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**Original Article**

# An Increase in Forearm Cortical Bone Size After Menopause May Influence the Estimated Bone Mineral Loss—A 28-Year Prospective Observational Study

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## Abstract

Areal bone mineral density (aBMD) is the most common estimate of bone mass, incorporated in the World Health Organization definition of osteoporosis. However, aBMD depends on not only the amount of mineral but also the bone size. The estimated postmenopausal decline in aBMD could because of this be influenced by changes in bone size.We measured bone mineral content (BMC; mg), aBMD (mg/cm$^2$), and bone width (mm) by single-photon absorptiometry at the cortical site of the forearm in a population-based sample of 105 Caucasian women. We conducted 12 measurements during a 28-yr period from mean 5 yr (range: 2−9) before menopause to mean 24 yr (range: 18−28) after menopause. We calculated individual slopes for changes in the periods before menopause, 0−<8, 8−<16, and 16−28 yr after menopause. Data are presented as means with 95% confidence intervals. The annual BMC changes in the 4 periods were −1.4% (−0.1, −2.6), −1.1% (−0.9, −1.4), −1.2% (−0.9, −1.6), and −1.1% (−0.8, −1.4) and the annual increase in bone width 0.4% (−1.2, 1.9), 0.7% (0.5, 0.9), 0.1% (−0.2, 0.4), and 0.1% (−0.2, 0.4). BMC loss was similar in all periods, whereas the increase in bone width was higher in the first postmenopausal period than in the second ($p = 0.003$) and the third ($p = 0.01$) postmenopausal periods. Menopause is followed by a transient increase in forearm bone size that will influence the by aBMD estimated cortical loss in bone minerals.

**Key Words:** Bone loss; bone mineral density; bone size; forearm; postmenopausal.

## Introduction

Areal bone mineral density (aBMD; g/cm$^2$) estimated by dual-energy X-ray absorptiometry (DXA) is the most used estimate of bone mass, also included in the World Health Organization (WHO) definition of osteoporosis *(1−11)*. After menopause, there is a transient increased loss in aBMD *(1−10)*. The cortical loss is verified by 3-dimensional scanning techniques and volumetric BMD (vBMD; g/cm$^3$) *(12−15)*, a loss that includes loss of bone minerals, trabecular thinning, loss of trabecular connectivity, increased cortical porosity, and thinning of the cortex *(1−10)*. There is also with aging an increase in bone size that has been shown in forearm *(2,4−6)*, femoral neck *(6−9)*, tibia *(10,16)*, and spine *(11)*, and this may be attenuated at menopause *(1,2,4)*. As aBMD depends on both the amount of mineral (bone mineral content [BMC]) and the bone size (bone area) *(2,4,11,17−19)*, an increased bone width would influence the DXA and single-photon absorptiometry (SPA) estimated aBMD changes.

Estrogen suppresses bone resorption *(20)* and bone turnover *(21)* and inhibits bone widening *(22−25)*, at least partly explaining why boys at puberty grow a wider skeleton than

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girls (22,23). Also menopause is followed by a bone widening, shown in cross-sectional (5,6,10) and short-term prospective studies (2,4). It should therefore be resolved if (1) the postmenopausal decline in aBMD is influenced by increased bone width, (2) an increased bone width is a transient phenomenon, and (3) there is an association with low estrogen and increased bone width. We therefore extended the evaluation of our cohort (1,26,27).

## Methods

We evaluated in this prospective observational study changes in BMC and bone width from before menopause to after menopause in a population-based sample of 241 Caucasian women aged 48 at baseline (1,26,27). Forty-nine women were excluded at study start as they were perimenopausal or postmenopausal or had conditions or medications that interfered with bone metabolism. The prospective study included 192 women who had cyclic menstrual bleedings at age 48. During follow-up, 30 women died, 17 had surgically induced menopause, 5 relocated, 24 received estrogen, corticosteroids, or other antiresorptive osteoporosis therapy, and 11 had unreadable baseline or endpoint data. This report therefore includes 105 women followed for 28 yr through their spontaneous menopause with measurements on 12 separate occasions, initially every second year and thereafter at intervals of 3−5 yr (27). From 48 to 76 yr, the women participated on average in 10 measurements (range: 3−12), and the women experienced menopause at a mean age of 52 yr (range: 48−57). The measurement done closest before menopause was defined as the menopausal measurement. Because age at menopause differed and all were measured until age 76, the women consequently had different premenopausal and postmenopausal follow-up periods. The mean premenopausal period was 5 yr (range: 2−9), and the median number of premenopausal measurements was 3 (range: 2−4). The mean postmenopausal period was 24 yr (range: 19−28), and the median number of postmenopausal measurements was 9 (range: 2−11).

Menopause was defined according to WHO as permanent cessation of menstruation because of the loss of ovarian follicular activity. The onset of menopause was determined when 12 mo of spontaneous amenorrhea was reported in conjunction with elevated serum levels of follicle-stimulating hormone. Follicle-stimulating hormone was analyzed by double-antibody radioimmunoassay (28) every 3 mo during the first year, then every 6 mo until 1 yr after menopause, and then yearly. Serum level of estradiol was also determined annually until 8 yr after menopause (28). As serum levels of estradiol in the cohort decreased during the first 3 postmenopausal years, but not after this, the postmenopausal estradiol level was defined as the mean value from 3 to 8 yr postmenopausal. Duration of amenorrhea and general health were evaluated through questionnaire and by interviews conducted by research nurses.

We measured BMC (mg), aBMD (g/cm$^2$), and bone width (mm) in the forearm at the cortical site 6 cm proximal to the ulnar styloid process by SPA (1,2). Both forearms were scanned, and the average value of BMC, bone width, and aBMD was registered. The same densitometer was used at all study periods (1,2), a scanner with no long-term drift evaluated with standardized phantom measurements every other week (1,2,27). The radiation source was replaced in 1980s; all measurements thereafter were adjusted by use of phantom data (1,2,27). The coefficient of variation for BMC and BMD was 1.7% and for bone width 1.6% with the standard phantom and for BMC and BMD 4.0% and bone width 8% by repeated measurements after reposition of 20 women.

We used STATISTICA software, version 12.0 (StatSoft, Tulsa, OK). Data are presented as means with 95% confidence intervals. To compare changes in bone parameters between different phases of the premenopausal and postmenopausal periods, we divided the study period in 4 subperiods, premenopausal, 0−<8, 8−<16, and 16−28 yr after menopause. We used all measurements, in relation to days since menopause, within each period in each woman to calculate a regression coefficient (individual slope) for changes. We used all measurements done before the menopausal measurement for calculating the premenopausal changes. To make calculation of an individual slope possible, there had to be at least 2 measurements in the evaluated period. Because the women reached menopause at different ages, we ended up with 56 women with at least 2 measurements in the premenopausal period, 105 women in the first postmenopausal period, 92 in the second, and 82 in the third. Relative changes in each interval were estimated based on the regression line in each period. Paired Student's $t$ test between means was used to compare the mean changes between the different periods. Pearson correlation was used to compare the correlations between changes in the traits in the different periods. Without a correlation between changes in BMC and bone width, it would be possible to use multiple linear regressions and the determination coefficients to estimate the proportion of variance in the aBMD loss explained by changes in BMC and bone width. We used linear regression to examine the association between postmenopausal estrogen levels and changes in bone traits.

At study start in 1977, all women gave informed oral consent, but no permission from the review board and no consent forms were required. Approval of the study was granted by the Ethics Committee of Lund University in 1999, and written informed consent was then obtained.

## Results

BMC, bone width, and aBMD at study start and study end and annual changes in these traits in the premenopausal and the different postmenopausal periods are presented in Table 1. A young chronological menopausal age was correlated with a greater loss in BMC ($r = -0.42$, $p < 0.001$) and a greater gain in bone width ($r = 0.48$, $p < 0.001$) but only in the first postmenopausal period.

Before menopause, there was a significant loss in BMC but no increase in bone width (Table 1). After menopause, there