

Bone density in women with spinal and hip fractures

Bone density in the lumbar spine and distal radius of 98 postmenopausal women was measured by quantitative computed tomography and in the distal radius by gamma ray attenuation. Nineteen had spinal fragility fractures, 30 had recent hip fractures while 49 were healthy control subjects. The trabecular bone density in spines of the control subjects showed a linear correlation with age corresponding to an annual decrease of 1 per cent and total decrease of 44 per cent between 46 and 86 years of age. Both patient groups had bone density reduction at the spine and peripheral measuring sites as compared with controls. In the distal radius, the reduction in bone density was of the same magnitude in both patients groups but in the spine, the reduction in patients with spinal fracture was more extensive than that in patients with hip fracture. Trabecular bone density in the distal radius and spine correlated in control and hip fracture patients, but not in spinal fracture patients. The results support the opinion that two forms of osteoporosis exist. One is characterised by excessive trabecular bone loss in the axial skeleton leading to spinal fractures; the second is due to equal extents of axial and peripheral osteopenia, found in connection with hip fractures.

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It has been suggested that patients with spinal osteoporosis have a disproportionate loss of trabecular bone, whereas hip fracture patients have a predominant loss of cortical bone of the appendicular skeleton (Nordin 1971, Wahner et al. 1977, Mazess 1979). Studies applying dual photon absorptiometry of the spine support this concept (Riggs et al. 1981, Krølner & Pors Nielsen 1982). Quantitative computed tomography is another noninvasive method of quantifying bone density in the spine (Genant et al. 1981) and the relationship of cortical and trabecular bone in the peripheral and central skeleton (Härmä 1983). We have studied peripheral and spinal bone densities in patients with spinal and hip fracture as compared to control subjects. A new modification of bone quantification in the spine by quantitative computed tomography (QCT) was developed. QCT was used for spinal measurements while QCT as well as gamma ray attenuation (GRA) were made for measuring the distal radius. The relationship of bone density to histomorphometric analysis of the iliac bone biopsies of the same individuals was studied.

Patients and methods

Nineteen females (mean age 65 (34–84) years with at least one (mean two) compression fractures in the spine, 30 females with recent hip fractures (mean age 78 (64–93) years, and 49 postmenopausal female volunteers (mean age 72 (45–86) years) were studied. All subjects with recognisable secondary causes of osteoporosis, metabolic bone disease or using drugs known to alter calcium metabolism were excluded. Control subjects and patients were ambulatory postmenopausal women, who were not institutionalised. Patients with spinal fracture were studied in the outpatient department; patients with hip fracture while hospitalised, within 1 week of operative treatment; and controls while hospitalised for cataract surgery or other minor operative procedures. Twenty-two of the hip fractures were cervical and eight were trochanteric. Four patients with hip fracture also had compression fractures of the spine.

The vertebral bone density was measured by x-ray computed tomography (CT) with a standard scanner from 4 mm consecutive slices with an energy of 96 kV, 300 mAs and 720 projections. The first three lumbar vertebrae were scanned thoroughly (Figure 1). If there were compression fractures in these particular vertebrae, the most proximal non-fractured vertebra was selected. A calibration phantom of wa-

CT NUMBERS (HU)

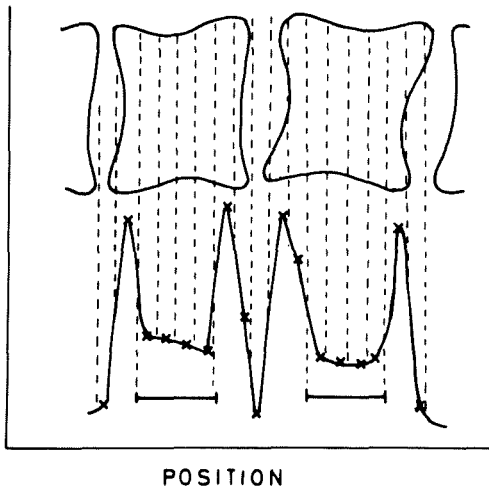


Figure 1. The accepted density values in QCT of the spine according to the position of consecutive 4 mm slices.

ter, air, ethanol and various potassium phosphate concentrates was scanned together with the subjects. The trabecular bone area of each 4 mm slice was manually limited as the region of interest and the mean densities of these areas in the Hounsfield scale were recorded. Each value of these slices was corrected by the formula:

$$HU = \frac{1000 (HU_b - HU_w)}{HU_w - HU_a},$$

where HU_b = mean density of the trabecular bone area, HU_w = mean density of the water standard in the phantom, and HU_a = mean density of the air standard in the phantom. The result of each subject was calculated using the equation:

$$HU = \frac{P_1 HU_1 + P_2 HU_2 + \dots + P_n HU_n}{P_1 + P_2 + \dots + P_n},$$

where P_n 's are the pixel numbers of accepted slices in three vertebrae and HU_n 's the mean Hounsfield units, respectively.

The distal radius was a second point for bone measurement with QCT. One slice was obtained at the 1.5 cm site and the other slice at the 3 cm site. The mean density in the Hounsfield scale was obtained from these slices after limiting manually the region of interest; the calibration was the same as in the spinal measurement.

The reproducibility of the QCT measurements was tested by seven measurements in a volunteer patient

with inoperable retroperitoneal tumour and no skeletal affections. The coefficient of variation of the results was 2.8 per cent in the spine, 1.7 per cent in the total slice of the radius at the 1.5 cm site, 3.4 per cent in the total slice of the radius at the 3 cm site and 15.2 per cent in the trabecular bone area of the radius at the 1.5 cm site.

The bone mineral density (BMD, g/cm^3) was measured by the Am-241 gamma ray attenuation method at the distal radius of the patient's non-dominant forearm (Karjalainen 1973). Control values were obtained from an age- and sex-matched group of healthy persons (Karjalainen & Alhava 1977).

The histomorphometric values of bone biopsy specimens from the iliac crest cancellous bone were determined from 16 spinal fracture and 25 hip fracture patients according to Merz & Schenk (1970a & b). The volumetric density of trabecular bone (V_v , %) and the percentage of trabecular bone occupied by osteoid (V_{vo} , %) were determined. Age- and sex-matched control values were obtained from a control material (Hoikka & Arnala 1981).

Results

The vertebral bone density of the 49 control subjects is plotted against age in Figure 2. The mean value of the controls is illustrated by a linear regression line as a function of age: $(HU) = 290 - 2.16 \times \text{age}$, $r = 0.42$, $p < 0.01$. This line

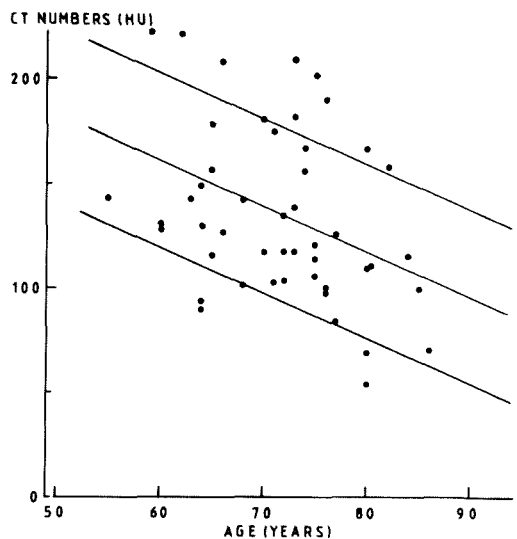


Figure 2. Vertebral bone density values of the 49 control subjects and the regression line ± 1 SD of the mean value as a function of age.

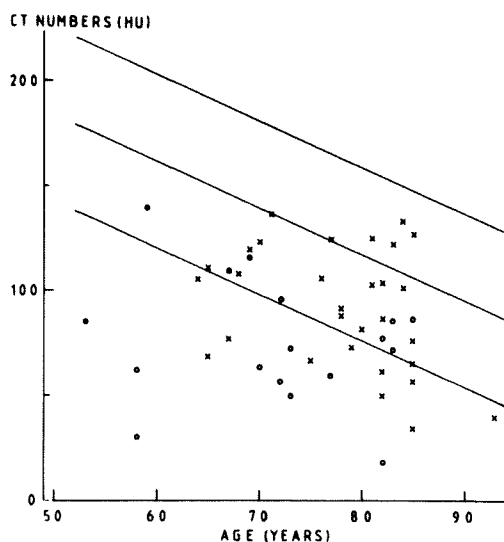


Figure 3. Individual bone density values of the 18 spinal fracture (○) and 30 hip fracture (×) patients. The lines denote the age regression of the control subjects ± 1 SD from the mean.

corresponds to an annual 1.1 per cent decrease in trabecular bone density and a reduction of one standard deviation (SD) of the mean value

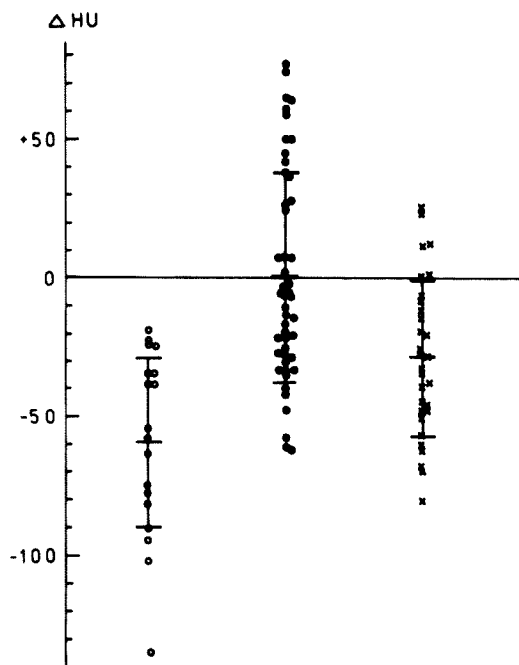


Figure 4. The difference of each individual vertebral bone density value from the age regression line of the controls. (○) spinal fracture patients, (×) hip fracture patients, (●) controls.

in 19 years. The individual values of the hip and spinal fracture patients are plotted on the regression line of the controls, Figure 3. In Figure 4, the individual values for each patient and control subject are expressed as the difference from this linear regression line of the control subjects, i.e., the difference from the age-adjusted mean of the controls. In both patient groups, the age-corrected mean trabecular bone density of the spine was significantly lower than that of the controls and the mean density of the spinal fracture patients was lower than that of the hip fracture patients ($t = 3.26$, $p < 0.005$).

The results of the measurements made in the distal radius by QCT and GM are summarised in Table 1. By both methods a significant osteopenia of less than one SD of the controls was found in the distal radius of the patients. There was no difference between the two patient groups in the peripheral measurements.

In the QCT of the distal radius, the total slice measurement was made in the same position as in the GT measurements, and the correlation of these two methods was significant ($r = 0.57$, $p < 0.001$). The GT and total slice QCT measurements of the distal radius correlated with the spinal QCT measurements in both patient groups. The trabecular bone density in the distal radius correlated with the trabecular

Table 1. The reduction of bone density in the distal radius of spinal and hip fracture patients, measured by gamma ray attenuation (GM) and quantitative computed tomography (QCT). The values are given as the difference from the age-adjusted mean of the control subjects using one standard deviation of the controls as a unit (z-score)

	Spinal fracture patients	Hip fracture patients
GM		
Radius 1.5 cm	-1.0 (± 0.9) ^c	-0.8 (± 1.6) ^a
QCT		
Radius 1.5 cm		
Total slice	-0.5 (± 0.8) ^a	-0.6 (± 0.8) ^b
Radius 1.5 cm		
Trabecular bone area	-0.7 (± 0.9) ^b	-0.6 (± 0.9) ^a
Radius 3 cm		
Total slice	-0.7 (± 1.2) ^a	-0.7 (± 0.8) ^b

^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.005$. Two-sided *t*-test.

Table 2. The relationship of histomorphometrically increased osteoid (the percentage of trabecular bone occupied by osteoid over 2 SD of the mean of the age- and sex-matched controls) to trabecular bone density in spine, bone mineral density (BMD) in the distal radius and volumetric density of trabecular bone (Vv) in the iliac crest biopsy. The values are given as the difference from the age-adjusted mean of the control subjects using one standard deviation of the controls as a unit (z-score)

	Trabecular bone density in spine ± 1 SD	BMD in distal radius ± 1 SD	Vv in iliac crest biopsy ± 1 SD
Spinal fracture patients (all)	-1.6 ± 0.9^d (n = 18)	-1.0 ± 0.9^c (n = 19)	-0.6 ± 0.9 (n = 14)
With normal osteoid (n = 11)	-1.9 ± 0.8^d	-1.2 ± 1.0^c	-1.5 ± 0.7^d
With increased osteoid (n = 3)	-0.7 ± 0.2^d	$+0.04 \pm 0.4$	-0.3 ± 0.9
Hip fracture patients (all)	-0.8 ± 0.8^d (n = 30)	-0.8 ± 1.6^a (n = 29)	-0.5 ± 1.0 (n = 25)
With normal osteoid (n = 14)	-0.8 ± 0.7^d	-1.2 ± 1.9^a	-0.6 ± 1.0
With increased osteoid (n = 11)	-0.4 ± 0.7	-0.8 ± 1.0^a	-0.5 ± 1.0

^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.005$, ^d $p < 0.0001$. Two-sided *t*-test.

bone density in the lumbar spine in the controls ($r = 0.53$, $p < 0.001$) and hip fracture patients ($r = 0.55$, $p < 0.01$). However, in the spinal fracture patients there was no correlation in the trabecular bone density between the spinal and the peripheral measurements ($r = 0.36$, n.s.).

In histomorphometric analysis of the iliac crest biopsies, the mean volumetric density of trabecular bone in the spinal and hip fracture patients was not lower than the value of the age- and sex-matched controls. The percentage of trabecular bone occupied by osteoid was increased by more than two SD of the control values in three of the 14 spinal fracture and in 11 of the 25 hip fracture patients. Regardless of the method used, the bone density values of the patients with increased osteoid were higher than the values of those with osteoid in the normal range (Table 2).

Discussion

The mean ages of the two patient groups and the control subjects were different and therefore the comparisons of the bone density between the groups were adjusted using the linear regression calculated from the control values. This type of estimation is valid as long as the linear regression is in force. In previous studies of peripheral (Hui et al. 1982, Karjalainen & Alhava 1977) and spinal (Riggs et al.

1981, Genant et al. 1983) bone measurements, the slope of the bone density values in the cross-sectional material was found to be steeper soon after the menopause and more gradual in old age. Most of the control values here are from age 60 to 85 and, hence, the linear regression is valid for this age group, but for ages under 60 and over 85 our control values are slightly low. With a larger control material and a non-linear regression equation, the oldest hip fracture patients could probably have been more osteopenic in the spinal measurement.

The accuracy of the single energy QCT has been 1 to 2 per cent for K_2HPO_4 solutions and 8 per cent for human vertebral specimens spanning a wide age range (Genant & Boyd 1977, Genant et al. 1981, Rohloff et al. 1982). In our study, the QCT of the spine was modified by scanning through the measured vertebral bodies with consecutive 4 mm slices, thereby increasing the sampling volume and improving reproducibility; the precision of this method in the spine was 2.8 per cent. For measuring the distal radius, only one 4 mm slice was used, and the patient was positioned beside the scanner which was uncomfortable, reducing the precision. The large precision error of trabecular bone area measurement in the distal radius (15 per cent) is due to manual limiting of the trabecular bone area in the small sampling volume.

The bone density of spinal fracture patients

was reduced in both spinal and peripheral measurements. The mean value was 1.6 SD below the age-corrected value of the control subjects in the spine and 0.5–1 SD in the distal radius. The results in the peripheral skeleton agreed with those made by the gamma ray attenuation method (Goldsmith et al. 1971, Cohn et al. 1974, Smith et al. 1975, Wahner et al. 1977). In spinal measurements the QCT distinguishes between spinal fracture patients and control subjects of comparable age in a similar manner to dual photon absorptiometry (DPA) (Riggs et al. 1981, Krølner & Pors Nielsen 1982). In this respect, our results agree with the earlier spinal QCT findings of Genant et al. (1983). The effect of the increasing amount of fat in osteoporotic trabecular bone seems to cancel out the accuracy error of QCT when compared with DPA. The simultaneous decrease in the amount of trabecular bone replaced by fat affects single energy QCT more than DPA (Mazess 1983). This change in trabecular bone constitution is specific for osteoporosis and overcomes the intra-individual variation in marrow fat content (Dunnill et al. 1967). QCT is also unaffected by aortic calcification and spondylotic hyperostosis, which may lead to overestimation of the true vertebral body mass in persons measured by DPA (Krølner et al. 1982).

As our patients with hip fracture were older than controls and patients with spinal fracture, comparisons were made with the age-adjusted mean values. The bone density values of the hip fracture patients were reduced in the spine and distal radius even after this correction. Alhava & Karjalainen (1973) and Nilsson & Westlin (1977) arrived at the same bone density results for the distal radius of patients with hip fracture by the gamma ray attenuation method. However, Riggs et al. (1982), Krølner & Pors Nielsen (1982) and Bohr & Schaad (1983) did not find differences in the spinal and peripheral bone mineral density of patients with hip fracture compared with age-matched controls. These different results are probably due to patient selection and the dissimilarity of the hip fracture groups studied.

The patients with hip fracture in this study were selected from the larger number of patients attending our hospital during the study

period, excluding those who had a secondary cause for osteoporosis and institutionalised patients. In spite of this selection, hyperosteoidosis suggesting osteomalacia was found in 11 of the 25 patients, studied histomorphometrically. Hip fracture patients with increased osteoid differed from other hip fracture cases in showing no reduction of bone density in their spinal QCT measurement. This difference in the QCT and gamma ray attenuation results for patients with increased osteoid may arise from secondary hyperparathyroidism and consequent osteitis fibrosa as an early sign of hypovitaminosis D (Parfitt et al. 1982). QCT was sensitive to this change in marrow constituents, as no correction for marrow fat was used in our QCT method, which had been done with the gamma ray attenuation values.

We conclude that two forms of osteoporosis occurred in this study. Patients with hip fracture had a slight but significant osteopenia of both the peripheral and axial skeleton. In patients with spinal fragility fractures, a comparable loss of cortical and trabecular bone was found in the peripheral skeleton, but they had lost more marked and disproportionate amounts of trabecular bone from the spine.

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