Cortical bone mineral content in primary hyperparathyroidism. Changes after parathyroidectomy

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Abstract. The bone mineral content (BMC) of 35 patients with primary hyperparathyroidism (PHPT) was measured at the mid radius (95% cortical bone) by photon absorptiometry of a $^{241}$Am source. The majority of the patients had an overt disease of moderate to severe degree. Average serum calcium of the group was 12.3 mg/100 ml (range 10.6 to 18.0 mg/100 ml). The percentage of normality of the BMC was (Av ± 1 sd) 75.1 ± 13.0% for the whole group.

The average increment of BMC in 14 patients 9 to 26 months after parathyroidectomy was 9.9%, with a wide dispersion. However a highly significant negative correlation ($r$: 0.83; $P < 0.01$) was found between the initial bone mass and the percentage increment per month after surgery. No further gain was observed 2 years after parathyroidectomy except in one patient with an extremely severe bone loss. In spite of the gain obtained after surgery the bone mass remained markedly diminished in most patients showing that the cortical bone loss caused by PHPT is mainly irreversible.

Bone loss is a well known complication of primary hyperparathyroidism (PHPT). However conventional radiological means of assessment are insensitive and cannot quantify the changes that occur after parathyroidectomy. The non-invasive techniques for the measurement of bone mineral content (BMC) are useful tools for the above mentioned estimation. Two different approaches have been used up to the present time: photon absorptiometry to assess the BMC at different skeletal sites (Forland et al. 1968; Pak et al. 1975; Dalén & Hjern 1974; Tougaard et al. 1977; Ringe et al. 1980; Leppla et al. 1982; Seeman et al. 1982; Kleerekoper et al. 1983) and neutron activation analysis to measure the total body calcium content (Hosking et al. 1972; Cohn et al. 1973; Jiménez et al. 1984). Different results have been obtained regarding the extent of the bone loss before surgery and its recovery after parathyroidectomy.

In the present report the cortical BMC of a group of patients with relatively severe PHPT has been determined before and after surgery by photon absorptiometry. The recovery after parathyroidectomy was directly related to the extent of the bone loss before surgery.

Patients and Methods

Thirty-five Caucasian patients (12 men, mean age 45 years; 23 women mean age 50 years) were studied. Average age of the whole group was 48 years with a range from 18 to 82 years. The symptoms that led to the study of the patients were the following: renal stones: 17 patients; skeletal symptoms: 5 patients; both symptoms: 5 patients; neonatal hypocalcaemia in one son: 1 patient; non-specific reasons: 9 patients. Paget's bone disease was associated in 2 patients. Creatinine clearance was above 40 ml/min in all patients. Radiological examination of hands or clavicles disclosed the presence of subperiosteal resorption in 10 patients. The films of the other patients were read as normal. The determination of the serum levels of calcium, phosphate and parathyroid hormone (PTH) was broadly typical of PHPT. Calcium was measured by atomic absorption spectrophotometry. Serum PTH was determined employing an antisera that recognizes the C-terminal
and the mid portion of the hormone molecule. The cortical BMC was measured in all patients at the distal third of the radius of the non-dominant arm by $^{241}$Am absorptiometry. Each reading represented the mean value of 4 to 6 consecutive determinations. The coefficient of variation of ten independent readings made on the same subject during a 1 year period was 1.9% for the BMC and 1.4% for the BMC/width ratio (Mautalen et al. 1984). The results obtained were referred to the values of our normal population (Mautalen et al. 1984) to obtain the percentage of normality.

The BMC was assessed before and at different times after parathyroidectomy in 14 of the 35 mentioned patients. The duration of the follow-up evaluation after surgery varied among the patients with an average of 20.4 months (range 9 to 26). In 4 patients measurements were moreover obtained at 26 to 55 months after successful parathyroidectomy.

The fractional change from the value obtained before parathyroidectomy (time zero) was calculated as the difference in BMC/width at time t and time zero divided by the value at time zero.

## Results

Serum values (Av ± 1 SD) of the whole group were as follows: calcium: 12.35 ± 1.46 mg/100 ml (range 10.6 to 18.0 mg/100 ml) (normal values: 8.9 to 10.4 mg/100 ml); phosphate: 2.46 ± 0.71 mg/100 ml (range 1.5 to 4.6 mg%) (normal values: 2.8 to 4.6 mg/100 ml) and PTH: 1012 ± 567 pg/ml (range 400 to 2400 pg/ml) (normal values: 50 to 450 pg/ml).

Fig. 1 shows the cortical BMC for 35 patients with PHPT. Only 9 cases were within the normal range but below the mean for corresponding sex and age. The (Av ± 1 SD) percentage of normality was 75.1 ± 13.0%. The loss of bone mass was greater in women than in men but the difference was not statistically significant. Results were as follows: women 72.6 ± 12.5%; men 79.9 ± 12.5%; the decrease of the BMC was however significantly greater in 14 post-menopausal compared with 9 pre-menopausal women (67.8 ± 11.2% vs 80.0 ± 10.8%, $P < 0.05$). No significant correlations were found between bone mass and serum PTH or serum calcium levels.

The average bone mass in 14 patients after parathyroidectomy increased from 511 ± 30 mg/cm² to 553 ± 25 mg/cm² ($P < 0.01$) with a marked dispersion from +114 mg/cm² to −11 mg/cm². However when the results were expressed as the percentage change per month after parathyroidectomy and correlated with the bone mass at time zero a highly significant negative correlation was found between these two variables ($r$: −0.83; $P < 0.01$) (Fig. 2). The increment per month after surgery was 0.62 ± 0.67 in percentage values and 2.66 ± 2.53 μg/cm² in absolute values.

In spite of the above mentioned increment, the
bone mass was still markedly decreased in the majority of the patients (Fig. 1) since only a portion of the initial deficit was repaired. The values in percentage of normality was as follows: time zero 71.9 ± 18.8% and at the time of the last measurement (average 20 months after surgery) 78.0 ± 10.1% ($P < 0.01$).

The measurement made on 4 patients from 24 to 55 months after surgery revealed no changes or minor losses in 3 patients, meanwhile one patient still gained 9.5% of bone mass during the third year after parathyroidectomy. It is important to mention that this was the patient with the greatest bone loss of the whole group. The percentage of normality rose from 40.8% at the initial determination up to 62.7% 35 months after surgery.

**Discussion**

The results obtained in patients with PHPT showed a significant cortical bone loss in both sexes although the deficit was greater in postmenopausal women. These results differ from those reported by Pak et al. (1975) who found that the skeleton was not affected in men and premenopausal women with PHPT.

The average cortical BMC loss found in the present study (± 25%) was similar to the 20% diminution found by Ringe et al. (1980) in a group of 46 patients (35 women and 11 men) in Germany. The deficit was markedly less in studies made in the USA (Leppla et al. 1980; Seeman et al. 1982; Kleerekoper et al. 1983). In the last mentioned study the investigators found an average loss of 14.6% in 115 women with a median age of 57 years, markedly less than the average of 27.4% in 23 women, median age 50 years, of the present study. The difference is most likely due to the delay in making the diagnosis and to the failure to detect the asymptomatic patients with PHPT in our community.

In opposition to the relative agreement observed in the studies that had evaluated cortical bone mass in PHPT patients, the measurements of the total body calcium have been somewhat contradictory, specially regarding the changes that occur after parathyroidectomy (Hosking et al. 1972; Cohn et al. 1973; Jiménez et al. 1984). The discrepancy could be due to technical reasons or due the fact that the cortical bone measurement is more sensitive to small changes than the total body calcium.

Another point that deserves further investigation is the effect of PHPT on trabecular bone mass. The exogenous administration of parathyroid hormone has been reported to increase trabecular bone mass (Reeve et al. 1980) and vertebral osteosclerosis was found in some patients with primary (Connor et al. 1973; Genant et al. 1975) or secondary (Campos et al. 1976) hyperparathyroidism. Charhon et al. (1982) and Marcus et al. (1984) on iliac crest biopsies in patients with PHPT found that the trabecular bone volumen was similar to the values predicted in the controls. However, Seeman et al. (1982) using dual photon absorptiometry reported that the BMC in patients with PHPT was lower in trabecular than in cortical bone sites.

We have observed an average increase of 9.9% on the cortical BMC in 14 patients 20 months after parathyroidectomy. The range of the recovery was wide since it was directly related to the extent of the bone loss found before surgery ($r$: 0.83; $P < 0.01$). The gain observed was somewhat greater than that found by Leppla et al. (1982) – 6.4% – or Ringe et al. (1980) – 5.1% – consistently with the greater extent of the bone loss found in our patients before surgery. The recovery that could be accomplished was completed within 2 years after parathyroidectomy in all cases except some exceptionally severely affected patients with PHPT. In spite of this recovery the cortical BMC was still significantly diminished in the patients studied. The excessive
levels of parathyroid hormone cause an increased tunnelization of the cortical bone that is reversible but also enhance the endosteal resorption of the cortex. This thinning of the cortex is largely irreversible and accounts for the failure to regain a normal BMC after healing of the PHPT.

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References

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