Natural History and Correlates of Hip BMD Loss With Aging in Men of African Ancestry: The Tobago Bone Health Study

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ABSTRACT: Little is known about the magnitude, pattern, and determinants of bone loss with advancing age among men, particularly among those of African descent. We examined the rate of decline in hip BMD and identified factors associated with BMD loss among 1478 Afro-Caribbean men ≥ 40 yr of age. BMD was measured at baseline and after an average of 4.4 yr by DXA. The rate of decline in femoral neck BMD was $0.29 \pm 0.81\%/yr$ in the total sample ($p < 0.0001$). However, a U-shaped relationship between advancing age and the rate of decline in BMD was observed. The rate of decline in BMD at the femoral neck was $-0.38 \pm 0.77\%/yr$ among men 40–44 yr of age, decelerated to $-0.15 \pm 0.81\%/yr$ among men 50–54 yr of age, and then accelerated to $-0.52 \pm 0.90\%/yr$ among those 75+ yr of age (all $p < 0.003$). Men who lost $\geq 5\%$ of their body weight during follow-up had significantly greater BMD loss than those who remained weight stable or gained weight ($p < 0.0001$). The relationship between weight loss and BMD loss was more pronounced among men who were older and leaner at study entry ($p < 0.03$). We also observed a strong impact of advanced prostate cancer and its treatment with androgen deprivation on BMD loss. Men of African ancestry experience substantial BMD loss with advancing age that seems to be comparable to the rate of loss among white men in other studies. Additional studies are needed to better define the natural history and factors underlying bone loss with aging in men of African ancestry.

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INTRODUCTION

ALTHOUGH OSTEOPOROSIS is more prevalent among women than men, men also experience substantial bone loss and an increase in fracture incidence with advancing age. However, little information exists about the natural history, magnitude, and correlates of bone loss with aging among men, especially among men of African ancestry. Osteoporosis is a global public health problem and, as the population ages, more men throughout the world will develop osteoporosis and its associated fractures, including men of African ancestry.⁽¹⁾ Indeed, individuals of African ancestry are expected to comprise a growing proportion of the incidence and economic burden of osteoporosis-related fractures over the next 20–50 yr in the United States⁽²⁾ and worldwide.⁽¹⁾ These demographic trends underscore the importance of better understanding the natural history and determinants of bone loss and osteoporosis in men of all ages and racial/ethnic background.

Most longitudinal studies of BMD changes with aging in men have been conducted among white men in North America,^(3–8) Europe,^(9–11) and Australia.⁽¹²⁾ These studies

have identified body weight and changes in body weight as the major correlates of bone loss with aging. Smoking has also been reported as a potential risk factor for bone loss in some studies,^(3,4,7,13,14) whereas other lifestyle factors such as alcohol consumption, calcium intake, and physical activity have been inconsistently related to bone loss.^(3,4,7,12) To our knowledge, only a single study has characterized the magnitude and correlates of bone loss in men of African ancestry.⁽¹⁴⁾ In this study, older age, lower initial body weight, and smoking were correlated with a greater decline in BMD among 119 African-American men ≥ 65 yr of age. The aim of this study was to further examine the magnitude, age-related patterns, and correlates of the decline in hip BMD with aging in a large cohort of middle-aged and elderly men of African ancestry.

MATERIALS AND METHODS

Study population

The population-based Tobago Bone Health Study was first conducted on the Caribbean island of Tobago in 2000.^(15,16) In brief, recruitment was accomplished by word of mouth, hospital flyers, and radio broadcasting. To be

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eligible, men had to be ≥ 40 yr of age, ambulatory, and not terminally ill. Questionnaires were administered to obtain information on demographic characteristics, occupation, medical history, and lifestyle-related factors. A total of 2652 men completed an initial DXA scan for assessment of BMD and body composition at that visit. Self-reported ethnicity of the cohort is 97% African, 2% East Indian, <1% white, and <1% "other."

Beginning in 2004, participants were recontacted for a second DXA scan to assess the rate of change in BMD. A total of 1748 men (70% of survivors) returned for the follow-up exam. We later excluded 36 men who identified themselves with ethnicity other than Afro-Caribbean and 21 men who had incomplete data. The Institutional Review Boards of the University of Pittsburgh and the Tobago Ministry of Health and Social Services approved this study, and all participants provided written informed consent before data collection.

Densitometry

BMD was measured at the proximal femur and subregions at both the baseline and follow-up visits using a single Hologic QDR 4500W densitometer (Hologic, Bedford, MA, USA). The left hip was scanned unless the participant had a fracture or a total hip replacement. Trained and certified technicians performed the DXA scans and followed a strict protocol for both visits. Longitudinal machine stability was assessed from plots of daily spine phantom scans and reviewed monthly. A weekly print out of quality control (QC) plots was generated to detect short-term inconsistencies and long-term drift. The scanner was stable throughout the course of the study. The long-term CV for BMD was 0.499%.

Anthropometric and body composition assessments

Body weight was measured in kilograms with participants wearing light clothing and without shoes, using a calibrated balance beam scale at both visits. Height was measured in centimeters without shoes, using a wall-mounted height board. Whole body fat and lean mass were also measured using DXA. Left and right grip strength was measured with a hand-grip dynamometer as a surrogate for upper body and overall strength (Preston Grip Dynamometer; JA Preston 136 Crop.). Average grip strength was based on two repeated measurements from the left and right hands.

Other measurements

Questionnaires were administered by trained interviewers and nurses to obtain information on demographic characteristics, lifestyle factors, and medical history. In this analysis, we used information from the baseline exam to assess potential factors related to the subsequent rate of decline in BMD. Mixed African ancestry was defined by self-report of one to three African-descent grandparents. Other factors that were assessed included history of cigarette smoking, alcohol consumption, time spent watching television, time spent walking, and medical history of fracture, hypertension, coronary heart disease, stroke,

diabetes, chronic bronchitis, and arthritis. We also asked participants to rate their overall health compared with others of their age. Diagnosis of prostate cancer, advanced prostate cancer (prostate specific antigen > 40 or Gleason score > 7), and androgen deprivation therapy (ADT; use of leuporelin or orchiectomy) were also recorded at baseline.

Statistical analysis

The annualized rate of change in BMD during follow-up was calculated as the percent BMD change from baseline to follow-up divided by duration in years between the two scans. Percent change in body weight or body composition was calculated as the difference between baseline and follow-up measures divided by baseline measures and multiplied by 100. We also categorized percent weight change into three groups: weight gain (>5% weight gain), weight stable (weight change between -5% and 5%), and weight loss (>5% weight loss).

We first compared the baseline characteristics between men who did ($n = 1748$) and did not ($n = 901$) return for the follow-up visit using analysis of covariance (ANCOVA) for continuous variables with age adjustment and χ^2 tests for dichotomous variables. ANOVA and ANCOVA were used to evaluate the annualized percentage rate of change in BMD across different age categories (e.g., 5-yr age groups or >55 yr) and across weight change groups. The distribution of BMD change in each age group satisfied the criteria of ANOVA. We evaluated the age-adjusted and age- and weight-adjusted contribution of each individual variable to the annualized rate of change in BMD using linear regression analysis. The strength of the association is expressed as an absolute difference in units of change chosen to approximate 1 SD in the distribution for each continuous variable or null category for dichotomous variables. The formula used to calculate the absolute difference in rate of change in BMD per unit change (SD) of the independent variable was $\beta = \text{unstandardized } \beta \times \text{unit change in independent variable}$. The corresponding 95% CIs were calculated using the following formula: $\beta \times (\pm 1.96 \times \text{SE}) \times \text{unit change}$. We also evaluated the interactions between weight change and age as well weight change and BMI on the rate of change in BMD using ANCOVA. We first performed the above analyses in 1691 participants with complete data. Because the effects of ADT and prostate cancer on BMD change were substantial, we excluded the 233 men on ADT or who had prostate cancer from subsequent analyses.

Multiple linear regression analysis was performed using a stepwise procedure to determine the potential independent correlates of the annualized rate of change in BMD. Variables from the age- and weight-adjusted univariate model with $p < 0.10$ were further entered in the multiple linear regression model. Age was forced into all models. We assessed multi-collinearity by inspecting the variance inflation factor (VIF). Because of the high correlation of body weight with lean and fat mass, we developed two different multiple linear regression models: (1) models with body weight only and (2) models substituting fat and lean mass for body weight. Statistical analyses were performed using SAS (version 9.1; SAS Institute, Cary, NC, USA).

TABLE 1. Comparison of Selected Baseline Characteristics Among Men Who Participated and Did Not Participate in the Follow-Up Examination

	Participants (n = 1748)	Nonparticipants (n = 904)	p
Age (yr)	56.4 ± 10.5	59.1 ± 12.0	<0.0001
Height (cm)	174.8 ± 6.6	174.6 ± 6.7	0.3810
Weight (kg)	83.6 ± 14.2	81.2 ± 14.6	<0.0001
BMI (kg/m ²)	27.3 ± 4.1	26.5 ± 4.2	<0.0001
Grip strength (kg)	43.0 ± 9.8	40.6 ± 11.1	<0.0001
Whole body fat (%)	20.1 ± 5.8	19.9 ± 6.2	0.5877
Total hip BMD (g/cm ²)*	1.150 ± 0.147	1.123 ± 0.155	<0.0001
Femoral neck BMD (g/cm ²)*	0.998 ± 0.147	0.961 ± 0.150	<0.0001
Worse health compared with men the same age (%)	2.5	5.5	0.0001
Ever smoker (%)	38.2	48.8	<0.0001
Current smoker (%)	11.6	18.8	<0.0001
Drink alcohol >4 times/wk	16.2	18.8	0.0975
Fracture (%)	19.8	20.8	0.5385
Hypertension (%)	28.9	34.2	0.0052
Heart disease (%)	3.4	5.9	0.0026
Diabetes (%)	11.2	14.8	0.0084
Arthritis (%)	11.7	15.5	0.0064
Prostate cancer (%)	13.8	14.2	0.7633

* Adjusted for age.

RESULTS

Table 1 shows the baseline characteristics of men who did and did not attend the follow-up exam. As expected, men who did not return were older, weighed less, and had lower baseline BMI and BMD than those who participated in the follow-up exam. Nonparticipants also were more likely to smoke, report poorer health status, and have a greater prevalence of hypertension, heart disease, diabetes, and arthritis.

Rate of change in BMD and androgen deprivation

The average length of time between DXA scans was 4.4 ± 0.8 yr (range, 1.1–6.9 yr). Men with advanced prostate cancer and men who had a history of ADT for prostate cancer had a significantly greater decline in BMD compared with their counterparts. For example, the average rate of decline in BMD was 0.137 ± 0.588%/yr at the total hip and 0.333 ± 0.841%/yr at the femoral neck (data not shown) for all men. The rate of decline in BMD was 0.78%/yr greater at the total hip and 0.58%/yr greater at the femoral neck for men with advanced prostate cancer compared with men without prostate cancer ($p < 0.0001$ for both). Men with nonadvanced prostate cancer had a 0.08% greater ($p = 0.08$) rate of decline in BMD at the total hip and 0.15% greater rate ($p = 0.02$) at the femoral neck compared with men without prostate cancer. Approximately 6% of the study population reported that they had either taken leuprolerin or underwent orchiectomy for prostate cancer. Men on either of these treatments

FIG. 1. Rate of decline in total hip and femoral neck BMD by 5-yr age groups among men of African Ancestry. *Rate of BMD change is not significantly different from zero. At the total hip, all age groups, except ages 45–49, have significantly different BMD changes compared with the 50- to 54-yr age group. At the femoral neck, age groups 40–44, 65–69, 70–74, and 75+ have significantly greater BMD changes compared with the 50- to 54-yr age group.

experienced an ~0.4%/yr greater rate of decline in total hip and femoral neck BMD compared with men who had neither of these treatments ($p < 0.0001$ for both). Because prostate cancer and its treatment by androgen deprivation had a strong impact on the rate of decline in BMD, we excluded the 233 men with prostate cancer or who had undergone androgen deprivation from subsequent analyses.

Rate of change in BMD and age group

Total hip and femoral neck BMD declined by $0.10 \pm 0.55\%/yr$ and $0.29 \pm 0.81\%/yr$ among the men who did not have prostate cancer or who had not undergone ADT ($p < 0.0001$ for both). To examine the age-related patterns in the rate of decline in BMD among these men, we stratified the total sample by 5-yr age groups using age at study entry (Fig. 1). The rate of decline in BMD across age groups appeared to have a U-shape relationship. Men 40–44 yr of age had a significantly greater rate of decline in BMD than those 45–49 and 50–54 yr of age at both the total hip and femoral neck. Thereafter, the rate of decline in BMD accelerated with advancing age. For example, the rate of decline in total hip BMD was $-0.10 \pm 0.55\%/yr$ among men 55–59 yr ($p = 0.009$) and increased to $-0.48 \pm 0.60\%/yr$ among men 70+ yr of age ($p < 0.0001$). Similar results were observed at the femoral neck. Moreover, this U-shaped relationship persisted after adjusting for baseline weight and weight change (data not shown). Additional adjustment for hypertension, diabetes, arthritis, grip strength, and current smoking status yielded similar results (data not shown).

Peak BMD reference data for the Afro-Caribbean population is not available. Thus, we used the non-Hispanic black BMD reference data from NHANES III to determine the prevalence of osteoporosis in our cohort. The prevalence of proximal femur osteoporosis at study entry

TABLE 2. Correlates of the Rate of Change in Hip BMD Among Men of African Ancestry

Variable	Mean $\pm$ SD or prevalence (%)	Unit	Age-adjusted rate of change in BMD (95% CI)*	
			Total hip	Femoral neck
Demographic characteristics				
Age (yr)	54.8 $\pm$ 10.0	10	−0.084 (−0.112, −0.055)	−0.053 (−0.095, −0.011)
Mixed African ancestry	11.2%	1	0.037 (−0.052, 0.126)	0.105 (−0.028, 0.238)
Occupational history				
Ever work on farm	51.1%	1	−0.009 (−0.065, 0.048)	−0.023 (−0.107, 0.061)
Ever work on fishing boat	17.0%	1	−0.012 (−0.087, 0.062)	−0.061 (−0.172, 0.051)
Anthropometric and DXA measures				
Body weight (kg)	84.0 $\pm$ 14.2	10	0.040 (0.020, 0.059)	0.065 (0.035, 0.094)
BMI (kg/m ²)	27.3 $\pm$ 4.1	4.1	0.057 (0.029, 0.085)	0.094 (0.052, 0.137)
Height (cm)	175.1 $\pm$ 6.5	6.5	0.029 (0.000, 0.058)	0.032 (−0.011, 0.075)
Grip strength (kg)	44.0 $\pm$ 9.6	9.6	0.030 (−0.003, 0.063)	0.074 (0.025, 0.124)
Total hip BMD (g/cm ²)	1.16 $\pm$ 0.14	0.14	0.004 (−0.024, 0.032)	—
Femoral neck BMD (g/cm ²)	1.00 $\pm$ 0.15	0.15	—	0.008 (−0.037, 0.052)
Fat mass (kg)	16.3 $\pm$ 6.5	6.5	0.069 (0.041, 0.097)	0.101 (0.059, 0.143)
Lean mass (kg)	64.9 $\pm$ 8.5	8.5	0.034 (0.005, 0.064)	0.064 (0.021, 0.108)
Body fat (%)	19.7 $\pm$ 5.7	5.7	0.079 (0.051, 0.108)	0.104 (0.061, 0.146)
Weight change (%)	0.2 $\pm$ 6.2	6.2	0.108 (0.078, 0.137)	0.158 (0.114, 0.201)
Fat mass change (%)	6.4 $\pm$ 18.1	18.1	0.062 (0.033, 0.091)	0.101 (0.059, 0.143)
Lean mass change (%)	−0.1 $\pm$ 3.6	3.6	0.132 (0.103, 0.161)	0.136 (0.092, 0.180)
Lifestyle characteristics				
Ever smoke	38.5%	1	0.009 (−0.049, 0.066)	0.029 (−0.057, 0.115)
Current smoker	12.0%	1	−0.064 (−0.150, 0.023)	−0.091 (−0.220, 0.038)
Watch TV $\geq$ 21 h/wk	31.1%	1	0.036 (−0.025, 0.097)	0.027 (−0.063, 0.118)
Drink alcohol $\geq$ 4 times/wk	15.9%	1	0.001 (−0.078, 0.080)	0.026 (−0.093, 0.144)
Medical history				
Ever fracture	20.2%	1	−0.015 (−0.085, 0.055)	−0.007 (−0.111, 0.098)
Hypertension	27.6%	1	0.037 (−0.027, 0.102)	0.065 (−0.031, 0.161)
Diabetes	10.7%	1	−0.102 (−0.195, −0.008)	−0.028 (−0.167, 0.111)
Arthritis	10.6%	1	0.015 (−0.080, 0.111)	0.053 (−0.089, 0.195)

$p < 0.05$ is shown in bold.

*Expressed as absolute difference in annualized rate of change in BMD per unit of the predictor variable. Men with prostate cancer or who had undergone androgen deprivation therapy were excluded from the analysis

was 0.41% and increased to 0.75% at the follow-up exam (data not shown).

Age-adjusted correlates of the rate of change in BMD

Table 2 shows the age-adjusted association of participant characteristics with the rate of decline in BMD at the total hip and femoral neck. Age was inversely and significantly correlated with the decline in BMD. For example, the rate of decline in total hip BMD increased by 0.084%/yr every 10 yr.

A 10-kg increase in body weight was associated with a slower rate of decline in total hip BMD. Body composition measures from DXA were also significantly associated with the rate of decline in hip BMD. Whole body fat, lean mass, and percent body fat were all positively and significantly associated with the decline in hip BMD in age-adjusted analysis. Initial BMD was not related to the subsequent rate of decline in BMD.

We also evaluated the relationship between change in body weight and body composition and the rate of decline in BMD. Men gained an average of $0.2 \pm 6.2\%$ body weight during follow-up ($p = 0.20$). As expected, fat mass increased ($p < 0.0001$), whereas lean mass decreased

nonsignificantly ($p = 0.25$) during the follow-up period. In age-adjusted analysis, men who lost weight during follow-up had a significantly greater rate of decline in BMD. For example, every 6% decrease in body weight from baseline was associated with a 0.11%/yr faster total hip and a 0.16%/yr faster femoral neck BMD loss. Similar associations were observed for the change in fat mass and lean mass.

None of the lifestyle-related characteristics examined were significantly associated with the rate of decline in BMD including current and past smoking history, time spent watching television, and alcohol intake. Diabetes was present in $\sim 11\%$ of the cohort and was associated with a greater decline in total hip, but not femoral neck, BMD in age-adjusted analysis. Because there was a U-shaped relationship between age and the rate of decline in BMD, we also examined the correlates of bone loss in stratified analyses among men 40–54 and ≥ 55 yr of age. We also included age as a dichotomous variable in adjusted analyses. We found similar results in these analyses as in the total cohort (data not shown).

We further evaluated the association of age, BMI, weight change, and the interactions of these variables with the rate of decline in BMD in stratified analyses (Tables 3

TABLE 3. Mean Rate of Change in Hip BMD by Category of Age at Study Entry and Percent Weight Change During Follow-Up

Category of weight change	Mean annualized percent change in BMD (95% CI)*		
	Overall cohort	Age	
		Age 40–54	Age 55+
Total hip		<i>n</i> = 768	<i>n</i> = 590
Weight loss (<i>n</i> = 210)	−0.340 (−0.413, −0.267)	−0.204 (−0.325, −0.085)	−0.418 (−0.509, −0.326)
Stable weight (<i>n</i> = 847)	−0.062 (−0.097, −0.026)	−0.030 (−0.077, 0.016)	−0.106 (−0.162, −0.051)
Weight gain (<i>n</i> = 274)	0.003 (−0.031, 0.067)	0.070 (−0.009, 0.149)	−0.122 (−0.230, −0.015)
Femoral neck†		<i>n</i> = 765	<i>n</i> = 596
Weight loss (<i>n</i> = 214)	−0.609 (−0.716, −0.502)	−0.437 (−0.615, −0.259)	−0.705 (−0.839, −0.572)
Stable weight (<i>n</i> = 874)	−0.252 (−0.305, −0.199)	−0.273 (−0.342, −0.204)	−0.222 (−0.304, −0.141)
Weight gain (<i>n</i> = 273)	−0.088 (−0.182, 0.007)	−0.048 (−0.165, 0.069)	−0.161 (−0.321, −0.002)

Weight loss was defined as a loss of 5% or more of body weight from baseline. Weight gain was defined as a gain of 5% or more of body weight from baseline.

* Adjusted for BMI.

† The interaction term between weight change and age category was significant for femoral neck only ($p = 0.03$). Men with prostate cancer or who had undergone androgen deprivation therapy were excluded from the analysis.

TABLE 4. Mean Rate of Change in Hip BMD by Category of Initial BMI and Percent Weight Change

Category of weight change	Mean annualized percent change in hip BMD (95% CI)*			
	Overall cohort	BMI		
		BMI < 25 kg/m ²	BMI = 25.0–29.9 kg/m ²	BMI ≥ 30 kg/m ²
Total hip†		<i>n</i> = 385	<i>n</i> = 655	<i>n</i> = 318
Weight loss (<i>n</i> = 216)	−0.308 (−0.381, −0.235)	−0.279 (−0.447, −0.112)	−0.289 (−0.393, −0.186)	−0.327 (−0.458, −0.196)
Stable weight (<i>n</i> = 878)	−0.066 (−0.102, −0.030)	−0.186 (−0.253, −0.118)	−0.043 (−0.093, 0.007)	0.037 (−0.039, 0.113)
Weight gain (<i>n</i> = 276)	−0.014 (−0.078, 0.051)	−0.027 (−0.132, 0.078)	−0.091 (−0.190, 0.008)	0.140 (0.004, 0.276)
Femoral neck		<i>n</i> = 390	<i>n</i> = 657	<i>n</i> = 314
Weight loss (<i>n</i> = 220)	−0.585 (−0.692, −0.478)	−0.598 (−0.841, −0.355)	−0.663 (−0.816, −0.510)	−0.436 (−0.630, −0.242)
Stable weight (<i>n</i> = 878)	−0.252 (−0.305, −0.199)	−0.381 (−0.481, −0.282)	−0.228 (−0.303, −0.154)	−0.146 (−0.260, −0.032)
Weight gain (<i>n</i> = 275)	−0.106 (−0.201, −0.011)	−0.271 (−0.427, −0.113)	−0.049 (−0.196, 0.099)	0.079 (−0.125, 0.283)

Weight loss was defined as a loss of 5% or more of body weight from the baseline exam. Weight gain was defined as a gain of 5% or more of body weight from the baseline exam. Men with prostate cancer or who had undergone androgen deprivation therapy were excluded from the analysis.

* Adjusted for age.

† The interaction term between BMI at study entry and weight change during follow-up was statistically significant at the total hip only ($p = 0.02$).

and 4). At both the total hip and femoral neck, men who lost 5% or more of their baseline body weight had a significantly greater decline in BMD compared with men who had remained weight stable or who gained 5% or more body weight. There was also a significant loss of BMD among men who remained weight stable during follow-up. However, men who gained at least 5% body weight during follow-up did not experience a significant decline in hip BMD.

We also found a significant interaction effect of age at study entry and weight change on the rate of decline in hip BMD (Table 3). The effect of weight loss on the decline in BMD was significantly greater (total hip, $p = 0.006$; femoral neck, $p = 0.018$) among older (age ≥ 55 yr) than younger (age < 55 yr) men. Finally, we also observed a significant interaction effect of initial BMI and subsequent weight change on the rate of decline in total hip BMD (Table 4). Although weight gain was associated with an overall slower rate of decline in femoral neck BMD, this effect was not apparent among the leanest men. Men with a low initial BMI (BMI < 25.0 kg/m²) experienced a more pronounced

rate of decline in BMD even if they had gained weight during follow-up.

Multiple linear regression analyses

The results from multiple linear regression analyses of the independent correlates of the rate of decline in BMD are shown in Table 5. Age (−), BMI (+), weight change (+), and grip strength (+) were significant correlates of the rate of decline in BMD in multiple regression analysis. Diabetes was no longer a statistically significant correlate of the rate of decline in total hip BMD in the multivariable model. Multivariable models explained 5–6% of the variance in the rate of decline in BMD.

DISCUSSION

Compared with women, much less is known about the natural history, magnitude, and correlates of bone loss with aging in men, especially among nonwhite men. To our knowledge, only a single longitudinal study to date has evaluated age-related bone loss in men of African ancestry

TABLE 5. Multivariable Correlates of the Rate of Change in Hip BMD

Variable	Unit	Rate of change in BMD (95% CI) per unit	
		Total hip*	Femoral neck†
Age (yr)‡	10	-0.056 (-0.0856, -0.027)	0.026 (-0.025, 0.078)
BMI (kg/m ²)	4.1	0.073 (0.043, 0.102)	0.101 (0.057, 0.146)
Weight change (%)	6.2	0.112 (0.082, 0.142)	0.167 (0.123, 0.211)
Grip strength (kg)	9.6	—	0.055 (0.004, 0.106)
Model R ²		0.07	0.06

p < 0.05 is shown in bold. Men with prostate cancer or who had undergone androgen deprivation therapy were excluded from the analysis.

* Age, BMI, weight change, grip strength, and diabetes were entered into the model.

† Age, BMI, weight change, and grip strength were entered into the model.

‡ Age was forced into the models.

and that study only included 119 men ≥ 65 yr of age.⁽¹⁴⁾ Thus, one aim of this study was to examine the pattern of bone loss at the proximal femur over 4 yr in a large population sample of middle-aged and elderly men of African ancestry. A primary finding was that the rate of decline in proximal femur BMD is substantial and may begin early in life among men of African ancestry. This early decline in BMD may reflect, in part, an early loss of trabecular bone mass from the proximal femur. Indeed, others have recently observed a loss of trabecular BMD beginning by the third decade of life among white men.^(17,18) However, the pattern of BMD loss with advancing age in our study seemed to be nonlinear, with a deceleration in the rate of loss between ages 40 and 54 and an acceleration in the rate of loss thereafter that continued unabated into the seventh decade of life. A progressive acceleration of bone loss with advancing age has also been observed among white men.^(3,13) Past epidemiological studies of the decline in BMD have largely focused on white men ≥ 65 yr of age and may have thus missed this early decline in hip BMD.

In our study of Afro-Caribbean men 40–92 yr of age, the overall unadjusted rate of decline in BMD at the femoral neck was $-0.29 \pm 0.81\%/yr$ and was $-0.47 \pm 0.89\%/yr$ among men ≥ 65 yr of age. The rate of decline in BMD was surprisingly very similar to the rate of decline reported in other longitudinal studies of white men.^(3–5,7,9) For example, in the Framingham Osteoporosis Study, the rate of decline in femoral neck BMD was $-0.38\%/yr$ among 278 white American men 67–90 yr of age.⁽⁴⁾ In the Rotterdam Study, the rate of decline in femoral neck BMD was $-0.4\%/yr$ among 1856 white European men >55 yr of age.⁽³⁾ In the Rancho Bernardo study, the rate of decline in BMD at the femoral neck was $-0.34\%/yr$ among 500 white American men 45–92 yr of age.⁽⁷⁾ In the Network in Europe for Male Osteoporosis study, the rate of decline in BMD at the femoral neck was $-0.48\%/yr$ among ~ 1300 white European men 50–80 yr of age.⁽¹¹⁾ In the Baltimore Men's Osteoporosis Study, the rate of decline in femoral

neck BMD was $2.1\%/yr$ in 349 white American and $1.1\%/yr$ in 119 black men 60–74 yr of age.⁽¹⁴⁾ The higher rate of decline in BMD in this later study may reflect the use of different densitometers at the initial and follow-up exams. Comparisons across these studies are difficult because of the differences in follow-up time, densitometers used, sample sizes, geographic areas, and age distributions of the populations studied. Nonetheless, the rate of decline in femoral neck BMD with aging in our cohort of Afro-Caribbean men is very consistent with the majority of these other studies of white men.

To better understand the factors that might influence the rate of bone loss with age in men of African ancestry, we characterized a number of anthropometric, lifestyle, and medical variables and examined the relation of these variables to the rate of decline in BMD at the proximal femur. In addition to advanced age, leanness at study entry and weight loss during follow-up were independent correlates of an increased rate of BMD decline with age. A positive association between body weight or BMI and BMD among middle-aged and elderly men has been well-documented in whites and blacks.^(19–24) Weight loss with aging is also a consistent predictor of bone loss in studies of white men.^(4,6–8,25) In this study, men who lost 5% or more of their baseline body weight had an accelerated rate of decline in BMD compared with men who remained weight stable or gained weight. The effect of weight loss on BMD loss was more profound among men ≥ 55 yr of age in our study. In the Framingham, Rancho Bernardo, Osteoporotic Fractures in Men (MrOS), and EPIC studies, white men who lost 5% or more of their baseline weight also experienced significantly greater bone loss at the proximal femur than those who gained 5% or more of their baseline weight.^(4,6–8) The importance of weight loss as a risk factor for accelerated loss of BMD among middle-aged and elderly men may be explained by underlying illness that results in poor health and physical inactivity,^(8,25) to declines in muscle mass and strength, to decreased mechanical loading on weight-bearing skeletal sites,^(26,27) to a decrease in adipose tissue mass, which is an important source of estrogens in men,⁽²⁸⁾ or to a combination of these factors. In addition, the interaction between age and weight loss on bone loss also suggests an important role of weight maintenance for bone health among older men.

Other frequently examined predictors of bone loss such as physical activity, smoking, calcium intake, and medical conditions have yielded inconsistent results across studies.^(3,4,7,12) We also examined several of these variables in this study. We found that greater grip strength was associated with a slower decline in BMD, even after adjusting for age, body weight, and weight change. This association may be indirectly caused by physical activity level.

We were unable to document an association between smoking and the rate of decline in BMD. Some^(22,29–31) but not all^(19,32,33) studies suggest that smokers have lower BMD than nonsmokers. In some studies of white men, smokers had a greater decline in hip BMD with age compared with nonsmokers.^(3,4,7,25) We were also unable to document an association between alcohol intake and the rate of decline in BMD. Moderate alcohol consumption

has been associated with greater BMD in several^(22,23,34) but not all^(13,19) studies of middle-aged and elderly white men. Alcohol consumption was associated with a slower rate of decline in BMD in some^(7,35) but not all^(4,25) longitudinal studies. The absence of a significant relationship with smoking and alcohol drinking in this study may be caused by a low prevalence of these behaviors in our cohort.

Two of the strongest correlates of the rate of decline in BMD were advanced prostate cancer and ADT for prostate cancer. This association was independent of other covariates including body weight and weight change during follow-up. Prostate cancer remains the most common cancer in American men and disproportionately afflicts more men of African ancestry worldwide than other ethnic and racial groups.^(15,36,37) ADT achieved surgically through orchiectomy or through gonadotropin-releasing hormone agonists, is a first-line treatment for metastatic prostate cancer and is increasingly being used in the treatment of localized, high-risk prostate cancer.⁽³⁸⁾ The prevalence of androgen deprivation therapy may be increasing⁽³⁹⁾; by 2000, ~3% of men in the U.S. Medicare fee-for-service program alone were androgen deprived.⁽³⁹⁾ Androgens are important for the development and maintenance of BMD in men. Androgen deprivation for prostate cancer has been associated with a rapid and marked loss of BMD in numerous studies^(40–47) and with an increased risk of fracture.^(38,48–53) The vast majority of men in these past studies were white. To our knowledge, ours is the first to document the association of ADT with the rate of decline in BMD exclusively among men of African ancestry.

This study has several potential limitations. The small proportion of men ≥ 75 yr of age may have limited our ability to estimate the rate of bone loss among these men. Although walking is a common form of physical activity in this population, our questionnaire-based estimates of walking might not have accurately reflected total physical activity levels. In addition, dietary calcium and vitamin D intake was not assessed, and only selected medication use was documented at study entry. Areal BMD may be confounded by bone size changes.⁽⁵⁴⁾ Bone mineral apparent density (BMAD) has been suggested as a surrogate for volumetric BMD. However, we found similar results for femoral neck BMAD (data not shown). Our DXA measures of areal BMD cannot provide insight on age-related loss of trabecular and cortical BMD or bone geometry. Finally, it will be important to examine fracture rates in relation to BMD and the rate of bone loss among men of African ancestry in the future.

In conclusion, although the prevalence of osteoporosis is higher among white men than men of African ancestry,⁽⁵⁵⁾ men of African ancestry seem to experience a substantial loss of BMD with aging that may be comparable to the rate of loss among white men. Advancing age, lower body weight, increased weight loss, and advanced prostate cancer and its treatment by androgen deprivation were identified as potential risk factors for accelerated BMD loss among men of African ancestry. However, these factors accounted for only a small fraction of the variation in BMD loss with aging. Many additional variables, including

genetic factors,^(56–60) may contribute to age-related BMD loss among men of African ancestry. A more complete understanding of BMD changes with aging in men of African ancestry will require a broader examination of the potential determinants.

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REFERENCES

- Cooper C, Campion G, Melton LJ III 1992 Hip fractures in the elderly: A world-wide projection. *Osteoporos Int* **2**:285–289.
- Burge R, Dawson-Hughes B, Solomon DH, Wong JB, King A, Tosteson A 2007 Incidence and economic burden of osteoporosis-related fractures in the United States, 2005–2025. *J Bone Miner Res* **22**:465–475.
- Burger H, de Laet CE, van Daele PL, Weel AE, Witteman JC, Hofman A, Pols HA 1998 Risk factors for increased bone loss in an elderly population: The Rotterdam Study. *Am J Epidemiol* **147**:871–879.
- Hannan MT, Felson DT, Dawson-Hughes B, Tucker KL, Cupples LA, Wilson PW, Kiel DP 2000 Risk factors for longitudinal bone loss in elderly men and women: The Framingham Osteoporosis Study. *J Bone Miner Res* **15**:710–720.
- Melton LJ III, Khosla S, Atkinson EJ, O'Connor MK, Ofallon WM, Riggs BL 2000 Cross-sectional versus longitudinal evaluation of bone loss in men and women. *Osteoporos Int* **11**:592–599.
- Kaptoge S, Welch A, McTaggart A, Mulligan A, Dalzell N, Day NE, Bingham S, Khaw KT, Reeve J 2003 Effects of dietary nutrients and food groups on bone loss from the proximal femur in men and women in the 7th and 8th decades of age. *Osteoporos Int* **14**:418–428.
- Bakhireva LN, Barrett-Connor E, Kritiz-Silverstein D, Morton DJ 2004 Modifiable predictors of bone loss in older men: A prospective study. *Am J Prev Med* **26**:436–442.
- Ensrud KE, Fullman RL, Barrett-Connor E, Cauley JA, Stefanick ML, Fink HA, Lewis CE, Orwoll E 2005 Voluntary weight reduction in older men increases hip bone loss: The osteoporotic fractures in men study. *J Clin Endocrinol Metab* **90**:1998–2004.
- Dennison E, Eastell R, Fall CH, Kellingray S, Wood PJ, Cooper C 1999 Determinants of bone loss in elderly men and women: A prospective population-based study. *Osteoporos Int* **10**:384–391.
- Emaus N, Berntsen GK, Joakimsen R, Fonnebo V 2006 Longitudinal changes in forearm bone mineral density in women and men aged 45–84 years: The Tromsø Study, a population-based study. *Am J Epidemiol* **163**:441–449.
- Kaptoge S, Reid DM, Scheidt-Nave C, Poor G, Pols HA, Khaw KT, Felsenberg D, Benevolenskaya LI, Diaz MN, Stepan JJ, Eastell R, Boonen S, Cannata JB, Glueck CC, Crabtree NJ, Kaufman JM, Reeve J 2007 Geographic and other determinants of BMD change in European men and women at the hip and spine: A population-based study from the Network in Europe for Male Osteoporosis (NEMO). *Bone* **40**:662–673.
- Jones G, Nguyen T, Sambrook P, Kelly PJ, Eisman JA 1994 Progressive loss of bone in the femoral neck in elderly people: Longitudinal findings from the Dubbo osteoporosis epidemiology study. *BMJ* **309**:691–695.
- Nguyen TV, Eisman JA, Kelly PJ, Sambrook PN 1996 Risk factors for osteoporotic fractures in elderly men. *Am J Epidemiol* **144**:255–263.

14. Tracy JK, Meyer WA, Flores RH, Wilson PD, Hochberg MC 2005 Racial differences in rate of decline in bone mass in older men: The Baltimore men's osteoporosis study. *J Bone Miner Res* **20**:1228–1234.
15. Bunker CH, Patrick AL, Konety BR, Dhir R, Brufsky AM, Vivas CA, Becich MJ, Trump DL, Kuller LH 2002 High prevalence of screening-detected prostate cancer among Afro-Caribbeans: The Tobago Prostate Cancer Survey. *Cancer Epidemiol Biomarkers Prev* **11**:726–729.
16. Hill DD, Cauley JA, Sheu Y, Bunker CH, Patrick AL, Baker CE, Beckles GL, Wheeler VW, Zmuda JM 2008 Correlates of bone mineral density in men of African ancestry: The Tobago bone health study. *Osteoporos Int* **19**:227–234.
17. Khosla S, Riggs BL, Atkinson EJ, Oberg AL, McDaniel LJ, Holets M, Peterson JM, Melton LJ III 2006 Effects of sex and age on bone microstructure at the ultradistal radius: A population-based noninvasive in vivo assessment. *J Bone Miner Res* **21**:124–131.
18. Riggs BL, Melton LJ, Robb RA, Camp JJ, Atkinson EJ, McDaniel L, Amin S, Rouleau PA, Khosla S 2008 A population-based assessment of rates of bone loss at multiple skeletal sites: Evidence for substantial trabecular bone loss in young adult women and men. *J Bone Miner Res* **23**:205–214.
19. Glynn NW, Meilahn EN, Charron M, Anderson SJ, Kuller LH, Cauley JA 1995 Determinants of bone mineral density in older men. *J Bone Miner Res* **10**:1769–1777.
20. Edelstein SL, Barrett-Connor E 1993 Relation between body size and bone mineral density in elderly men and women. *Am J Epidemiol* **138**:160–169.
21. George A, Tracy JK, Meyer WA, Flores RH, Wilson PD, Hochberg MC 2003 Racial differences in bone mineral density in older men. *J Bone Miner Res* **18**:2238–2244.
22. Bendavid EJ, Shan J, Barrett-Connor E 1996 Factors associated with bone mineral density in middle-aged men. *J Bone Miner Res* **11**:1185–1190.
23. Huuskonen J, Vaisanen SB, Kroger H, Jurvelin C, Bouchard C, Alhava E, Rauramaa R 2000 Determinants of bone mineral density in middle aged men: A population-based study. *Osteoporos Int* **11**:702–708.
24. Mazess RB, Barden HS, Drinka PJ, Bauwens SF, Orwoll ES, Bell NH 1990 Influence of age and body weight on spine and femur bone mineral density in U.S. white men. *J Bone Miner Res* **5**:645–652.
25. Knoke JD, Barrett-Connor E 2003 Weight loss: A determinant of hip bone loss in older men and women. The Rancho Bernardo Study. *Am J Epidemiol* **158**:1132–1138.
26. Hyldstrup L, Andersen T, McNair P, Breum L, Transbol I 1993 Bone metabolism in obesity: Changes related to severe overweight and dietary weight reduction. *Acta Endocrinol (Copenh)* **129**:393–398.
27. Svendsen OL, Hassager C, Christiansen C 1993 Effect of an energy-restrictive diet, with or without exercise, on lean tissue mass, resting metabolic rate, cardiovascular risk factors, and bone in overweight postmenopausal women. *Am J Med* **95**:131–140.
28. Kley HK, Deselaers T, Peerenboom H, Kruskemper HL 1980 Enhanced conversion of androstenedione to estrogens in obese males. *J Clin Endocrinol Metab* **51**:1128–1132.
29. Vogel JM, Davis JW, Nomura A, Wasnich RD, Ross PD 1997 The effects of smoking on bone mass and the rates of bone loss among elderly Japanese-American men. *J Bone Miner Res* **12**:1495–1501.
30. Nguyen TV, Kelly PJ, Sambrook PN, Gilbert C, Pocock NA, Eisman JA 1994 Lifestyle factors and bone density in the elderly: Implications for osteoporosis prevention. *J Bone Miner Res* **9**:1339–1346.
31. Lorentzon M, Mellstrom D, Haug E, Ohlsson C 2007 Smoking is associated with lower bone mineral density and reduced cortical thickness. *J Clin Endocrinol Metab* **92**:497–503.
32. Orwoll ES, Bevan L, Phipps KR 2000 Determinants of bone mineral density in older men. *Osteoporos Int* **11**:815–821.
33. Cauley JA, Fullman RL, Stone KL, Zmuda JM, Bauer DC, Barrett-Connor E, Ensrud K, Lau EM, Orwoll ES 2005 Factors associated with the lumbar spine and proximal femur bone mineral density in older men. *Osteoporos Int* **16**:1525–1537.
34. Holbrook TL, Barrett-Connor E 1993 A prospective study of alcohol consumption and bone mineral density. *BMJ* **306**:1506–1509.
35. Hansen MA, Overgaard K, Riis BJ, Christiansen C 1991 Potential risk factors for development of postmenopausal osteoporosis examined over a 12-year period. *Osteoporos Int* **1**:95–102.
36. Bunker CH, Patrick AL, Maharaj G, Keenan HA, Ramnarine S, Belle A, Richard JR, Dhir R 2002 Prostate cancer risk is three-fold higher among men, aged 50–64, of African descent compared with men of Asian-Indian descent in Trinidad and Tobago. *Ethn Dis* **12**:S3–S30.
37. Reddy S, Shapiro M, Morton R Jr, Brawley OW 2003 Prostate cancer in black and white Americans. *Cancer Metastasis Rev* **22**:83–86.
38. Higano CS 2008 Androgen-deprivation-therapy-induced fractures in men with nonmetastatic prostate cancer: What do we really know? *Nat Clin Pract Urol* **5**:24–34.
39. Barry MJ, Delorenzo MA, Walker-Corkery ES, Lucas FL, Wennberg DC 2006 The rising prevalence of androgen deprivation among older American men since the advent of prostate-specific antigen testing: A population-based cohort study. *BJU Int* **98**:973–978.
40. Conde FA, Sarna L, Oka RK, Vredevoe DL, Rettig MB, Aronson WJ 2004 Age, body mass index, and serum prostate-specific antigen correlate with bone loss in men with prostate cancer not receiving androgen deprivation therapy. *Urology* **64**:335–340.
41. Kiratli BJ, Srinivas S, Perkash I, Terris MK 2001 Progressive decrease in bone density over 10 years of androgen deprivation therapy in patients with prostate cancer. *Urology* **57**:127–132.
42. Preston DM, Torrens JI, Harding P, Howard RS, Duncan WE, McLeod DG 2002 Androgen deprivation in men with prostate cancer is associated with an increased rate of bone loss. *Prostate Cancer Prostatic Dis* **5**:304–310.
43. Maillefert JF, Sibilia J, Michel F, Saussine C, Javier RM, Tavernier C 1999 Bone mineral density in men treated with synthetic gonadotropin-releasing hormone agonists for prostatic carcinoma. *J Urol* **161**:1219–1222.
44. Goldray D, Weisman Y, Jaccard N, Merdler C, Chen J, Matzkin H 1993 Decreased bone density in elderly men treated with the gonadotropin-releasing hormone agonist decaptyl (D-Trp6-GnRH). *J Clin Endocrinol Metab* **76**:288–290.
45. Greenspan SL, Coates P, Sereika SM, Nelson JB, Trump DL, Resnick NM 2005 Bone loss after initiation of androgen deprivation therapy in patients with prostate cancer. *J Clin Endocrinol Metab* **90**:6410–6417.
46. Wei JT, Gross M, Jaffe CA, Gravlin K, Lahaie M, Faerber GJ, Cooney KA 1999 Androgen deprivation therapy for prostate cancer results in significant loss of bone density. *Urology* **54**:607–611.
47. Mittan D, Lee S, Miller E, Perez RC, Basler JW, Bruder JM 2002 Bone loss following hypogonadism in men with prostate cancer treated with GnRH analogs. *J Clin Endocrinol Metab* **87**:3656–3661.
48. Krupski TL, Foley KA, Baser O, Long S, Macarios D, Litwin MS 2007 Health care cost associated with prostate cancer, androgen deprivation therapy and bone complications. *J Urol* **178**:1423–1428.
49. Lopez AM, Pena MA, Hernandez R, Val F, Martin B, Riancho JA 2005 Fracture risk in patients with prostate cancer on androgen deprivation therapy. *Osteoporos Int* **16**:707–711.
50. Abrahamsen B, Nielsen MF, Eskildsen P, Andersen JT, Walter S, Brixen K 2007 Fracture risk in Danish men with prostate cancer: A nationwide register study. *BJU Int* **100**:749–754.
51. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS 2005 Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med* **352**:154–164.

52. Smith MR, Boyce SP, Moynour E, Duh MS, Raut MK, Brandman J 2006 Risk of clinical fractures after gonadotropin-releasing hormone agonist therapy for prostate cancer. *J Urol* **175**:136–139.
53. Smith MR, Lee WC, Brandman J, Wang Q, Botteman M, Pashos CL 2005 Gonadotropin-releasing hormone agonists and fracture risk: a claims-based cohort study of men with nonmetastatic prostate cancer. *J Clin Oncol* **23**:7897–7903.
54. Carter DR, Buxsein ML, Marcus R 1992 New approaches for interpreting projected bone densitometry data. *J Bone Miner Res* **7**:137–145.
55. Looker AC, Orwoll ES, Johnston CC Jr, Lindsay RL, Wahner HW, Dunn WL, Calvo MS, Harris TB, Heyse SP 1997 Prevalence of low femoral bone density in older U.S. adults from NHANES III. *J Bone Miner Res* **12**:1761–1768.
56. Kelly PJ, Nguyen T, Hopper J, Pocock N, Sambrook P, Eisman J 1993 Changes in axial bone density with age: A twin study. *J Bone Miner Res* **8**:11–17.
57. Christian JC, Yu PL, Slemenda CW, Johnston CC Jr 1989 Heritability of bone mass: A longitudinal study in aging male twins. *Am J Hum Genet* **44**:429–433.
58. Slemenda CW, Christian JC, Reed T, Reister TK, Williams CJ, Johnston CC Jr 1992 Long-term bone loss in men: Effects of genetic and environmental factors. *Ann Intern Med* **117**:286–291.
59. Hui SL, Koller DL, Foroud TM, Econs MJ, Johnston CC, Peacock M 2006 Heritability of changes in bone size and bone mass with age in premenopausal white sisters. *J Bone Miner Res* **21**:1121–1125.
60. Shaffer JR, Kammerer CM, Bruder JM, Cole SA, Dyer TD, Almasy L, Maccluer JW, Blangero J, Bauer RL, Mitchell BD 2008 Genetic influences on bone loss in the San Antonio Family Osteoporosis study. *Osteoporos Int* **19**:1759–1767.

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