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Clinical Investigations

Is Postmenopausal Bone Loss an Age-Related Phenomenon?

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Summary. Forearm bone mineral content (BMC), an index of skeletal mineralization, and lean body mass (LBM), an index of the muscle mass in the body, were calculated in 574 healthy, white subjects, aged 20–89 years. In women, there was no significant change in BMC with age until the menopause. Thereafter, a significant decline averaging 15% per decade was found up to the age of 70 years, after which it was 10% per decade. In men, there was a significant overall decline of about 4% per decade from the age of 20. When BMC was corrected for LBM, the age-related fall in men disappeared, while remaining without a significant trend in premenopausal women. This was, however, not the case in women after the menopause, where a significant decline of about 12% per decade was noted. These data clearly demonstrate that the major contribution to the well-known bone loss in postmenopausal women is not a simple age-related phenomenon. The development of osteoporosis must be due to some additional bone-diminishing effect on the female skeleton, most likely the absence of estrogen.

Key words: Bone mineral content — Lean body mass — Postmenopausal women — Age-related bone loss.

The measurement of forearm BMC by single photon absorptiometry is a noninvasive and reproducible method of *in vivo* estimation of the status of skeletal mineralization [1–3]. This, as well as other techniques, has been widely used to quantify the amount of bone and to establish bone mass as a function of age [4, 5]. Such methods have therefore become important tools in the study of osteoporosis.

The significance of osteoporosis is the increased risk of fracture, which at least in part must be due to an imbalance between bone mass and soft tissue weight. Both muscle [6–8] and bone mass [4, 5] decrease during normal aging, and these two variables are known to correlate [7–9] though the decrease in bone mass in perimenopausal women has been shown to be independent of muscle mass [10]. Mechanical loading and exercise increases both muscle and bone mass, whereas immobilization has the opposite effect [11–14].

We examined the BMC and LBM values in a large group of healthy, white subjects aged 20–89 years, to see if the age-related loss of bone and muscles is parallel in both sexes.

Materials and Methods

Normal Subjects

The study comprised 350 healthy, white women and 224 healthy, white men, aged 20–89 years. None of the participants had received hormones, diuretics, or drugs known to interfere with calcium metabolism. Research protocols were approved by the local ethical committee. In accordance with the Helsinki II Declaration, all participants gave their consent after receiving thorough information.

Bone mineral content (BMC) in the forearm, which is known to correlate well with total body bone mineral [1–3], was measured by single photon absorptiometry (^{125}I). BMC was calculated as the mean of 12 scans (6 on each arm) on the distal part of the forearm. The first scan site was selected as the most distal position where the ulna and radius are separated by 8 mm, the succeeding 5 scans being performed proximal to this site at intervals of 4 mm. BMC was expressed in arbitrary units (dimension mass/unit length). This method has a high (1.2%) long-term reproducibility in normal subjects [1] and BMC values correlate to the dry defatted bone weight of forearm bone slices with an r value of 0.98 [15]. The BMC was corrected for interference from

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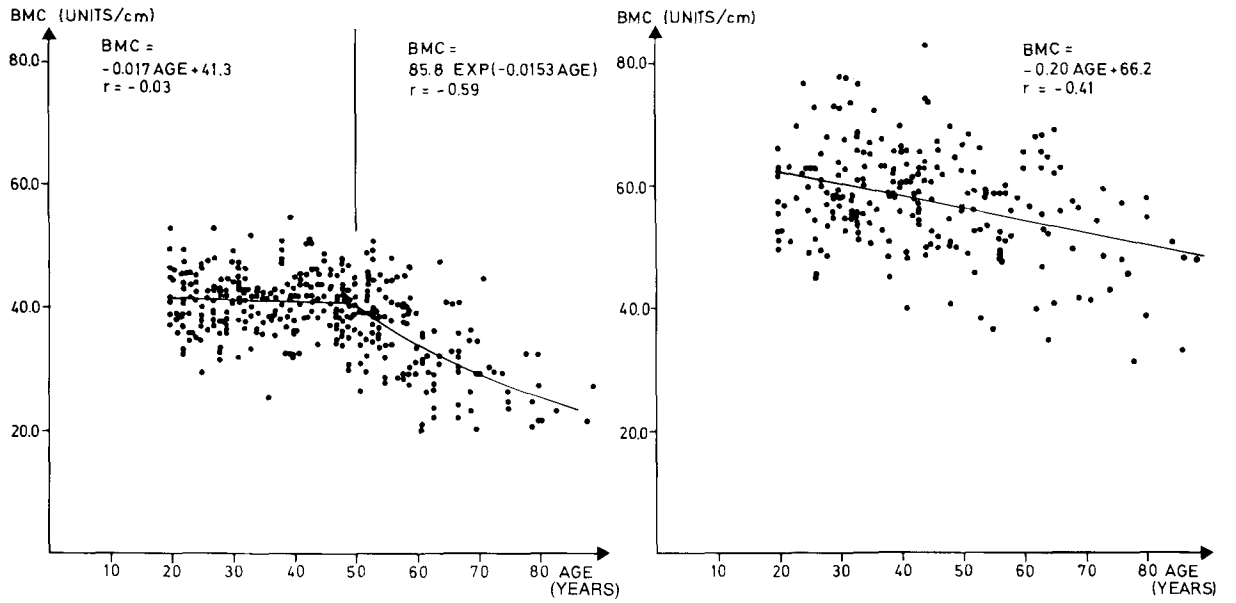

Fig. 1. Relationship between bone mineral content (BMC) and age in 350 normal women (left) and 227 normal men (right).

fat in the subcutaneous tissue according to the method of Nilas et al. [16].

The *height* and the *body weight* were measured, with the participants wearing indoor clothes, but no shoes. The *lean body mass* (LBM) was calculated according to the equations of Boddy et al. [17]. LBM is an index of muscle mass in the body [16–18] and, when calculated according to the Boddy equations, fits LBM by dual photon absorptiometry [19, 20].

Statistical Evaluation

The significance of differences was determined by Student's *t* test for unpaired data and by one way analysis of variance. Relations between variables were investigated by linear or exponential regression analysis.

Results

The BMC values in the age span 20–90 years of the female and male populations as a function of age are given in Fig. 1. In the women there was no significant change in BMC with age before the menopause. Thereafter a significant decline in bone mass was observed ($r = -0.59$, $P < 0.001$), the rate of loss amounting to 15% per decade up to the age of 70 years. In the last two decades, 70–79 years and 80–89 years, the decline was approximately 10% per decade. In the men there was a significant ($r = -0.41$, $P < 0.001$) decline in BMC of about 4% per decade from 20–90 years of age. In Table 1 the data have been divided into age groups. One-way analysis of variance revealed highly significant differences among age groups within the sexes (women $F = 39.6$, $P < 0.001$; men $F = 7.9$, $P < 0.001$).

Figure 2 shows the BMC values divided by LBM. This mode of calculation revealed moderate, although not significant increases in bone mass relative to muscle mass in men throughout life and in women before 50 years of age. This was not the case in the women after the menopause where a significant decline in BMC/LBM was noted. In the age group 50–69 years, the rate of loss was 1.2% per year ($P < 0.01$) and in the age group 70–89 years the loss was 0.8% per year (nonsignificant). Using one-way analysis of variance in the age-divided BMC/LBM data (Table 1), the differences within the women were highly significant ($F = 27.2$, $P < 0.001$), whereas in the men the age-dependent differences were small and not significant ($F = 1.4$).

Division of the population (both men and women) into two subsets according to the age decades, and including the age decade group of 40–49 years in both subdivisions, revealed the following pattern (analysis of variance Table 2): No difference was found between the first three age groups regarding both BMC and BMC/LBM in both men and women. In the last four age groups there were highly significant differences between the groups in the women regarding both BMC and BMC/LBM. In the men, however, the last four age groups differed significantly using BMC, whereas the difference disappeared after correction for LBM.

Discussion

In the present study, the data on men and on women up to the age of 50 were described by

Table 1. Bone mineral content (BMC) and bone mineral content corrected for lean body mass (BMC/LBM) of women and men divided into age groups

Age group (years)	Subjects		BMC		BMC/LBM	
	Women	Men	Women	Men	Women	Men
20–29	75	44	99.6 ± 12.3	142.5 ± 17.9	97.8 ± 10.8	104.3 ± 12.9
30–39	66	59	100.8 ± 12.3	147.2 ± 17.7	100.0 ± 11.8	109.7 ± 12.9
40–49	78	50	100.1 ± 11.3	143.5 ± 20.4	101.1 ± 11.8	108.6 ± 16.1
50–59	74	32	94.7 ± 14.2	134.4 ± 17.7	98.9 ± 15.1	110.8 ± 16.1
60–69	37	23	77.0 ± 15.7	136.9 ± 24.3	81.7 ± 16.1	112.9 ± 18.3
70–89	20	16	66.7 ± 14.7	115.5 ± 20.6	71.0 ± 18.3	106.5 ± 12.9

All values are calculated as a percentage of the mean value in the 20–49-year-old women ± 1 SD.
In all age subgroups the difference between women and men is significant for both BMC and BMC/LBM ($P < 0.001$)

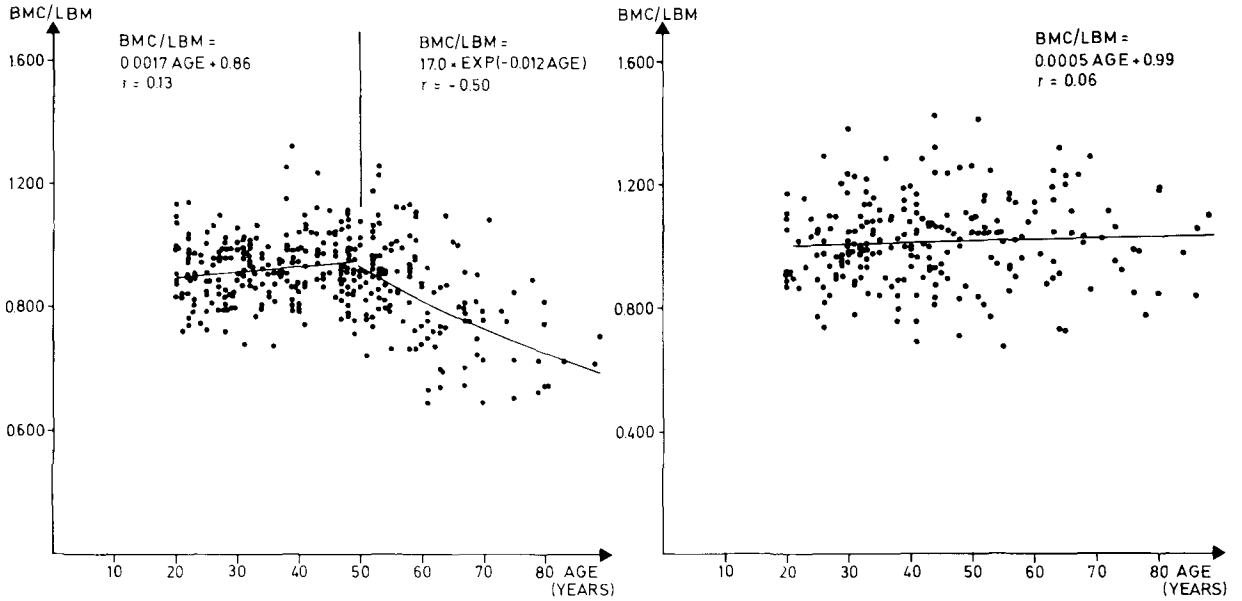

Fig. 2. Relationship between bone mineral content (BMC) corrected for lean body mass (LBM) in 350 normal women (left) and 227 normal men (right).

means of linear regressions. The bone mineral loss in women after age 50 has in previous studies been assumed to be linear [21], quadratic [22], or more or less complex exponential function [22, 23]. In this study, the data were fitted by a simple exponential regression (Figs. 1 and 2). However, for practical reasons we have chosen to interpret the female data in the age groups 50–69 years and 70–89 years by means of two linear regressions instead of an exponential regression.

Our study comprised a large sample of healthy white adults. The forearm BMC measurement was used which has been shown to give a valid estimate of the total mineral content of the skeleton [1–3]. The mean menopausal age in this population is 51.4 years [24]. For practical purposes it is therefore reasonable to consider the women of our sample over 50 years of age as postmenopausal. In women, the raw BMC values were stationary before the age of 50. The marked decline in BMC found in the women over 50 years is well known [4, 5, 25, 26]. The relatively moderate fall observed in the 50 to 59-year-old age group is probably caused by the fact that some of the subjects have not yet reached the menopause, and therefore have a relatively slow bone loss. The significant fall in between the 60–69 and 70–89 subgroups may reflect the so-called senile osteoporosis [27]. The mechanism of sensecent bone loss has been postulated to differ from that in the postmenopausal period. In the former, a major pathogenetic factor is thought to be simple aging of bone cells [27], whereas most evidence points towards falling estrogen production as the direct cause of bone loss related to the early

Table 2. Analysis of variance on bone mineral content (BMC) and bone mineral content corrected for lean body mass (BMC/LBM) in 350 women and 224 men divided into six age groups by decades

		Decade groups: 20–29, 30–39, and 40–49	Decade groups: 40–49, 50–59, 60–69, and 70–89
Men	BMC	$F = 0.94$ n.s.	$F = 7.60$ $P < 0.001$
	BMC/LBM	$F = 1.99$ n.s.	$F = 0.64$ n.s.
Women	BMC	$F = 0.18$ n.s.	$F = 48.31$ $P < 0.001$
	BMC/LBM	$F = 1.63$ n.s.	$F = 34.73$ $P < 0.001$

The difference between the first three age groups, and the difference between the last four age groups are tested separately by one-way analysis of variance
F = variance ratio; n.s. = not significant

postmenopausal years [26–28]. The findings by regression analysis were supported by the divided analysis of variance. In men, the BMC data throughout all ages were fitted by one linear, slightly falling slope, whereas the divided analysis of variance indicated stationary values before age 50 and a falling tendency thereafter.

LBM is a measure of the muscle mass [6, 16], one of the body components known to decline throughout life in man [6]. Correction of BMC with LBM is therefore at least partly an expression of the status of bone mineralization corrected for the physiological, age-related decline. Some of the age and sex characteristics indicated by the raw BMC data were changed when the BMC/LBM data were applied. In premenopausal women and men, the change in bone mass occurred parallel to a change in muscle mass as reflected by the lack of trends of BMC/LBM. A difference of almost 30% was found between the raw BMC values of the women up to age 50 and those of the men. When corrected for LBM, this difference was reduced to less than 10%.

In the postmenopausal women, the changes in BMC did not parallel the changes in LBM (Fig. 2, Table 1 and 2). A significant decline in BMC/LBM was seen after age 50, and at the age of 60, when wrist fractures are common [26], the fall was considerable. The decrease in BMC/LBM even continued in the 70- and 80-year-old women, a decrease that is concomitant with the increasing fracture risk found in this group [26].

Endogenous creatinine clearance (ECC), like muscle mass, shows a steady decline with age [29], and correction of BMC with ECC would, therefore, in much the same way as correction with LBM, give an expression of BMC corrected for age-related changes. We have corrected the present BMC data with age- and sex-matched ECC data from a study on a similar Danish population [29], and the picture was exactly the same as that found with BMC/LBM: no decline and a parallel course in the premenopausal women and the men, and a significantly negative slope in the postmenopausal women, with BMC/ECC decreasing with age.

Although the results of this study seem rather valid, one should bear in mind that they are obtained from a skeletal site with mainly cortical bone. Other investigators have found slightly different results, indicating that significant trabecular bone loss occurs from the central skeleton prior to the menopause [30–32]. We have recently published work demonstrating a generalized and parallel bone loss from all skeletal regions in the early menopause [33].

Our results clearly show that correction of BMC values for the age-dependent variable LBM was able to abolish the age-related change in men, but not in women over 50 years of age.

We therefore conclude that the bone loss in postmenopausal women cannot be explained as being a simple age-related phenomenon. Our data clearly demonstrate that the major contribution to this well-known loss must be an additional negative action on the skeleton, which is generally agreed to be estrogen deficiency resulting from declining ovarian function.

References

1. Christiansen C, Rødbro P (1977) Long-term reproducibility of bone mineral content measurements. Scand J Clin Lab Invest 37:321–323
2. Christiansen C, Rødbro P, Jensen H (1975) Bone mineral content in the forearm measured by photon absorptiometry. Scand J Clin Lab Invest 35:323–330
3. Gotfredsen A, Borg J, Nilas L, Tjellesen L, Christiansen C (in press) Representativity of regional to total bone mineral in healthy subjects and "anticonvulsive-treated" epileptic patients. Measurements by single and dual photon absorptiometry. Eur J Clin Invest
4. Smith DM, Khairi MRA, Johnston Jr CC (1975) The loss of bone mineral with aging and its relationship to risk of fracture. J Clin Lab Invest 56:311–318
5. Mazess RB (1982) On aging bone loss. Clin Orthop 165:239–252
6. Anderson EC (1963) Three-component body composition analysis based on potassium and water determinations. Ann NY Acad Sci 110:189–210
7. Doyle F, Brown J, Lachance C (1970) Relation between bone mass and muscle weight. Lancet i:391–393
8. Ellis KJ, Cohn SH (1975) Correlation between skeletal calcium mass and muscle mass in man. J Appl Physiol 38(3):455–460
9. Cohn SH, Aloia JF, Vaswani AN, Zanzi I, Vartsky D, Ellis KJ (1981) Age- and sex-related changes in bone mass measured by neutron activation. In: Osteoporosis, Proc Int

Symp, Jerusalem Osteoporosis Center, June 1981. John Wiley & Sons, Chichester, New York, Brisbane, Toronto, Singapore, pp 33–43
10. Meema HE (1966) Menopausal and aging changes in muscle mass and bone mineral content. 48A-2:1138–1144
11. Leusinki JA (1974) A comparison of the body composition estimated by densitometry and total body potassium measurement in trained and untrained subjects. Pflügers Arch 348:357–362
12. Åstrand P-O, Rodahl K (1977) Textbook of work physiology. Physiological bases of exercise. McGraw-Hill, New York
13. Krølner B, Toft B, Nielsen SP, Tøndevold E (1983) Physical exercise as prophylaxis against involutional vertebral bone loss: a controlled trial. Clin Sci 64:541–546
14. Whedon GD (1984) Disuse osteoporosis: Physiological aspect. Calcif Tissue Int 36:146–150
15. Nilas, L, Nørgaard H, Pødenphant J, Gotfredsen A, Christiansen C (in press) Bone composition in the distal forearm. Scand J Clin Invest
16. Nilas L, Borg J, Gotfredsen A, Christiansen C (1985) Comparison of single- and dual-photon absorptiometry in postmenopausal bone mineral loss. J Nucl Med 26:1257–1262
17. Boddy K, King PC, Hume R, Weyers E (1972) The relation of total body potassium to height, weight, and age in normal adults. J Clin Pathol 25:512–517
18. Womersley J, Durnin JVGA, Boddy K, Mahaffy M (1976) Influence of muscular development, obesity and age on fat-free mass of adults. J Appl Physiol 41:223–229
19. Mazess RB, Peppler WW, Gibbons M (1984) Total body composition by dual-photon (^{153}Gd) absorptiometry. Am J Clin Nutr 40:834–839
20. Gotfredsen A, Jensen J, Borg J, Christiansen C (1986) Measurement of lean body mass and total body fat using dual photon absorptiometry. Metabolism 35(1):88–93
21. Newton-John HF, Morgan DB (1970) The loss of bone with age, osteoporosis, and fractures. Clin Orthop Rel Res 71:229–251
22. Smith DM, Khairi MRA, Johnston CC Jr, Norton J (1976) The slowing of the rate of mineral loss with aging. Am J Roentgenol 1126(6):1298–1299
23. Nordin BEC (1984) Closing remarks. In: Christiansen C, Arnaud CD, Nordin BEC, Parfitt AM, Peck WA, Riggs BL, (eds) Osteoporosis, Proc Copenhagen Int Symp on Osteoporosis. Copenhagen, pp 403–406
24. Hagen C, Christiansen C, Christiansen MS, Transbøl I (1982) Climateric symptoms, fat mass, and plasma concentrations of LH, FSH, Prl, oestradiol-17, and adrostenedione in the early postmenopausal period. Acta Endocrinol 101:87–92
25. Cohn SH, Vaswani A, Zanzi I, Ellis KJ (1976) Effect of aging on bone mass in adult women. Am J Physiol 230(1):143–148
26. Nordin BEC, Crilly RG, Smith DA (1984) Osteoporosis. In: Nordin BEC (ed) Metabolic bone and stone disease. Churchill Livingstone, Edinburgh, pp 1–70
27. Riggs BL (1981) Evidence for etiologic heterogeneity of involutional osteoporosis. In: Menczel J, Robin GC, Makin M, Steinberg R (eds) Osteoporosis, Proc Int Symp, Jerusalem Osteoporosis Center, June 1981. John Wiley & Sons, Chichester, pp 3–14
28. Richelson LS, Wahner HW, Melton III LJ, Riggs BL (1984) Relative contributions of aging and estrogen deficiency to postmenopausal bone loss. N Engl J Med 311:1273–1275
29. Kampmann JP, Siersbaek-Nielsen K, Kristensen M, Hansen JM (1971) Aldersbetingede variationer i urinkreatinin og endogen kreatininclearance. Ugeskr laeger 43:2369–2372
30. Riggs BL, Wahner HW, Seeman E, Offord KP, Dunn WL, Mazess RB, Johnson KA, Melton III LJ (1982) Changes in bone mineral density of the proximal femur and spine with aging. Differences between the postmenopausal and senile osteoporosis syndromes. J Clin Invest 70:716–723
31. Marcus R, Kosek J, Pfefferbaum A, Horning S (1983) Age-related loss of trabecular bone in premenopausal women: a biopsy study. Calcif Tissue Int 35:406–409
32. Cann CE, Dinant HK, Kolt SU, Ettinger B (1985) Quantitative computing tomography for prediction of vertebral fracture risk. Bone 6:1–7
33. Gotfredsen A, Nilas L, Riis BJ, Thomsen K, Christiansen C (in press) Spontaneous- and oestrogen-caused bone changes in the early menopaused. A local or generalized phenomenon. Br Med J

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