HHS Public Access

Author manuscript

J Bone Miner Res. Author manuscript; available in PMC 2023 January 01.

Published in final edited form as:

J Bone Miner Res. 2022 January ; 37(1): 41–51. doi:10.1002/jbmr.4460.

Age-related changes in bone density, microarchitecture and strength in postmenopausal Black and White women: SWAN Longitudinal HR-pQCT Study

Fjola Johannesdottir[1,2], **Melissa S. Putman**[2,3,4], **Sherri-Ann M. Burnett-Bowie**[2,3], **Joel S. Finkelstein**[2,3], **Elaine W. Yu**[2,3,Ɨ], **Mary L. Bouxsein**[1,2,3,Ɨ]

[1]Center for Advanced Orthopedic Studies, Beth Israel Deaconess Medical Center, Boston, MA, USA

[2]Harvard Medical School, Boston, MA, USA

[3]Endocrine Unit, Massachusetts General Hospital, Boston, MA, USA

[4]Endocrine Division, Boston Children's Hospital, Boston, MA, USA

Abstract

Higher fracture risk in White versus Black women is partly explained by lower BMD and worse bone microarchitecture in White women. However, whether rates of decline in bone density, microarchitecture and strength differ between postmenopausal Black and White women is unknown. Further, factors that influence rates of age-related bone microarchitecture deterioration remain ill-defined. Thus, over 6.7 years, we measured longitudinal changes in peripheral volumetric bone mineral density (vBMD), microarchitecture and strength at the distal radius and tibia using high-resolution peripheral quantitative computed tomography (HR-pQCT) in postmenopausal Black (n=80) and White (n=137) women participating in the Study of Women's Health Across the Nation (SWAN). We assessed whether age-related changes in vBMD and microarchitecture were influenced by body weight, body composition, and/or weight change. We found that at the radius, whereas White women appeared to have slightly greater rates of loss in total vBMD, cortical bone volume and porosity than Black women, those differences were attenuated after adjusting for clinical covariates. At the tibia, Black and White women had similar rates of bone loss. Independent of race and other clinical covariates, women with the lowest baseline body weight experienced the greatest decline in total and trabecular vBMD at the radius. Further, women who lost weight over the follow-up period had higher rates of bone loss, particularly at the tibia, compared to those who maintained or gained weight. Higher baseline total body fat mass was also protective of bone loss at both radius and tibia. In conclusion, these findings indicate that lower fracture risk among postmenopausal Black women is not due to slower rates of bone deterioration and highlight the importance for postmenopausal women to avoid lower body weight and excessive weight loss to avert rapid bone loss and subsequent fractures.

Corresponding author: Fjola Johannesdottir, PhD, Center for Advanced Orthopaedic Studies, Beth Israel Deaconess Medical Center, RN112, 330 Brookline Avenue, Boston, MA 02215, fjohanne@bidmc.harvard.edu.

Ɨ EWY and MLB are joint senior authors

Disclosures

All authors have no conflicts of interest regarding this manuscript.

Keywords

HR-pQCT; bone loss; bone microarchitecture; race; postmenopausal; weight; Black; White; women

Introduction

Skeletal fragility increases with advancing age in all individuals [1,2], yet fracture rates differ markedly by racial/ethnic background [3]. For example, Black women have up to 50% lower risk of fracture than White women [1,2,4–6]. There are many potential explanations for these differing fracture rates, including consistent findings that Black women generally have higher bone density than White women [2,7–12]. Notably, however, the variation by race/ethnicity in areal bone mineral density (aBMD) by dual-energy X-ray absorptiometry (DXA) is greatly attenuated after accounting for differences in body weight, suggesting that racial/ethnic differences in obesity rates may explain these aBMD differences. Importantly, the reported differences in BMD by race/ethnicity only partially explain the observed differences in fracture risk, as Black women still have 35% lower risk of fracture than White women even after accounting for Black women's higher total hip aBMD by DXA [2].

Determinants of bone strength beyond aBMD include bone geometry, microarchitecture and bone material properties. Thus, differences in these factors could contribute to lower fracture rate among Black women. Indeed, a few studies using histomorphometry of iliac crest bone biopsies have shown that Black women have better cortical and trabecular microarchitecture than White women [13–15]. Furthermore, high resolution peripheral quantitative computed tomography (HR-pQCT) scans reveal that postmenopausal Black women have larger and denser bones than White women, as well as greater estimated bone stiffness and failure load, at both the radius and tibia [8,16]. Interestingly, Black women exhibited advantageous bone structure primarily in the cortical compartment, consistent with a prior report showing that older Black men have thicker cortices in the proximal femur than White men by QCT [17] and with studies reporting greater differences in aBMD by race/ethnicity in the cortical-rich hip than in the trabecular-rich lumbar spine [7,8].

The rates of age- and menopause-related bone loss may also contribute to variations in fracture risk [18]. The rate of aBMD decline is influenced by weight, weight change and physical activity [19–22], though relatively few studies have examined rates of aBMD loss in different racial/ethnic groups. In the Study of Osteoporotic Fractures (SOF) cohort, a longitudinal study among women 65 years and older, Black women had approximately 2-fold slower aBMD loss in the hip compared to White women [23]. In contrast, in the Study of Women's Health Across the Nation (SWAN) cohort, aBMD declines during menopause were similar across different racial/ethnic groups after accounting for differences in body weight [11]. However, no study has assessed whether age-related deterioration of cortical and trabecular microstructure varies by race/ethnicity among postmenopausal women.

To evaluate the rate and determinants of age-related changes in bone microarchitecture in a diverse cohort of postmenopausal women, we examined longitudinal changes in volumetric bone mineral density (vBMD), microarchitecture and estimated strength at the distal radius

and tibia using HR-pQCT among women participating in SWAN at the Boston site. We aimed to determine whether age-related declines in bone density, microarchitecture and strength at the radius and tibia are similar in Black and White postmenopausal women and to examine whether variations in body weight, body composition, physical activity and/or weight change may contribute to racial differences in longitudinal bone density and microarchitectural declines.

Materials and Methods

Participants

SWAN is a multisite, longitudinal community-based cohort study of Black, Chinese, Japanese, Latina, and White women, as previously described [24,25]. Briefly, 3302 premenopausal women ages 42–52 years and not taking hormonal therapies were enrolled between 1996–97. Participants were recruited at seven sites in the United States: Boston, Massachusetts; Chicago, Illinois; Detroit, Michigan; Los Angeles, California; Hudson County, New Jersey; Oakland, California; and Pittsburgh, Pennsylvania. Women were followed annually for ten years and then approximately every 2 years thereafter. Participants self-identified their race/ethnicity. The current study was conducted at the SWAN Boston site, which enrolled Black and White women only. The study sample included 217 postmenopausal women (80 Black and 137 White) who had a technically acceptable HR-pQCT scan at SWAN visit 16 (2016–2017) at either the radius, tibia or both, as well as at SWAN visit 11, 12 or 13 (2008–2013), here referred to as the baseline scan. The majority (93%) of baseline scans were performed at visit 12. The protocol was approved by the Mass General Brigham Institutional Review Board, and written informed consent was obtained from all participants.

Clinical covariates

At both the baseline and follow-up study visits, we acquired HR-pQCT scans of the radius and tibia, measured height using a stadiometer and weight using a balance scale. Clinical covariates were assessed using standardized interviewer-administered or self-administered questionnaires. Clinical covariates of interest included age, current tobacco use, current alcohol intake, menopause duration (years post menopause), physical activity [26] (as measured by modified Baecke questionnaire), diabetes status (as assessed by self-report, diabetes medication use, or fasting glucose ≥126 mg/dL), self-reported fracture history, and medication use (including any current or prior use of oral glucocorticoids, hormone replacement therapy and osteoporosis medications). Additionally, body composition was assessed at baseline by a whole body DXA scan (QDR Discovery, Hologic, Inc. Bedford, MA) and results for subtotal (i.e., minus head) body fat mass, percent fat and lean mass (minus bone mineral content) were recorded in kilograms.

Bone density and microarchitecture by HR-pQCT

HR-pQCT scans (XtremeCT, Scanco Medical AG, Brürtisellen, Switzerland) were used to assess volumetric bone density, microstructure and compressive stiffness and failure load by linear micro-finite-element-analysis (μFEA) at the distal radius and tibia, as previously described for the SWAN cohort at the Boston site [8]. Briefly, the scans (60 kVp, 1000 mA,

100ms integration time, isotropic voxel size of 82 μm) were acquired at the distal radius and tibia using the standard region of interest (ROI) placement of a fixed distance of 9.5 and 22.5mm from the radial and tibial endplate, respectively. Total area (Tt.Ar, mm^2), total and trabecular volumetric BMD (Tt.BMD, Tb.BMD; mg HA/cm^3), trabecular number (Tb.N; mm-1), thickness (Tb.Th; mm) and separation (Tb.Sp, mm) were obtained from the standard morphologic analysis using Scanco analysis software version 6.0. The extended cortical analysis [27–29] was performed to measure cortical volumetric BMD (Ct.BMD; mg HA/cm^3), cortical bone volume (Ct.BV, mm^3), cortical thickness (Ct.Th, mm), cortical tissue mineral density (Ct.TMD, mg HA/cm^3), cortical porosity (Ct.Po, %) and endocortical perimeter (mm). All scans were reviewed for motion artifacts at the time of scanning and were repeated up to two times if significant motion artifact was present. All scans were graded for movement artifact using a 5-point scale [30], and scans graded 4 or 5 were excluded from these analyses. Two-dimensional, slice-based image registration based on total bone cross-sectional area was performed and common regions between baseline and follow-up scans were compared. Individuals that had common region lower than 70% between baseline and follow-up were excluded from analyses. Quality control assessment was maintained with daily scanning of the manufacturer's phantom. Short term reproducibility (with repositioning) for HR-pQCT measurements at the radius and tibia in our laboratory has previously been reported, and ranges from 0.2%−1.4% for vBMD variables; 0.3–8.6% for trabecular microarchitecture; 0.6% to 2.4% for cortical microarchitecture; 7.3%−20.2% for cortical porosity; and 2.1%−3.0% for μFEA outcomes.[8]

The number of participants with acceptable HR-pQCT scans at the distal radius at both the baseline and follow-up visits was 186. Of those, one was excluded because of poor image quality and 3 were excluded because the common region between baseline and follow-up scans was lower than 70%, leaving a total study sample for distal radius of 182 (68 Black and 114 White). The number of women with acceptable HR-pQCT scans at the distal tibia at both the baseline and follow-up visits was 210; 3 were excluded because common region between baseline and follow-up scans was lower than 70%, resulting in a study sample for the distal tibia of 207 (78 Black and 129 White). The median and interquartile range of common region overlap of the baseline and follow-up scans was 93% (87 to 96%) for the radius and 94% (91 to 97%) for the tibia.

Statistical analysis

Standard descriptive statistics are reported as means and standard deviation. Baseline characteristics between Black and White women were compared using a two-sample t-test for continuous variables and a chi-square test for categorical variables. Longitudinal changes in HR-pQCT-derived measurements were assessed with linear mixed models (LMM), including both random intercepts and slopes. Two regressions were performed on each variable in the units of measurement: 1) unadjusted, and 2) with adjustment for clinical covariates (menopause duration, baseline weight, diabetes status, alcohol intake) and interaction terms, including follow-up time x menopause duration and follow-up time x baseline weight. Physical activity score was not included as a covariate because it had no association with changes in bone outcomes. Results were reported as 5-yr percent change from baseline. Potential differences in the rate of bone parameter change between racial

groups were tested by an interaction term between race/ethnicity and time in each model, with regressions performed on natural log-transformed HR-pQCT variables. To account for variable time between visits, the percent change from baseline in each variable was calculated and normalized to 5 years and the least-squares means in percent change in HR-pQCT-derived outcomes were assessed across tertiles of baseline weight, BMI and body composition with adjustment for race, menopause duration, and weight change over follow-up, and differences across tertiles were analyzed by one-way analysis of covariance (ANCOVA). Finally, we computed the least-squares means for percent changes in HR-pQCT-derived outcomes across weight change groups (< −3% weight loss, >3% weight gain, and 3% ≤ and ≥−3% maintained weight). A 3% threshold was chosen to reach sufficient numbers of individuals who experienced weight change during follow-up. Further we assessed the effect of body weight and race as well as percent change in body weight and race on changes in bone outcomes by including interaction terms in the ANCOVA models (weight x race and percent change in weight x race). All analyses were performed using R 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria) and p values <0.05 were considered significant.

Results

At the baseline visit, the average age of the cohort was 59.9 ± 2.7 years, and there were no differences in age, height and time since menopause between Black and White women (Table 1). Black women had a higher weight and BMI and were more likely to have diabetes than White women, whereas White women were more physically active and had higher alcohol intake. There was no difference in smoking nor use of glucocorticoids, osteoporosis medications or HRT. Prior history of fracture tended to be higher in the White (23%) versus Black (14%) women, but did not reach statistical significance (p=0.16). At the baseline scan, Black women had better cortical bone microarchitecture and higher bone strength than White women (Suppl. Table 1).

Postmenopausal changes in vBMD, bone microarchitecture and strength

The average length of time between baseline and follow-up HR-pQCT scans was 6.7 ± 0.8 years. Considering both the Black and White women together, age-related declines were apparent in nearly every bone microarchitectural parameter (Figure 1) and were generally greater at the radius than the tibia. For example, the rates of decline in total and trabecular vBMD were 1.8- and 6-fold higher, respectively, at the radius than tibia (p<0.0001 for both) (Figure 1). Cortical bone microarchitecture, including cortical bone volume, thickness and porosity, also deteriorated faster at the radius than the tibia (p<0.001 for all). In contrast, cortical vBMD declined faster at the tibia than radius (p>0.0001). All together, these microarchitectural changes contributed to significant declines in stiffness and failure load at the radius (p<0.0001), with little to no decline in stiffness and failure load at tibia.

Association between race and rate of bone loss

At the radius, the unadjusted rates of bone decline tended to be greater in White women than Black women. For example, the average percent loss in Tt.BMD was ~23% greater in White versus Black women (p=0.07, Table 2). Similar patterns were seen for the rate of decline in

cortical bone volume and Ct.BMD, which were 29% (p = 0.056) and 26% (p=0.12) greater, respectively, in White versus Black women, though the differences did not meet statistical significance. Similarly, cortical porosity tended to increase more in White than in Black women (+48 vs +41%/5 yr; p=0.09). After accounting for clinical covariates, the effect of race on rates of bone density and microarchitecture deterioration was attenuated for most outcomes. The decline in estimated failure load and stiffness at the radius was similar in both groups for both unadjusted and multivariate-adjusted analyses.

In contrast to the radius, age-related changes in density, microarchitecture and strength at the tibia were largely similar in Black and White women (all p>0.26, Table 2). For example, Tt.BMD declined about 2.5%/5yr in both Black and White women (p=0.67 between groups), while Ct.BMD declined by −4.9%/5yr and −4.5%/5yr in White and Black women respectively. On average, tibial Tb.BMD was maintained in Black and White women over the follow-up (p>0.6), whereas both Black and White women experienced deterioration in trabecular microarchitecture during the longitudinal study (p>0.26 between groups). Changes in cortical bone microarchitecture at the tibia were also similar between Black and White women (p>0.28). μFEA-derived tibia stiffness did not change in either Black or White women during follow-up after accounting for clinical covariates, and failure load declined by a minor amount in White women only. Rates of change in μFEA-derived estimates of bone strength were similar in White and Black women (p>0.85).

Association between baseline body weight and rate of bone loss

Among the full cohort, baseline weight was significantly associated with rates of bone loss in Tt.BMD and Tb.BMD at the radius, with women in the lowest weight tertile experiencing the greatest loss (Figure 2) even after adjusting for race and other covariates. For example, Tt.BMD and Tb.BMD declined by −5.7% and −3.2% over 5 yrs in the lowest weight tertile compared to −3.5% and −0.9% in the highest weight tertile, respectively (Figure 2A; p<0.02 for both). There was no evidence of an interaction between body weight and race for these rates of bone loss (p>0.22). Changes in cortical bone at the radius were similar across all tertiles of baseline body weight (p>=0.12). At the tibia, rates of bone density and microarchitectural changes did not differ among baseline body weight tertiles (p>=0.10 for all, Figure 2B). We observed similar patterns between baseline BMI and bone loss as with baseline body weight and bone loss (results not shown).

Association between baseline fat mass and rate of bone loss

Baseline fat mass was significantly associated with rates of Tt.BMD and Tb.BMD decline at both radius and tibia, with women in the lowest fat mass tertile at baseline showing the greatest rates of decline (Figure 3). Adjustment for race, menopause duration and weight loss did not change the results. Lower baseline fat mass was also significantly associated with greater rate of Ct.BMD decline at the tibia (Figure 3B). At the tibia, only women in the lowest tertile of fat mass exhibited significant declines in failure load. Changes in tibial bone microarchitecture were not associated with baseline fat mass (p>0.12). Baseline lean mass was not associated with bone loss at the tibia (p=0.13–0.99) or at the radius (p=0.15–0.66), with the exception of radius Tt.BMD, where higher lean mass was associated with slower decline (p=0.04).

Association between weight change over follow-up and bone loss

Overall, those who lost weight (>3% of body weight) over the follow-up period had the greatest rates of bone density and microstructure decline. Specifically, at the tibia, those who lost >3% of body weight over follow-up (n=55) experienced two-fold greater loss in Tt.BMD than those who gained weight (>3% of baseline body weight, n=54) over follow-up (−3.4%/5yr versus −1.6%/5yr, respectively; Figure 4 B). Women who gained weight during follow-up also maintained their tibial cortical bone microarchitecture, whereas those who lost weight during follow-up had significant declines in cortical bone volume (p=0.008). Similarly, the rate of deterioration in tibial trabecular number was also associated with change in body weight during follow-up (p=0.004). Those who lost weight had on average a 2-fold greater decrease in trabecular number than those who maintained weight and a 6-fold greater decrease than those who gained weight. At the radius, the association between change in body weight and rates of decline in bone density and structure followed similar patterns as the tibia, but did not reach statistical significance for microarchitecture (Figure 4 A). These associations between percent change in body weight and rates of bone loss did not differ between races (p>0.46 for interaction terms, % change in weight x race). Percent change in body weight was strongly correlated with percent change in both lean and fat mass, however the correlation was stronger for fat mass than lean mass (r=0.91 (95%CI: 0.88–0.93) vs r=0.80 (95%CI: 0.75–.084)). In addition, change in fat mass over follow-up was greater than lean mass among both those who lost weight and gained weight (p<0.001). The change in fat mass was 2-fold greater than in lean mass (9 %/5yr vs 5 %/5yr) among those who gained weight but was 3-fold greater in the weight loss group (−10 %/5yr vs −3 %/5yr).

Discussion

In this study, we characterized age-related changes in volumetric bone density, microarchitecture and strength at the distal radius and tibia in a cohort of Black and White postmenopausal women. We also determined whether age-related changes in these bone outcomes were influenced by race, weight, body composition and/or weight change. During an average of 6.7 years of follow-up, we found that age-related declines in bone density, structure and strength were similar in Black and White women at the tibia. At the radius there appeared to be greater rates of decline in White women, but these differences were eliminated after adjusting for clinical covariates. In particular, higher body weight was protective against bone loss, as women with the lowest baseline body weight experienced the highest rates of bone loss at the radius. Furthermore, women who lost weight over the follow-up period had accelerated rates of bone loss, particularly at the tibia, compared to those who maintained or gained weight. Higher total body fat mass was also protective of bone loss at both radius and tibia. Thus, the lower risk of fracture among postmenopausal Black versus White women does not appear to be due to slower rates of bone microstructure deterioration, at least at the peripheral skeleton. Rather, differential fracture incidence may be attributed to attainment of more favorable peak bone density, structure and strength in Black compared to White women [31,32] and/or other non-skeletal factors such as fall risk, muscle strength/power or body composition.

Our study is unique in that the few prior longitudinal studies assessing age-related changes in peripheral bone microstructure by HR-pQCT have been limited to predominantly White cohorts [33–35] and relatively short follow-up of one to three years [34,35]. Detailed comparisons across the studies are difficult due to use of different approaches for registration of follow-up images, as well as varied lengths of follow-up, study participants and sample sizes. Nonetheless, our finding that postmenopausal women experience significant declines in total, cortical and trabecular bone density, cortical structure, and strength at the distal radius is consistent with a prior 3-year study [35], but differed from a 5-year study [33] that reported no changes in trabecular bone density and microarchitecture. In line with most other studies, we observed notable increases in cortical porosity, but were unable to detect changes in trabecular microstructure, the latter likely due to resolution limitations inherent in the first-generation HR-pQCT scanner.

One consistent observation across all studies, including the current one, is a generally greater rate of age-related decline in bone density, structure and strength at the radius than at the tibia. Since the radius is a non-weight-bearing site it may reflect age-related alterations in hormonal status more than the tibia, which may be protected, in part, by its weight bearing status. Indeed, Khosla et al [36] have speculated that weight-bearing bones may have lower sensitivity to bioavailable estrogen, and thus a higher threshold to withstand deleterious skeletal effects of sex hormone deficiency.

At the radius, Black women appeared to have slightly slower rate of bone loss than White women in unadjusted analyses, particularly a slower deterioration of cortical microarchitecture. However, after accounting for clinical covariates, differences in rates of bone decline by race were attenuated. Thus, racial differences in bone microarchitectural decline are explained by differences in known clinical variables such as weight and body composition. At the tibia, rates of bone loss did not differ by race in either the unadjusted or adjusted analyses. These findings suggest that baseline differences in bone density and microarchitecture may contribute to variations in fracture rates by race/ethnicity, whereas postmenopausal changes in these parameters do not. Additional non-skeletal factors might also contribute to differential fracture rates; for example, older Black women have a lower risk of falling compared to White women [37,38].

Several studies have compared age-related rate of loss in aBMD in Black and White women at various skeletal sites [11,23,39,40] and a few have examined bone loss at each stage of the menopause transition [11,39]. Interestingly, White women had significantly more rapid loss in aBMD than Black women during transmenopause (i.e., 1 yr before to 2 yrs after the final menstrual period) [39]. However, in agreement with the current findings, there were no differences in postmenopausal rates of aBMD loss in Black and White women after adjustment for weight. In contrast, another study of women aged 65 yrs and older reported that White women have 2-fold more rapid bone loss at the femoral neck than Black women [23], even after multivariate adjustment. We detected only slight differences in rates of bone loss, restricted to the radius, and these differences were abrogated by adjustment for clinical covariates.

Notably, we found that both weight and weight-change had a large impact on age-related declines in peripheral bone density and microstructure. Our finding that lower baseline body weight is associated with faster rates of peripheral bone deterioration at the radius is consistent with several studies reporting that lower body weight or BMI is associated with more rapid aBMD declines at the radius, lumbar spine and hip by DXA [11,22,39,41–43]. However, the finding that body weight had a greater effect at the non-weight bearing radius than the tibia was unexpected, and suggests that weight may exert systemic effects on bone beyond direct mechanical loading and/or that low weight reflects aspects of poor health and nutrition that were not captured by our multivariate adjustment. Interestingly, higher total fat mass at baseline provided partial protection against bone loss at both radius and tibia, possibly due to estrogen production by adipose tissue [44]. Although in this study, there was no association between physical activity score and changes in bone outcomes it is worth noting that assessment of physical activity that is more osteogenic specific, such as the bone specific physical activity questionnaire [45] or skeletal loading score [46] might have exhibited different results.

Our observation that weight loss is associated with more rapid decline in peripheral bone density and microstructure is also consistent with prior studies reporting that weight loss is associated with faster declines in aBMD [20–22,47,48] and worse peripheral bone microarchitecture [49]. In our study, we found that weight loss during follow-up was associated with greater loss in total BMD and deterioration in trabecular and cortical microarchitecture at the weight-bearing tibia compared to those who gained weight. Our results are consistent with the observation that older women who experience weight loss have increased rates of bone loss at the hip regardless of body weight, even in the obese group [20]. Although the underlying causes for weight loss in older women can vary widely, both intentional and unintentional weight loss are associated with bone loss and increased risk of hip fracture [20]. It is possible that bone loss may be more deleterious in women who start with lower BMI and presumably lower bone strength. However, we were unable to investigate this issue, as our cohort did not have any women who were underweight at the start, had few who were normal weight (n=51), and had even fewer who were normal weight and lost weight during the follow-up period (n=9). Thus, a larger study is needed to explore this important issue. Additionally, we could not determine whether change in lean or fat mass is more important when comes to changes in bone outcomes due to insufficient sample in the each weight changing group. Overall, our findings indicate that independent of race, both lower body weight and weight loss can cause more rapid loss of peripheral bone density and microstructure in postmenopausal women.

This study has several important strengths. In particular, it is among the few longitudinal studies to assess age-related changes in bone density, microarchitecture and bone strength by HR-pQCT among postmenopausal women, and involves the longest prospective follow-up (6.7 ± 0.8 years). In addition, we studied Black and White women to investigate how age-related changes in bone fragility might be modified by the social construct of race, which has not been previously been examined. We also directly measured weight change, as opposed to relying on patient recall. Finally, we were able to take advantage of the highly detailed and prospectively collected menopause data from the SWAN cohort to accurately

adjust postmenopausal rates of bone loss for menopause duration, an important variable that is often not accounted for in other analyses.

This study also has several limitations. We acknowledge that the association between body composition and skeletal fragility is complex, and although we explored the contribution of fat and lean mass, we did not explore the role of other body composition variables such as visceral adipose tissue, which has been proposed to negatively influence bone outcomes [50,51]. Further, although this represents one of the largest longitudinal HR-pQCT studies published to date, the study may nevertheless have been insufficiently powered to detect small differences in rates of bone microstructure deterioration between Black and White women. However, the study should have had sufficient power to detect clinically relevant differences in rates of bone loss between Black and White women and the study had ~80% power to detect 2% difference over 5 years between the groups in rates of loss in total bone density and within the cortical bone compartment at the radius. As the cohort encompassed only Black and White postmenopausal women, we cannot make any conclusion regarding possible differences in men, other racial/ethnic groups or during the menopause transition. Moreover, we acknowledge that while the SWAN participants were initially recruited as a community-based cohort ~ 25 years ago, there is now potential for survivor bias such that rates of bone deterioration may be even greater in less healthy, less motivated postmenopausal women. Finally, we acknowledge that racial designations may primarily reflect differences in sociocultural factors, and that heterogeneity and fluidity within racial/ethnic designations may further complicate generalizations within racial groups.

In conclusion, we found largely similar rates of loss in peripheral bone density and microarchitecture deterioration in postmenopausal Black and White women after accounting for clinical covariates. Baseline weight and fat mass, as well as greater weight loss during follow-up, were associated with more rapid bone deterioration at the peripheral skeleton. As lower weight and weight loss are associated with increased risk of fracture [20,52–54], our findings reinforce the notion that it is important for postmenopausal women to maintain weight after menopause to avoid experiencing rapid bone loss and subsequent fractures. Additionally, older women who lose weight to achieve better health may need targeted interventions to prevent excessive bone loss due to weight loss.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495). The HR-pQCT scans were supported by an NCRR Shared Equipment Grant (1S10RR023405-01). The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

We thank the study staff at each site and all the women who participated in SWAN.

SWAN Clinical Centers: *University of Michigan, Ann Arbor – Siobán Harlow, PI 2011 – present, MaryFran Sowers, PI 1994–2011*; *Massachusetts General Hospital, Boston, MA – Joel Finkelstein, PI 1999 – present*; *Robert Neer, PI 1994 – 1999; Rush University, Rush University Medical Center, Chicago, IL – Howard Kravitz, PI 2009 – present*; *Lynda Powell, PI 1994 – 2009; University of California, Davis/Kaiser – Ellen Gold, PI*; *University of California, Los Angeles – Gail Greendale, PI*; *Albert Einstein College of Medicine, Bronx, NY – Carol Derby, PI 2011 – present, Rachel Wildman, PI 2010 – 2011; Nanette Santoro, PI 2004 – 2010; University of Medicine and Dentistry – New Jersey Medical School, Newark – Gerson Weiss, PI 1994 – 2004;* and the *University of Pittsburgh, Pittsburgh, PA – Karen Matthews, PI.*

NIH Program Office: *National Institute on Aging, Bethesda, MD – Chhanda Dutta 2016- present; Winifred Rossi 2012–2016; Sherry Sherman 1994 – 2012; Marcia Ory 1994 – 2001; National Institute of Nursing Research, Bethesda, MD – Program Officers.*

SWAN Central Laboratory: *University of Michigan, Ann Arbor – Daniel McConnell* (Central Ligand Assay Satellite Services).

SWAN Coordinating Center: *University of Pittsburgh, Pittsburgh, PA – Maria Mori Brooks, PI 2012 - present; Kim Sutton-Tyrrell, PI 2001 – 2012; New England Research Institutes, Watertown, MA - Sonja McKinlay, PI 1995 – 2001.*

Steering Committee: Susan Johnson, Current Chair; Chris Gallagher, Former Chair

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Barrett-Connor E, Siris ES, Wehren LE, Miller PD, Abbott TA, Berger ML, et al. Osteoporosis and fracture risk in women of different ethnic groups. J Bone Miner Res. 2005;20(2):185–94. [PubMed: 15647811]
2. Cauley JA, Wu L, Wampler NS, Barnhart JM, Allison M, Chen Z, et al. Clinical risk factors for fractures in multi-ethnic women: the Women's Health Initiative. J Bone Miner Res. 2007;22(11):1816–26. [PubMed: 17638574]
3. Cauley JA. Defining ethnic and racial differences in osteoporosis and fragility fractures. Clin Orthop Relat Res. 2011;469(7):1891–9. [PubMed: 21431462]
4. Baron JA, Barrett J, Malenka D, Fisher E, Kniffin W, Bubolz T, et al. Racial differences in fracture risk. Epidemiology. 1994;5(1):42–7. [PubMed: 8117781]
5. Griffin MR, Ray WA, Fought RL, Melton LJ, 3rd. Black-white differences in fracture rates. Am J Epidemiol. 1992;136(11):1378–85. [PubMed: 1488964]
6. Taylor AJ, Gary LC, Arora T, Becker DJ, Curtis JR, Kilgore ML, et al. Clinical and demographic factors associated with fractures among older Americans. Osteoporos Int. 2011;22(4):1263–74. [PubMed: 20559818]
7. Finkelstein JS, Lee ML, Sowers M, Ettinger B, Neer RM, Kelsey JL, et al. Ethnic variation in bone density in premenopausal and early perimenopausal women: effects of anthropometric and lifestyle factors. J Clin Endocrinol Metab. 2002;87(7):3057–67. [PubMed: 12107201]
8. Putman MS, Yu EW, Lee H, Neer RM, Schindler E, Taylor AP, et al. Differences in skeletal microarchitecture and strength in African-American and white women. J Bone Miner Res. 2013;28(10):2177–85. [PubMed: 23572415]
9. Taaffe DR, Cauley JA, Danielson M, Nevitt MC, Lang TF, Bauer DC, et al. Race and sex effects on the association between muscle strength, soft tissue, and bone mineral density in healthy elders: the Health, Aging, and Body Composition Study. J Bone Miner Res. 2001;16(7):1343–52. [PubMed: 11450711]
10. Cauley JA, Lui LY, Ensrud KE, Zmuda JM, Stone KL, Hochberg MC, et al. Bone mineral density and the risk of incident nonspinal fractures in black and white women. Jama. 2005;293(17):2102–8. [PubMed: 15870413]

11. Finkelstein JS, Brockwell SE, Mehta V, Greendale GA, Sowers MR, Ettinger B, et al. Bone mineral density changes during the menopause transition in a multiethnic cohort of women. J Clin Endocrinol Metab. 2008;93(3):861–8. [PubMed: 18160467]
12. Looker AC, Melton LJ 3rd, Harris TB, Borrud LG, Shepherd JA. Prevalence and trends in low femur bone density among older US adults: NHANES 2005–2006 compared with NHANES III. J Bone Miner Res. 2010;25(1):64–71. [PubMed: 19580459]
13. Han ZH, Palnitkar S, Rao DS, Nelson D, Parfitt AM. Effect of ethnicity and age or menopause on the structure and geometry of iliac bone. J Bone Miner Res. Dec 1996;11(12):1967–75. Epub 1996/12/01. [PubMed: 8970900]
14. Schnitzler CM, Mesquita JM. Cortical bone histomorphometry of the iliac crest in normal black and white South African adults. Calcified tissue international. Dec 2006;79(6):373–82. Epub 2006/12/13. [PubMed: 17160576]
15. Schnitzler CM, Pettifor JM, Mesquita JM, Bird MDT, Schnaid E, Smyth AE. Histomorphometry of iliac crest bone in 346 normal black and white South African adults. Bone and Mineral. 1990/09/01/ 1990;10(3):183–99. [PubMed: 2224205]
16. Putman MS, Yu EW, Lin D, Darakananda K, Finkelstein JS, Bouxsein ML. Differences in Trabecular Microstructure Between Black and White Women Assessed by Individual Trabecular Segmentation Analysis of HR-pQCT Images. J Bone Miner Res. 2017;32(5):1100–8. [PubMed: 27958659]
17. Marshall LM, Zmuda JM, Chan BK, Barrett-Connor E, Cauley JA, Ensrud KE, et al. Race and Ethnic Variation in Proximal Femur Structure and BMD Among Older Men. Journal of Bone and Mineral Research. 2008;23(1):121–30. [PubMed: 17892375]
18. Cawthon PM, Ewing SK, Mackey DC, Fink HA, Cummings SR, Ensrud KE, et al. Change in hip bone mineral density and risk of subsequent fractures in older men. J Bone Miner Res. Oct 2012;27(10):2179–88. Epub 2012/06/01. [PubMed: 22648990]
19. Nguyen TV, Sambrook PN, Eisman JA. Bone loss, physical activity, and weight change in elderly women: the Dubbo Osteoporosis Epidemiology Study. J Bone Miner Res. Sep 1998;13(9):1458–67. Epub 1998/09/17. [PubMed: 9738519]
20. Ensrud KE, Ewing SK, Stone KL, Cauley JA, Bowman PJ, Cummings SR. Intentional and unintentional weight loss increase bone loss and hip fracture risk in older women. J Am Geriatr Soc. 2003;51(12):1740–7. [PubMed: 14687352]
21. Macdonald HM, New SA, Campbell MK, Reid DM. Influence of weight and weight change on bone loss in perimenopausal and early postmenopausal Scottish women. Osteoporos Int. 2005;16(2):163–71. [PubMed: 15185065]
22. Uusi-Rasi K, Sievänen H, Pasanen M, Oja P, Vuori I. Maintenance of body weight, physical activity and calcium intake helps preserve bone mass in elderly women. Osteoporos Int. 2001;12(5):373–9. [PubMed: 11444085]
23. Cauley JA, Lui LY, Stone KL, Hillier TA, Zmuda JM, Hochberg M, et al. Longitudinal study of changes in hip bone mineral density in Caucasian and African-American women. J Am Geriatr Soc. 2005;53(2):183–9. [PubMed: 15673339]
24. Santoro N, Sutton-Tyrrell K. The SWAN song: Study of Women's Health Across the Nation's recurring themes. Obstetrics and gynecology clinics of North America. 2011;38(3):417–23. [PubMed: 21961710]
25. Sowers MR, Jannausch M, McConnell D, Little R, Greendale GA, Finkelstein JS, et al. Hormone predictors of bone mineral density changes during the menopausal transition. J Clin Endocrinol Metab. 2006;91(4):1261–7. [PubMed: 16403818]
26. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. The American journal of clinical nutrition. Nov 1982;36(5):936–42. Epub 1982/11/01. [PubMed: 7137077]
27. Burghardt AJ, Buie HR, Laib A, Majumdar S, Boyd SK. Reproducibility of direct quantitative measures of cortical bone microarchitecture of the distal radius and tibia by HR-pQCT. Bone. 2010;47(3):519–28. [PubMed: 20561906]

28. Burghardt AJ, Kazakia GJ, Ramachandran S, Link TM, Majumdar S. Age- and gender-related differences in the geometric properties and biomechanical significance of intracortical porosity in the distal radius and tibia. J Bone Miner Res. 2010;25(5):983–93. [PubMed: 19888900]
29. Nishiyama KK, Macdonald HM, Buie HR, Hanley DA, Boyd SK. Postmenopausal women with osteopenia have higher cortical porosity and thinner cortices at the distal radius and tibia than women with normal aBMD: an in vivo HR-pQCT study. J Bone Miner Res. 2010;25(4):882–90. [PubMed: 19839766]
30. Pialat JB, Burghardt AJ, Sode M, Link TM, Majumdar S. Visual grading of motion induced image degradation in high resolution peripheral computed tomography: impact of image quality on measures of bone density and micro-architecture. Bone. Jan 2012;50(1):111–8. Epub 2011/10/25. [PubMed: 22019605]
31. Popp KL, Xu C, Yuan A, Hughes JM, Unnikrishnan G, Reifman J, et al. Trabecular microstructure is influenced by race and sex in Black and White young adults. Osteoporos Int. Jan 2019;30(1):201–9. Epub 2018/11/07.
32. Popp KL, Hughes JM, Martinez-Betancourt A, Scott M, Turkington V, Caksa S, et al. Bone mass, microarchitecture and strength are influenced by race/ethnicity in young adult men and women. Bone. Oct 2017;103:200–8. [PubMed: 28712877]
33. Burt LA, Hanley DA, Boyd SK. Cross-sectional Versus Longitudinal Change in a Prospective HR-pQCT Study. J Bone Miner Res. 2017;32(7):1505–13. [PubMed: 28294405]
34. Kawalilak CE, Johnston JD, Olszynski WP, Kontulainen SA. Characterizing microarchitectural changes at the distal radius and tibia in postmenopausal women using HR-pQCT. Osteoporos Int. 2014;25(8):2057–66. [PubMed: 24781379]
35. Shanbhogue VV, Brixen K, Hansen S. Age- and Sex-Related Changes in Bone Microarchitecture and Estimated Strength: A Three-Year Prospective Study Using HRpQCT. J Bone Miner Res. 2016;31(8):1541–9. [PubMed: 26896351]
36. Khosla S, Riggs BL, Robb RA, Camp JJ, Achenbach SJ, Oberg AL, et al. Relationship of volumetric bone density and structural parameters at different skeletal sites to sex steroid levels in women. The Journal of clinical endocrinology and metabolism. 2005;90(9):5096–103. Epub 2005/07/05. [PubMed: 15998772]
37. Geng Y, Lo JC, Brickner L, Gordon NP. Racial-Ethnic Differences in Fall Prevalence among Older Women: A Cross-Sectional Survey Study. BMC Geriatr. 2017;17(1):65–. [PubMed: 28284206]
38. Sun DQ, Huang J, Varadhan R, Agrawal Y. Race and fall risk: data from the National Health and Aging Trends Study (NHATS). Age and Ageing. 2016;45(1):120–7. [PubMed: 26764401]
39. Greendale GA, Sowers M, Han W, Huang MH, Finkelstein JS, Crandall CJ, et al. Bone mineral density loss in relation to the final menstrual period in a multiethnic cohort: results from the Study of Women's Health Across the Nation (SWAN). J Bone Miner Res. 2012;27(1):111–8. [PubMed: 21976317]
40. Luckey MM, Wallenstein S, Lapinski R, Meier DE. A prospective study of bone loss in African-American and white women--a clinical research center study. J Clin Endocrinol Metab. 1996;81(8):2948–56. [PubMed: 8768857]
41. Ravn P, Cizza G, Bjarnason NH, Thompson D, Daley M, Wasnich RD, et al. Low body mass index is an important risk factor for low bone mass and increased bone loss in early postmenopausal women. Early Postmenopausal Intervention Cohort (EPIC) study group. J Bone Miner Res. 1999;14(9):1622–7. [PubMed: 10469292]
42. Guthrie JR, Ebeling PR, Hopper JL, Barrett-Connor E, Dennerstein L, Dudley EC, et al. A prospective study of bone loss in menopausal Australian-born women. Osteoporos Int. 1998;8(3):282–90. [PubMed: 9797914]
43. Sowers MR, Zheng H, Jannausch ML, McConnell D, Nan B, Harlow S, et al. Amount of bone loss in relation to time around the final menstrual period and follicle-stimulating hormone staging of the transmenopause. J Clin Endocrinol Metab. 2010;95(5):2155–62. [PubMed: 20215399]
44. Reid IR. Relationships between fat and bone. Osteoporos Int. May 2008;19(5):595–606. Epub 2007/10/30. [PubMed: 17965817]
45. Weeks BK, Beck BR. The BPAQ: a bone-specific physical activity assessment instrument. Osteoporos Int. Nov 2008;19(11):1567–77. Epub 2008/04/17. [PubMed: 18414964]

46. Popp KL, Turkington V, Hughes JM, Xu C, Unnikrishnan G, Reifman J, et al. Skeletal loading score is associated with bone microarchitecture in young adults. Bone. Oct 2019;127:360–6. Epub 2019/07/03. [PubMed: 31265923]

47. Johannesdottir F, Aspelund T, Reeve J, Poole KE, Sigurdsson S, Harris TB, et al. Similarities and differences between sexes in regional loss of cortical and trabecular bone in the mid-femoral neck: the AGES-Reykjavik longitudinal study. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2013;28(10):2165–76.

48. Knoke JD, Barrett-Connor E. Weight loss: a determinant of hip bone loss in older men and women. The Rancho Bernardo Study. Am J Epidemiol. 2003;158(12):1132–8. [PubMed: 14652297]

49. Liu CT, Sahni S, Xu H, McLean RR, Broe KE, Hannan MT, et al. Long-Term and Recent Weight Change Are Associated With Reduced Peripheral Bone Density, Deficits in Bone Microarchitecture, and Decreased Bone Strength: The Framingham Osteoporosis Study. J Bone Miner Res. Oct 2018;33(10):1851–8. Epub 2018/05/31. [PubMed: 29813182]

50. Bredella MA, Lin E, Gerweck AV, Landa MG, Thomas BJ, Torriani M, et al. Determinants of bone microarchitecture and mechanical properties in obese men. J Clin Endocrinol Metab. Nov 2012;97(11):4115–22. [PubMed: 22933540]

51. Sheu Y, Cauley JA. The role of bone marrow and visceral fat on bone metabolism. Curr Osteoporos Rep. Jun 2011;9(2):67–75. Epub 2011/03/05. [PubMed: 21374105]

52. Ensrud KE, Harrison SL, Cauley JA, Langsetmo L, Schousboe JT, Kado DM, et al. Impact of Competing Risk of Mortality on Association of Weight Loss With Risk of Central Body Fractures in Older Men: A Prospective Cohort Study. Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research. 2017;32(3):624–32. Epub 2016/11/07.

53. Ensrud KE, Cauley J, Lipschutz R, Cummings SR. Weight change and fractures in older women. Study of Osteoporotic Fractures Research Group. Arch Intern Med. 1997;157(8):857–63. [PubMed: 9129545]

54. De Laet C, Kanis JA, Odén A, Johanson H, Johnell O, Delmas P, et al. Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int. 2005;16(11):1330–8. [PubMed: 15928804]

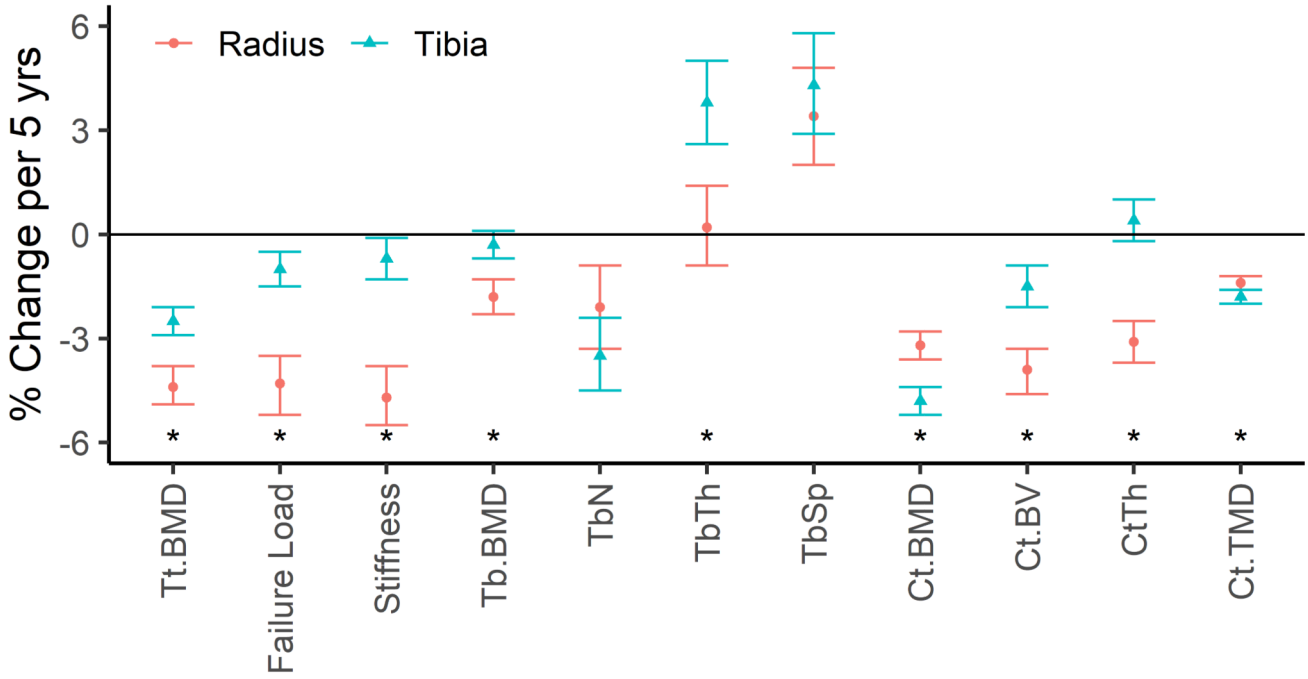

Figure 1.

Average percent change (with 95% confidence interval) over 5 years in HR-pQCT variables at the radius and tibia among postmenopausal women. *indicates a significant difference in changes at the radius and tibia (p-value <0.05) Changes were always significant except Tb Th at the radius and CtTh and Tb.BMD at the tibia.

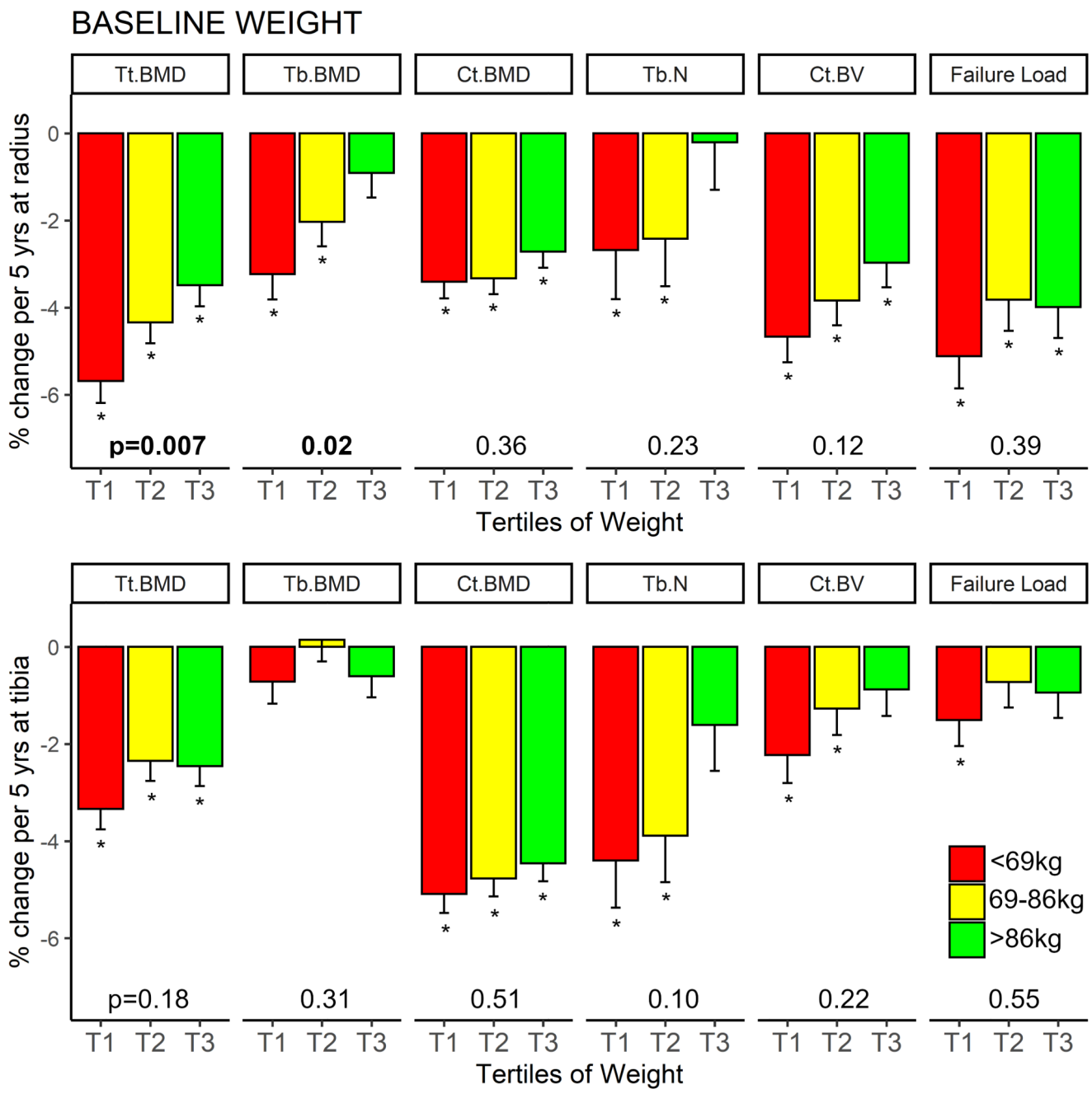

Figure 2.

Average percent change (± SE) over 5 years for bone microarchitectural variables analyzed by tertiles of baseline body weight (tertile 1 (T1): <69 kg, tertile 2 (T2): 69–86 kg; tertile (T3): >86kg) at (A) distal radius, tertile 1 (T1) n: 60, tertile 2 (T2) n: 61, tertile 3 (T3) n: 61; and (B) distal tibia, T1 n: 69, T2 n: 69, T3 n: 69. Models are adjusted for race/ethnicity, time since menopause and weight change over the follow-up time. ANCOVA p-values comparing tertiles are shown. * indicate significant change from baseline within each tertile. Tt, total; Tb, trabecular; N, number; Ct, cortical; BV, bone volume.

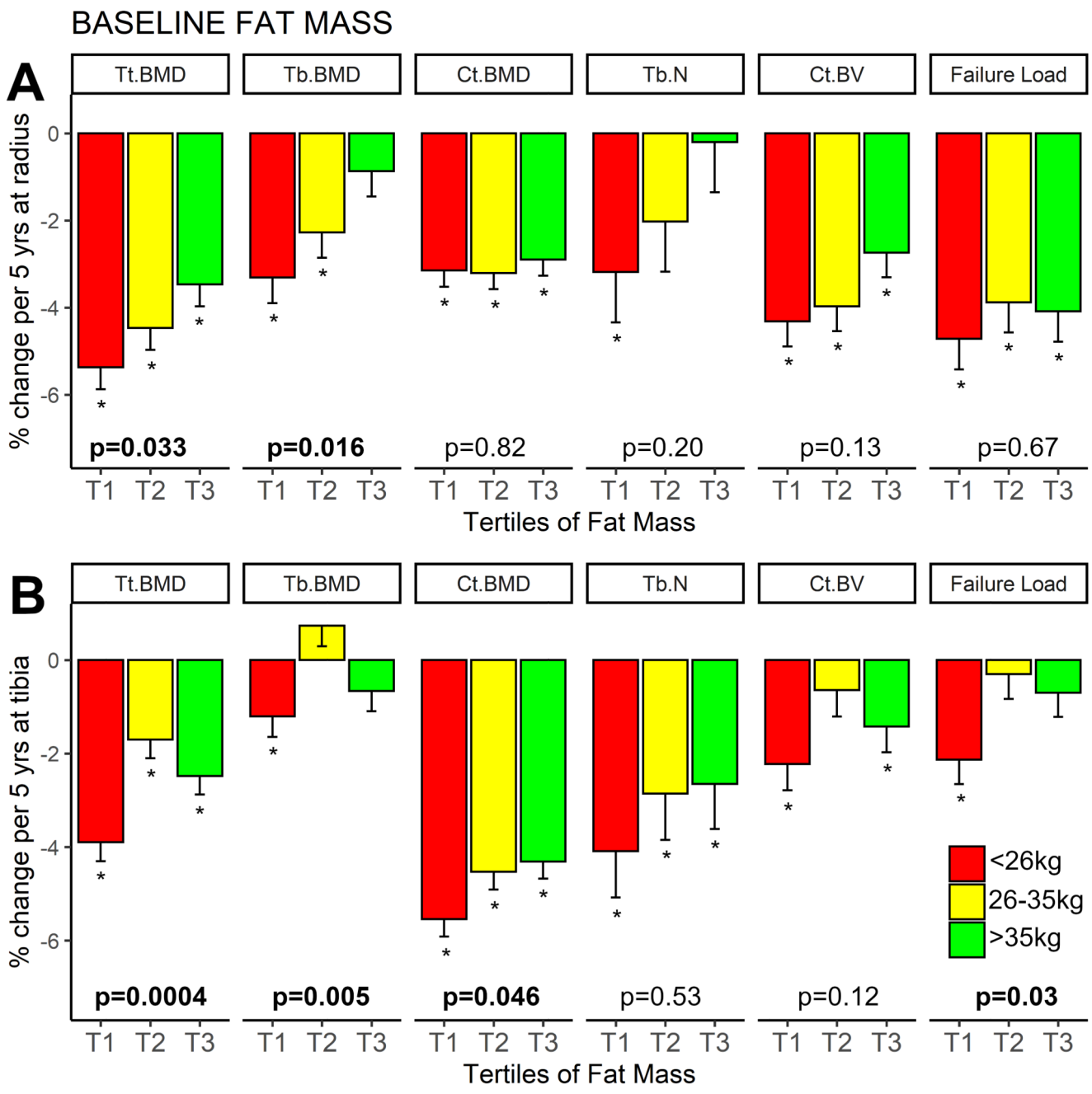

Figure 3.

Average percent change (± SE) over 5 years for bone microarchitectural variables analyzed by tertiles of baseline fat mass (tertile 1 (T1): <26 kg, tertile 2 (T2): 26–35 kg; tertile 3 (T3): >35kg), at (A) distal radius, T1 n: 57, T2 n: 57, T3 n: 56; and (B) distal tibia, T1 n: 68, T2 n: 68, T3 n: 68. Models are adjusted for adjusted for race/ethnicity, time since menopause and weight change over the follow-up time. ANCOVA p-values comparing tertiles are shown. * indicate significant change from baseline within each tertile. Tt, total; Tb, trabecular; N, number; Ct, cortical; BV, bone volume.

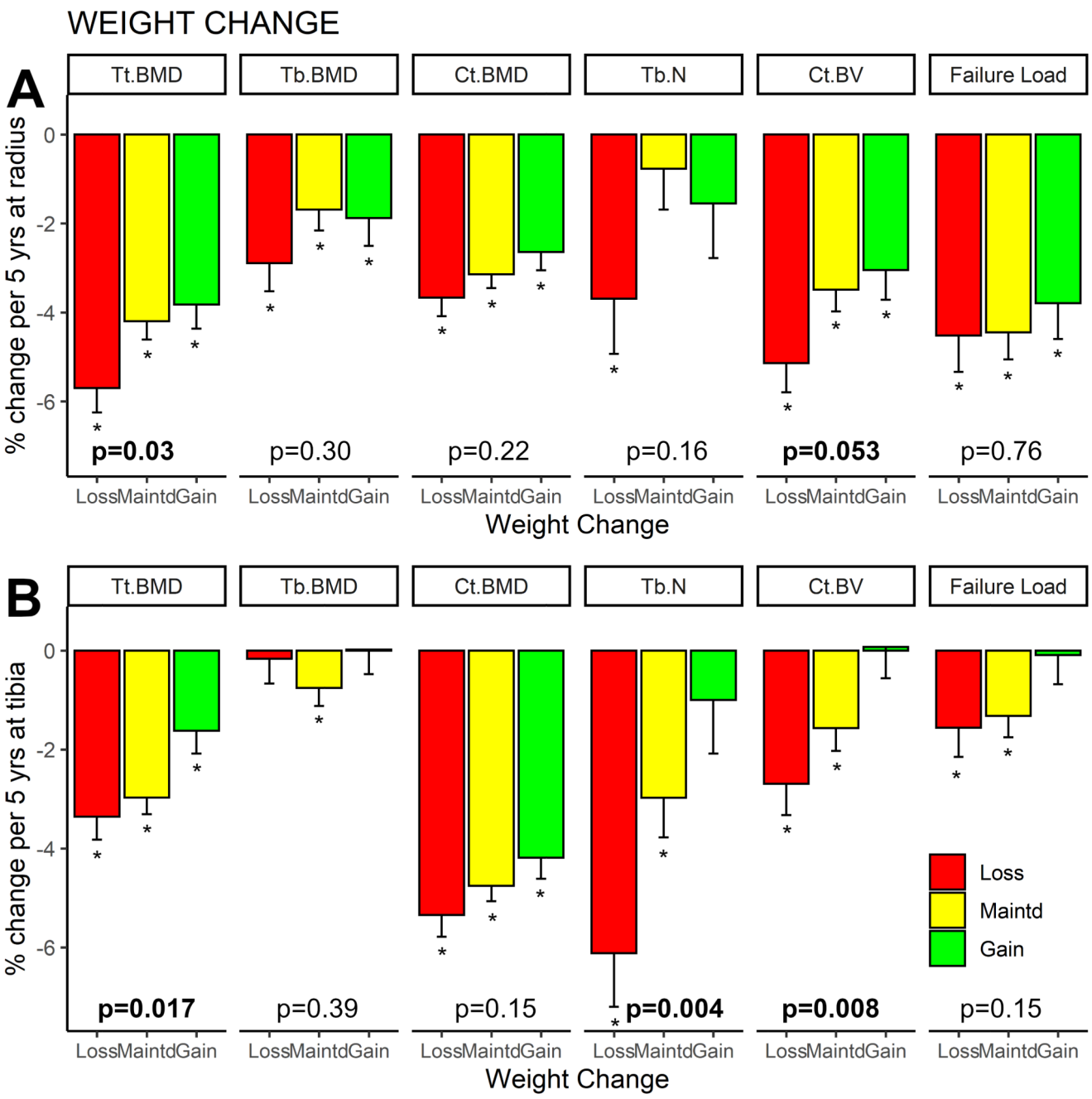

Figure 4.

Average percent change (± SE) over 5 years for bone microarchitectural variables analyzed by percent change over 5 years in body weight (Loss: −3%; <, Maintained: => −3% and =<3%; Gain: >3%), at (A) distal radius (loss n: 49, maintained n: 85, gain n: 48); and (B) distal tibia (loss n: 55, maintained n: 98, gain n: 54). Models are adjusted for race/ethnicity, time since menopause, and baseline body weight. ANCOVA p-values comparing tertiles are shown. * indicate significant change from baseline within each tertile. Tt, total; Tb, trabecular; N, number; Ct, cortical; BV, bone volume.

Table 1:

Characteristics of study cohort at the baseline HR-pQCT visit (mean ± SD, or n (%)).

	All (n=217)	Black (n=80)	White (n=137)	p-value
Age, yrs	59.9 ± 2.7	59.8 ± 2.5	60.0 ± 2.8	0.50
Weight, kg	79.6 ± 17.7	84.4 ± 17.8	76.7 ± 17.1	**0.002**
Height, cm	164.0 ± 6.1	163.5 ± 6.8	164.3 ± 5.7	0.40
Body mass index, kg/m^2	29.5 ± 6.1	31.5 ± 6.0	28.4 ± 5.9	**0.0003**
Fat mass, kg	31.3 ± 10.3	33.7 ± 9.9	29.9 ± 10.2	**0.008**
Lean mass, kg	41.7 ± 7.1	43.7 ± 7.8	40.5 ± 6.4	**0.003**
Fat %	42.0 ± 5.4	43.0 ± 4.6	41.5 ± 5.8	**0.04**
Weight change over 5 yrs, n (%)				0.47
Lose >3% vs. baseline weight	59 (27)	22 (28)	37 (27)	
Maintained weight	102 (47)	41 (54)	61 (45)	
Gain >3% vs. baseline weight	56 (26)	17 (21)	39 (28)	
Menopause duration, yrs	7.9 ± 3.2	8.3 ± 3.3	7.7 ± 3.2	0.21
Physical activity score[26]	8.2 ± 1.9	7.6 ± 1.9	8.5 ± 1.7	**0.0006**
Tobacco, n (%)	22 (10)	11 (14)	11 (8)	0.27
Alcohol, n (%)				**<0.0001**
None	45 (21)	31 (39)	14 (10)	
<2/day	149 (69)	48 (60)	101 (74)	
≥2/day	23 (11)	1 (1)	22 (16)	
Glucocorticoid use, n (%)	23 (11)	12 (15)	11 (8)	0.17
Osteoporosis medication ever use, n (%)	19 (9)	6 (8)	13 (9)	0.80
Systemic HRT ever use, n (%)	82 (38)	32 (40)	50 (36)	0.71
Diabetes, n (%)	27 (12)	19 (24)	8 (6)	**0.0003**
Prevalent fracture (yes/no), n (%)	42 (19)	11 (14)	31 (23)	0.16
Follow-up time btw HR-pQCT, yrs	6.7 ± 0.8	6.8 ± 0.9	6.7 ± 0.7	0.46
With HR-pQCT at tibia, n (%)	207 (95)	78 (98)	129 (94)	–
With HR-pQCT at radius, n (%)	182 (84)	68 (85)	114 (83)	–

HRT, hormone replacement therapy

[26]Scores range 3–15 with higher scores indicating increased physical activity

Table 2:

Longitudinal changes in peripheral bone density, microarchitecture and strength at the radius and tibia by race, unadjusted and with multivariate (MV) adjustment. Changes presented as mean percent (%) change over 5 years (95% confidence interval)

	Black (n=68)	White (n=114)		Black (n=68)	White (n=114)	
RADIUS	% change (unadjusted)	% change (unadjusted)	*p* for difference between groups	% change * (MV adjusted)	% change * (MV adjusted)	*p* for difference between groups
Tt.BMD	**−3.9 (−4.8, −3.0)**	**−4.8 (−5.5, −4.1)**	0.07	**−4.2 (−5.1, −3.3)**	**−4.6 (−5.3, −3.9)**	0.22
Tb.BMD	**−1.6 (−2.4, −0.9)**	**−1.8 (−2.6, −1.1)**	0.63	**−1.9 (−2.6, −1.1)**	**−1.7 (−2.4, −0.9)**	0.86
Ct.BMD	**−2.7 (−3.3, −2.2)**	**−3.4 (−4.0, −2.9)**	0.12	**−2.8 (−3.5, −2.2)**	**−3.4 (−3.9, −2.9)**	0.19
Tb.N	−1.1 (−3.2, 1.0)	**−2.7 (−4.2, −1.1)**	0.13	−1.2 (−3.4, 1.0)	**−2.7 (−4.3, −1.1)**	0.16
Tb.Th	−1.1 (−3.1, 1.0)	1.0 (−0.4, 2.3)	0.14	−1.4 (−3.4, 0.7)	1.1 (−0.2, 2.4)	0.08
Tb.Sp	2.0 (−0.4, 4.4)	**4.3 (2.4, 6.1)**	0.15	2.0 (−0.5, 4.4)	**4.0 (2.2, 5.8)**	0.20
Ct.BV	**−3.4 (−4.4, −2.3)**	**−4.4 (−5.3, −3.6)**	0.056	**−3.5 (−4.6, −2.4)**	**−4.4 (−5.2, −3.5)**	0.11
Ct.Th	**−2.6 (−3.6, −1.6)**	**−3.3 (−4.2, −2.5)**	0.21	**−2.7 (−3.7, −1.7)**	**−3.3 (−4.1, −2.5)**	0.30
Ct.TMD	**−1.4 (−1.7, −1.1)**	**−1.4 (−1.7, −1.2)**	0.80	**−1.4 (−1.7, −1.1)**	**−1.4 (−1.7, −1.2)**	0.96
Ct.Por	**41.0 (30.9, 51.0)**	**48.3 (38.9, 57.8)**	0.088	**46.3 (35.0, 57.5)**	**53.7 (43.2, 64.2)**	0.21
EndoCt perim	−0.1 (−0.3, 0.1)	−0.1 (−0.2, 0.1)	0.95	−0.1 (−0.3, 0.1)	−0.1 (−0.3, 0.1)	0.98
Failure load	**−4.0 (−5.3, −2.7)**	**−4.7 (−5.6, −3.8)**	0.34	**−4.1 (−5.4, −2.8)**	**−4.4 (−5.3, −3.6)**	0.45
Stiffness	**−4.3 (−5.7, −2.9)**	**−5.0 (−6.0, −3.9)**	0.33	**−4.5 (−5.9, −3.0)**	**−4.7 (−5.8, −3.7)**	0.52
	Black (n=78)	White (n=129)		Black (n=78)	White (n=129)	
TIBIA	% change (unadjusted)	% change (unadjusted)	*p* for difference between groups	% change * (MV adjusted)	% change * (MV adjusted)	*p* for difference between groups
Tt.BMD	**−2.5 (−3.1, −1.8)**	**−2.6 (−3.1, −2.0)**	0.67	**−2.4 (−3.1, −1.7)**	**−2.4 (−2.9, −1.9)**	0.98
Tb.BMD	−0.2 (−0.8, 0.5)	−0.3 (−0.9, 0.2)	0.71	0.1 (−0.6, 0.8)	−0.3 (−0.9, 0.2)	0.73
Ct.BMD	**−4.5 (−5.2, −3.9)**	**−4.9 (−5.3, −4.4)**	0.43	**−4.7 (−5.4, −3.9)**	**−4.8 (−5.3, −4.4)**	0.60
Tb.N	**−3.0 (−4.5, −1.4)**	**−4.0 (−5.6, −2.4)**	0.26	**−3.4 (−5.4, −1.4)**	**−3.8 (−5.4, −2.2)**	0.42
Tb.Th	**2.7 (0.7, 4.7)**	**4.1 (2.6, 5.6)**	0.31	**3.3 (0.7, 6.0)**	**4.1 (2.8, 5.4)**	0.44
Tb.Sp	**3.1 (0.7, 5.5)**	**5.2 (3.4, 7.0)**	0.26	**3.3 (1.0, 5.6)**	**4.9 (3.2, 6.7)**	0.42
Ct.BV	**−1.7 (−2.7, −0.7)**	**−1.4 (−2.1, −0.6**)	0.52	**−1.6 (−2.7, −0.6)**	**−1.2 (−1.9, −0,4)**	0.30
Ct.Th	0.2 (−0.7, 1.1)	0.7 (−0.03, 1.3)	0.29	0.3 (−0.7, 1.2)	0.7 (−0.03, 1.5)	0.28
Ct.TMD	**−1.9 (−2.2, −1.5)**	**−1.8 (−2.0, −1.6)**	0.66	**−1.9 (−2.3, −1.6)**	**−1.8 (−2.0, −1.6)**	0.61
Ct.Por	**30.7 (25.1, 36.3)**	**30.6 (27.0, 34.3)**	0.53	**31.8 (26.4, 37.2)**	**31.5 (28.1, 34.8)**	0.66

EndoCt perim	**−0.6 (−1.0, −0.1)**	**−0.7 (−1.1, −0.3)**	0.68	−0.5 (−1.5, 0.5)	**−0.8 (−1.2, −0.4)**	0.55
Failure load	−0.8 (−1.7, 0.03)	**−1.2 (−1.9, −0.4)**	0.62	−0.8 (−1.7, 0.1)	**−1.0 (−1.7, −0.2)**	0.85
Stiffness	−0.5 (−1.4, 0.5)	**−0.9 (−1.7, −0.1)**	0.56	−0.5 (−1.5, 0.5)	−0.7 (−1.5, 0.09)	0.98

Values are reported as mean change with 95% confidence interval. Bold text indicate significant change from baseline within each group over the follow-up time (p-value <0.05).

*Multivariate adjustment includes menopause duration, baseline weight, **diabetes** status, current alcohol intake and interaction terms (time*menopause duration) and (time*baseline weight).