
<tr>
<td>Spine BMD</td>
<td>21.0 ± 6.8</td>
<td>53.6 ± 8.3</td>
</tr>
<tr>
<td>Spine BMC</td>
<td>0.31 ± 0.13</td>
<td>64.1 ± 6.2</td>
</tr>
<tr>
<td>Forearm BMC</td>
<td>11.8 ± 5.2</td>
<td>63.0 ± 7.2</td>
</tr>
</tbody>
</table>
Table 3. Estimated rates of bone loss in the premenopausal, perimenopausal and osteoporotic groups as determined by each of the measurements

The *r* value for the correlation of each measurement with age is given in parentheses. Statistical significance: *P* < 0.05.

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Premenopausal (<em>n</em> = 24)</th>
<th>Perimenopausal (<em>n</em> = 10)</th>
<th>Osteoporotic (<em>n</em> = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-44</td>
<td>0.30</td>
<td>0.60</td>
<td>1.40</td>
</tr>
<tr>
<td>(−1.414)</td>
<td>(−3.024)*</td>
<td>(−2.488)*</td>
<td></td>
</tr>
<tr>
<td>BMD (DPA)</td>
<td>0.25</td>
<td>1.50</td>
<td>0.40</td>
</tr>
<tr>
<td>(0.331)</td>
<td>(−1.055)</td>
<td>(−0.683)</td>
<td></td>
</tr>
<tr>
<td>BMC (DPA)</td>
<td>0.03</td>
<td>1.50</td>
<td>0.50</td>
</tr>
<tr>
<td>(−0.055)</td>
<td>(−1.049)</td>
<td>(−0.576)</td>
<td></td>
</tr>
<tr>
<td>BMC (SPA)</td>
<td>0.20</td>
<td>2.20</td>
<td>1.60</td>
</tr>
<tr>
<td>(−0.348)</td>
<td>(−0.958)</td>
<td>(−1.675)</td>
<td></td>
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</tbody>
</table>

Fig. 4. Relationship between sensitivity (●) and specificity (■) of BUA in discriminating between normal control subjects (pre- and peri-menopausal women) and osteoporotic patients. At 70 dB/MHz, which corresponds to 2 SD below the mean of the normal control subjects, the sensitivity and specificity of BUA are 81% and 94%, respectively.

Similarly shown an apparently parallel reduction in BUA, vertebral mineral density and femoral neck mineral density in women with vertebral or femoral neck fracture when compared with age-matched control subjects [14].

The correlation between BUA in the os calcis and BMC (measured by SPA) in the distal forearm (*r* = 0.77) is similar to that reported previously (*r* = 0.80) [15], and is also comparable with radial shaft BMC measured by QCT (*r* = 0.85) [16]. The correlations of BUA with vertebral BMC (*r* = 0.66) and BMD (*r* = 0.72), although statistically significant, are not sufficiently close to be predictive. Evans *et al.* [17] obtained a similar correlation with spinal QCT (*r* = 0.66) and concluded that BUA did not provide a better indication of vertebral trabecular BMD than BMC (determined by SPA) of the distal forearm. This does not necessarily mean that BUA is less able to predict the risk of vertebral fracture, since factors other than BMD contribute to this risk [18–20].

The study of any given technique to predict fracture would, ideally, require a prospective study of fracture incidence. A more immediate assessment of the diagnostic power can be provided by examining the ability of a technique to discriminate between patients with and without an osteoporotic fracture. In this study, we found that BUA was at least as accurate if not more so than either SPA or DPA in detecting the presence of vertebral fracture. The value of BUA at which optimal sensitivity and specificity occurs obviously depends on the choice of normal control subjects. Thus the most discriminate or optimal value of BUA in this study (70 dB/MHz) differs from that of Baran *et al.* [14] (50 dB/MHz) because of the different age structure of the control populations. If, as has been suggested [21] the definition of osteoporosis depends on a value of BMC or BMD at least 2 SDs below...
the mean of young adults of the same sex, then the sensitivity of BUA at this point (81%) is higher than that of measurements at other skeletal sites including the spine, with similar specificity (>93%).

It is perhaps surprising that a measurement in the os calcis should be superior to direct measurements at the lumbar spine. Wasnich et al. [22], utilizing SPA to measure BMC, have suggested that the os calcis is the optimal skeletal site for the prediction of combined non-spinal and spinal fractures. Unlike the distal forearm, the os calcis consists of predominantly trabecular bone with a thin surrounding cortex. Like the vertebrae, it is subjected to the stresses of load-bearing. Therefore the high sensitivity and specificity of BUA for vertebral fracture might be related in part to the site of measurement. Although the numbers studied are relatively small, it is of interest that there is a significant difference in the relationship between BUA and forearm BMC (SPA) in the normal and osteoporotic subjects. Thus, for a given reduction in forearm BMC (measured by SPA), there is a greater change in BUA in the os calcis in patients with osteoporotic fracture than in normal control subjects. A possible explanation might be that there is a greater rate of loss of bone mineral in the trabecular bone of the os calcis, similar to that in axial sites of predominantly trabecular bone. An alternative explanation, which does not necessarily exclude this, is that BUA may be more sensitive to other osteoporosis-induced changes in trabecular bone. BUA, unlike photon absorptiometry, does appear to be dependent on factors other than absorption by bone mineral [12, 12a, 23]. As BUA is much more marked in cancellous bone than in cortical bone [24, 25], and there is little or no BUA by marrow fat [12a], it is likely that BUA is dependent on scattering and reflection of ultrasound by trabecular elements within cancellous bone. The decrease in BUA in osteoporosis may therefore reflect disruption of the normal trabecular architecture, the integrity of which plays a vital role in maintaining skeletal strength [19, 26]. In this regard it is of interest that the decrease in BUA showed a significant correlation with age in osteoporotic females, whereas no significant correlations with age were observed with the other measurements. If the above hypothesis is correct, this might be due to a disproportionate decrease in the quality of the trabecular architecture with age rather than a decrement in bone mineral with age.

The reproducibility of BUA in this study is comparable with that reported elsewhere [15, 17], and also compares very favourably with that of other non-invasive methods [27]. The os calcis is a readily accessible site for measurement, and BUA has the added advantages of being relatively inexpensive, rapid and radiation-free. If in addition to correlating with bone mineral at other skeletal sites it can also provide clinically significant information about bone quality, it could play a useful role in the evaluation of osteoporosis.

ACKNOWLEDGMENTS

We are grateful to Dr C. M. Langton for his assistance and advice, and Mr M. Morter of Walker Sonix Ltd for the loan of the ultrasound scanner. We also thank Mr D. Wright and Miss S. Hilditch for their statistical advice and assistance. E. McC. is in receipt of an MRC Training Fellowship. This study was supported in part by an MRC Programme Grant and by Rorer Central Research.

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