Influence of Body Weight on Rates of Change in Bone Density of the Spine, Hip, and Radius in Postmenopausal Women

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Summary. Interrelationships between percent of ideal body weight (%IBW), serum estrogen levels, and change in bone mineral density (ΔBMD) and bone mineral content (ΔBMC) were studied in 288 postmenopausal women aged 41–71 years who participated in a 2-year calcium supplement trial. The spine (L2–L4) and femoral neck were measured by dual-photon absorptiometry, and the radius was measured by single-photon absorptiometry. Years since menopause, calcium intake, and initial BMD or BMC were included as independent variables in two-phase regressions of ΔBMD and ΔBMC on %IBW. Increased %IBW protected against loss of spine BMD [regression slope estimate = 0.05, 95% C.I.: (0.03, 0.26)] and BMC in women up through about 106 %IBW but not in heavier women. Increased %IBW was not significantly related to ΔBMD or ΔBMC at the femoral neck or radius. Women above 106 %IBW had significant gains in spine and femoral neck area (P < 0.05). Serum estrone and estradiol were positively correlated with ΔBMD and ΔBMC at the femoral neck only.

Key words: Bone mineral density – Body weight – Menopause – Dual-photon absorptiometry – Bone area.

Longitudinal studies of postmenopausal women have shown positive correlations of serum estrone and estradiol concentrations with change in radius or forearm BMD [9, 10, 12] and no correlation with change in spine BMD [12]. The effect of estrone and estradiol levels on change in femoral neck BMD has not been established.

Here, we examine the influence of %IBW on rates of change BMD and BMC of the lumbar spine, femoral neck, and radius in 288 healthy postmenopausal women who completed a 2-year calcium supplement trial. We also examine serum estrogen levels in relation to %IBW and to rates of bone change at the three sites.

Methods

Subjects

As described previously [13], women with habitually low dietary calcium intakes (half less than 400 mg/day, half between 400 and 650 mg/day) were enrolled in the calcium trial, and randomly assigned to treatment with placebo or 500 mg of calcium as calcium citrate malate (Procter and Gamble, Cincinnati, OH) or calcium carbonate. Tablet compliance was 98% in each supplement group over the 2-year study period. The study group for these analyses includes the 288 women who completed the calcium field trial, knew their exact age at menopause, and had complete scan data at one or more bone sites. The protocol was approved by the Human Investigation Review Committee at Tufts University, and all subjects gave written informed consent. The women had no history of nontraumatic fracture and no evidence of vertebral compression fracture on lateral thoracic or lumbar spine radiographs. None used estrogen or other steroids or had a history of disorders associated with bone metabolism.

Measurements

The bone measurements used in this analysis were made at enrollment and after 1 and 2 years of treatment. BMD and BMC of the lumbar spine (L2–L4) and femoral neck were measured by dual-photon absorptiometry using a DP-3 model scanner (Lunar Radiation Corp., Madison, WI) with a coefficient of variation of 2.3% at the spine and 3.3% at the femoral neck. Subjects with calcification of the aorta or osteophytes in the lumbar scan field were excluded from spine analyses [14]. Spine measurements were corrected for drift resulting from 153-gadolinium source changes, and source decay, and for variability related to subject thickness [15]. No drift was observed in the femoral neck measurements [16]. BMD and BMC of the nondominant radius (two-thirds distal site) were measured by single-photon absorptiometry using an SP-2 model scanner (Lunar Radiation Corp.) with a coefficient of variation of 1.0%. Percent changes in BMD (ΔBMD) and BMC (ΔBMC) were calculated for the 2-year period between the first and last study visits and then annualized.

Height in centimeters and weight in kilograms were measured at each visit. Percent of ideal body weight was computed from actuarial weight-for-height tables [17]. Physical activity during waking
hours was measured in kcals/hour with Caltrac accelerometers (Hemokinetics Inc., Madison, WI) worn for 1 week.

Serum estrone and estradiol concentrations were measured at the first study visit. Estradiol was analyzed in duplicate by radioimmunoassay in the laboratory of Dr. Longcope (74% of sample) [18] or with kits from Serono Laboratories, Braintree, MA. Intra- and interassay coefficients of variation were 3.6 and 7.1% (Dr. Longcope) and 5.0 and 7.5% (Serono), respectively. Estrone was measured in the laboratory of Dr. Longcope [18]. Intra- and interassay coefficients of variation were 4.6 and 9.9%. As significant amounts of estradiol in the serum can produce upwardly biased measures of estrone, we limited the study of serum estrone to the 263 women whose serum estradiol levels were below 111 pmol/liter. Dietary calcium intake (mg/day) was assessed at enrollment and at four semi-annual visits with a food frequency questionnaire [19].

Simple correlations, partial correlations, linear regressions, t-tests and chi-square tests were performed with SPSS-X [20]. Adjusted means from analysis of covariance were computed with SAS PROC GLM [21]. Years since menopause, total calcium intake, and initial BMD or BMC were included as independent variables in multiple regressions and covariance analyses because they were significantly correlated with ∆BMD or ∆BMC at one or more bone sites. The logarithm of years since menopause was used in linear and two-phase models because of a nonlinear relation of years since menopause to ∆BMD and ∆BMC of the spine. Although results of the calcium field trial [13] showed differences in the effects of the two calcium supplements on ∆BMD, analysis of covariance showed no significant interaction between %IBW and supplement type, and supplement type was therefore not controlled for in final analyses. The SPSS-X constrained nonlinear regression procedure (CNLR) was used to perform two-phase regression analyses in which separate linear regression lines are fitted to data below and above an estimated changepoint value where the lines are constrained to intersect. This least squares regression procedure estimates the regression slopes and changepoint value simultaneously. We have reported the 95% trimmed range of 100 bootstrap estimates for each parameter as the 95% confidence interval (CI) because bootstrap estimates of variability are superior to those obtained by using asymptotic standard errors [22]. The letter “b” signifies “regression slope estimate” in the presentation of statistics from multiple and two-phase regressions.

The P-values in the text and tables are two-tailed. P-values below 0.05 were considered to indicate significance.

Results

The 288 women in this study ranged in age from 41 to 71 years (mean 59 ± 6) and were 1–30 years postmenopausal (mean 11 ± 7) at enrollment. Mean and median %IBW were 118 ± 19 and 115%, respectively, and ranged from 78 to 208%. Scatterplots of change in BMD with %IBW are shown in Figure 1.

Because our cross-sectional results indicated that the relationship between BMD and %IBW was different in subjects above and below 115 %IBW [1], we used a two-phase regression procedure to determine if there was a similar changepoint in %IBW with respect to ∆BMD and ∆BMC. Percent IBW was controlled for total calcium intake, initial BMD, and the logarithm of years since menopause in regressions that identified the best changepoint in %IBW at each bone site and estimated the slope of %IBW at values above and below the changepoint.

At the spine, there was a changepoint in the ∆BMD regression of 106.2 %IBW (95% CI: 89, 110) (Table 1). In this data set, 106.2 %IBW corresponds to a body mass index of 23.6 (kg/m²). Below 106.2 %IBW, the slope of %IBW was significantly positive (95% CI: 0.03, 0.26) whereas above, the slope was not significantly different from zero (95% CI: −0.02, 0.01). As there was no overlap in the 100 bootstrap estimates (Fig. 2) of the %IBW slope for women above and below the changepoint, the two slopes were significantly different from each other. The changepoint and slopes for ∆BMC were similar to those for ∆BMD. The fraction of variability in spine ∆BMD accounted for by years since menopause, total calcium intake, and initial BMD in the lighter subjects (R²) increased from 0.14 to 0.19 when %IBW was added as an independent variable. In the heavier group, the R² was 0.08 both with and without inclusion of %IBW as an independent variable.

At the femoral neck, the changepoint estimate for the ∆BMD regression was 110.6 %IBW (95% CI: 87, 125), but the slopes of %IBW below and above 110.6 were not significantly different. Furthermore, the slope of %IBW calculated in a linear model was not significantly different from zero (b = 0.01, 95% CI: −0.01, 0.03; r = 0.09 N.S.). The results for ∆BMC were similar.