Circulating PTH, Vitamin D and IGF-I Levels in Relation to Bone Mineral Density in Elderly Women*

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Abstract. Age and reduced bone mineral density (BMD) represent major risk factors for vertebral fracture risk, especially in post-menopausal women, and measurement of BMD is currently considered of value in estimating bone mineralization. BMD correlates with demographics and anthropometric parameters, as well as with several markers of bone metabolism and calcium-regulating hormones, such as leptin, osteoprotegerin, parathyroid hormone (PTH), vitamin D, insulin-like growth factor-I (IGF-I) and sex steroid hormones. The aim of this study was to evaluate the relationship between PTH, 25(OH) vitamin D [25(OH)D], IGF-I and BMD in a selected group of elderly women. Thirty-one post-menopausal women over the age of 65, who were not estrogen, vitamin D or bisphosphonate users and did not have a history of fracture, bone disease or malignancy, were prospectively enrolled in the study. All the patients underwent lumbar spine dual-energy x-ray absorptiometry (DXA) and serum calcium, creatinine, PTH, 25(OH)D and IGF-I measurements. As expected, a weakly-inverse correlation between age and 25(OH)D (R=–0.50, p=0.020), and between BMD and PTH (R=–0.48, p=0.027) was found. There was a strong relationship between IGF-I and BMD (R=0.64, p=0.0016), and between age and IGF-I (R=–0.70, p<0.001), while IGF-I did not correlate with 25(OH)D (R=–0.16, p=0.48) or BMI (R=–0.089, p=0.70). In conclusion, in this selected group of elderly women, we found a strong relationship of increased bone resorption, expressed as BMD, to calcium-regulating hormones PTH and IGF-I, while 25(OH)D and BMI seem to be independent of bone mineralization status.

Secondary hyperparathyroidism (HPT) is a frequent condition in elderly women that may lead to increased bone resorption. Secondary HPT may also affect up to 50% of patients who underwent successful kidney transplantation, representing the most frequent cause of hypercalcemia in the transplant recipient (1, 2). Age and reduced bone mineral density (BMD) represent major risk factors for vertebral fracture risk, especially in post-menopausal women and measurement of BMD is currently considered of value in estimating bone mineralization (3). BMD correlates with demographics (i.e., age and gender) and anthropometric parameters, such as weight, height and body mass index (BMI), as well as with several markers of bone metabolism and calcium-regulating hormones, such as leptin, osteoprotegerin, parathyroid hormone (PTH), vitamin D, insulin-like growth factor-I (IGF-I) and sex steroid hormones (4-7).

The aim of this study was to investigate the relationship between serum levels of parathyroid hormone (PTH), 25(OH) vitamin D [25(OH)D] and IGF-I, and BMD in a selected group of elderly women who were not estrogen, vitamin D or bisphosphonate users.

Patients and Methods

A group of 31 post-menopausal women over the age of 65 (median age=68 years, range=65-74 years) was prospectively enrolled in the study and informed consent was obtained from each participant. Patients who used bisphosphonates, estrogens, calcium or vitamin D and those who had a history of fracture, bone diseases or malignancy, were excluded from the study. The factors examined were age, age at menarche and menopause, weight, height and body


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mass index (BMI, calculated as weight in kilograms divided by the square of height in meters). Serum calcium, creatinine, PTH, 25(OH)D and IGF-I measurements were performed in all the patients, who also underwent dual-energy x-ray absorptiometry (DXA, Hologic QDR 4500 C; Whaltham, MA, USA) and subsequently lumbar spine (L2-L4) BMD measurement (8, 9). In vitro, a coefficient of variation (CV) of 0.6% (calculated performing 20 scans of the Hologic Anthropometric Spine Phantom) and in vivo the CV was 1.2% (calculated performing two lumbar scans in 10 healthy volunteers), as previously reported (10).

Both serum calcium and creatinine were measured spectrophotometrically, by standard laboratory methods. Serum intact PTH was analyzed by an immunometric assay (Intact PTH Bridge; Adaltis, Bologna, Italy), with a detection limit 10 pg/ml, and inter- and intra-assay CV of 4% and 3.5%, respectively. 25(OH)D was determined by a radioimmunoassay (RIA) (25-hydroxyvitamin D 125I RIA kit; DiaSorin, Stillwater, MN, USA), detection limit 1.5 ng/ml, and inter- and intra-assay CV of 9% (10, 11). Serum IGF-I was measured by an immunoradiometric method (IGF-1 kit; Immunotech, Marseille, France), with detection limit 10 ng/l, and inter- and intra-assay CV of 11% and 4%, respectively (12, 13).

The reported data are expressed as mean±standard deviation (SD) and the relationship between pairs of variables was determined using Pearson’s correlation coefficient (R) calculation. Each association was considered statistically significant when the p-value was less than 0.01.

### Results

Table I lists the main parameters recorded for the overall population. There were no hypertensive patients and both serum calcium and creatinine were within the normal range (2.10-2.55 mmol/l and 53-97 μmol/l, respectively) in all patients. As expected, a weakly inverse correlation between age and 25(OH)D (R=-0.50, p=0.020) and between BMD and PTH (R=-0.48, p=0.027) was found (Table II).

There was a strong relationship (R=0.70, p<0.001) between age and IGF-I and an inverse relationship between IGF-I and BMD (Figure 1), while serum IGF-I levels did not correlate with 25(OH)D (R=-0.16, p=0.48) or BMI (R=-0.089, p=0.70).

### Discussion

Calcium metabolism mainly depends on the activity of PTH and vitamin D (2). Secondary HPT is the principal mechanism whereby vitamin D deficiency can be involved in the pathogenesis of pathological fractures in the elderly (14). Vitamin D is hydroxylated to 25-hydroxyvitamin D [25(OH)D] and further 1α-hydroxylated to 1,25(OH)2 vitamin D (calcitriol), which is under the direct control of PTH (15, 16). It has long been observed that serum 25(OH)D inversely correlates with serum PTH and that under physiological conditions PTH stimulates both bone resorption and formation, although given intermittently for therapeutic purposes it has anabolic effects on the bone (17-19). The measurement of 25(OH)D, which reflects the total body vitamin storage, is currently considered the best clinical indicator describing vitamin D status (15, 16, 20). IGF-I is a polypeptide hormone involved in the regulation of growth and development, also playing a role in carcinogenesis (21-23).

It is well-known that both BMD and serum concentration of IGF-I decrease with age and that IGF-I should be considered a potential marker of bone loss, changing many years before a decrease of BMD (24). Thus, IGF-I plays an important role in the pathogenesis of osteoporosis, especially in women (14, 25). Studies performed in patients with male idiopathic osteoporosis are controversial, usually showing no relationship between serum IGF-I and BMD (26, 27), or a weak correlation with BMD at the lumbar spine (LS) only and in men younger than 60 years (28, 29).

In menopausal women, bone loss proceeds more rapidly in the LS than in the femoral neck (FN) and osteoporosis at the FN is rare in 60-year-old women, whereas, osteoporosis at the LS is not (30, 31).

Our study confirmed previous data reported by Salminen et al. (12), showing a positive relationship (p<0.001) between BMD and serum IGF-I in this selected group of elderly women. Both in vitro and in vivo, IGF-I and PTH have synergistic actions and the anabolic actions of PTH on bone require the presence of IGF-I (32). Low serum levels of IGF-I increase the risk of pathological fractures in post-menopausal women, independently of BMD (24, 33). We found a significant relationship between serum IGF-I and BMD (R=0.64, p=0.0016), but no correlation (p=NS) was found between IGF-I and 25(OH)D.

### Conclusion

In this selected group of elderly women, we found a strong relationship of increased bone resorption, expressed as BMD, to calcium-regulating hormones PTH and IGF-I, while BMI and 25(OH)D seem to be independent of bone mineralization status.
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