Bone mineral content of the lumbar spine in normal and osteoporotic women: cross-sectional and longitudinal studies

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Summary

1. Bone mineral content of the second, third and fourth lumbar vertebrae was determined in normal women and women with clinical osteoporosis by using dual-photon ($^{133}$Gd) absorptiometry.

2. A cross-sectional study of 70 normal women (aged 19–88 years) showed a bone loss of 44% from the age of around 34 years throughout life.

3. Longitudinal data from 59 normal women confirmed that the vertebral bone loss started before the menopause. An accelerated bone loss amounting to nearly 6% per year was seen immediately after the menopause. The bone loss of older women was slower.

4. Mean lumbar bone mineral content of 36 women (aged 48–93 years) with recent fractures of their femoral neck after minor trauma equalled that of age-matched normal women. Lumbar bone mineral content of the women with intratrochanteric femoral neck fractures was lower than that of the women with medial femoral neck fractures.

5. Mean lumbar bone mineral content of 72 women (aged 58–89 years) with primary osteoporosis was 41% lower than that of normal premenopausal women and 18% lower than that of age-matched controls. A weak inverse relationship between lumbar bone mineral content and the number of compression fractures was found. A weak inverse relationship between lumbar bone mineral content and the number of compression fractures was found.

6. Women with lumbar bone mineral content values below the 95% confidence limits for normal premenopausal women are at risk of future vertebral compression fractures, the fracture risk being inversely related to lumbar bone mineral content.

Key words: bone mineral content, dual-photon absorptiometry, lumbar spine, osteoporosis, spine.

Introduction

A rational approach to the clinical problem of osteoporosis would require reliable measures of the dynamic and static strength of the skeleton. Measurement of bone mineral content is generally accepted as an appropriate estimate of bone strength [1]. In bone disease prediction of bone mineral content of parts of the axial skeleton from the currently used forearm bone mineral content is poor [2]. It is preferable to study the bones of interest, and the vertebral and the femoral neck. Dual-photon absorptiometry makes possible a determination of bone mineral content is poor [2]. It is preferable to study the bones of interest, the vertebral and the estimate of vertebral strength is as yet uncertain.

The main object of the present study was to investigate whether lumbar bone mineral content could separate normal women and women with 'spontaneous' vertebral compression fractures or femoral neck fractures (i.e. women with clinical osteoporosis), and perhaps also identify women at risk of future fractures. Cross-sectional and longitudinal data were obtained in normal women and postmenopausal women with clinical osteoporosis.
Materials and methods

Patients

Three groups of women were investigated. They all gave informed consent to participation according to the Helsinki Declaration.

Group 1 (normal subjects). This group consisted of 70 generally healthy women (aged 19–88 years) having been referred to the hospital because of hallux valgus or simple (non-toxic, non-myxoedematous) goitres. None had a previous history of fractures. All had normal serum levels of calcium, inorganic phosphate, alkaline phosphatase and creatinine. They were considered to be normal for their age as regards calcium metabolism and skeletal mass. Radiographic examination of the spine was performed in the postmenopausal women, none of whom showed signs of vertebral wedging or severe spondylarthrosis. There were 32 premenopausal women (aged 19–51 years; mean 36 years) and 38 postmenopausal women (aged 42–88 years; mean 62 years).

Group 2 (spinal osteoporosis). This group comprised 72 postmenopausal women (aged 58–89 years; mean 73 years) successively referred to the department because of spinal osteoporosis. The disease was classified as primary, and the diagnosis was made clinically from recurrent back pain, and radiographically from decreased radiodensity of the vertebral bodies and at least one compression fracture (i.e. height reduction of the vertebral body by at least one-third) of the thoracic or lumbar spine. Fig. 1 shows the location of the fractures ranked according to the number of fractures in the individual patient. The patients were otherwise healthy, and none had received drugs known to interfere with calcium metabolism.

Group 3 (femoral neck fractures). This group consisted of 36 unselected postmenopausal women (aged 48–93 years; mean 77 years) who were successively referred for investigation because of a femoral neck fracture after a minor trauma. The patients were measured within 3–34 days (mean 16 days) of the injury. Six women of this group were also included in group 2 because of clinical and radiographic signs of primary spinal osteoporosis.

Repeated measurements. A group of 27 premenopausal women, 32 postmenopausal women without vertebral compression fractures and 15 women with obvious spinal osteoporosis not receiving any specific treatment was investigated twice within 3–19 months (mean 10.5 months).

BMC method

A collimated beam of photons from a 40 GBq $^{153}$Gd source was transmitted through the body in a rectilinear scanning mode across the lumbar vertebrae. The attenuations of the 44 keV and 100 keV radiation were simultaneously registered, and a bone-density profile corrected for soft tissue absorption was recorded for each scan. The area of this profile, i.e. the scan integral (SCI), represented the bone mineral mass per unit length of a vertebral cross-section [5]. Lumbar bone mineral content was expressed as the integral of SCI over the second, third and fourth lumbar vertebrae in arbitrary units, and has the dimension of mass. The couch of the bone mineral content analyser was translucent and the correct positioning of the spine was ensured by marking the vertebral spines on the skin. During sequential measurements the specific configuration of each density profile confirmed exact anatomical repositioning without additional radiological examination. The coefficient of variation of repeated measurements within 3 months equalled 1.9% at the bone mineral content range 36.5–65.3 units. The mean radiation dose to the uterus during one examination was 0–6 mrem (6 μSv).

Premenopausal women were measured within the menstrual or the early postmenopausal phases.

Statistical evaluation

The distribution of lumbar bone mineral content of normal premenopausal women showed
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a moment coefficient of skewness of 0·47 (i.e. skewness to the right). This figure was reduced to 0·12 when logarithmic transformation was used. Bone mineral content of each patient was expressed in two ways:

1. Relative to that of normal premenopausal women, to give the bone mineral index \[\text{BMI} = (\ln \text{bone mineral content} - \ln y_s)/\text{SD}_y,\] where \(\ln y_s\) and \(\text{SD}_y\) are the mean and SD of ln bone mineral content of the 32 normal premenopausal women of group 1.

2. Relative to that of normal women at the same age, to give the age-normalized bone mineral index \[\text{BMI}_n = (\ln \text{bone mineral content} - \ln y_e)/\text{SEE},\] where \(\ln y_e\) is the estimated bone mineral content at a given age \((x)\), and \(\text{SEE}\) is the residual SD of ln bone mineral content about the regression equation of a gamma variate fit of bone mineral content versus age, applied on the 70 normal women of group 1 \((\ln y = a_0 + a_1x + a_2\ln x)\) [5, 6].

The normal ranges of BMI and \(\text{BMI}_n\) (95% confidence intervals) are then -2.00 to 2.00, \(\text{SD}_y\) and \(\text{SEE}\) are measures of the inter-individual (biological) variation of lumbar bone mineral content.

The obtained mean BMI (or mean \(\text{BMI}_n\)) of a group of patients was retransformed to a non-logarithmic term as

\[e^{\text{BMI}_n} \cdot s \cdot 5 \cdot 5 \cdot (\text{SD}^2 - 1),\]

where \(\text{BMI}\) and \(\text{SD}\) indicate the mean and SD of BMI (or \(\text{BMI}_n\)) of the group, and \(s\) indicates \(\text{SD}_y\) (or \(\text{SEE}\)).

The possible age-dependency of lumbar bone mineral content was evaluated by the use of different linear and polynomial regression equations (Table 1). The method of least squares was used to calculate the regression lines. The residual variance about each line was a measure of the goodness of the fit [6]. Student’s \(t\)-test or analysis of variance (ANOVA) was used for comparison of mean values. The 95% confidence limits (CL95) of a probability was determined from tables of exact confidence limits; that of a mean was defined as mean \(\pm t_{95} \cdot \text{SE} \). The longitudinal data were analysed according to the CUSUM theory (A. Horsman, F. Armes & M. Simpson, unpublished work).

### Results

**Cross-sectional studies**

Fig. 2 shows lumbar bone mineral content of the normal women as a function of age. Bone mineral content of premenopausal women was not related to age \((r = 0.1, \text{N.S.})\), whereas a significant reduction was observed in the postmenopausal group \((r = -0.66, P < 0.001)\). The annual postmenopausal decline in this cross-sectional study was 1·4·% (CL95 0·9-2·0%). It was hypothesized that the skeletal mass decreased immediately after its maximum had been reached, and that the relative bone loss of old age was constant. Such a relationship can be described by a gamma variate function. The present data from normal women showed a maximum lumbar bone mineral content at the age of 34 years (CL95 18-40 years) [6], if such a fit was used.

<table>
<thead>
<tr>
<th>Table 1. Age-relationship of lumbar spine bone mineral content in empirical equations</th>
</tr>
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<tbody>
<tr>
<td>(y), Lumbar bone mineral content; (x), age: (x_m), years after the menopause ((x_m) of premenopausal women = 0). N.S., Not significant.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regression equation</th>
<th>Residual variance</th>
<th>(F^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(y = 60.35 - 0.31x)</td>
<td>71.42</td>
<td>1.04 (N.S.)</td>
</tr>
<tr>
<td>(y = 42.10 + 0.46x - 0.001x^2)</td>
<td>67.04</td>
<td>1.02 (N.S.)</td>
</tr>
<tr>
<td>(y = 13.05 + 2.39x - 0.035x^2 + 2.46x^3)</td>
<td>65.81</td>
<td>1.04 (N.S.)</td>
</tr>
<tr>
<td>(y = 48.89 - 0.56x)</td>
<td>59.59</td>
<td>1.15 (N.S.)</td>
</tr>
<tr>
<td>(y = e^{0.89 \cdot x + 0.05 \cdot w^2} + 0.46)</td>
<td>68.41</td>
<td>—</td>
</tr>
</tbody>
</table>

* Calculated in relation to the residual variance of the gamma variate fit [6].

![Fig. 2. Lumbar spine bone mineral content (BMC) in 70 normal women, in relation to age: ▲, premenopausal women; ○, postmenopausal women. The stippled area denotes the normal range for the premenopausal women. The curves indicate limits of the age-related normal range (i.e. 95% confidence intervals).](image-url)
Bone mineral content values below the normal range of premenopausal women (34.8–67.0 units) was considered to be reduced and defined as lumbar osteopenia. Lumbar osteopenia within the age-related normal range was termed ‘simple lumbar osteopoenia’ and lumbar osteopenia below this range was termed ‘accelerated’ or ‘pathological’ lumbar osteopenia. With these criteria the present normal data suggested a prevalence of lumbar osteopenia of 7% at the age of 50 years, 18% at the age of 60 years, 41% at the age of 70 years and 70% at the age of 80 years. The suggested total bone loss from the measured vertebrae throughout life was 44%. The interindividual variation of lumbar bone mineral content of premenopausal women (SDN) was 17.4%; the age-independent interindividual variation (SEE) was 20.9%.

The data from patients with spinal osteoporosis are summarized in Figs. 1 and 3 and Tables 2 and 3. The lack of complete separation between lumbar bone mineral content of patients and that of age-matched normal women is obvious. Lumbar osteopenia was observed in 55 patients

**TABLE 2. Lumbar spine bone mineral content in patients with clinical osteoporosis, compared with that of normal premenopausal women (BMI) and that of normal women of the same age (BMI,)**

Values are expressed as a deviation from the normal mean by using the normal SD as unit (calculations based on ln bone mineral content). Values in parentheses denote measured bone mineral content relative to normal mean bone mineral content of premenopausal and age-matched women respectively (as percentages). Significance of differences (t-test): ***P < 0.001; **P < 0.01; *P < 0.05. a From mean value for normal women, b from mean values for women with medial femoral neck fractures.

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>No. of patients</th>
<th>Bone mineral content</th>
<th>BMI</th>
<th>BMI,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Spinal osteoporosis</td>
<td>72</td>
<td>-3.54*** (59)</td>
<td>1.98</td>
<td>1.75</td>
</tr>
<tr>
<td>Femoral neck fractures</td>
<td>36</td>
<td>-1.73*** (77)</td>
<td>1.43</td>
<td>1.12</td>
</tr>
<tr>
<td>Medial</td>
<td>20</td>
<td>-1.19*** (83)</td>
<td>1.13</td>
<td>0.80*** (116)</td>
</tr>
<tr>
<td>Petrochanteric</td>
<td>16</td>
<td>-2.42*** (69)</td>
<td>1.50</td>
<td>0.00*** (100)</td>
</tr>
<tr>
<td>Normal women</td>
<td></td>
<td>0.00 (100)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**TABLE 3. Lumbar spine bone mineral content in 72 women with primary osteoporosis, related to the numbers of compression fractures**

Values are expressed in relation to bone mineral content of normal premenopausal women (BMI) and bone mineral content of age-matched normal women (BMI,) as a deviation from the normal mean by use of the normal SD as unit (calculations based on ln bone mineral content). Values in parentheses denote measured bone mineral content relative to normal mean bone mineral content of premenopausal and age-matched women respectively (as percentages). Probability estimated by ANOVA: † F = 4.41, P < 0.01; ‡ F = 6.16, P < 0.01.

<table>
<thead>
<tr>
<th>No. of fractures</th>
<th>No. of patients</th>
<th>Mean age (years)</th>
<th>Bone mineral content</th>
<th>BMI</th>
<th>BMI,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>75</td>
<td>3.05 † (63)</td>
<td>1.63</td>
<td>0.73 (89)</td>
</tr>
<tr>
<td>2–3</td>
<td>17</td>
<td>74</td>
<td>3.07 † (63)</td>
<td>1.75</td>
<td>0.81 (88)</td>
</tr>
<tr>
<td>4</td>
<td>14</td>
<td>74</td>
<td>3.58 † (58)</td>
<td>1.66</td>
<td>1.24 (80)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>14</td>
<td>68</td>
<td>5.02 † (47)</td>
<td>2.12</td>
<td>2.92 (60)</td>
</tr>
<tr>
<td>Normal women</td>
<td></td>
<td>0.00 (100)</td>
<td>1.00</td>
<td>0.00 (100)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
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FIG. 4. Lumbar spine bone mineral content (BMC) in 36 women with recent fractures of their femoral necks, in relation to age. ●, Women with medial femoral neck fractures; ○, women with pertrochanteric femoral neck fractures. The stippled area denotes the normal range for premenopausal women. The lines indicate limits of the age-related normal range (i.e. 95% confidence intervals).

(CL95 65–86%) and classified as pathological in 24 (CL95 24–47%). BMI of the patients showed a slight decrease with increasing number of compression fractures, but only those patients who had more than four fractures differed significantly from the others. The changes of BMI were more distinct, reflecting the fact that the clinically most severe osteoporosis was seen in the younger individuals. The patients (n = 31) with fractures within the measured vertebrae had twice as many fractures as patients with fractures in other parts of the spine (four vs two, P < 0.001) (Fig. 1), and their measured bone mineral content was on average 16% lower (P < 0.05).

The data from women with femoral neck fractures are summarized in Fig. 4 and Table 2. Lumbar bone mineral content of these patients was identical with that of age-matched normal women. Lumbar osteopenia was proved in 16 patients (CL95 28–62%), and classified as pathological in one (CL95 0–15%). Bone mineral content of the patients with pertrochanteric fractures was, however, lower than that of the patients with medial fractures, even if the obvious difference in age was eliminated.

Longitudinal studies

Fig. 5 shows the results of the longitudinal measurements of lumbar bone mineral content. The weighted mean change in the 27 premenopausal women was a decrease of 0.45 unit/year (0.9%). This change was not significant (P < 0.3). However, if the individuals were separated according to the age of maximum lumbar bone mineral content, i.e. 34 years, suggested by the cross-sectional data, the eight women below the age of 34 years showed a significant increase of 0.93 unit/year (2.0%), [CL95 0.01–1.85 units/year (0.01–3.9%) (P < 0.001)]1, and the 19 women, older than 34 years, showed a decrease of 1.07 units/year (2.2%) [CL95 0.07–2.06 units/year (0.1–4.2%) (P < 0.05)].

The 32 postmenopausal women showed a weighted mean decrease of 1.83 units/year (4.4%) [CL95 0.68–2.97 units/year (1.6–7.1%) (P < 0.01)]. Twelve women were within 5 years...
of the menopause, and their mean decrease was 3·25 units/year (6·5%) |CL: 1·44–5·07 units/year (3·2–9·8%) (P < 0·01). The 20 women whose menopausal age exceeded 5 years showed an insignificant mean decrease of 0·88 unit/year (2·4%) (P < 0·3). The obviously accelerated bone loss of the early postmenopause differed significantly from that of the late premenopause (P < 0·05) and from that of the late postmenopause (P < 0·05).

The 15 women with non-treated spinal osteoporosis, all being late menopausal, showed a mean bone loss of 1·46 units/year (4·4%). This change was not significant (P < 0·1).

Discussion

The amount of bone mineral within parts of the axial skeleton can be determined in vivo by the use of dual-photon absorptiometry or computed tomography [1]. The present dual-photon method measures the total bone mineral mass of the second, third and fourth lumbar vertebrae, unlike the developmental technique of computed tomography of the spine which gives an index of the bone mineral density within cubes of the bodies of the first and second lumbar vertebrae [7].

The degree of age-dependent bone loss from lumbar vertebrae is a matter of controversy. The cross-sectional data of Madsen [8] showed an unchanged bone mineral content until the age of 50–60 years, followed by a decrease of less than 1% per year, whereas Riggs et al. [9] reported a linear reduction of 47% from young adulthood throughout life. Our previously reported data suggest a continued bone loss from the age of 30–35 years, probably accelerated in the years immediately after the menopause [5]. The present results confirm this complex age-relationship, which is in accordance with the pattern demonstrated in iliac-crest biopsies [10]. Differences in the populations studied may account for this obvious discrepancy. However, bone mineral content versus age relations can be described by several mathematical models, owing to a substantial biological variation (Table 1), and the discrepancy might be a matter of statistics [6]. Nevertheless, estimation of longitudinal changes from cross-sectional results is not feasible, since life styles of different age strata change continuously.

The present longitudinal data confirm the previously hypothesized 'gamma variate' relationship of lumbar bone mineral content versus age. It is therefore questionable whether lumbar bone mineral content of any individual (unlike forearm bone mineral content) is ever constant. We cannot yet exclude the possibility that lumbar bone mineral content of women outside the age range 35–65 years for several years remains nearly unchanged. To our knowledge no other longitudinal investigation of lumbar bone mineral content has been published.

The accelerated bone loss immediately after the menopause, observed in the present study, equals that described in oophorectomized women examined by computed tomography of the spine [7]. The data clearly suggest that physiological changes related to the menopause are major determinants of lumbar bone mineral content of postmenopausal women. Further knowledge of those changes might improve the chances of successful prevention of postmenopausal bone loss [11, 12].

The present data show a large overlapping between patients with clinical spinal osteoporosis and age-matched normals. The occurrence of vertebral compression fractures is related to bone mass [13], but the significance of this quantitative approach in vivo remains uncertain. Qualitative properties of the vertebrae as tissues, and differences in the musculo-ligamental support of the spine, are certainly to be considered. Lumbar bone mineral content is a measure of the total amount of bone mineral within the scanning field, and each bone mineral content unit will obviously not contribute to the strength of the vertebrae to the same extent. A minor loss of transverse trabeculae within the vertebrae [14] might hardly be detectable by the present method, although it might contribute considerably to the weakening of the bone [13]. Nor would a change in the volume of the trabecular framework be distinguishable from a change in the degree of mineralization of an unchanged bone volume. The slight increase in lumbar bone mineral content with increasing age observed in the osteoporotic women (Table 3) may in part reflect an increased degree of mineralization of old age [15], a change which is known to reduce the dynamic strength of the bones at the tissue level [16]. Arteriosclerosis of the lumbar aorta may account for nearly 15% of the measured bone mineral content in severe osteopenia (unpublished work). The errors due to spondylarthrosis need to be investigated.

When discussing differences in bone mass between patients and normals most authors regard osteoporosis as an all-or-none state. However, osteoporosis, like other diseases, represents a continuum, and any observed difference will certainly depend on the severity of the disease in the population of patients studied. Mean lumbar bone mineral content of patients with one
compression fracture was in the present study reduced by 11% compared with normal women at the same age and the quantitative difference between non-fracture and incipient fracture cases is supposed to be immaterial. Our data suggest that the majority of patients with clinical spinal osteoporosis are indistinguishable from age-matched normals, in accordance with the hypothesis of Newton-John & Morgan [117], although a subgroup evinces accelerated bone loss from the lumbar vertebrae. Whether this accelerated bone loss is the cause or the consequence of fractures is unknown. Our longitudinal results are yet inconclusive as to whether there is a differential bone loss in postmenopausal women with and without compression fractures. However, it should be emphasized that the observed differences in lumbar bone mineral content between patients and age-matched normals of 18% (Table 2) could be explained by a difference in the duration of accelerated bone loss in the early postmenopause of approximately 3 years, the bone loss being 6% per year. An early recognition of those rapid bone losers would be of great advantage, but the appropriate procedure has not yet been worked out.

The vertebral bone mass is supposed to give a poor estimate of the strength of the femoral neck [18], and the present patients with femoral neck fractures might have had accelerated osteopenia in the proximal femur, although their lumbar bone mineral content equals that of age-matched normals. The dual-photon method can be used for measurement of bone density in the narrowest part of the femoral neck (unpublished work). It is questionable, however, if such measures will yield valuable data on the complicated biomechanical properties of that region. The fact that neither forearm bone mineral content shows any significant clinical distinction between women with femoral neck fractures and age-matched controls [19], makes it conceivable that the occurrence of femoral neck fractures depends on an increased incidence of falls and minor trauma rather than bone loss per se [20]. The present difference in lumbar bone mineral content of women with medial and pertrochanteric fractures suggests that the pertrochanteric fracture mainly reflects loss of trabecular bone.

The clinical diagnosis of spinal osteoporosis implies vertebral compression fractures. Measurement of lumbar bone mineral content is of benefit if existence of a condition of pre-osteoporosis or asymptomatic osteopenia is acknowledged. It seems reasonable to advocate a definition of osteopenia as a bone mineral content below the 95% confidence interval of normal premenopausal women, since the prevalence of compression fractures amongst such women after minor trauma is less than 2-5%. Women with bone mineral content values below that normal range are considered by us to be at risk. The existence of a fracture threshold [9] is rather speculative. The fracture risk represents, a continuum inversely related to bone mass [21]. Logarithmic transformation of lumbar bone mineral content is justified by the fact that the static strength of a vertebra declines more quickly than its bone mass [13]. The scattergrams of the present study should therefore reflect the estimated variable of interest, i.e. vertebral bone strength, on a simple linear scale.

Determination of a lumbar bone mineral content or a rate of bone loss at which prophylactic measures should commence awaits further investigation.

Acknowledgments

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