Osteoporosis Int (1993) 3:314–321

Osteoporosis International

Original Article

Body Size, Estrogen Use and Thiazide Diuretic Use Affect 5-year Radial Bone Loss in Postmenopausal Women

M. R. Sowers[1], M. K. Clark[2], M. L. Jannausch[1] and R. B. Wallace[3]

[1]Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan, USA, [2]College of Nursing, and [3]Department of Preventive Medicine and Environmental Health, College of Medicine, University of Iowa, Iowa City, Iowa, USA

Abstract. Understanding factors associated with more rapid bone mineral loss among aging women is important for establishing preventive strategies for intervention. This study reports factors associated with the 5-year change in radial bone mineral density (BMD) determined prospectively in 435 women aged 55–80 years at baseline. The baseline study included measurement of radial BMD (gm/cm^2) by single photon densitometry and personal interview. The baseline protocol was replicated 5 years later in a follow-up study. Women with a lower baseline weight or Quetelet index, smaller triceps skinfold and less arm muscle area had significantly greater 5-year bone loss ($p = 0.001$). Current users of estrogens had less radial bone loss (2.8% vs 7.3%, $p = 0.0005$) than women not currently using estrogens. Current users of estrogen had significantly less 5-year loss if use had been for 5 years or longer (−1.0% vs −6.9%, $p = 0.05$). Current users of the thiazide class of medications had less 5-year radial bone loss (5.0% vs 7.4%, $p = 0.0035$) than women without current thiazide use. Baseline dietary calcium, alcohol consumption and smoking were not associated with BMD change. This suggests that greater body size, and current use of estrogens or thiazide antihypertensives are associated with less radial bone mass loss in a 5-year period among postmenopausal women.

Correspondence and offprint requests to: MaryFran R. Sowers, Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI 48109, USA.

Keywords: Bone; Bone loss; Epidemiology; Estrogen; Prospective study; Thiazide

Introduction

Because of the social, health and economic impact of fractures, loss of bone mass and osteoporosis are important. The lifetime risk of hip fracture is estimated to be 15% in women and 5% in men; this is equivalent to the lifetime risk of developing breast, uterine and ovarian cancer in women and prostate cancer in men. The cost of health care associated with fractures was estimated to be $6.1 billion in 1984 [1,2] and has been projected to be more than $100 billion by the year 2020 [3], driven, in part, by the increasing proportion of elderly persons in society.

The magnitude of bone loss is important in understanding the process that may ultimately lead to fracture. There have been few prospective studies of bone mineral density (BMD) which characterized bone loss with aging using contemporary, precise bone measurement methodology [4–9] and which considered multiple risk factors for rate of bone loss simultaneously. We have recently reported that the average 5-year radial bone mineral loss was 6% among women aged 55–80 years at baseline [9]. Understanding factors associated with more rapid bone mineral loss among aging women is important for establishing preventive strategies for intervention.

This report describes those factors associated with 5-year change in radial BMD determined prospectively in women who were aged 60–85 years at follow-up

Table 1. Baseline characteristics (mean ± SEM) of follow-up participants and nonrespondents in three communities

	Participated	Moved	Died	Refused	*p* value
n	435	26	33	29	
Radial BMD (g/cm^2)	0.62±0.005	0.612±0.020	0.587±0.018	0.578±0.019	0.0561
Age (yr)	66.9±0.3	68.1±1.4	69.6±1.2	69.5±1.3	0.0404
Height (cm)	159.1±0.3	160.2±1.1	159.9±0.9	158.0±1.1	0.4392
Weight (kg)	70.4±0.7	68.2±2.7	69.0±2.4	69.2±2.6	0.7815
Quetelet index (kg/m^2)	27.8±0.3	26.6±1.0	27.0±0.9	27.7±1.0	0.5906
Muscle area (cm^2)	54.1±0.8	55.1±3.1	52.3±2.8	57.2±3.0	0.6682
Skinfold thickness (mm)	18.7±0.2	17.7±0.9	17.6±0.8	17.0±0.8	0.1267
Age at menopause (yr)	47.4±0.3	47.9±1.2	48.1±1.1	46.4±1.1	0.7148

measurement. This study is an extension of our earlier work and includes data from an additional 164 women, making a total study group of 435 elderly women.

Methods

The study population included women living in three demographically similar rural communities in northwest Iowa. State-specific census data from 1970 and 1980 indicated that the communities were similar with respect to population size, age distribution, proportion of foreign-born subjects, mean income and occupational categories. The population of each community was less than 2000 persons. The municipal drinking water supplies in the three communities had divergent calcium and fluoride content. The drinking water in one community had an elemental calcium concentration of 15 ± 3 mg/l and a naturally occurring fluoride concentration of 4 ± 0.1 mg/l; drinking water in the second community averaged 375 ± 8 mg/l elemental calcium and was fluoridated to a level of 1 mg/l; drinking water in the third community had an average elemental calcium content of 67 ± 4 mg/l and was fluoridated to a level of 1 mg/l, as determined by the state public health laboratory.

Women were eligible for the baseline study if they had lived in their respective communities for the 5 years prior to the survey. All participants were ambulatory and had not experienced wrist or forearm fractures in the 2 years prior to baseline radial BMD assessment. All participants were aged 55–80 years at the baseline measurement, postmenopausal, and of northern European origin, as has been described [10]. Baseline information was gathered in the communities from May to August 1983 or from May to August 1984. Each woman was re-examined exactly 5 years after her initial measurement. To simplify presentation, all data collected in 1983 or 1984 will be labeled 'baseline' while data collected in 1988 or 1989 will be labeled 'follow-up'.

Selected characteristics for women who participated in both the baseline and follow-up studies (n = 435) were compared with the characteristics of those women who participated only in the baseline study because they had moved from their communities (n = 26), died (n = 33) or refused participation at follow-up (n = 29). The characteristics are summarized in Table 1. Participants in the follow-up study had greater radial BMD, were younger, and had been menopausal for a shorter time (p = 0.05).

Bone Mass and Physical Measurements

Radial bone mass was measured, at both time points, using a Norland 278 photon absorpiometer (Norland, Madison, WI) with a ^{125}I source. Bone mass, expressed as the bone mineral to bone width ratio (g/cm^2), was measured distally at a site one-third the distance between the styloid process and the olecranon, a site which is at least 95% cortical bone. The same procedures and instrumentation were used at both baseline and follow-up examinations. A single observer measured bone mass of all persons at baseline while a different single observer measured bone mass at follow-up. Bone mass loss was calculated on an individual basis not on a summary basis across the entire group of women.

At each time point, one trained observer measured each participant for height, weight, triceps skinfold thickness and mid-arm circumference according to standardized procedures. Subjects were weighed in light clothing without shoes to the nearest 0.1 kg using an electronic scale; height was measured to the nearest 0.1 cm using an anthropometric plane and scale. Triceps skinfold thickness was measured with Lange calipers and recorded in millimeters using the mean of three consecutive readings; mid-arm circumference was measured to the nearest 0.1 cm and used with triceps skinfold to estimate muscle area. Quetelet index was calculated as weight/height^2 in kilograms and meters, respectively.

Nutrient Intake Assessment

At baseline, each participant responded to a food frequency instrument to characterize intake of foods high in calcium and vitamin D; they also recalled their intake of food over the preceding 24 h. Interviewers were trained in techniques to elicit recall of food and beverage intake, including the use of color photographs

to enhance the recall of portion sizes. To promote accuracy, food and beverage intakes from each recall and the food frequency were independently coded twice. The correlation between calcium intake at baseline estimated by the two methods was 0.56.

Nutrient values were assigned to coded foods and beverages using the US Department of Agriculture (USDA) Food Composition Tape #456. This computer tape provides 20 nutrient values, including calcium, for more than 2600 foods. It does not include values for vitamin D, so a supplemental computer program was developed to assign vitamin D values to foods and beverages. These values were based on information from the food composition tables published in *McCance and Widdowson's Composition of Foods* [11] or on other information sources about fortified products such as milk and dry cereals. Nutrient values for the food frequency were based on the algorithms from the NCI food frequency [12].

The interviewer gathered information about nutritional supplements by observing the labels of currently used preparations and asking the participant to recall the number, frequency and individual duration of use of the preparations. These estimates of supplements were added to nutrient intake from food and water to calculate total intake.

Reproduction, Climacteric and Medical History

Interviews at baseline and follow-up included questions about estrogen replacement therapy (including time intervals of use) and surgical menopause. Detailed medication use histories were taken at both points in time. We compared responses to questions about ever use of perimenopausal estrogen (Premarin, Wyeth) and the duration of that use as reported at both baseline and follow-up interviews. Data analysis describing a role for estrogen was limited to those women who were consistent in their report of estrogen use and whose reported duration of use was congruent (± 1 year).

Procedures followed were approved by the Universities of Michigan and Iowa Committees on Human Experimentation and Radiation Protection Subcommittees.

Data Analysis

Chi-squared tests of homogeneity were used to ascertain whether women who did not participate in the follow-up were different in terms of marital status, self-perception of health, education, parity and medication use compared with women who did participate. Students' *t*-test and analysis of variance were used to test whether baseline measures of age, body size, age of menopause and BMD were comparable between respondents and non-respondents in the re-examination.

All continuous variables were evaluated for normalcy of distribution; those variables identified as not having a normal distribution (such as nutrient intake) were either logarithm transformed or changed into categorical variables (such as alcohol intake). Continuous radial BMD variables were: radial BMD (1983), radial BMD (1988), and 5-year BMD change expressed as the difference between measured BMD in 1983 and 1988 (g/cm^2) and the percentage change in 5 years.

Univariate summaries were produced for continuous BMD variables, overall and according to community. *F*-test values from multiple variable linear regression and logistic regression analyses were used to test for a difference in bone and physical measurements according to community status. Because a community difference in BMD was identified, all subsequent analyses included adjustment for community. Multiple variable regression and multiple response conditional logistic regression analyses were used to assess relationships between 5-year BMD change and baseline BMD value, body size measures, medication use and nutrient intake, after adjusting for age [13, 14].

Results

The mean radial BMD at baseline and follow-up, as well as the difference (both absolute and percentage) between baseline and follow-up measures, are shown in Table 2. There is remarkable consistency in associations between the risk factors and the two measures of 5-year bone mineral, the absolute change or percentage change; therefore, risk factor associations in this paper will be related to percentage loss for ease of presentation.

Baseline radial BMD was highly associated (r^2 =

Table 2. Radial bone mineral density (mean±SD) measured at baseline and follow-up, with percentage change and BMD difference (g/cm^2) in 5 years among 435 postmenopausal women

Age group at baseline)yr)	*n*	Baseline BMD (g/cm^2)	Follow-up BMD (g/cm^2)	% BMD change in 5 years	BMD difference in 5 years
55–80	435	0.620±0.099	0.577±0.102	−6.9±0.7	−0.043±0.042
55–59	85	0.677±0.082	0.629±0.076	−7.9±0.6	−0.048±0.044
60–64	85	0.654±0.087	0.604±0.096	−7.8±0.6	−0.050±0.038
65–69	97	0.621±0.096	0.580±0.098	−6.5±0.7	−0.041±0.041
70–74	84	0.590±0.098	0.553±0.105	−6.4±0.7	−0.037±0.040
75–80	84	0.560±0.090	0.520±0.098	−7.1±0.8	−0.039±0.047

0.86, $p < 0.0001$) with radial BMD observed at follow-up, after adjusting for age and community of residence. However, there was no important relationship between baseline BMD and percentage BMD change ($p = 0.30$), suggesting that lower BMD was not a risk factor for more rapid bone loss in a 5-year period among women of this age group. We explored the possibility of a quadratic relationship between baseline radial BMD and percentage 5-year radial bone loss, and found no evidence of non-linearity when age or baseline radial BMD were evaluated using quadratic terms.

Several measures of body size were evaluated as possible risk factors for increased rate of radical bone loss (Fig. 1). Women with a lower baseline weight or Quetelet index, smaller triceps skinfold and less humeral muscle area were significantly more likely to experience a greater percentage bone loss either with or without adjustment for community ($p = 0.001$). Thus, a 60-year-old woman who weighed 65 kg could be expected to lose an additional 1.0% or 0.005 g/cm^2 more radial bone in a 5-year period than another woman of the same age who weighed 73 kg.

Ever use and duration of estrogen use were evaluated for possible impact on 5-year rate of radial bone loss. This analysis was undertaken among the 86% of women who were consistent reporters (i.e. consistent reports of whether or not they had ever used estrogens and the dates of use at baseline and follow-up). The consistently reporting group included current users at the time of follow-up investigation ($n = 24$), previous users ($n = 71$) and never users ($n = 244$); mean baseline age, Quetelet index and years of estrogen use are shown in Table 3 for each subgroup. As shown in Table 3, following adjustment for age, community and body size, use of estrogens at follow-up was associated with less 5-year bone loss. Current users lost less radial bone mass (2.8% vs 7.3% and 7.4%, $p = 0.005$) than did women in either of the other two categories.

However, duration of estrogen use was an important factor among current users (see Table 4). Current users of estrogen had significantly less 5-year loss is use had been for 5 years or longer (−1.0% vs −6.9%, $p = 0.05$). Duration of use was not associated with either follow-up

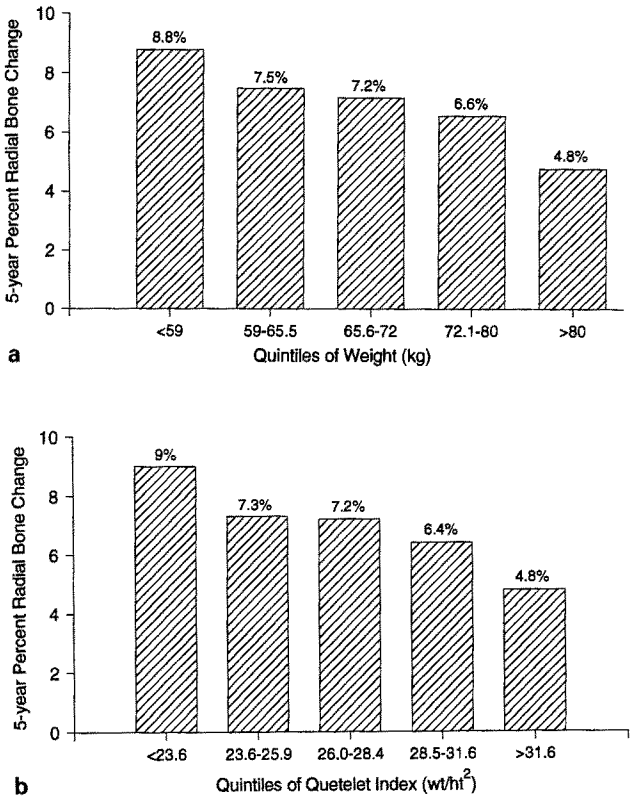

Fig. 1a,b. Five-year percentage bone change by quintiles of weight (**a**) and Quetelet index (**b**) in women aged 55–80 years in three Iowa communities ($n = 432$).

BMD or 5-year BMD loss among past users of estrogens.

We compared the bone loss of women in four categories of thiazide use as shown in Table 5. There was significantly less 5-year bone loss among women who had a current thiazide prescription. When women who had never used thiazides and past-only users ($n = 343$) were compared with women who reported current use ($n = 88$), the current users had less 5-year radial bone loss (7.4% vs 5.0%, $p = 0.0035$).

Factors which might influence this relationship are shown in Table 6. After adjustment for age, commun-

Table 3. Selected characteristics of women aged 55–80 years, after classification by estrogen use status

	Estrogen use status			
	Current use	Past use	Never used	p value
n	24	71	244	
Age (yr)	63.1±1.4	66.5±0.8	67.5±0.4	0.0107
Quetelet index (kg/m^2)	25.7±1.1	27.7±0.6	28.0±0.3	0.1203
Years of use	11.4±1.4	4.1±0.8	—	—
Years since menopause	23.7±1.8	23.4±1.1	24.3±0.6	0.7221
Baseline BMD (g/cm^2)[a]	0.634±0.018	0.618±0.011	0.618±0.006	0.6921
Follow-up BMD (g/cm^2)[a]	0.620±0.018	0.574±0.011	0.572±0.006	0.4890
% Radial BMD change[a]	2.8%±1.3	7.4%±0.7	7.3%±0.4	0.0005

[a] Adjusted for age, community and Quetelet index.

Table 4. Duration of estrogen use and 5-year rate of BMD loss

Use status	*n*	Duration of use (yr)	Age at baseline (yr)	Years since menopause	Years of perimenopausal estrogen use	Years since estrogen use	5-year % bone loss (mean±SEM)
Past	51	<5	66.8±0.9	23.4±1.2	1.3±0.3	20.8±1.3	−7.4±1.0
	20	≥5	65.7±1.4	23.4±1.8	11.1±0.5	12.8±2.1	−7.3±1.6
Current	8	<5	65.2±2.2	23.1±2.9	1.4±2.8	—	−6.9±2.2
	16	≥5	62.0±1.5	23.9±2.1	16.4±2.0	—	−1.0±1.5*

Five-year percentage age loss is adjusted for age, Quetelet index and community in regression analysis.
*$p=0.05$.

Table 5. Duration and ever use of thiazide antihypertensive medication, BMD and 5-year rate of radial BMD loss

Use status	*n*	Baseline BMD (g/cm^2; mean±SEM)	Follow-up BMD (g/cm^2; mean±SEM)	5-year % bone loss (mean±SEM)
Never	287	0.60±0.005	0.56±0.005	−7.2±0.4
Past only	56	0.64±0.018	0.60±0.011	−7.4±1.0
Current	21	0.64±0.019	0.62±0.019	−4.9±1.5
Current and past	67	0.65±0.011	0.61±0.011	−5.9±0.8

Follow-up BMD and 5-year percentage age loss are adjusted for age, Quetelet index, estrogen use and community in regression analysis.

Table 6. Description of population attributes according to thiazide use characteristics

	Thiazide use				
	Never used	Past only	Now only	Past and now	*p* value
Smoked					
Ever (%)	19	20	15	12	
Never (%)	81	80	85	88	0.51
Age (yr)	65.9	68.0	69.5	68.7	0.06
Years since menopause	18.5	19.8	20.7	21.7	0.06
Quetelet index (kg/m^2)	26.9	28.8	30.1	30.0	0.0001
Calcium intake (mg)					
Food frequency: follow-up	853	911	933	822	0.71
baseline	807	797	828	777	0.12
24-h recall: follow-up	807	735	825	686	0.06
baseline	903	830	975	840	0.34

ity, Quetelet index and estrogen use, thiazide use still explained a significant proportion of variation in 5-year percentage change ($p = 0.05$).

Baseline intakes of protein, dietary/supplement calcium and dietary/supplement vitamin D intake were not predictive of 5-year radial bone percentage change. The age-adjusted models of bone change and these nutrients were non-significant whether dietary intake was estimated from a food frequency instrument or a 24-h recall. Likewise, there was no relationship when calcium intake was expressed per 1000 kilocalories and related to percentage bone mass change.

As shown in Table 7, calcium and vitamin D intake were each dichotomized with Recommended Dietary Allowance as the criterion [calcium <800 mg ($n = 199$) vs ≥800 mg ($n = 233$); vitamin D <400 IU ($n = 269$) vs ≥400 IU ($n = 163$)]. There was no significant relationship between radial bone loss and either two-level variable. When women were categorized by their joint calcium and vitamin D intake [dietary calcium <800 mg and vitamin D <400 IU ($n = 130$); calcium intake ≥800 mg but vitamin D <400 IU ($n = 139$); calcium <800 mg and vitamin D ≥400 IU ($n = 69$); and calcium intake ≥800 mg with vitamin D ≥400 IU ($n = 94$)], no relationship was found between calcium/vitamin D intake and percentage bone loss.

As shown in Table 8, there was no association of alcohol intake with bone change, but women with greater alcohol use were younger and had fewer years since menopause. There was no association between

Table 7. Five-year radial bone change by categories of dietary calcium and vitamin D (including the contribution of supplements)

Nutrient	*n*	% change[a]	*p* value
Calcium intake (mg)			
<800	199	6.8±0.5	0.6210
≥800	233	7.1±0.4	
Vitamin D intake (IU)			
<400	269	6.5±0.4	0.1221
≥400	163	7.6±0.5	
Combined calcium and vitamin D intake			
<800 mg <400 IU	130	6.4±0.6	0.4643
<800 mg ≥400 IU	69	7.5±0.5	
≥800 mg <400 IU	139	6.7±0.6	
≥800 mg ≥400 IU	94	7.7±0.7	

[a] Adjusted for age, community and Quetelet index.

Table 8. Characteristics of study population according to alcohol use at baseline

	Never	<4 drinks/ week	≥4 drinks/ week
n	118	122	192
%Bone loss[a]	7.2±0.6	6.6±0.6	7.0±0.5
% bone loss, adjusted[b]	7.2±0.6	6.6±0.6	6.8±0.5
Age (yr)	68.2	68.4	64.9
Years since menopause	20.5	21.0	17.5
Quetelet index (kg/m^2)	27.4	27.7	27.7
% now smoke	4	4	12.5

[a] Unadjusted; p=0.77.
[b] Adusted for community, age and Quetelet index; p=0.79.

alcohol consumption (never drank, less than 4 drinks/ week, or 4 or more drinks/week) and rate of bone mineral change after adjusting for age, menopause, body size and community.

Smoking was not associated with 5-year bone change when categorized as never smoker, previous smoker or smoker in the 5-year interval (p = 0.72). As shown in Table 9, classification according to pack-years was not associated with a significant difference in 5-year bone loss. The median number of packs smoked in this population is 4500.

Reproduction and the climacteric were evaluated for association with 5-year rate of bone loss. We observed no association between age at menopause or time since menopause and 5-year BMD change following adjustment for age, body size and community. When women were classified according to parity (nulliparous, parity >1–3 or parity >3 live births), there was no association with rate of change. Similarly, women who had had two or more miscarriages had no difference in 5-year bone loss among these postmenopausal women.

Table 9. Characteristics of study population according to smoking behaviour and duration

	Never	<median pack-years	>median pack-years
Number	353	40	36
% of bone loss[a]	6.2	8.5	5.6
% of bone loss, adjusted[b]	6.8	8.3	5.1
Age (yr)	67.7	63.0	62.0
Years since menopause	20	16	14.5
Quetelet index (kg/m^2)	27.6	28.3	27.6
% now smoke	0	48	74

[a] Unadjusted; p=0.1728.
[b] Adusted for age, community and Quetelet index; p=0.1113.

Discussion

Given the limited number of interventions currently available to treat bone loss with aging, identification of factors which minimize 5-year bone change is important. Estrogens have been identified as slowing or curtailing bone loss in a number of clinical studies (see [15] and [16] for reviews). We have found that current estrogen use was associated with less bone loss in a group whose average age is 63 years, which is 15 years after the average age of menopause in this population. Other studies, including those using estradiol implants, have confirmed a positive effect of estrogens on bone mineral density and fracture among older women [17–19]. It is important to note that the most potent effect of these estrogens appeared to be associated with current use, but that the duration of current use had to be in excess of 5 years. These data suggest that prior use of estrogens does not delay bone loss beyond the time of use, even if that prior use was of relatively long duration. Furthermore, these data suggest that protection is associated with estrogen even in the period of time beyond the perimenopause. Although there is relatively low prevalence of estrogen use in this study, this finding in a community-based population supports an accumulating body of literature.

We observed that current thiazide use was associated with less radial bone loss, though the reduction was not as substantial as that observed with the use of estrogens. The impact of thiazides was associated with current but not previous thiazide use. This impact is also independent of current estrogen use as only 4 women were using thiazides and estrogens concurrently. It has been proposed that thiazide use might forestall bone loss by curtailing urinary calcium excretion [20]. There was no difference in baseline dietary calcium intake between users and non-users of thiazides. Therefore, the contrast in rate of 5-year bone loss between current and past thiazide users would suggest that urinary calcium loss resumed its previous rate among those women who were past users of thiazides. While we [21] and others [22] have previously reported an association, a clinical trial of thiazide use suggested this might be a transitory effect [23].

It is well recognized that body size is associated with level of bone mass, and we observed that measures of greater body size, including measures of both obesity and muscle area, were associated with less 5-year bone change. Whether obese women have greater bone mass because of aromatization of adrostenedione to estrone in the adipocytes [24] or a mechanical role associated with bone loading has not been defined. Ribot et al. [25] have reported a protective effect of obesity in postmenopausal bone loss. However, levels of estradiol and testosterone did not differ between obese and nonobese postmenopausal women, suggesting that body size may have a mechanical rather than a hormonal role in bone change.

We can only speculate as to why dietary calcium and vitamin D intake at baseline were not associated with subsequent rates of radial bone change. While many may be disappointed at our failure to find a relationship between bone mass change and calcium intake, the lack of an observed relationship is consistent with many other studies which included various study designs [26]. Several factors may account for these findings. First, in a widely cited study of calcium supplementation [27] no effect of supplementation was observed in women whose baseline intake exceeded 400 mg calcium per day. Further, the most promising supplement was in a citrate complex, a chemical configuration not widely available in foods. Second, assessment of calcium, like that of other dietary nutrients, has been plagued with methodological problems. For example, Sempos et al. [28] have estimated that six 24-h recalls per individual are needed to assure that the efficiency of estimating the true population correlation coefficient is greater than or equal to 90%. A single 24-h recall used to estimate an individual's calcium intake has an efficiency of 50%. Thus, findings from studies based on 24-h food recalls should be regarded with caution unless accompanied by other methodologies. We took this approach to evaluating diet in our study population, and utilized both the 24-h recall method and the food frequency method. In addition, calcium intake from supplements and drinking water were considered. Even when considering vitamin D contribution or adjustment for total calories consumed, we could not identify a statistically significant relationship with bone mineral change in this well-nourished population.

This prospective study and its implementation have several limitations. It describes cortical bone of the radius measured by single photon absorptiometry and does not provide measures of the spine and hip. BMD was measured at the radius with single photon densitometry for historical reasons. When the study began, single photon densitometry was the only technique available with minimal radiation exposure that was acceptable to the ethics committee for community-based studies. It is a highly precise methodology, a characteristic desirable in longitudinal studies with repeated measurements, where each subsequent measure can be associated with potential for error. The follow-up examination included measures of both radial BMD by single photon densitometry and femoral neck BMD by dual photon absorptiometry.

A second limitation is the relatively short 5-year follow-up – a limitation shared with many studies. There are two other reported longitudinal studies of BMD, using the more precise photon densitometric methodology, which has reported data from a longer time interval. The study by Johnston et al. [4,5] reports an average follow-up of approximately 6.5 years. The study of 73 women by Falch and Sandvik [29] was 10 years in duration.

Loss to follow-up is a major concern in all prospective studies. The refusal rate for re-examination was extremely low (6%), although an additional 12% of the baseline study group did not participate because of death (7%) or moving (5%).

In summary, we reiterate that understanding the factors associated with more rapid bone mineral loss among aging women is important for establishing preventive strategies for intervention and risk profiles for women who may need frequent follow-up. Baseline radial BMD was highly associated with follow-up radial BMD; however, there was no relationship between baseline BMD and percentage BMD change, suggesting that lower BMD was not a risk factor for more rapid bone loss in a 5-year period among these women. These data suggest that greater body size, and current use of estrogens or thiazide antihypertensive medication are associated with less radial bone mass loss in a 5-year period among postmenopausal women. Baseline dietary calcium, alcohol consumption and smoking were not associated with BMD change.

Acknowledgement. This work was supported by grant NIH-NIA 1-R01 AG07094.

References

1. Melton LJ III. Epidemiology of fractures. In: Riggs BL, Melton LJ III, editors. Osteoporosis: etiology, diagnosis, and management. New York: Raven Press, 1988:133–54.
2. Holbrook TL, Grazier K, Kelsey JL, et al. The frequency of occurrence, impact, and cost of selected musculoskeletal conditions in the United States. Chicago, IL: American Academy of Orthopaedic Surgeons, 1984:1–187.
3. Mack TM, Ross RK. A current perception of HRT risks and benefits. In: DeLuca HF, Mazess R, editors. Osteoporosis: physiological basis, assessment, and treatment. Madison, WI: University of Wisconsin, 1990:161–78. (Proceedings of the 19th Steenbock Symposium, Madison, Wisconsin, 5–8 June 1989.)
4. Johnston CC, Jr., Norton JA, Khairi RA, Longcope C. Age-related bone loss. In: Barzel U, editor. Osteoporosis II. New York: Grune and Stratton, 1979:91–100.
5. Hui SL, Wiske PS, Norton JA, Johnston CC, Jr. A prospective study of change in bone mass with age in postmenopausal women. J Chronic Dis 1982;35:715–25.
6. Davis JW, Ross PD, Wasnich RD, Maclean CJ, Vogel JM. Comparison of cross-sectional and longitudinal measurements of age-related changes in bone mineral content. J Bone Miner Res 1989;4:351–7.
7. Riggs BL, Wahner HW, Melton LJ III, et al. Rates of bone loss in the appendicular and axial skeletons of women: evidence of

substantial vertebral bone loss before menopause. J Clin Invest 1986;77:1487–91.
8. Ruegsegger P, Dambacher MA, Ruegsegger E, Fischer JA, Anliker M. Bone loss in premenopausal and postmenopausal women. J Bone Joint Surg [Am] 1984;66:1015–23.
9. Sowers MF, Clark K, Wallace R, Jannausch M, Lemke J. Prospective study of radial bone mineral density in a geographically defined population of postmenopausal Caucasian women. Calcif Tissue Int 1991;48:232–9.
10. Sowers MFR, Wallace RB, Lemke JH. The relationship of bone mass and fracture history to fluoride and calcium intake: a study of three communities. Am J Clin Nutr 1986;44:889–98.
11. Southgate PPA, Southgate DAT editors. McCance and Widdowson's composition of foods. 4th edition. Amsterdam: Elsevier/North-Holland Biomedical Press, 1978.
12. Block G, Hartman AM, Dresser CM, et al. A data-based approach to diet questionnaire design and test. Am J Epidemiol 1986;123:453–69.
13. Schlesselman JJ. Case–control studies: design, conduct, analysis. New York: Oxford University Press, 1982.
14. Kleinbaum DG, Kupper LL. Applied regression analysis and other multivariable methods. North Scituate, MA: Duxbury Press, 1988.
15. Riggs BL, Melton LJ. The prevention and treatment of osteoporosis. N Engl J Med 1992;327:620–7.
16. Lindsey R. Sex steroids in the pathogenesis and prevention of osteoporosis. In Riggs BL, Melton LJ, editors. Osteoporosis: etiology, diagnosis, and management. New York: Raven Press, 1988:333–58.
17. Lindsay R, Tohme JF. Estrogen treatment of patients with established postmenopausal osteoporosis. Obstet Gynecol 1990;72:290–5.
18. Savvos M, Studd JWW, Normon S, et al. Increase in bone mass after one year of percutaneous oestradiol and testosterone implants in post-menopausal women who have previously received long-term oral estrogens. Br J Obstet Gynecol 1992;99:757–60.
19. Spector TD, Brennan P, Harris PA, et al. Do current regimes of hormone replacement therapy protect against subsequent fracture? Osteoporosis Int 1992;2:219–24.
20. Ivanovich P, Fellows H, Rich C. The absorption of calcium carbonate. Ann Intern Med 1967;66:917–23.
21. Sowers MFR, Wallace RB, Lemke JH. Correlates of mid-radius bone density among postmenopausal women: a community study. Am J Clin Nutr 1985;41:1045–53.
22. Wasnich RD, Benfante RJ, Yano K, Heilbrun L, Vogel JM. Thiazide effect on the mineral content of bone. N Engl J Med 1983;309:344–7.
23. Transbol I, Christianson GF, Jensen GF, Christensen C, McNair P. Thiazide for the postponement of postmenopausal bone loss. Metabolism 1982;31:383–6.
24. Siiteri PK, MacDonald PC. Role of extraglandular estrogen in human endocrinology. In: Greep RO, Astwood E, editors. Handbook of physiology: endocrinology. Washington, DC: American Physiological Society, 1973;615–22.
25. Ribot C, Tremollieres F, Pouilles JM, et al. Obesity and postmenopausal bone loss: the influence of obesity on vertebral density and bone turnover in postmenopausal women. Bone 1987;8:327–31.
26. Cumming RG. Calcium intake and bone mass: a quantitative review of evidence. Calcif Tissue Int 1990;47:194–201.
27. Dawson-Hughes B, Dallal GE, Krall EA, Sadowski L, Sahyoun N, Tannebaum S. A controlled trial of the effect of calcium supplementation on bone density in postmenopausal women. N Engl J Med 1990;232:878–83.
28. Sempos CT, Johnson NE, Smith EL, Gilligan C. Effect of intraindividual and interindividual variation in repeated dietary records. Am J Epidemiol 1985;121:120–30.
29. Falch JA, Sandvik L. Perimenopausal appendicular bone loss: a 10-year prospective study. Bone 1990;11:425–8.

Received for publication 22 January 1992
Accepted in revised form 11 February 1993