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Evidence for Negative Correlation Between Quantitative Histological Studies and Microradiography of Iliac Crest Bone and Forearm Osteodensitometry in Elderly Women with Osteoporosis

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Summary. Quantitative histomorphometric and microradiographic analysis of iliac crest bone biopsy specimens of 10 unselected and untreated postmenopausal women with osteoporosis was performed and the results were correlated with the values measured by osteodensitometry on the right forearm. No positive correlation between histomorphometry or microradiography and osteodensitometry was observed. Moreover, the data of various histomorphometric parameters and those of the bone mineral content measured by microradiography revealed a significant negative correlation when compared to the values obtained by osteodensitometry. Our results suggest, that evaluation of one skeletal site is not necessarily representative of the entire skeleton in patients with postmenopausal osteoporosis.

Key words: Osteoporosis — Histomorphometry — Microradiography—Osteodensitometry

Quantitative histomorphometric and microradiographic analysis of bone biopsy specimens, as well as osteodensitometry, are well established techniques for investigation of osteoporosis. However, no linear correlation was found when the trabecular mineral content, assessed by osteodensitometry, was correlated with volume density quantified by histomorphometric means [1]. In primary osteoporosis, subnormal values of both these parameters were found in only 60% of the patients examined [1]. Because of the discrepancy of these findings and in order to specify the diagnostic and clinical value of osteodensitometry, as well as histomorphometric and microradiographic analysis of bone biopsy, we correlated these parameters in untreated women with primary osteoporosis.

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Patients and Methods

Ten unselected and untreated postmenopausal patients aged 53 to 78 years (mean 67.2) with clinical symptoms of osteoporosis and radiologic evidence of osteopenia were investigated. Radiologic osteopenia was defined by the presence of at least one crush fracture of the spine. The definition of a crush fracture is based on a decrease of one third or more in the anterior vertebral height. No patient revealed biochemical evidence for osteomalacia, as indicated by normal values of calcium, phosphate, creatinine, and alkaline phosphatase in the plasma and normal levels of parathyroid hormone in the serum. Bone samples for histomorphometric analysis and evaluation of bone mineral content were taken from the iliac crest [2, 3]. The histomorphometric analysis of bone structure was carried out on Goldner-stained, undecalcified microtome sections [4, 5]. The structural parameters of the bone biopsy, which were used for correlation with bone mineral content assessed by osteodensitometry, were calculated and determined according to Merz and Schenk [5]:

Volume density (Vv%): volume of the mineralized and nonmineralized bone trabeculae as a percentage of the total volume measured

Volume density of osteoid (Vvo%): volume of the nonmineralized (osteoid) parts of the bone trabeculae as a percentage of the total volume

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Surface density (Sv mm^2/mm^3): surface area of the interface between trabeculae and bone marrow per unit volume of cancellous bone

Specific surface (S/Vmm^2/mm^3): surface area of bone trabeculae per unit absolute volume of cancellous bone; this parameter is the reciprocal value of the average diameter of the bone trabeculae.

The quantitation of bone mineral content of iliac crest biopsies has been performed according to a method described by Eschberger and Hartenstein [6]. Microradiographs were prepared from consecutive ground sections, with a thickness of 30 μm each. Using a computer-assisted photometer microscope with a scanning table (Leitz MPV-2, Digital PDP-12), at least 3 fields of view (with 7056 reference points in 2,8 mm^2, each) were evaluated. The maximum content of hydroxyapatite/unit volume of bone, mineral distribution within the bone trabeculae present in the biopsy, and hydroxyapatite content per total volume of bone trabeculae measured was calculated. The latter parameter was correlated with volume density assessed by histomorphometric analysis of the iliac crest and with the bone mineral content measured by osteodensitometry of the forearm.

For evaluation of the bone density of the forearm we used osteodensitometry with a dual radioisotope method using two radioactive sources of different gamma-ray energy (Am^{241} and I^{125}, Studsvik-Sweden). Measurements were performed at the right distal forearm 1 cm proximal of the processus styloideus of the distal ulna, a point that is thought to be representative in a major part for trabecular bone, and the results were expressed as mass of bone mineral per unit length of bone (g/cm CaOH-apatite) [7]. To test the precision of our apparatus we measured aluminum tubes of different weight in a water tank. A highly significant correlation between known and measured density as mass of mineral per unit length ($r = 0{,}999$) indicates the high precision of the instrument used. In a normal control, the coefficient of variation for measurements on 7 consecutive days was found to be 5.7%. For statistical analysis of the data, linear regression analysis was used.

Results

The individual data of osteodensitometry, percent hydroxyapatite per total volume, volume density, osteoid volume density, surface density, and specific trabecular surface are shown in Table 1. The histomorphometric values for osteoid volume density, though relatively high (0.65–4.23%) compared to the values published by Delling [8] (0.2–1.1%), range below the values found in our patients with osteomalacia. Comparison of computer-assisted evaluation of microradiographs and histomorphometric analysis of consecutive sections of identical iliac crest biopsies yielded a highly significant positive correlation between hydroxyapatite content and volume density in the patients examined ($p < 0.0005$).

Comparison of bone density, measured by osteodensitometry of the right forearm and histomorphometric and microradiographic parameters of the iliac crest, however, showed a negative correlation between osteodensitometry and volume density ($r = -0.88$, $p < 0.0005$), osteoid volume density ($r = -0.62$, $p < 0.05$), surface density ($r = -0.88$, $p < 0.005$), and percent hydroxyapatite content per total volume ($r = -0.92$, $p < 0.0005$). A positive correlation was found between osteodensitometry and specific trabecular surface ($r = 0.72$, $p < 0.01$) (Fig. 1).

Discussion

Summarizing the results in 10 unselected and untreated postmenopausal osteoporotic patients we found 1) a highly significant correlation between histomorphometric and microradiographic values of identical bone biopsy specimens; and 2) a significant negative correlation between bone density of the right forearm assessed by osteodensitometry and quantitative histomorphometric and microradiographic parameters of the iliac crest.

In our study, we found high reproducibility of bone density assessed by histomorphometric or

Table 1. Individual data of osteodensitometry (PAD g/cm CaOH-apatite), percent hydroxyapatite per total volume (% OH-apatite/t.V.), volume density (Vv%), osteoid volume density (Vvo%), surface density (Sv), and specific trabecular surface density (S/V) in 10 unselected and untreated patients with postmenopausal osteoporosis.

Patient	PAD g/cm CaOH-apatite	% OH-apatite/t.V.	Vv%	Vvo%	Sv	S/V
1	1.28	3.38	10.93	0.69	2.25	20.54
2	1.05	5.53	25.95	1.27	3.12	12.04
3	1.26	4.59	13.76	1.19	2.80	20.32
4	0.92	7.52	18.79	2.12	2.46	13.11
5	0.82	6.11	19.53	0.74	3.33	17.06
6	0.95	6.64	20.16	1.44	3.00	14.89
7	0.78	8.70	30.54	3.64	4.02	13.14
8	1.68	2.99	7.14	0.99	1.33	18.68
9	0.85	7.55	26.58	4.23	3.90	14.73
10	1.37	3.76	11.44	0.65	2.59	22.69

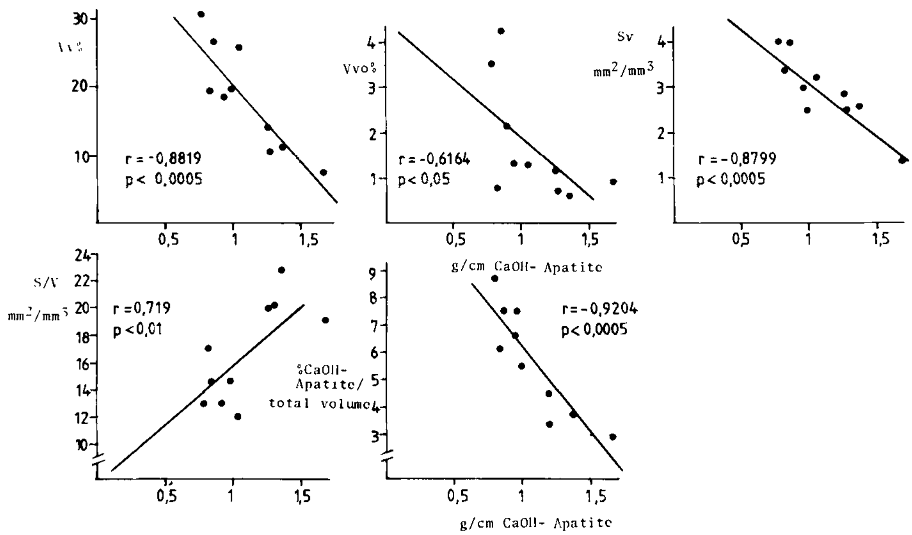

Fig. 1. Correlation between osteodensitometry of the forearm (g/cm CaOH-apatite) and histomorphometric parameters as well as microradiography of the iliac crest bone biopsy specimen.

microradiographic analysis of an identical iliac crest biopsy specimen. However, marked differences of histomorphometric parameters were found when different sections of iliac crest biopsies of one individual were studied [9]. In contrast to metabolic bone disease [10], there is evidence that normal or subnormal bone mineral density of the forearm may not necessarily reflect uniform changes of the structural parameters of the iliac crest in primary osteoporosis [1]. An unexplained negative correlation between osteodensitometry of the forearm and a radiological index obtained by subjective assessment of conventional skeletal x-ray readings has been reported [1]. Our findings of a negative correlation between gamma-ray densitometry and volume density, osteoid volume density, surface density achieved by histomorphometric means, and mineral content computed by microradiography agree with this report.

We conclude that evaluation of one skeletal site is not necessarily representative of the entire skeleton in patients with postmenopausal osteoporosis. Moreover, bone density measurements of the iliac crest and of the forearm can be inversely correlated. The pathophysiological and clinical significance of these findings remain to be established.

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