Increased fracture risk in hypercalcemia

Bone mineral content measured in hyperparathyroidism

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In the present study, 39 women with mild hypercalcemia, which had been detected 18 years earlier during a health survey, and presumably caused by primary hyperparathyroidism (HPT), were investigated together with 34 age-matched controls. The bone mineral content (BMC) of the nondominant distal forearm was measured by single-photon absorptiometry, and the occurrence of fractures was recorded.

Among women up to the age of 70 years, those with hypercalcemia had lower BMC than the controls ($P < 0.05$), whereas among the older women, there was no difference. Twelve of the women with probable primary HPT had suffered a distal radius fracture as compared with 3 of the controls ($P < 0.05$).

Thus, also mild hypercalcemia is a risk factor for bone loss and distal forearm fractures. The findings constitute arguments in favor of early detection and treatment of primary HPT.

Primary hyperparathyroidism (HPT) is a common disorder. Because many patients only have mild hypercalcemia and do not develop clinical symptoms, there is no uniform opinion as to the optimal management of this disease.

We have investigated bone mineral content (BMC) and the incidence of fractures in patients with mild hypercalcemia and presumably primary HPT, which was originally detected in a health survey 18 years earlier.

Materials and methods

On two separate occasions in 1969 and 1970, and in 1971, all the men and women 25 years and older living in a central district in the city of Gävle, Sweden, were invited to attend a health screening. At both events, 16,401 individuals, or 68 percent of the original population, were examined (Palmér et al. 1988). In retrospect, 176 persons with serum calcium levels exceeding 2.60 mmol/L in both examinations were identified. For 172 of them, 146 women and 26 men, no other cause for elevated serum calcium levels was established, and therefore they were considered to have primary HPT. For the present study, 39 women who were still alive and eligible were summoned together with 34 normocalcemic controls from the health survey. The mean age in both groups was 68 years (52–82).

At the present examination, all the participants replied to a questionnaire concerning fractures, medication, smoking, pregnancies, and menstruations. Blood samples were taken for measurement of serum concentration of calcium, phosphate, alkaline phosphatase, and creatinine, as well as for parathyroid hormone (PTH) and vitamin D metabolites.

The patients and controls were comparable regarding body mass index, smoking, parity, fertile years, and the number of years after menopause that the examination was performed.

The groups differed in serum calcium (2.58 ± 0.11 [SD] mmol/L vs. 2.43 ± 0.07 mmol/L, $P < 0.0001$) and PTH (0.85 ± 0.19 U/L vs. 0.79 ± 0.12 U/L, $P < 0.05$), but not in other laboratory values.

Twenty probands had virtually all previous serum calcium values above 2.60 mmol/L, whereas 19 only had displayed intermittent elevation of serum calcium.

BMC in the distal radius was measured with single-photon absorptiometry. The scanner used was ND 1100 A. This equipment makes 10 scans of the distal forearm using the point where the space between the radius and ulna is 8 mm as a standard for scan number 5 (no. 1 being the most distal scan). Scans nos. 1–4 (in-

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terval width 2 mm) were used to calculate distal BMC (D-BMC) and scans nos. 5–10 (interval width 4 mm) proximal BMC (P-BMC). The measurements of 1 patient and 1 control were technically unsatisfactory, and could not be used.

The Student's *t*-test and the Mann-Whitney test were used for the statistical evaluation.

Results

For both probands and controls, there was an inverse relationship between the BMC values and age (Figure 1). This was most evident in the control group (Table 1).

In the entire material, regardless of age, there was no difference for BMC in the distal radius among the women with hypercalcemia and the controls (Table 1). When age was taken into account and the values analyzed separately for subjects below the age of 70, it turned out that the probands had lower proximal BMC measurements.

Twelve of the probands had suffered at least one distal radius fracture compared with three in the control group ($P < 0.05$). The probands who had suffered a distal radius fracture had lower BMC (Table 1) and higher PTH values (0.91 ±0.09 U/L as compared to 0.82±0.14 U/L; $P < 0,05$) than those who had not had a fracture, but there was no difference in serum calcium or alkaline phosphatase.

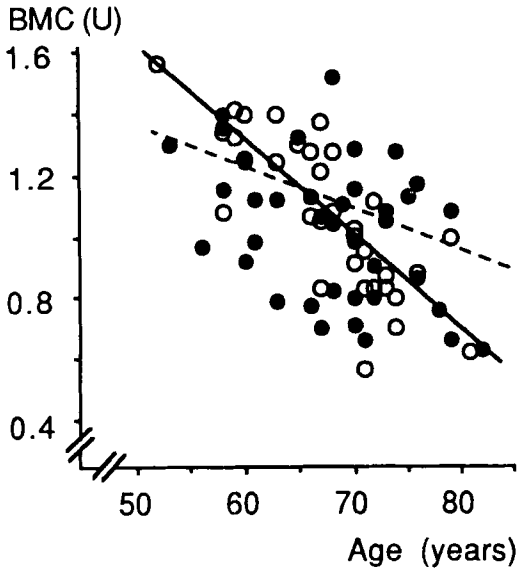

Figure 1. Proximal bone mineral content (BMC) of the forearm in relation to age in females with mild primary HPT (sold symbols, *r* 0.41) and controls (open symbols, *r* 0.80).

Table 1. Values for proximal (P) and distal (D) bone-mineral content (BMC) of the forearm in female patients with mild primary HPT and age-matched controls. (Mean, *SD*)

	HPT patients		Controls	
	P-BMC (U)	D-BMC (U)	P-BMC (U)	D-BMC (U)
All women	1.01 *0.23* n 38	0.71 *0.17*	1.06 *0.25* n33	0.76 *0.17*
≤aged 70	1.06 *0.22*[a] n25	0.75 *0.17*	1.20 *0.19* n21	0.83 *0.15*
>aged 70	0.92 *0.22* n13	0.64 *0.15*	0.82 *0.15* n12	0.62 *0.10*
fracture	0.87 *0.16*[b] n12	0.62 *0.12*[c]		
no fracture	1.08 *0.23* n26	0.75 *0.17*		

[a] $P < 0.05$ compared with age matched controls (Student's *t*-test).
[b] $P < 0.01$ compared with nonfractured patients (Mann-Whitney).
[c] $P < 0.05$ compared with nonfractured patients (Mann-Whitney).

When the probands were separated into two groups, one with virtually constant and the other with intermittent hypercalcemia, there were differences for the current values of serum calcium (2.64 ± 0.10 mmol/L and 2.51 ±0.08 mmol/L, $P < 0.01$), and also for 25(OH)-vitamin D (54 ±27 µg/L and 16 ±6 µg/L; $P < 0.01$). No differences were found for $1,25(OH)_2$-vitamin D, BMC, fractures, or PTH.

Discussion

Bone disease is a classical complication of severe primary HPT (Peacock et al. 1984, Devogelaer et al. 1984).

The present study material includes individuals with mild hypercalcemia without apparent symptoms, who were detected in a health survey 18 years ago; no patient had any other obvious cause for their hypercalcemia. Previous studies have shown that the vast majority of such patients have primary HPT.

The subgroup of patients with constant hypercalcemia had higher values of 25(OH)-vitamin D as compared with those with intermittent hypercalcemia. A low vitamin D intake thus might conceal mild primary HPT.

Together with the knowledge that BMC can increase after parathyroidectomy (Mautalen et al. 1986, Martin et al. 1986), our findings argue in favor of early detection and treatment also in women with mild primary HPT.

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