Bone mineral changes in primary hyperparathyroidism

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Abstract. We studied 34 patients with primary hyperparathyroidism in order to assess their bone mineral status, to determine its relationship to biochemical parameters (serum calcium and parathyroid hormone) and surgical status, and to determine the relationship between peripheral cortical bone and spinal trabecular bone in this disease. These patients were studied with radiogrammetry of the metacarpals, Norland-Cameron photon absorptiometry of the radius, quantitative computed tomography (QCT) of the spine, industrial radiography of the hands, and conventional radiography of the thoracolumbar spine. We also calculated a spinal fracture index from thoracolumbar spine films. We found that the appendicular measurements correlated well together, but less well with spinal QCT. The spinal fracture index correlated best with QCT (r = -0.55), although significant dispersion was noted. We found that, in general, these hyperparathyroid patients had statistically significant decrements in bone mineral content in both the appendicular and the axial portions of the skeleton. However, the decrement in the appendicular skeleton did not correlate well with that in the axial skeleton. Therefore we conclude that it is necessary to measure both peripheral and central bone mineral content in order to reliably assess the skeletal demineralizing effects of primary hyperparathyroidism in an individual patient.

Key words: Hyperparathyroidism, primary – Bone mineral analysis – Quantitative computed tomography – Radiogrammetry, metacarpal – Norland-Cameron photon absorptiometry

With the widespread use of automated techniques for measuring serum calcium and parathyroid hormone levels, primary hyperparathyroidism is now usually diagnosed by laboratory means. The detection of the skeletal changes in this disease by conventional radiography has become diagnostically less important [13, 21, 36, 48]. Since evidence of demineralization by conventional radiography requires a loss of bone mineral of 25 to 60% [12, 17, 27, 52], it is not surprising that such abnormalities are now infrequently observed. Nevertheless, routine iliac crest biopsies have shown bone abnormalities in most cases of primary hyperparathyroidism [3, 27, 38].

Several methods have been used to measure bone mineral changes in primary hyperparathyroidism. These include radiogrammetry of the metacarpals [1, 22, 28, 43], photon absorptiometry of the forearm and phalanges [13, 21, 22, 41, 44, 51, 58], total body neutron activation analysis [7, 8, 30], X-ray spectrophotometry of the spine [9], gamma-ray computed tomography of the forearm [11, 53], and recently, X-ray quantitative computed tomography of the radius [32].

Data on quantitative spinal mineral content in primary hyperparathyroidism have been limited [5, 46, 56], and studies have shown variable results when comparisons between cortical and trabecular bone mass have been made. We have used quantitative computed tomography (QCT) of the spine and standard peripheral cortical bone measurements to determine the relationship between peripheral cortical and spinal trabecular bone mass in patients with primary hyperparathyroidism. We have also studied the relationship between bone mineral content, biochemical parameters (serum calcium and parathyroid hormone), and surgical status.

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Materials and methods

Thirty-four patients with primary hyperparathyroidism were studied. Of these, six were male with an average age of 61 years, and 28 were female with an average age of 59 years. All but three of the females were 50 years of age or older. All patients had increased serum parathyroid hormone levels on more than one examination. All but three patients had elevated serum calcium levels. However, these three patients had been treated with oral phosphate therapy with resulting normalization of their serum and urine calcium levels. To date, 17 of 34 patients have undergone parathyroidectomy, which has demonstrated single adenomas in 15 patients and parathyroid hyperplasia in two patients.

Bone mineral analyses included industrial radiographs of the hands, measurement of combined cortical thickness of the second metacarpal, conventional radiography of the lateral thoracolumbar spine, Norland-Cameron single photon absorptiometry of the radial diaphysis and distal metaphysis, and QCT of the lumbar spine.

Radiographic examinations

The presence of subperiosteal resorption (Fig. 1), intracortical resorption (tunnelling) (Fig. 2), generalized osteopenia, and juxta-articular osteopenia was evaluated on the industrial radiographs using optical magnification (4 x). The findings were graded: 0 - normal; 1/2 - equivocal; 1 - mild; 2 - moderate; and 3 - severe. Generalized osteopenia on the lateral thoracolumbar spine films was graded by the same scale. A fracture index (FXI) was then calculated (as previously reported [26, 45]) for the thoracolumbar spine in the following manner: each vertebral body between T3 and L5 was graded as to the degree of compression fracture present using the same scoring system as for osteopenia (Fig. 3). The score for each vertebral body was then summed and added to the generalized spinal osteopenia score to yield the FXI. This semiquantitative FXI can range from 0 for a normal spine to 48 for a severely osteopenic spine with severe compression fractures in all vertebral bodies between T3 and L5. All radiographic examinations were interpreted by the same observer.

Quantitative bone mineral analyses

Norland-Cameron single photon absorptiometry [6] was used to measure the mineral content (g/cm) of the right and left radius in two locations: the radial diaphysis at the junction of its middle and distal thirds (NCD) (>95% cortical bone), and the distal radial metaphysis (NCM) (roughly 75% cortical and 25% trabecular bone in normal patients) [55]. NCD measurements were obtained on only 32 patients. The NCD and NCM measurements were then divided by bone width at each site to yield size-corrected measurements, NCDW and NCMW (g/cm²), which were then compared with published normal values [40]. The ratio of these two new measurements was then calculated for each patient (NCDW/NCMW) [29]. Normal values for this ratio were calculated by dividing those for NCDW by those for NCMW.

The combined cortical thickness (CCT) of the right and left second metacarpals was measured on industrial radiographs of the hands. These measurements were taken at the midpoint of the metacarpal and the values for each side were then averaged to yield one measurement for each patient. These values were expressed in millimeters and compared with published normal values [16, 20].

The vertebral cancellous mineral of the first and second lumbar vertebrae was measured using a modified General Electro-nuclear Corporation (GEC) QCT/T 7800 scanner (Fig. 4). The details of this method of quantitative computed tomography (QCT) were described elsewhere [4, 18, 28]. For age and sex-matched normal values, we used our own normal subjects, which included 120 males ranging in age from 18 to 80 years and 203 females ranging in age from 19 to 77 years. None of these controls had evidence of metabolic bone disease [5].

Data analysis

A Spearman nonparametric correlation matrix was calculated for QCT, CCT, NCDW, NCMW, and NCDW/NCMW. A similar matrix was calculated for serum calcium and parathyroid hormone levels versus CT, CCT, NCDW, NCMW, and NCDW/NCMW. An unpaired t-test was used to assess whether any significant difference existed between the serum calcium, serum parathyroid hormone, QCT, CCT, NCDW, NCMW, or NCDW/NCMW of the surgical patients and those of the non-surgical patients. A paired t-test was used to compare the QCT, CCT, NCDW, NCMW, and NCDW/NCMW values for each patient with those of their age and sex matched controls. Z-scores were calculated as follows: the observed value in a patient minus the age and sex-matched normal value divided by the standard deviation for age and sex. The methods used in the Statistical Analysis System [54] were used to carry out all statistical computations.

Results

The mean serum calcium at the time of the bone mineral studies was 11.2 mg/dl (11.8 mg/dl in the surgically treated group and 10.8 mg/dl in the non-surgical group). The calcium levels for these two groups are shown graphically in Fig. 5, and were statistically different at the p < 0.0001 level. Among surgical patients, two patients had values in the normal range and had parathyroid hyperplasia at surgery. Among nonsurgical patients, all had elevated parathyroid hormone levels on more than one examination. No statistically significant difference was noted between the parathyroid hormone levels of the surgical and the non-surgical patients.

Radiographic findings

The industrial radiographs of the hands showed mild subperiosteal resorption in seven cases (Fig. 6). Intracortical resorption (tunnelling) was seen in 21 cases. The grade was mild in nine of the cases, moderate in nine, and severe in three. Generalized osteopenia and juxta-articular osteopenia were seen in most patients (24 and 29 respectively), principally of a mild to moderate degree. There was no evidence of cystic erosions or brown tumors.

The radiographs of the thoracolumbar spine qualitatively showed a mild grade of osteopenia in eight patients and a moderate grade in 13. No case showed severe osteopenia. Fifty-four vertebral compressions were seen in 18 patients. The com-