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Clinical Investigations

Cortical Bone Senescence and Mineral Bone Density of the Humerus

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Summary. Study of the humeral cortex of 89 acute cadavers showed that an important factor contributing to the physiologic bone loss of aging is increasing bone porosity. Mean cortical porosity increases in both sexes with age, from 4.6% in men and 4% in women at 40 years of age to 10% and more at age 80. In the population studied, no significant difference of porosity was observed between men and women. Apparent mineral density is linked to porosity, and decreases markedly with age in women. Changes in men are lesser in magnitude and show a larger difference of density values. Correction of the apparent mineral density, by a factor reflecting the proportion of vascular and resorption spaces in the cortical bone, produces a true mineral density which does not vary significantly with age in either sex. The density values obtained for the proximal humerus differ from those in the literature which represent the femur. However, they are more readily compared with the results of clinical densitometry and may have greater clinical applications.

Key words: Bone density — Bone mineral — Humerus — Porosity — Aging.

The aging process is manifested by bone loss involving the entire skeleton. The alterations are both qualitative and quantitative and vary somewhat at different sites. It is evident that the study of bone density and its variation with aging is rather different for compact bone, such as the humeral cortex, than it is for the cancellous bone of the axial skeleton.

In the strict sense of its definition, the density of a bone sample is its specific mass, that is, mass per unit volume of whole bone. This is to be distinguished from apparent mineral density (AMD) which is the ashweight per cm^3 and the true mineral density (TMD) which is the ashweight per unit volume of bone freed of its canals and spaces. The TMD is derived by correcting the AMD for the volume occupied by spaces. It represents a *true* density in the sense of *point* mineral content.

The senescent change in cortical bone appears largely related to a decrease in bone volume. With age, there is a decrease in cortical thickness and in the cortico-diaphyseal index which is similar for metacarpal, radius, humerus, femur, and tibia [1–5]. There is also a tendency to increased porosity which may not be uniform [6–8]. Sometimes the alterations of the endosteal surface make the inner margin of the cortex difficult to define, thus complicating measurement of cortical thickness and radiologic density.

It is not clear to what extent bone density (AMD) decreases because of the loss of bone due to intracortical porosity, and to what extent it may reflect alterations in the degree of calcification (TMD) at a given point in the remaining bone. The implications of quantifying these changes in normal and pathologic populations are evident.

The cortical bone chosen for this *in vitro* study is the proximal humeral shaft. The humerus is a site readily used for clinical measurements of bone density [9, 10] and cortical thickness [11]. It presents the advantages of having an easily defined area free of muscular insertions, a rounded cross-section, and a cortical thickness and surface large enough for accurate measurements. Studies of the trabecular bone of the iliac crest and lumbar vertebral bodies obtained from the same subjects will be the subject of future discussions.

Material and Methods

The proximal humerus was removed from the cadavers of 89 subjects (44 women and 45 men) who died in hospital from trauma or acute diseases not affecting the skeleton. Samples

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were taken from an area free of muscular insertions 8–10 cm below the humeral head. Two contiguous transverse sections were obtained, one for histomorphometric study and the other for determination of ash weight.

Porosity

Contact microradiographs were made of a thin (100 μ) transverse section of humeral shaft. Histomorphometric measure of the proportion of the cortical bone area occupied by vascular and resorption cavities was performed using a semiautomatic Leitz ASM system. Osteoid seams are not visible in microradiographs and are included in the measurement of porosity. The mean value of measurements from areas evenly distributed around the circumference of cortical bone was calculated (Fig. 1). The total area of measurements represents 50% of total section area.

Cortical Area

This is the cross-sectional area derived from computer reading of the microradiograph using 9111 graphic table and HP 85 computer. Data are fed into the system with a 11.65 × magnification. The algorithm had been described by Meunier et al [12], and the system's accuracy had been evaluated to less than 1%.

Mineral Density

Thick (5 mm) transverse sections were scraped free of periosteal fibers and endosteal bone spicules. A light coating of polyester varnish was applied to seal off the vascular cavities. Volume was obtained by displacement in water, ethanol, and cyclohexane. The bone was ashed at 800°C in an oxygenated atmosphere for 4 h. The ashes were weighed after cooling in a dessicator.

The weight of ashes was divided by the volume of the bone sample to obtain the AMD. True mineral density was derived by correcting for porosity.

$$\text{TMD} = \frac{\text{AMD} \times 100}{100 - \text{porosity}}$$

Statistical Methods

Multiple analyses, including linear and polynomial regressions and analyses of variance, were performed (Table 2) following the program GENSTAT V (Mark 4.01) of the CNRS Computing Center (CIRCE Orsay—France). Between decades, Student's *t* test were performed using the "General Statistic Pac" of HP 85.

Results

(See Table 1 for summary of all numerical results)

Porosity

The measurements of porosity, defined as the percentage of cortical bone occupied by vascular and resorption cavities, increased with age in both sexes (Fig. 2). For younger persons (33–50 years) the values were relatively homogeneous and less than 6%. It was only after 50 years that a significant increase of porosity was seen. The *t* test between means of porosity values becomes significant ($P < 0.005$) at 60 years for men and 50 years for women. The distribution of values shows a great dispersion after 70 years in men and 60 years in women. The regression curves are almost identical for either sex (Fig. 2), but the correlation coefficient is better for women ($r = 0.70$) than men ($r = 0.67$). To the increase of porosity of women, the best fitted function is an exponential one.

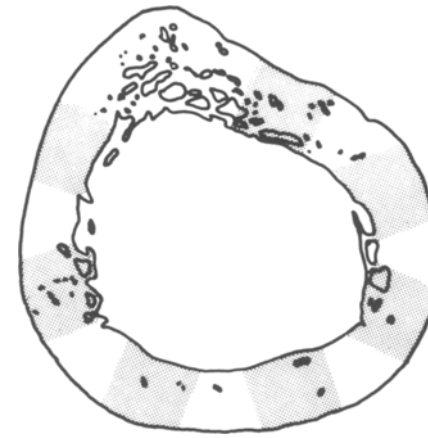

Fig. 1. Section of the humerus showing 7 sites for measurement of porosity.

Total and Corrected Bone Area

Two values were obtained: the area of the section and a *true* area corrected for porosity. The area of the humeral section was related to body size and was larger in men. For men, we did not prove a significant modification of areas with age. For women, bone loss related to aging was manifested by decreased cortical thickness as well as by increased intracortical porosity. The total cross-sectional area and the corrected area decrease significantly after 60 years of age ($P < 0.001$).

Apparent Mineral Density (AMD)

The measured AMD reflects both the true mineralization of the bone and its porosity. Apparent mineral density was seen to decrease with age in both sexes (Fig. 3). The mean value of AMD of young women (under 50) is not significantly higher than

Table 1. Summary of results

Men												
Age group	42–49		50–59		60–69		70–79		80–89		90	Grand mean
Mean age	45.5	± 2.7	53.9	± 2.8	65.9	± 2.3	74.3	± 1.7	84.0	± 3.3	90	66.1 ± 13.8
Number of cases	6		10		11		8		9		1	(total: 45)
Porosity (%)	4.6	± 0.8	5.5	± 2.0	6.6	± 1.1	8.1	± 4.0	10.1	± 2.9	11.1	7.1 ± 3.0
Cortical area (cm^2)	1.76	± 0.35	1.61	± 0.24	1.90	± 0.26	1.86	± 0.41	1.71	± 0.31	1.87	1.77 ± 0.31
Corrected area (cm^2)	1.68	± 0.33	1.52	± 0.22	1.77	± 0.24	1.71	± 0.36	1.53	± 0.28	1.66	1.63 ± 0.29
Cortical diameter (cm)	2.35	± 0.10	2.11	± 0.28	2.27	± 0.22	2.18	± 0.16	2.34	± 0.18	2.40	2.25 ± 0.21
Specific mass (g/cm^3)	1.888	± 0.037	1.912	± 0.066	1.885	± 0.048	1.858	± 0.102	1.824	± 0.098	1.812	1.873 ± 0.077
AMD (g/cm^3)	1.161	± 0.069	1.133	± 0.057	1.118	± 0.046	1.093	± 0.080	1.058	± 0.090	1.038	1.109 ± 0.073
TMD (g/cm^3)	1.216	± 0.070	1.199	± 0.043	1.198	± 0.047	1.189	± 0.079	1.176	± 0.081	1.168	1.194 ± 0.062
Women												
Age group	33–49		50–59		60–69		70–79		80–89		90–96	Grand mean
Mean age	41.5	± 6.5	54.8	± 3.5	65.2	± 3.7	73.0	± 2.8	83.6	± 3.0	94.7 ± 1.5	69.98 ± 16.3
Number of cases	6		6		6		10		12		4	(total: 44)
Porosity (%)	4.0	± 0.8	6.5	± 1.1	7.7	± 4.6	7.5	± 3.2	11.8	± 4.3	13.9 ± 4.3	8.7 ± 4.5
Cortical area (cm^2)	1.63	± 0.13	1.37	± 0.31	1.26	± 0.16	1.19	± 0.27	1.09	± 0.16	0.86 ± 0.09	1.22 ± 0.28
Corrected area (cm^2)	1.57	± 0.13	1.29	± 0.30	1.16	± 0.17	1.12	± 0.26	0.96	± 0.16	0.74 ± 0.11	1.12 ± 0.33
Cortical diameter (cm)	1.95	± 0.22	1.90	± 0.11	1.91	± 0.15	1.93	± 0.22	1.89	± 0.18	1.88 ± 0.11	1.91 ± 0.21
Specific mass (g/cm^3)	1.950	± 0.053	1.892	± 0.042	1.888	± 0.083	1.878	± 0.120	1.782	± 0.078	1.721 ± 0.113	1.849 ± 0.110
AMD (g/cm^3)	1.195	± 0.056	1.125	± 0.038	1.142	± 0.072	1.117	± 0.080	1.050	± 0.060	0.956 ± 0.067	1.097 ± 0.091
TMD (g/cm^3)	1.244	± 0.053	1.202	± 0.031	1.236	± 0.040	1.207	± 0.064	1.190	± 0.034	1.110 ± 0.046	1.201 ± 0.056

Table 2. Statistical results

	Measure precision	Group	Anova F Ratio	Regression versus age	r	F Ratio
Porosity	6%	men	7.6[d]	Polynomial-2	0.67	17.3[d]
		women	6.7[d]	Exponential	0.70	40.3[d]
Cortical area	1%	men	1.1[a]	Linear	−0.08	0.3[a]
		women	10.3[d]	Polynomial-2	0.70	18.8[d]
Apparent mineral density	0.5%	men	2.7[b]	Polynomial-2	0.51	7.2[b]
		women	8.3[d]	Polynomial-2	0.69	12.0[c]
True mineral density	6.5%	men	0.4[a]	Linear: TMD = −0.001[a] age + 1.263	−0.20	1.8[a]
		women	4.8[c]	Linear: TMD = −0.002[a] age + 1.318	−0.48	12.5[c]
AMD versus porosity		men		Linear: AMD = −0.016 P + 1.222	−0.66	32.4[d]
		women		Linear: AMD = −0.017 P + 1.249	−0.86	63.3[d]

r = regression coefficient
[a] No significance
[b] Significance at $P < 0.05$
[c] Significance at $P < 0.01$
[d] Significance at $P < 0.001$

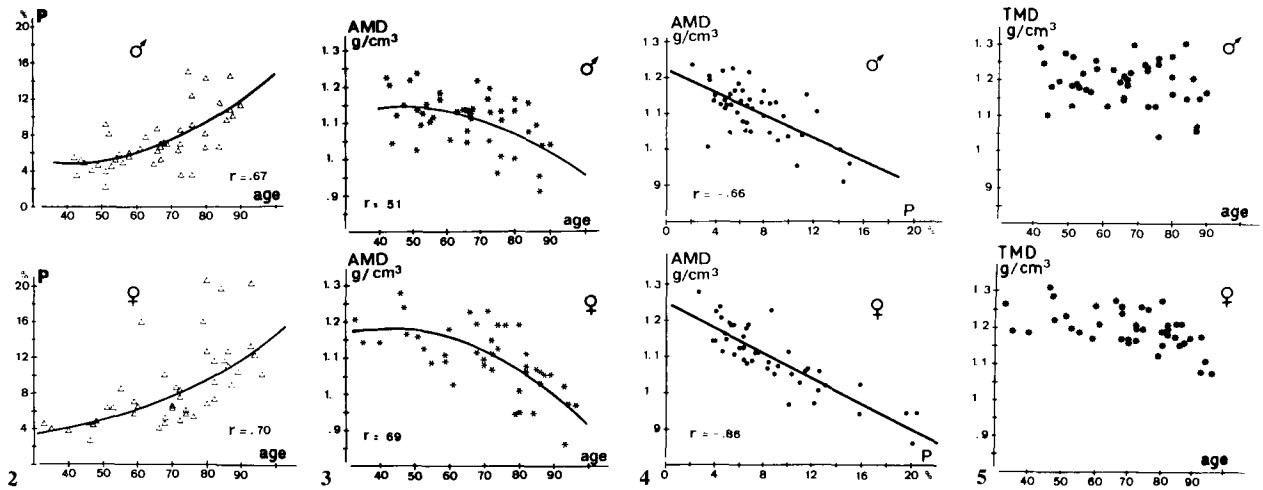

Fig. 2. Porosity (expressed as the percentage of cortical bone occupied by vascular cavities) versus age in men and women. **Fig. 3.** Apparent mineral density (g/cm³) versus age. AMD is ashweight per volume unit of cortical bone. **Fig. 4.** Apparent mineral density (g/cm³) versus porosity (%). **Fig. 5.** True mineral density (g/cm³) versus age. TMD is ashweight per volume unit of bone freed of its canals and resorption spaces.

AMD of men of the same age. After 50 years, the decrease is faster in women. There was a clear relationship between porosity and AMD (Fig. 4) in women ($r = -0.86$) and men ($r = -0.66$).

True Mineral Density

Correcting apparent mineral density for the presence of vascular and resorption spaces enables us to derive the true mineral density (TMD). It does not decrease with age in men (Fig. 5) and shows only a slight decrease after 80 years of age in women ($P < 0.01$).

Discussion

Although age-related cortical bone loss has been studied for many years [1–3] the increase of *bone porosity* has been diversely appreciated. Jowsey [6, 13] found 3–40% of incompletely closed osteons, and an increasing number in women, but not in men. Martin et al [8] evaluated an increase of femoral porosity from about 9–18% in men between ages 40 and 90. Currey [14] found a constant osteonic canal diameter, and Singh and Gunberg [15] found a decrease of canal diameter with aging. Thompson [16] showed that increased porosity in both sexes correlates with bone mineral index. All these studies used femoral cortical bone from different sites, whereas Atkinson and Weatherell [17] demonstrated the density differences between the quadrants of the femoral shaft. This fact could explain the discrepancies between, for instance, the values of Thompson (anterior shaft) and Currey (total shaft including linea aspera). We feel that the measurement of the total porosity, all around the section, may be a better index.

From our data, there is much evidence also that supports the view that a nonbearing bone is more homogeneous and more significant for age-related loss [18]. Lindahl and Lindgren [19] made a similar observation: the loss of density with age is earlier and greater for the humerus than for the femur. Martin et al [8] show similar porosity trends in men, but their values for humeral porosity were higher than ours; these differences can be due to differences in methods of valuation. As in the femur [20], the distribution of the porosity throughout the humeral cortex is not uniform [8, 21]. Porosity increase is linked to the increase of canal number and the widening of their individual area [21]. With aging, the modified activity of the Haversian systems is reflected by variation in the form and the size of the osteons which may become irregular and even confluent [7, 13]. The differences between the haversian systems and the spaces of Volkmann become less obvious than in young bone. Both types of vascular spaces contribute significantly to porosity. We have not considered the canaliculi or the osteocyte spaces because the absolute magnitude of their area is small [22, 23]. Also, their variations seem more closely to reflect reversible metabolic changes than bone senescence [24].

Age-related decrease of cortical area in women

accompanies the preservation of the bone diameter. The decrease of cortical area is due to thinning. In men, we could not demonstrate a decrease of cortical area or diameter. Martin found decrease in area after 80 years of age [8].

The *mineral density* values described, as well as the aging variations in porosity, cannot be related to values in the literature except in a very general fashion, principally because they usually relate to the femur. The values for humeral cortical density reported by Lindahl and Lindgren [19] were obtained for a differently oriented site and relate to intact hydrated bone. They are of the same order as our figures for specific mass.

Significant cortical AMD decrease only becomes apparent in normal women after about age 60, and in men after age 70. The changes are less marked in men, and more gradual in onset. For the humeral cortex, our results indicate that the principal factor responsible for aging variations in AMD is the increase of the porosity. This is observed in both sexes. Increased porosity also explains the variations in X-ray densitometric measurements in older subjects and contributes to the decrease of the bone mineral index.

Finally, it becomes obvious that measurements of mineral density (AMD) must be corrected to reflect the presence of intracortical vascular spaces if an accurate value is desired for mineral content of the bone substance remaining (TMD). Furthermore it appears that aging changes in humeral TMD are not significant until advanced ages, when a small decrease is observed only in women.

In women, aging is characterized by cross-sectional area shrinking (due to cortical thinning) and by increasing porosity. Between ages 40 and 80, women lose 28% of humeral bone mass by cortical thinning and only 2% by increase of porosity. The mineral content of the remaining bone (TMD) is maintained until advanced ages.

In men, we observed an almost identical increase of porosity without provable loss of cortical area and with preservation of the true mineral density.

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