In Vivo SPECT Quantitation of Bone Metabolism in Hyperparathyroidism and Thyrotoxicosis

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Bone metabolism was assessed in vivo and noninvasively using quantitative SPECT. The effect of endocrine abnormalities on bone metabolism was studied in 27 patients with primary hyperparathyroidism (HPT) and 12 patients with thyrotoxicosis (TTX). Quantitative bone scintigraphy (QBS) values of ^{99m}Tc-MDP uptake were compared to normal values matched for sex and age. Bones with significantly increased QBS values indicating increased bone metabolism were identified in the two patient groups. Fifty-one percent of the bones in patients with HPT and 78% in patients with TTX showed significantly increased QBS values. Increase in bone metabolism was highest in the femoral shaft. Seven patients with HPT and five with TTX were successfully treated. Six patients with HPT and four patients with TTX showed significant decrease of bone metabolism with normal QBS values after three months. The results indicate that QBS can be used to evaluate bone metabolism and its response to treatment in individual bones in patients with endocrine abnormalities.

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Technetium-99m-MDP uptake is a sensitive indicator of bone metabolism (*1–6*). Bone scintigraphy has been used extensively for detection of focal bone abnormalities such as metastases or infection. Generalized abnormalities of bone metabolism necessitate quantitation. The methods that have been used previously (*7–11*) can be affected by uptake in nonosseous tissues and do not provide information on uptake in separate bones, especially those prone to bone loss and fractures. Often there is increased uptake in non-relevant bones such as the skull or sternum. Recently, it has been shown that SPECT can be used for in vivo quantitation of radionuclide uptake in various tissues (*12*). Quantitative SPECT for bone has been validated by phantom studies and the very good correlation between in vivo measurements of uptake in bones and in vitro measurements of samples of the same bones obtained during surgery (*13*). This method enables measurement of the individual bone at risk for osteopenic fractures.

Increased bone metabolism has been reported to cause bone loss and osteopenia in patients with hyperparathyroidism (HPT) and thyrotoxicosis (TTX) (*14–18*). In the present study, the ability of quantitative SPECT to detect abnormalities in bone metabolism in patients with HPT and TTX was evaluated. Quantitative bone scintigraphy (QBS) values in patients were compared with values of normal age- and sex-matched individuals. The effect of treatment of these endocrine abnormalities on bone metabolism also was studied.

MATERIALS AND METHODS

Quantitative Bone Scintigraphy

Quantitative scintigraphy has been previously described in detail (*12,13*) and will be discussed here only briefly. The patient was injected with 20–25 mCi of Tc-MDP and SPECT was performed after 2–4 hr. The amount of Tc-MDP was corrected for decay to the time the study was actually performed. A complete rotation of 360° of the detector, 120 projections, 3° apart with a study time of 20 min was used. About 6×10^6 counts were acquired for each study. Raw data were reconstructed using filtered backprojection with a Hanning filter with a cutoff point of 0.5 cycle/cm. Data were stored on an Elscint SP-1 computer with an optical disk. This 32-bit computer utilized our program for quantitative calculations. After reconstruction, each image was sectioned at 1-pixel (0.68 cm) intervals in the transaxial, coronal, and sagittal planes using a 64×64 byte matrix. For concentration measurements, calculations were performed on the reconstructed data using the threshold method (*12*). A threshold of 43%, which was found to give the smallest error in a wide range of phantom studies, was used to measure radioactivity in the bone (*13*). This threshold is suitable for the range of Tc-MDP concentrations encountered in the present study (*12*). QBS measurements of the ilium and the sacroiliac region, the lumbar and thoracic spine, the femoral neck, and femoral shaft were performed as reported previously (*13*). Counts/voxel were converted to concentration units (μCi/cc) and then to percent of injected dose per cc (%ID/cc) using the identity line of counts/voxel and μCi/cc (*12*).

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Patients

Normal data have been obtained in 240 individuals who had no clinical, laboratory, radiologic, or scintigraphic evidence of bone disease. These individuals were classified according to sex and age groups with increments of 10 yr. Two groups of patients had QBS measurements. One group included patients with primary HPT and the other included patients with TTX. All patients had normal renal function. Twenty-seven patients with clinical and laboratory evidence for primary HPT were investigated. There were 10 men and 17 women, aged 28 to 79 yr (mean age 56 yr). Seven of the patients in this group had surgery to remove a hyperfunctioning adenoma. All patients had a repeat study at 3 mo after surgery. Twelve patients with newly diagnosed or recurrent TTX were also investigated. There were three men and nine women, aged 26 to 74 yr (mean age 39 yr). All patients had Graves' disease with typical clinical and laboratory findings. Five patients had repeat SPECT studies 3 mo after their thyroid function tests returned to normal following treatment.

QBS values of the ilium, sacroiliac region, lumbar and thoracic spine, and the femoral neck and shaft in the patients with HPT and TTX were compared with the values obtained in measurements of normal controls matched for sex and age using a t-test. QBS values in patients were also analyzed as % increment/decrement from the mean values in normals using the equation:

$$\frac{QBSP - QBSN}{QBSP} \times 100,$$

where QBSP = QBS value in patients and QBSN = QBS value in normals.

The age- and sex-matched normals of the same control population were used for comparison of both patient groups.

QBS values in the seven patients with HPT were compared after surgery with the values in the same patients before surgery using the paired t-test. QBS values in the five patients who became euthyroid also were compared with the measurements before treatment using the same test. The changes in QBS induced by surgical removal of the parathyroid adenoma or treatment of TTX were also expressed as % increment/decrement from the baseline study using the equation:

$$\frac{QBS2 - QBS1}{QBS1} \times 100,$$

where QBS2 = QBS value after treatment and QBS1 = QBS value before treatment.

Changes were considered significant if they were beyond the 95% limit of confidence established for each bone (*19*).

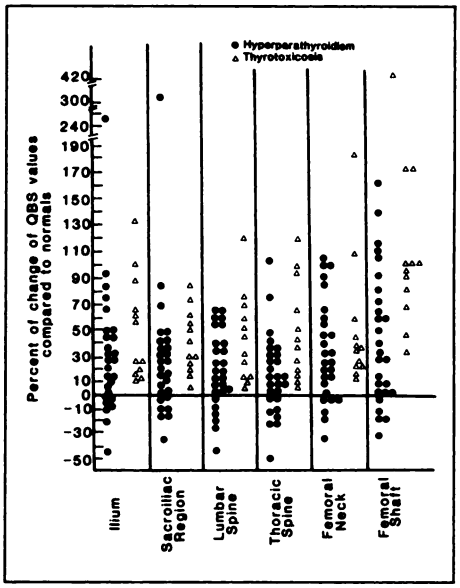

FIGURE 1. Percent change QBS values in 27 patients with HPT and 12 patients with TTX as compared with normals.

RESULTS

Patients with primary HPT, as a group, had significantly higher QBS values in the ilium, sacroiliac region, femoral neck, and femoral shaft as compared to their sex- and age-matched controls (Table 1). Fifty-one percent of the measured bones in all patients showed significantly increased

TABLE 1
Comparison of QBS Values (%ID/cc × 10^{-3}) in 27 Patients with Primary HPT and Normal Controls Matched for Age and Sex

	Ilium	Sacroiliac	Lumbar spine	Thoracic spine	Femoral neck	Femoral shaft
HPT						
mean ± s.d.	7.97 ± 3.78	6.87 ± 3.98	5.49 ± 1.45	6.69 ± 1.69	4.24 ± 1.30	3.84 ± 1.35
n	27	27	27	27	27	27
Normal: age- and sex-matched						
mean ± s.d.	6.03 ± 2.28	5.11 ± 1.77	4.81 ± 1.94	5.79 ± 2.38	3.18 ± 1.44	2.68 ± 1.17
n	42	41	41	33	37	33
Significance (p)	<0.01	<0.02	ns*	ns	<0.01	<0.001
Average percent change (%)	31	29	19	14	33	44
Patients with significantly increased QBS						
n	16	14	12	11	14	15

* Not significant.

TABLE 2
Comparison of Baseline (Study 1) QBS Measurements (%ID/cc × 10^{-3}) in Seven Patients with Primary HPT at 3 Months After Surgical Removal of Parathyroid Adenoma (Study 2)

Patient no.	Sex/Age	Ilium	Sacro-iliac	Lumbar spine	Thoracic spine	Femoral neck	Femoral shaft	Significance (p)
1	F 60 yr							
	Study 1	9.6	7.3	5.4	6.9	5.2	4.6	<0.01
	Study 2	4.6	4.1	4.3	4.5	2.7	2.2	
2	M 28 yr							
	Study 1	24.3	25.7	8.6	10.3	6.3	5.8	<0.05
	Study 2	5.1	5.3	3.2	3.8	2.1	2.6	
3	F 52 yr							
	Study 1	7.4	5.8	4.5	6.5	4.8	4.2	<0.01
	Study 2	4.1	4.3	3.7	4.8	2.3	3.0	
4	M 47 yr							
	Study 1	6.1	7.3	6.6	8.2	3.8	2.4	ns
	Study 2	6.6	7.0	7.6	8.2	3.3	2.3	
5	M 70 yr							
	Study 1	6.9	4.7	4.9	6.7	4.0	3.8	<0.01
	Study 2	5.2	3.5	4.1	4.2	2.9	2.3	
6	M 38 yr							
	Study 1	4.4	4.0	2.5	3.3	1.7	1.5	<0.05
	Study 2	3.2	3.0	2.2	2.8	1.5	1.5	
7	M 60 yr							
	Study 1	9.9	8.6	6.4	7.8	5.2	4.8	<0.01
	Study 2	5.7	4.9	4.0	5.7	3.4	3.2	

QBS values: 16 out of 27 (59%) in the ilium, 14 (52%) in the sacroiliac region, 12 (44%) in the lumbar spine, 11 (41%) in the thoracic spine, 14 (52%) in the femoral neck, and 15 (56%) in the femoral shaft (Table 1, Fig. 1). The mean percent of change from the mean normal values in patients with HPT varied between 14% in the thoracic spine to 44% in the femoral shaft (Table 1). At 3 mo after surgery for parathyroid adenoma removal, there was a significant decrease in QBS values in six patients who had high values before operation (Table 2, Fig. 2). In one patient, QBS did not change after surgery (Patient 4, Table 2, Fig. 2). In all patients, QBS values at 3 mo after surgery were not significantly different from the normal population.

Patients with TTX as a group had significantly higher QBS values in the ilium, sacroiliac region, lumbar and thoracic spine, and the femoral shaft. Seventy-eight percent of the bones measured in all patients had significantly increased QBS values: 10 out of 12 (83%) in the ilium and sacroiliac region, 9 (75%) in the lumbar and thoracic spine, 6 (50%) in the femoral neck, and 12 (100%) in the femoral shaft (Table 3, Fig. 1). The mean percent of change from normal varied in individual bones between 40% in the sacroiliac region to 123% in the femoral shaft (Table 3, Fig. 1). Five patients had repeat QBS measurements 3 mo after successful treatment of TTX. There was a significant decrease in QBS values in all bones in four patients compared to the baseline pretreatment study (Table 4, Fig. 3). QBS values after treatment of TTX were not significantly different from the normal control group.

TABLE 3
Comparison of QBS Values (%ID/cc × 10^{-3}) in 12 Patients with TTX and Normal Controls Matched for Age and Sex

	Ilium	Sacroiliac	Lumbar spine	Thoracic spine	Femoral neck	Femoral shaft
TTX						
mean ± s.d.	9.71 ± 2.55	7.87 ± 1.74	7.21 ± 1.90	8.42 ± 2.24	4.87 ± 1.40	5.07 ± 2.34
n	12	12	12	12	12	12
Normal age- and sex-match						
mean ± s.d.	6.84 ± 1.95	6.35 ± 2.05	5.31 ± 2.05	5.99 ± 1.89	3.90 ± 1.57	2.74 ± 1.23
n	16	16	15	14	13	13
Significance (p)	<0.01	<0.05	<0.05	<0.01	ns	<0.001
Average percent change (%)	49	40	45	48	49	123
Patients with significantly increased QBS (n)	10	10	9	9	6	12

TABLE 4
Comparison of Baseline (Study 1) QBS Measurements (%ID/cc × 10^{-3}) in 5 Patients with TTX and at 3 Months After Treatment (Study 2)

Patient no.	Age/Sex	Ilium	Sacro iliac	Lumbar Spine	Thoracic Spine	Femoral Neck	Femoral Shaft	Significance (p)
1	F 35 yr							
	Study 1	10.8	8.5	8.4	9.3	4.3	3.9	<0.001
	Study 2	6.1	5.0	4.4	5.7	2.1	2.2	
2	F 74 yr							
	Study 1	13.3	9.5	11.7	13.0	5.8	6.2	<0.001
	Study 2	6.4	4.5	6.9	4.5	2.1	2.0	
3	F 49 yr							
	Study 1	7.6	6.1	6.1	9.3	4.1	2.9	ns
	Study 2	8.0	6.3	6.1	7.0	3.2	2.4	
4	F 31 yr							
	Study 1	6.2	6.9	5.5	5.4	4.1	3.6	<0.001
	Study 2	3.9	4.0	3.0	3.1	1.9	1.3	
5	M 27 yr							
	Study 1	14.0	10.1	8.1	10.1	4.4	4.2	<0.001
	Study 2	5.9	5.1	4.1	5.0	1.6	1.1	

DISCUSSION

Technetium-99m MDP uptake is an indicator of bone metabolism (*1–6*). Both phantom studies and in vivo/in vitro comparison studies show quantitative SPECT to be an accurate technique for measuring Tc-MDP uptake (*13*). The technique showed very small interobserver variability and very high repeatability in studies performed at different times in the same patient (*13*). The technique can therefore be used to monitor bone metabolism in individual bones in patients with endocrine abnormalities. Histomorphometric analysis which necessitates bone biopsy is invasive and cannot be used routinely. A recent study on histomorphometry in 11 patients with HPT before and after treatment shows complete agreement with our findings (*20*). Long-term high bone turnover in adult bones may cause mineral loss and osteopenia, and this should be a consideration in patient management. As a rule, bone metabolism is not routinely evaluated in patients with HPT and TTX, although it is well established that these diseases may sometimes cause osteopenia (*14–18,21,22*). It is now becoming evident that even replacement therapy hypothyroidism may cause excessive bone loss (*23,24*).

Fifty-one percent of all measured bones in patients with HPT in the present study showed increased bone turnover when compared with a normal population. Since the incidence of primary HPT is now believed to be one to two cases per thousand per year (*25*), the contribution of HPT to osteopenia in the general population may be important. In TTX, the problem appears to be even more significant, and this correlates with data indicating long-standing osteopenia increased thyroid function (*16,17,21–26*). All the patients with TTX in our study showed varying degrees of high bone turnover (Fig. 1, Table 3), although not all increases in bone turnover were significant. The femoral

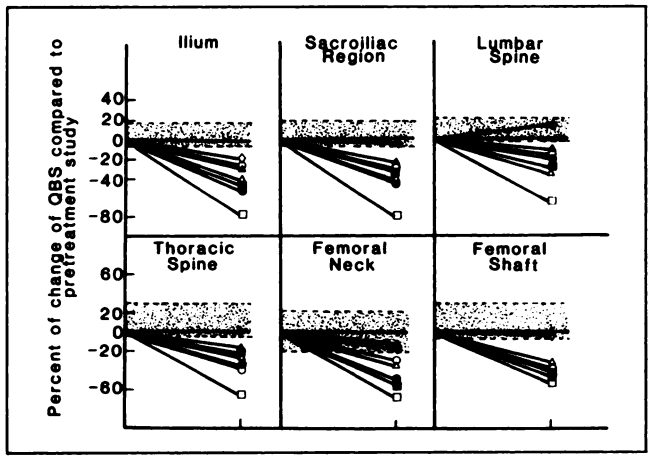

FIGURE 2. Percent of change of QBS values after removal of parathyroid adenoma in seven patients with HPT. The dotted lines and shaded areas represent 95% confidence of repeatability of the test.

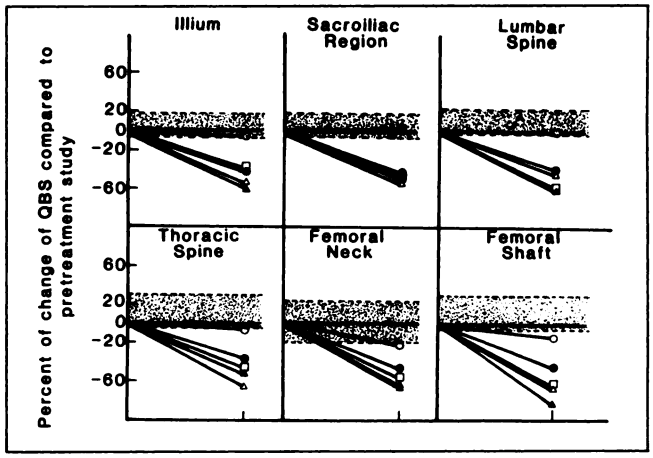

FIGURE 3. Percent change of QBS values after treatment of TTX in five patients. The dotted lines and shaded areas represent 95% confidence of repeatability of the test.

shaft was the region of the skeleton most affected by the disease. This is a surprising finding since the femoral shaft consists of cortical bone that is metabolically less active.

Treatment of both HPT and TTX in our patients resulted in significant decreases in bone metabolism (Figs. 2 and 3 and Tables 2 and 4) and the return of QBS values to normal. It indicates that the treatment of the primary endocrine abnormality affects bone metabolism, which returns to normal within 3 mo after successful treatment.

Presently, bone loss can be demonstrated by bone densitometry (*26*). This technique, however, shows only the end result of high bone metabolism. Increased bone metabolism detected by quantitative SPECT should be a consideration in the management of patients with HPT and TTX.

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