Bone Turnover in Cortical and Trabecular Bone in Normal Women and in Women with Osteoporosis

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This study is based on the assumption that if bone turnover, shown by the uptake of ^{99m}Tc-MDP, indicates a high rate of bone loss in patients with osteoporosis, it could potentially predict bone loss in patients at risk before significant bone loss has occurred. **Methods:** Quantitative bone SPECT (QBS) using ^{99m}Tc-MDP, expressed as the %ID/cc $\times 10^{-3}$, was performed in 71 women who had osteoporosis in the lumbar vertebrae, the femoral neck or both, and in 54 age-matched normal female controls. Of the women with osteoporosis, 42 had postmenopausal osteoporosis and 29 had primary hyperparathyroidism (HPT) and osteoporosis. **Results:** QBS increased with age in the cortical bone and decreased in the trabecular bone of the normal women. Quantitative bone SPECT in the femoral neck was 3.18 ± 1.20 and was 2.73 ± 1.06 in the femoral shaft in 20 women with postmenopausal osteoporosis of the femoral neck. In 19 women with HPT and osteoporosis of the femoral neck, the QBS value in the femoral neck was 3.57 ± 0.92 and in the femoral shaft 3.38 ± 1.12. These values were also significantly higher for the femoral neck and for the femoral shaft than those of normals. Although QBS values were higher in the lumbar region in 39 women with postmenopausal osteoporosis (4.59 ± 1.45) and in 27 women with HPT (4.30 ± 1.52), as compared with the normal group (4.28 ± 1.61), the difference was not statistically significant. **Conclusion:** This study shows that bone turnover is significantly higher in the cortical bone of women with osteoporosis than in normal women.

Key Words: osteoporosis; bone metabolism; SPECT

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The impact of osteoporosis on health care has drawn much attention in recent years (*1,2*). Prevention, diagnosis and treatment are intensely studied (*2–6*). Diagnosis is made by measuring bone density with single-photon absorptiometry, CT, dual-energy x-ray absorptiometry (DEXA), or, recently, ultrasound (*4*). Diagnosis of decreased bone mineral density (BMD) suggests a higher risk of fracture (*4,6*). There is, however, little that can be done to restore lost bone in older osteoporotic patients (*1*), although there is some evidence that estrogen treatment can stabilize (*7*) or even increase BMD somewhat (*8*). The aim in handling osteoporosis should be to predict the population at risk of bone loss before it occurs. Potential candidates for bone loss should then be treated prophylactically before a significant amount of bone is actually lost. Presently, there are difficulties in achieving this by using BMD measurements (*4,9*). The test has to be performed at least twice during unspecified but long enough intervals to show a significant decrease in BMD and indicate the rate of bone loss. It has been suggested that a number of measurements over a period of several years should be done (*5*). This is inconvenient and often impossible to achieve.

Quantitative bone SPECT (QBS) to measure bone turnover is a potential technique to determine the rate of bone loss before a large amount of bone is lost (*10*). Bone turnover must be abnormally high with an excess of bone loss over bone formation for a long enough time before significant bone is lost. In this study, we have measured QBS values in 42 women with postmenopausal osteoporosis and 29 women with hyperparathyroidism and osteoporosis and compared them to the QBS values of 54 age-matched normal controls.

MATERIALS AND METHODS

Fifty-four women (age 55.8 ± 7 yr) investigated for musculoskeletal pain or routinely scanned for bone metastases with no clinical, laboratory or radiologic evidence for bone disease served as the normal control population. BMD values measured by DEXA were normal and the chance for fracture in the lumbar vertebrae or femoral neck was smaller then 5%. There were 71 women with osteoporosis on DEXA who had measurements of their bone metabolism. Forty-two were postmenopausal women (age 58.3 ± 8 yr) with osteoporosis. Of these, 39 had osteoporosis of the lumbar spine and 20 had osteoporosis of the femoral neck. Twenty-nine women with primary hyperparathyroidism (HPT) (age 59.2 ± 8.8 yr), in whom BMD measurements of the lumbar spine (27 women) and femoral neck (19 women) showed de-

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creased values, were also included in the study. Diagnosis of HPT was based on elevated serum levels of calcium, low phosphorus levels and elevated serum parathormone values. The study was approved by the Helsinki Committee for Human Investigations of our institution.

BMD—the ratio of bone mineral content-to-area—was measured by the routine DEXA technique (Lunar Radiation, Madison, WI). Bone density studies were performed on the same day or within 14 days of the SPECT study. BMD was measured as g/cm^2. The short-term and long-term variability of BMD measurements was less than 1%. BMD was considered abnormally low when below the standard deviation of the age- and sex-matched normal values.

The SPECT technique for quantitative bone scintigraphy has been discussed in detail in previous publications (*10–13*). Quantitative bone SPECT values were expressed as the percent of injected dose of ^{99m}Tc-MDP per cc of bone tissue × 10^{-3}. The study was performed after the intravenous injection of 20 mCi ^{99m}Tc-MDP using a digital gamma camera with a rotating gantry (Apex 415 ECT, Elscint, Haifa, Israel) and a low-energy, multipurpose collimator (Elscint, APC-3). SPECT studies of the pelvis were performed. QBS values of the lumbar vertebrae, femoral neck and femoral shaft were obtained. The whole vertebra was included in the measurement. The same area as that used for BMD, L-2 to L-4 vertebrae, was measured. QBS precision of measurement in a phantom is 2%. The age-dependent normal population data were fitted using a power function. The fit and the standard deviation were plotted on the same graph displaying the low and the high normal limits. This is the normal shaded area in Figures 1–4. The data obtained from osteoporotic women (mean value ± standard deviation) were compared with the matched normal controls. An unpaired t-test and Mann-Whitney test were used to evaluate the significance of the difference in QBS values between normal women and osteoporotic women.

RESULTS

The BMD in the lumbar vertebrae in women with postmenopausal osteoporosis (0.88 ± 0.12 g/cm^2) and in women with HPT and osteoporosis (0.84 ± 0.11) was significantly lower ($p < 0.001$ respectively) than the BMD of the lumbar spine in the normal controls (1.17 ± 0.15). The BMD in the femoral neck of women with postmenopausal osteoporosis (0.68 ± 0.10) and with HPT osteoporosis (0.68 ± 0.09) was also significantly lower ($p < 0.001$ respectively) than the mean BMD of the normal control group (0.93 ± 0.10).

The normal lumbar vertebrae showed a decrease in QBS values over the years, whereas the femoral neck showed an increase in QBS values over the years (Figs. 1–4). In women with postmenopausal osteoporosis, there was a significantly higher percent of injected dose of ^{99m}Tc-MDP per cc of bone in the femoral neck of 20 women with femoral neck osteoporosis in comparison with normal controls 3.18 ± 1.20 versus 2.44 ± 0.71 ($p < 0.01$) (Fig. 1). QBS measurements of the femoral shaft in women with postmenopausal osteoporosis of the femoral neck were also significantly higher when compared to normal controls 2.73 ± 1.06 versus 2.14 ± 0.68 ($p < 0.01$). Although the QBS values of the lumbar vertebrae (Fig. 2) in 39 women

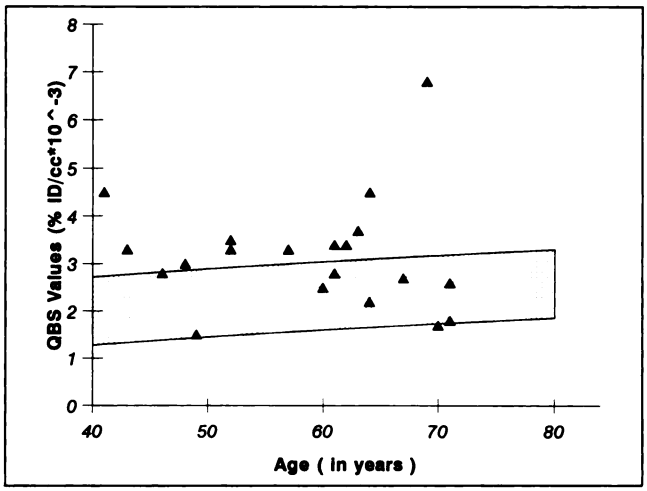

FIGURE 1. Percent of injected dose per cc of bone tissue × 10^{-3} in the femoral neck of 54 normal women (shaded area) and in 20 women with osteoporosis of the femoral neck (▲).

with postmenopausal osteoporosis were higher than those in normal controls, the difference was not statistically significant (4.59 ± 1.45 versus 4.28 ± 1.61).

There was a significantly higher percent of injected dose of ^{99m}Tc-MDP per cc of bone in the femoral neck (Fig. 3) in 19 women with HPT and femoral neck osteoporosis in comparison with normal controls 3.57 ± 0.92 versus 2.44 ± 0.71 ($p < 0.001$). This was also true for QBS in the femoral shaft in women with HPT and osteoporosis of the femoral neck as compared to normal controls (3.38 ± 1.12 versus 2.14 ± 0.68, $p < 0.001$). Although the QBS values of the lumbar vertebrae were higher in 27 women with HPT and osteoporosis of the vertebrae than those in normal controls (Fig. 4), the differences were not significant (4.30 ± 1.52 versus 4.28 ± 1.61). The results of BMD and QBS measurements are summarized in Table 1.

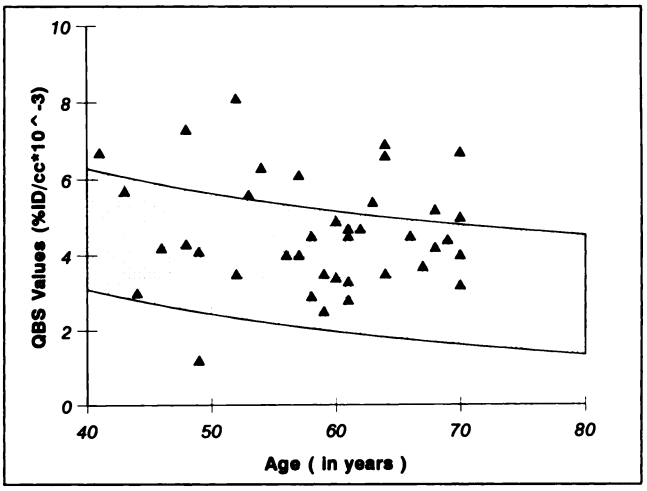

FIGURE 2. Percent of injected dose per cc of bone tissue × 10^{-3} in the lumbar vertebrae of 54 normal women (shaded area) and in 39 women with osteoporosis of the lumbar vertebrae (▲).

DISCUSSION

Technetium-99m-MDP uptake indicates bone formation. Since bone formation is coupled with bone loss in most diseases, it is also an indicator of bone turnover (*14*). Technetium-99m-MDP uptake can therefore be considered an indicator of local bone loss in patients with bone metastases. Technetium-99m-MDP uptake is also diffusely increased in the bones of patients with metabolic bone diseases (*13*) known to cause bone loss.

The measurement of ^{99m}Tc-MDP uptake by QBS has proven to be an accurate test. Using the ultimate gold standard of comparing in vivo SPECT measured uptake in the bones of patients before surgery with in vitro measurements of the same bone obtained during surgery, a very high correlation has been obtained (*10*). The technique also has high repeatability and precision (*10*). For these reasons, QBS provides a reliable parameter in evaluating osteoporosis in a clinical setting.

Although BMD tests are widely used in patients suspected of osteoporosis, their utilization poses significant problems. The main disadvantage of bone density measurement is that one measurement is diagnostic only when a significant amount of bone is lost. A long period of follow-up for an individual patient with still normal bone mass may be necessary to collect significant information about the rate of bone loss and the possibility of osteoporosis. There is an obvious need for a single test which will diagnose abnormal bone turnover without the need for a long waiting period to document significant bone loss.

In 1980, Fogelman (*14*), in a pioneer study measuring 24-hr whole-body retention of ^{99m}Tc-MDP in young women after oophorectomy, showed that increased retention of MDP was associated with low BMD. However, there was no continuation of this line of research. Thomsen et al. (*15*) and Riis et al. (*16*) measured ^{99m}Tc-MDP whole-body retention and urinary excretion over a period of 24 hr as an overall estimate of bone turnover. The problem with using ^{99m}Tc-MDP retention or excretion measurements in the evaluation of bone turnover is that these techniques measure the average uptake in all the different bones of the body. Such techniques may be able to detect only major changes occurring in extreme states such as oophorectomy in young women (*14*). Whole-body retention of ^{99m}Tc-MDP does not allow, for example, the differentiation between cortical and trabecular bone which the present study shows is critical in patients with osteoporosis. Blood and urine tests, such as measurement of osteocalcin or hydroxyproline, suffer the same disadvantage.

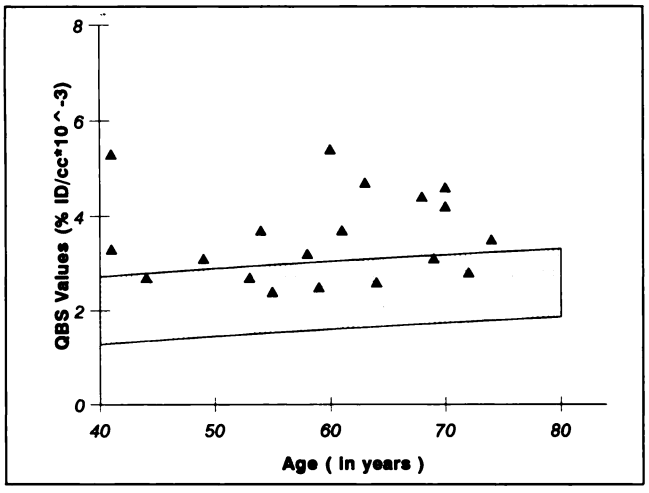

FIGURE 3. Percent of injected dose per cc of bone tissue × 10^{-3} in the femoral neck of 54 normal women (shaded area) and in 19 women with primary hyperparathyroidism and osteoporosis of the femoral neck (▲).

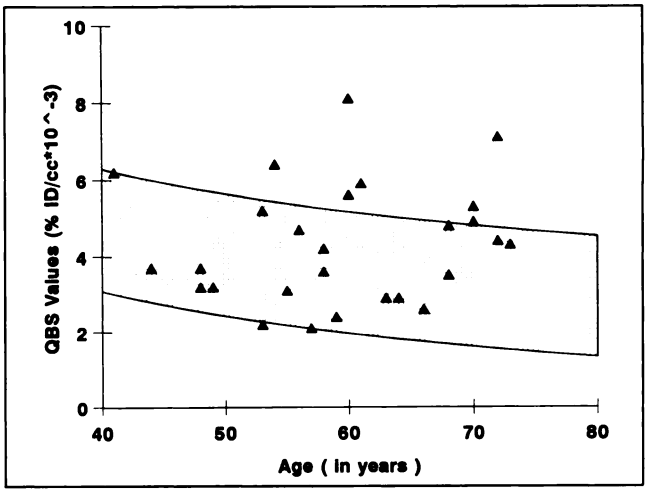

FIGURE 4. Percent of injected dose per cc of bone tissue × 10^{-3} in the lumbar vertebrae of 54 normal women (shaded area) and in 27 women with primary hyperparathyroidism and osteoporosis of the lumbar vertebrae (▲).

Quantitative bone SPECT values, mainly in the cortical bone of the femur, increase with age in normals, in contrast to QBS values mainly in the trabecular bone of the lumbar vertebrae (Figs. 1–4). This is in accord with the fact that the level of parathyroid hormone affecting the cortical bone increases with age (*1*), causing an increase in the number of bone remodeling units and bone turnover. When there is some uncoupling of formation and resorption with greater bone loss than formation, this leads to a net bone loss (*17,18*). In spite of the variations in QBS values in the normal population, patients with osteoporosis showed significantly higher QBS values in the femoral neck and shaft than in the normal controls. The values in the predominantly trabecular bone of the lumbar vertebrae were higher in patients with osteoporosis than in normal controls but the difference was not statistically significant. The same results have been previously shown in a smaller number of patients with hyperparathyroidism and in patients with thyrotoxicosis, where QBS values were significantly elevated in the femoral neck and shaft but not significantly in the lumbar spine (*13*). However, the failure to find a significant difference in the lumbar spine in this patient population might also be due to a relatively small number of patients or because of the wide range of normal values with age.

TABLE 1

BMD (g/cm^2 ± s.d.) and QBS (%ID/cc × 10^{-3} ± s.d.) Measurements in Women with Postmenopausal Osteoporosis and with Primary Hyperparathyroidism and Osteoporosis in Comparison to Normal Age-Matched Women

	Postmenopausal osteoporosis	Hyperparathyroidism osteoporosis	Normals	Significance (p)
BMD				
LS	0.88 ± 0.12	0.84 ± 0.11	1.17 ± 0.15	p1 < 0.001*
	n = 39	n = 29	n = 54	p2 < 0.001†
FN	0.68 ± 0.10	0.68 ± 0.09	0.93 ± 0.10	p1 < 0.001
	n = 20	n = 19	n = 54	p2 < 0.001
QBS				
LS	4.59 ± 1.45	4.30 ± 1.52	4.28 ± 1.61	p1, ns
	n = 39	n = 29	n = 54	p2, ns
FN	3.18 ± 1.20	3.57 ± 0.92	2.44 ± 0.71	p1 < 0.01
	n = 20	n = 19	n = 54	p2 < 0.001
FS	2.73 ± 1.06	3.38 ± 1.12	2.14 ± 0.68	p1 < 0.01
	n = 20	n = 19	n = 54	p2 < 0.001

*p1 is significance of comparison between women with postmenopausal osteoporosis and normal population.
†p2 is significance of comparison between women with primary hyperparathyroidism and normal population.
LS = lumbar spine; FN = femoral neck; FS = femoral shaft; n = number of patients.

The reasons why cortical bone shows significantly higher-than-normal bone turnover in patients with osteoporosis while the trabecular bone does not, may also be due to differences in bone cells, particularly osteoclasts in different parts of the body. Therefore, there may be more pronounced uncoupling of formation and loss in the trabecular than the cortical bone with formation not significantly high in the trabecular bone. Since ^{99m}Tc-MDP indicates only bone formation, the increase in QBS values in the trabecular bone is not very large.

CONCLUSIONS

A difference was observed in ^{99m}Tc-MDP uptake in cortical and trabecular bone in normal controls and in patients with osteoporosis. Women with osteoporosis due to HPT or with postmenopausal osteoporosis showed significantly higher QBS values in the femoral neck and shaft than the controls.

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