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Pre- and Postmenopausal Differences in Bone Microstructure and Mechanical Competence in Chinese-American and White Women

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Abstract

Introduction—Compared to white women, premenopausal Chinese-American women have more plate-like trabecular (Tb) bone. It is unclear whether these findings are relevant to postmenopausal women and if there are racial differences in the deterioration of bone microarchitecture with aging.

Methods—We applied individual trabecula segmentation and finite element analysis to high-resolution peripheral quantitative computed tomography images in pre- and postmenopausal Chinese-American and white women to quantify within-race age-related differences in Tb plate-versus rod-microarchitecture and bone stiffness. Race-menopause interactions were assessed. Comparisons between races within menopause status were adjusted for age, height and weight. Comparisons between pre- and postmenopausal women were adjusted for height and weight.

Results—Adjusted analyses at the radius indicated that premenopausal Chinese-Americans had a higher plate bone volume fraction (pBV/TV), Tb plate-to-rod ratio (P-R Ratio), and greater plate-plate junction densities (P-P Junc.D) versus white women (all $p < 0.01$), resulting in 27% higher Tb stiffness ($p < 0.05$). Greater cortical thickness and density (Ct.Th & Dcort) and more Tb plates led to 19% greater whole bone stiffness ($p < 0.05$). Postmenopausal Chinese-Americans had similar pBV/TV and P-P Junc.D, yet higher P-R ratio versus white women. Postmenopausal Chinese-American versus white women had greater Ct.Th, Dcort and relatively intact Tb plates, resulting in similar Tb stiffness but 12% greater whole bone stiffness ($p < 0.05$). In both races, Ct.Th and Dcort were lower in post- versus premenopausal women and there were no differences between races. Tb plate parameters were also lower in post- vs. premenopausal women, but age-related differences in pBV/TV, P-R ratio and P-P Junc D were greater ($p < 0.05$) in Chinese-Americans versus white women.

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Conclusion—There are advantages in cortical and Tb bone in premenopausal Chinese-American women. Within-race cross-sectional differences between pre- and postmenopausal women suggest greater loss of plate-like Tb bone with aging in Chinese-Americans, though thicker cortices and more plate-like Tb bone persists.

Keywords

race; HR-pQCT; microarchitecture; Chinese; white; individual trabecula segmentation; age-related differences

Introduction

Over the last decade, the Asian population, a group traditionally considered at high risk for osteoporosis, grew faster than any other race group in the United States (1). While Asian individuals tend to have lower areal BMD than white and other racial groups, their risk of hip and forearm fractures is paradoxically low. In contrast, vertebral fracture rates are similar or higher in Asian as compared to white women (2–8). These observations have been elucidated, in part, by prior analyses of skeletal microstructure and mechanical competence, which favor the Asian skeleton. For example, we and others recently reported that while pre- and post-menopausal Chinese-American women have smaller bone size than white women, they have thicker, and more dense cortices as well as thicker trabeculae at the radius and tibia as measured by high resolution peripheral quantitative computed tomography (HR-pQCT) (9–11). Premenopausal, but not postmenopausal, Chinese-American women also have higher trabecular bone density compared to white women (9,10).

Using individual trabecula segmentation (ITS), a new analytical tool that can assess the plate- and rod-like characteristics of individual trabeculae (12,13), as well as micro-finite element analysis (μ FEA), we have also found that premenopausal Chinese-American women have microstructural advantages leading to greater mechanical competence as compared to white women (14). Specifically, we demonstrated that premenopausal Chinese-American women have higher plate bone volume fraction and higher plate number density at the distal radius and tibia as compared to white women, leading to a greater plate to rod ratio and greater trabecular connectivity. These striking differences in trabecular microstructure translate into greater trabecular and whole bone competence in Chinese-American versus white premenopausal women (14).

Since our previous work has shown that postmenopausal Chinese-American and white women do not differ in trabecular volumetric bone density by HR-pQCT (10), it is unclear if the plate-like trabecular advantages in Chinese-American pre-menopausal women revealed by ITS would also be seen in postmenopausal Chinese-American women. Additionally, our prior HR-pQCT findings suggest that there may be racial differences in age-related deterioration of bone microarchitecture. The purpose of this study was, therefore, 3-fold: 1) to determine whether postmenopausal Chinese-American women, similar to their pre-menopausal counterparts, have more plate-like trabecular bone compared to post-menopausal white women, 2) to assess pre- and post-menopausal differences in microstructure and mechanical competence within each racial group, and 3) to examine whether there are race-specific differences between pre- and postmenopausal women in their skeletal microstructure.

Material and Methods

Subjects

Ninety-five premenopausal (49 Chinese and 46 white) and 97 (29 Chinese and 68 white) postmenopausal women were studied. Participants in the current report represent those included in our prior studies utilizing HR-pQCT (9,10,14). As previously described, participants were recruited by newspaper and internet advertisements, flyers, and directly at primary care physician offices. Inclusion criteria were self-reported Chinese or white descent (all 4 grandparents) (9,10). Specific country of birth was not an inclusion/exclusion criterion. The cohort represents women born in the United States, China and other countries. Premenopausal status was evaluated by history as regular menses with >6 cycles per year. We further limited inclusion to premenopausal women who were 29–40 years old in order to study women who had reached peak bone mass but in whom the perimenopausal transition or menopause had not yet influenced skeletal metabolism. Postmenopausal status was defined as the absence of periods for > 1 year. Postmenopausal women who were 59–70 years old were included in order to study women who were past the perimenopausal transition period but who had not yet reached an advanced age when co-morbid conditions/medications would be more likely to affect bone metabolism. Women were screened by history and biochemical evaluation for conditions or medications known to affect bone metabolism. Exclusion criteria included untreated hyperthyroidism; renal or liver dysfunction; current pregnancy or lactation; intestinal malabsorption due to any cause; history of malignancy other than non-melanomatous skin cancer; metabolic bone diseases; HIV disease; organ transplantation; fragility fracture; and drug exposures affecting bone metabolism (current or past use of glucocorticoids, tacrolimus, cyclosporine, methotrexate, teriparatide, calcitonin, or aromatase inhibitors; current use or use within the last 12 months of hormone replacement therapy, raloxifene, or bisphosphonates; cumulative bisphosphonate use > 6 months duration). Over 500 women were screened for the study; overall, 70% of white women versus 76% of Chinese-American women were eligible ($p=0.20$). 82% of premenopausal white women versus 80% of premenopausal Chinese-American women were eligible ($p=0.72$); 56% of white postmenopausal versus 63% of Chinese-American postmenopausal women were eligible ($p=0.35$). All participants gave written, informed consent. Participants were compensated for study participation and travel expenses within the guidelines of the Columbia University Institutional Review Board, who approved this study.

Clinical Evaluation

Information regarding past medical history, lifestyle, and medications was collected. Daily dietary calcium was assessed with a standardized food frequency questionnaire (15). Weight and height were measured by balance beam and a wall-mounted, calibrated Harpenden stadiometer, respectively (Holtain Ltd, Crymch, UK).

Biochemical Evaluation

Serum intact parathyroid hormone (PTH) was measured by chemiluminescence assay and 25-hydroxyvitamin D was measured by liquid chromatography tandem mass spectrometry.

Volumetric bone density and microarchitecture

HR-pQCT (XtremeCT, Scanco Medical AG, Bassersdorf, Switzerland) of the non-dominant distal radius and distal tibia was performed as previously described (16–18). The HR-pQCT measurement included 110 slices, corresponding to a 9.02 mm section along the axial direction, with a nominal voxel size of 82 μm . Quality control was provided by scanning the European Forearm Phantom at the time subjects were scanned. Volumetric bone density and

microarchitecture were measured at the non-dominant forearm and tibia from these HR-pQCT images as previously described (9,16,18–21).

Individual Trabecula Segmentation (ITS)-Based Morphological Analyses

The trabecular bone compartment of each HR-pQCT image was manually extracted from cortex (22). All trabecular bone images were then subjected to ITS-based morphological analyses. It should be noted that the ITS results of premenopausal Chinese-American and White women reported in Liu *et al.* (14) were evaluated based on a central cubic sub-volume of the trabecular compartment. However, the same methodology is not suitable for analyses of postmenopausal trabecular bone, as the deterioration of trabecular structure often begins from the center of the trabecular compartment (23), making structural distribution highly heterogeneous (24). Therefore, in the current study, all the ITS analyses were applied to the whole trabecular compartment for both pre- and post-menopausal groups as shown in Figure 1.

Briefly, digital topological analysis (DTA)-based skeletonization (25) was applied first to transform a trabecular bone image into a representation composed of surfaces and curves skeleton while preserving the topology (*i.e.*, connectivity, tunnels, and cavities) (26,27) as well as the rod and plate morphology of the trabecular microarchitecture. Then, digital topological classification was applied in which each skeletal voxel was uniquely classified as either a surface or a curve type (28). Using a newly developed iterative reconstruction method, each voxel of the original image was classified as belonging to either an individual plate or rod. Based on the 3D evaluations of each individual trabecular plate and rod, bone volume and number of plates and rods were evaluated by plate and rod bone volume fraction (pBV/TV and rBV/TV), as well as plate and rod number densities (pTb.N and rTb.N, 1/mm). Plate-to-rod ratio (P-R Ratio), a parameter of plate *versus* rod characteristics of trabecular bone, was defined as plate bone volume divided by rod bone volume. The average size of plates and rods was quantified by plate and rod thickness (pTb.Th and rTb.Th, mm). Intactness of trabecular network was characterized by plate-plate junction density (P-P Junc.D, 1/mm³) and plate-rod junction density (P-R Junc.D, 1/mm³), calculated as the total junctions between trabecular plate-plate or plate-rod normalized by the bulk volume. Trabecular bone volume fraction, mean number density, and mean thickness (BV/TV, Tb.N, and Tb.Th) for all trabeculae were also calculated. Detailed methods of the complete volumetric decomposition technique and ITS-based measurements can be found in our recent publications (12,29).

Micro Finite Element Analysis (μFEA)

Each thresholded HR-pQCT whole bone segment image and trabecular bone compartment image of the distal radius and distal tibia was converted to a μFE model. Bone tissue was modeled as an isotropic, linear elastic material with a Young's modulus (E_s) of 15 GPa and a Poisson's ratio of 0.3 (30). For each model of whole bone or trabecular bone segment, a uniaxial compression was imposed to calculate the reaction force under a displacement equal to 1% of bone segment height along the axial direction. Whole bone stiffness, defined as total reaction force divided by the applied displacement, characterizes the mechanical competence of both cortical and trabecular compartments and is closely related to whole bone strength (31) and fracture risk (23,32,33). Trabecular stiffness was defined as reaction force of the trabecular bone model divided by the applied displacement.

Statistics

Data are expressed as mean $\pm$ SD. Criterion values were adjusted for unequal variances where appropriate. Bone density, ITS, and μFEA results for each site were compared between the two racial groups within menopause status and between the two menopause

states within racial group using generalized linear models. Interaction effects were analyzed using generalized linear models to examine the effect of race and menopause status on each variable. Comparisons between races within menopausal status were adjusted for age, height and weight. Comparisons between pre- and postmenopausal women within race were adjusted for height and weight. For all analyses, a two-tailed $p < 0.05$ was considered to indicate statistical significance. In order to evaluate the contribution of age and years since menopause to trabecular structure, we evaluated each as predictors separately in univariate regression models for ITS parameters. Statistical analysis was performed using STATA (StataCorp. 2007. *Stata Statistical Software: Release 10*. College Station, TX: StataCorp LP) and SAS version 9.2 (SAS Institute, Cary, NC).

Results

As shown in Table 1, there were no significant differences in age between races within each menopausal group. Chinese-American women were shorter and weighed less than white women. Additionally, within each race, post-menopausal women were shorter than their pre-menopausal counterparts. Chinese-American women had lower calcium intake and lower vitamin D levels than their white counterparts (Table 1). PTH level was higher in Chinese-American versus white premenopausal women but there was no difference among postmenopausal women. White postmenopausal women had higher PTH levels than their premenopausal counterparts ($p = 0.004$), while there was no difference between pre- and postmenopausal Chinese-American women (interaction $p = 0.05$; Table 1).

Chinese-American versus White women

Pre-menopausal women—As shown in Table 2, among premenopausal women, bone area was 9% lower at the radius in Chinese-American compared with white women ($p = 0.03$). A similar trend was apparent at the tibia. Cortical thickness was higher at both radial and tibial sites in Chinese-American women (radius: +18%, $p < 0.0001$; tibia: +10%, $p = 0.03$) compared with their white counterparts. Trabecular volumetric bone density (D_{trab}) was also higher in Chinese-American women at the radius (+15%, $p = 0.005$) and tibia (+8%, $p = 0.05$; Table 2).

As shown in Table 3, the plate bone volume fraction (pBV/TV) was higher (radius: +38%, $p < 0.0001$, tibia: +46%, $p < 0.0001$) while the rod bone volume fraction (rBV/TV) was lower in Chinese-American compared with white women (radius: -6%, $p = 0.04$; tibia: -19%, $p < 0.0001$), leading to a higher plate-to-rod ratio (radius: +63%, $p < 0.0001$, tibia: +79%, $p < 0.0001$; Table 3). Additionally, plate number (pTb.N) was higher and thickness (pTb.Th) was greater at both sites in Chinese-American versus white women (pTb.N-radius: +8.0%, $p = 0.002$ and tibia: +5%, $p < 0.001$; pTb.Th-radius: +5%, $p < 0.0001$ and tibia: +5%, $p < 0.0001$). Chinese-American women also had greater rod thickness (rTbTh) at the radius (+5%, $p = 0.0007$) but not the tibia; Table 3). Plate-to-plate junction density (P-P Junc.D) was higher in pre-menopausal Chinese-American women compared with their white counterparts (radius: +23%, $p = 0.002$; tibia: +11%, $p = 0.02$), but there was no difference in P-R Junc.D (Table 3). Whole bone (radius: +14%, $p = 0.0004$; tibia: +8%, $p = 0.03$) but not trabecular stiffness was greater in Chinese-American versus white women at the radius and at the tibia (Table 4).

After adjustment for age, height and weight, racial differences in bone area (Table 2) and radius rBV/TV (Table 3) were attenuated and no longer significant. After adjustment, radial P-R Junc.D as well as trabecular stiffness at both sites were significantly higher in Chinese-American versus white women ($p < 0.05$ for all).

Postmenopausal women—In postmenopausal women as in premenopausal women (Table 2), Chinese-American women had smaller bone area than their white counterparts (radius: -10% , $p=0.01$; tibia: -9% , $p=0.01$) while cortical thickness was higher in Chinese-American women (radius: $+18\%$, $p=0.0005$; tibia: $+17\%$, $p=0.006$). Unlike pre-menopausal women however, in the postmenopausal group, Dtrab did not differ between Chinese-American and white women (Table 2).

Despite the same Dtrab between both postmenopausal cohorts, pBV/TV was higher in Chinese-American compared with white women at the tibia ($+27\%$, $p=0.004$). The difference at the radius did not reach significance. Higher pBV/TV was accompanied by lower rBV/TV in Chinese-American postmenopausal versus white women (radius: -13% , $p=0.006$; tibia: -27% , $p<0.0001$), leading to a higher P-R ratio (radius: $+36\%$, $p=0.002$; tibia: $+67\%$, $p<0.0001$; Table 3). While pTb.N was not different at either site between groups, pTb.Th was greater (radius: $+3.0\%$, $p=0.003$, tibia: $+4.6\%$, $p<0.001$) in Chinese-American women than white women. There was no difference in rTb.Th at the radius while it was 2% greater at the tibia in Chinese women ($p=0.03$; Table 3).

In contrast to premenopausal women, P-P Junc.D did not differ by race. P-R Junc.D was lower in Chinese-American women than their white counterparts at the tibia (-17% , $p<0.001$) but not the radius (Table 3). Neither whole bone nor trabecular stiffness differed between races at either bone site (Table 4).

After adjustment for age, height and weight, racial differences in bone area (Table 2) and rTb.Th at the tibia (Table 3) were attenuated and no longer significant. After adjustment, whole bone stiffness at the radius (Table 4) was significantly higher in Chinese-American versus white women ($p<0.05$).

Postmenopausal vs. Pre-menopausal women

Chinese-American women—As shown in Table 2, bone area did not differ between pre- and postmenopausal Chinese-American women at either the radius or tibia. However, cortical thickness was 11% and 18% lower at the radius and tibia respectively ($p<0.01$ for both) in the postmenopausal group. Likewise, Dtrab was lower in Chinese-American postmenopausal versus premenopausal women at both bone sites (radius: -28% , tibia: -17% , $p<0.0001$ for both; Table 2, Figures 2a and 2b).

pBV/TV was 36% lower in postmenopausal versus premenopausal Chinese-American women at the radius ($p<0.0001$) and 13% lower at the tibia ($p=0.04$). rBV/TV was 13% and 15% lower in postmenopausal versus premenopausal Chinese-American women at the radius and tibia ($p<0.05$ for both). P-R ratio was lower in the post-menopausal group at the radius (radius: -29% , $p<0.001$; Table 3, Figure 3) but not the tibia. pTb.N was lower at both bone sites in the postmenopausal group (radius: -13% , $p<0.001$; tibia: -4% , $p<0.01$). pTb.Th was lower at the radius ($p=0.02$) but not the tibia. Rod thickness was 3% lower in postmenopausal women at the radius ($p<0.001$) but no different at the tibia (Table 3, Figure 3). P-P Junc.D (radius: -34% , tibia: -15% , $p<0.001$ for both; Table 3, Figure 3) and P-R Junc.D (radius: -29% , tibia: -16% , $p<0.01$ for both; Tables 3, Figure 3) were lower in post- versus premenopausal Chinese-American women at both bone sites. Whole bone (radius: -24% , tibia: -17% , $p<0.0001$ for both) and trabecular stiffness (radius -57% , $p<0.0001$; tibia -17% , $p=0.03$) was lower at both sites in post-menopausal Chinese-American women compared to their pre-menopausal counterparts (Table 4; Figure 3).

After adjustment for height and weight, differences in tibial pBV/TV (Table 3) were no longer significant while differences in rTb.N at the radius and rTb.Th at the tibia (Table 3) were accentuated ($p<0.05$).

White women—At both the radius and tibia, there was no difference in bone area between pre- and postmenopausal white women (Table 2). Cortical thickness was 11% and 23% lower in postmenopausal versus premenopausal women at the radius and tibia ($p<0.01$ and $p<0.0001$) respectively. Additionally, D_{trab} was 12% lower at the radius but not the tibia in postmenopausal white women (Table 2, Figure 2).

Post- versus premenopausal women had 25% lower pBV/TV at the radius ($p=0.02$) and a 6% lower rBV/TV at the radius ($p=0.04$), but there were no differences at the tibia. There were no differences in P-R ratio at either site (Table 3, Figure 3). pTb.N was 9% lower at the radius ($p<0.001$) in post- versus premenopausal women but did not differ at the tibia (Tables 3, Figures 2). There was no difference in pTb.Th or rTb.Th at either bone site (Table 3, Figure 3). At the radius, P-P Junc.D was 22% ($p=0.001$) lower in post- versus premenopausal white women but not different at the tibia (Table 3, Figure 3). P-R Junc.D was 19% lower at the radius ($p=0.002$) in the postmenopausal group but did not differ at the tibia (Table 3, Figure 3). Whole bone stiffness was lower in postmenopausal white women than their premenopausal counterparts at both sites (radius: -17%, $p<0.0001$; tibia: -11%, $p=0.001$; Table 4 and Figure 3). Trabecular stiffness was 40% lower at the radius ($p<0.001$) but not different at the tibia.

Adjustment for height and weight did not change the direction or significance of comparisons between white pre- and postmenopausal women.

Comparisons of post- and premenopausal differences between Chinese-American and White women

There were several interactions between race and menopause status for ITS variables at the radius and tibia (Table 3 and Figure 3). At the radius, there were greater age-related differences in pBV/TV (-36% vs. -25%, $p=0.02$) and rTb.Th (-3% vs. -1%, $p=0.03$) in Chinese-American versus white women. The race-menopause status interactions for P-R ratio (-29% vs. -15%) and P-P Junc.D (-34% vs. -22%) were of borderline significance at the radius ($p=0.06$, Table 3). At the tibia, there were greater age-related differences in P-R Junc.D (-16% vs. -2%, $p=0.03$) and P-P Junc.D (-15% vs. -3%, $p=0.04$) in Chinese-American versus white women. There were no significant race-menopause interactions for whole bone or trabecular stiffness (Table 4 and Figure 3). All interactions terms remained significant after adjusting models for height and weight. Additionally, the race-menopause status interactions for P-R ratio and P-P Junc.D became significant after adjusting for covariates ($p<0.05$).

Multiple Regression modeling of ITS variables

In order to evaluate the contribution of age and years since menopause to trabecular structure, we evaluated age and years since menopause as predictors separately in univariate regression models for ITS parameters (pBV/TV, rBV/TV, P-R ratio, pTb.N, pTb.Th, P-R Junc.D, P-P Junc.D) and stiffness at the radius and tibia. Age was a significant predictor in all radius ITS and FEA models ($p<0.05$), while years since menopause was not significant in any model. Similar trends were apparent at the tibia except for the models for rBV/TV, tibial P-R ratio, tibial pTb.Th and tibia Tb stiffness where neither age nor years since menopause were significant predictors.

Discussion

Utilizing HRpQCT and ITS, this is the first study to assess whether there are racial differences in age-related microarchitectural deterioration. Additionally, we also utilized a newer ITS methodology for assessing the entirety of the trabecular compartment rather than

just a cubic subvolume (34). Utilizing this newer technique, our study confirms our prior findings that premenopausal Chinese-American women have more plate-like trabecular bone and greater plate connectivity than their white counterparts, leading to greater trabecular and whole bone stiffness at both the radius and tibia (14). In this study we extend our observations to postmenopausal women. The advantages observed in trabecular morphology in premenopausal Chinese vs. white women were less apparent among postmenopausal women, yet several key plate-like trabecular characteristics, such as greater plate-to-rod ratio and greater plate thickness persisted. While Tb stiffness was similar, thicker and denser cortices were present in postmenopausal Chinese-American versus white women, leading to greater whole bone stiffness at the radius (but not the tibia). Though racial differences in bone size were attenuated and no longer significant after adjusting for covariates, we suspect that racial differences in weight and height are mediators for differences in bone size rather than confounders.

Within each race, there were expected age-related differences in microarchitecture such as reduced cortical thickness and density, decreased plate number, lower fractional volume of plate-like bone and decreased trabecular connectivity. Our findings, however, further suggest that there are greater age-related differences in trabecular bone including plate bone volume fraction, plate to rod ratio, rod thickness and plate connectivity, in Chinese-American versus white women. Given the strong correlations between HR-pQCT and central QCT of the spine and hip (35), these findings could explain the lower rates of fracture at predominantly cortical sites (hip and forearm) but similar or higher rates of trabecular (vertebral) fracture in Chinese versus white women.

While our data are cross-sectional and we can not rule out the possibility that age-related differences are due to secular changes, one alternative explanation for this finding is that the rate of menopause- or age-related trabecular bone loss is greater in the Chinese-American versus white group. Few studies have assessed racial differences in bone loss and even fewer have included Asian groups. Consistent with our findings, Duan et al. reported greater “declines” in trabecular vBMD at the lumbar spine as calculated from DXA in Chinese versus white women in a large cross-sectional study (36). Another cross-sectional study reported greater “rates” of bone loss in the proximal femur in native Chinese versus white, Hispanic and Black women, utilizing data from the third National Health and Nutrition Examination Survey (37).

Longitudinal studies assessing racial differences in age- or menopause related bone loss between Asian and other racial groups are even more uncommon. All have utilized DXA rather than HR-pQCT. Finkelstein *et al.* reported that Chinese and Japanese women had higher rates of areal bone density loss at the lumbar spine compared with white and African-American women, a finding that was mediated by their lower weight which has been shown to be a risk factor for greater loss in other studies (38,39). This finding is consistent with our results indicating greater trabecular “deterioration” among Chinese-American versus white women. In contrast, another study indicated that Asian men had a slower rate of decline in areal bone density at the femoral neck and hip (40). This finding is not necessarily inconsistent since this site has a significant amount of cortical bone and our data suggest that ethnic differences in rates of bone loss could be compartment-specific. Alternatively differences in gender or the racial make-up of the study groups could account for such differences.

Our study did not address pathophysiological mechanisms that might explain the greater age-related differences in trabecular bone in Chinese-American vs. white women. Published data suggest lower, rather than higher, levels of bone turnover markers in Asian versus white women and thus do not support the concept that greater trabecular bone loss in Asians is due

to greater turnover (41). One study suggested that greater trabecular bone loss in Asian women is due to lower weight rather than race per se (38). Whether this mechanism is mediated by reduced mechanical loading in those with lower weight or perhaps lower estrone levels after menopause due to less peripheral aromatization (42–44) or other pathways is unclear and requires further study.

Our study has several limitations. This study used a convenience sample of women, which could have led to sampling bias. Additionally, exclusion criteria limit the generalizability of these results to all pre- and postmenopausal populations. Certain exclusion criteria (HRT and fracture) would make postmenopausal women less likely to be eligible than premenopausal women; however, there is no evidence that this differed by race. Previous studies by Walker *et al.* and others (8,9,13) have used this sample of women and have corroborated findings with other studies in Australia (11). Given that this is a cross-sectional study and women were not followed longitudinally, there may be unknown differences between the pre- and post-menopausal groups that could lead to confounding through generation-specific differences such as diets and risk factors for osteoporosis. Despite these limitations, our study has several notable strengths. This study is the first to provide data regarding racial variation in age-related differences in bone microarchitecture utilizing HR-pQCT and its related techniques including ITS and μ FEA. Future longitudinal studies are needed to confirm the findings suggested by these results. Demonstration of differing patterns of age-related bone loss between races would be important. Such data may explain differences in risk for certain types of fracture, enhance our knowledge of the pathophysiology of osteoporosis and better equip clinicians to diagnosis and treat osteoporosis among minorities.

In summary, there are microstructural advantages in both cortical and trabecular bone in premenopausal Chinese-American versus white women. However, within-race cross-sectional differences between pre- and postmenopausal women suggest that there may be greater loss in plate-like trabecular bone and plate connectivity with aging in Chinese-American women. However, advantages such as thicker cortices and more plate-like trabecular bone still persist in postmenopausal Chinese-American versus white.

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Figure 1. Representative images indicating ITS analyses of individual trabecular plates (green) and rods (red) in A) premenopausal Chinese-American; B) premenopausal white; C) postmenopausal Chinese-American; and D) postmenopausal white women.

Figure 2. Percent differences in HR-pQCT parameters between postmenopausal and premenopausal women within each race at the A) radius and B) tibia. *p < 0.05 for White post- vs. premenopausal women; **p < 0.05 for Chinese post- vs. premenopausal women; † p < 0.05 for interaction

Figure 3. Percent differences in ITS parameters and stiffness between postmenopausal and premenopausal women within each race at the A) radius and B) tibia. *p 0.05 for White post- vs. premenopausal women; **p 0.05 for Chinese post- vs. premenopausal women; † p 0.05 for interaction

Anthropometric and Biochemical Characteristics

Table 1

	Chinese-American		White		Comparison by Menopausal Status within Race	
	Premenopausal	Chinese-American Postmenopausal	Premenopausal	White Postmenopausal	p-value Chinese-American Post- vs. Premenopausal	p-value White Post- vs. Premenopausal
Age (years)	36±7	61±2	35±4	64±3	<0.0001	<0.0001
Height (inches)	64±2	62±2	65±3 ^a	64±2 ^a	0.0002	0.01
Weight (lbs.)	125±22	128±17	139±38 ^a	146±27 ^a	0.69	0.19
Years menopausal (years)	N/A	10±4	N/A	12±5	N/A	N/A
Calcium intake (mg/day)	885±557	901±544	1394±1570 ^a	1557±730 ^a	0.94	0.40
Current smoking (%)	6.5%	0.0%	4.1%	1.5%	0.12	0.42
Baeke sport index	1.08±0.61	1.23±0.68	1.59±0.70 ^a	1.24±0.54	0.36	0.02
PTH (pg/ml) [*]	37±13	37±11	31±13 ^a	38±12	0.96	0.004
Vitamin D level (ng/ml) ^{**}	25±9	31±10	36±14 ^a	38±14 ^a	0.02	0.41

Values represent mean ± SD; N/A = not applicable;

^a p<0.05 between race within menopausal status;

^{*} data available for 174/192 and

^{**} 152/192 women.

Table 2
Volumetric Bone Density and Geometry in Chinese-American and White Pre- and Postmenopausal Women.

	Chinese-American Premenopausal	White Premenopausal	Chinese-American Postmenopausal	White Postmenopausal	p-value Chinese-American Post- vs. Premenopausal	p-value White Post- vs. Premenopausal	p-value Interaction
Radius							
Bone area (mm ²)	211±50	231±37 ^a	201±33	224 ± 40 ^a	0.32	0.34	0.86
Cortical thickness (mm)	0.97±0.15	0.82 ± 0.15 ^{a, b}	0.86 ± 0.14	0.73 ± 0.20 ^{a, b}	<0.01 ^c	<0.01 ^c	0.78
Cortical Density (mmHg/ccm)	962 ± 38	923 ± 43 ^{a, b}	916 ± 54	862 ± 77 ^{a, b}	0.001 ^c	<0.0001 ^c	0.40
Drab (mmHg/ccm)	164 ± 42	142 ± 33 ^{a, b}	118 ± 36	125 ± 34	<0.0001 ^c	0.009 ^c	0.01 ^c
Tibia							
Bone area (mm ²)	625±122	663 ± 82	613 ± 83	670 ± 103 ^a	0.62	0.69	0.52
Cortical thickness (mm)	1.21 ± 0.25	1.10 ± 0.21 ^{a, b}	0.99 ± 0.20	0.85 ± 0.24 ^{a, b}	<0.0001 ^c	<0.0001 ^c	0.61
Cortical Density (mmHg/ccm)	921 ± 33	901 ± 34	828 ± 57	789 ± 68 ^{a, b}	<0.0001 ^c	<0.0001 ^c	0.22
Drab (mmHg/ccm)	166 ± 32	153 ± 32 ^{a, b}	138 ± 29	148 ± 29	<0.0001 ^c	0.38	0.01 ^c

Values represent unadjusted mean ± SD;

^a p<0.05 between race within menopausal status;

^b p<0.05 between race within menopausal status after adjustment for height, weight and age;

^c p<0.05 between pre- vs. postmenopausal women within race after adjustment for height and weight

Plate versus Rod-like Trabecular Bone Characteristics in Chinese-American and White Pre- and Postmenopausal Women

Table 3

	Chinese-American Premenopausal	White Premenopausal	Chinese-American Postmenopausal	White Postmenopausal	p-value Chinese-American Post- vs. Premenopausal	p-value White Post- vs. Premenopausal	p-value Interaction
Radius							
pBV/TV	0.11±0.04	0.08±0.03 ^{a,b}	0.07±0.04	0.06±0.03	<0.0001 ^c	0.02 ^c	0.02 ^c
±BV/TV	0.16±0.03	0.17±0.02 ^a	0.14±0.03	0.16±0.03 ^{a,b}	0.02 ^c	0.04 ^c	0.56
P-R ratio	0.75±0.32	0.46±0.19 ^{a,b}	0.53±0.33	0.39±0.21 ^{a,b}	<0.001 ^c	0.16	0.06 ^c
rTb.N (1/mm)	1.49±0.18	1.38±0.17 ^{a,b}	1.29±0.19	1.26±0.18	<0.001 ^c	0.001 ^c	0.12
rTb.N (1/mm)	1.78±0.17	1.87±0.15 ^{a,b}	1.72±0.17	1.81±0.15 ^{a,b}	0.06 ^c	0.04 ^c	0.84
rTb.Th (mm)	0.212±0.01	0.202±0.01 ^{a,b}	0.208±0.01	0.202±0.01 ^{a,b}	0.02 ^c	0.68	0.11
rTb.Th (mm)	0.219±0.01	0.215±0.01 ^{a,b}	0.213±0.01	0.213±0.01	<0.001 ^c	0.25	0.03 ^c
P-R Junc.D (1/mm ²)	3.76±1.17	3.35±0.99 ^b	2.67±0.98	2.72±1.00	<0.001 ^c	0.002 ^c	0.15
P-P Junc.D (1/mm ²)	1.96±0.65	1.59±0.56 ^{a,b}	1.28±0.57	1.24±0.53	<0.001 ^c	0.001 ^c	0.06 ^c
TbIa							
pBV/TV	0.16±0.05	0.11±0.04 ^{a,b}	0.14±0.04	0.11±0.04 ^{a,b}	0.04	0.60	0.18
±BV/TV	0.13±0.03	0.16±0.03 ^{a,b}	0.11±0.03	0.15±0.03 ^{a,b}	0.04 ^c	0.70	0.19
P-R ratio	1.40 ± 0.74	0.78 ± 0.37 ^{a,b}	1.3 ± 0.62	0.78 ± 0.40 ^{a,b}	0.57	0.94	0.69
pTb.N (1/mm)	1.57±0.10	1.50±0.13 ^{a,b}	1.50±0.09	1.48±0.13	<0.01 ^c	0.50	0.09
rTb.N (1/mm)	1.68±0.18	1.82±0.16 ^{a,b}	1.58±0.16	1.80±0.17 ^{a,b}	0.02 ^c	0.64	0.12
pTb.Th (mm)	0.227±0.02	0.217±0.01 ^{a,b}	0.226±0.01	0.216±0.01 ^{a,b}	0.74	0.59	0.93
rTb.Th (mm)	0.216±0.01	0.216±0.01	0.220±0.01	0.216±0.01 ^a	0.06 ^c	0.85	0.18
P-R Junc.D (1/mm ²)	3.58±0.74	3.69±0.72	3.00±0.55	3.60±0.80 ^{a,b}	0.001 ^c	0.52	0.03 ^c
P-P Junc.D (1/mm ²)	2.20±0.41	1.98±0.46 ^{a,b}	1.87±0.34	1.92±0.47	0.002 ^c	0.50	0.04 ^c

Values represent unadjusted mean ±SD;

^a p<0.05 between race within menopausal status;

^b p<0.05 between race within menopausal status after adjustment for height, weight and age;

c_p between pre- vs. postmenopausal women within race after adjustment for height and weight

Table 4

Whole and Trabecular Bone Stiffness in Chinese-American and White Pre- and Postmenopausal women.

	Chinese-American Premenopausal	White Premenopausal	Chinese-American Postmenopausal	White Postmenopausal	p-value Chinese-American Post- vs. premenopausal	p-value White Post- vs. Premenopausal	p-value Interaction
Radius							
Whole Bone Stiffness (kN/mm)	94.0 ± 16.8	82.6 ± 15.5 ^{a,b}	71.6 ± 12.5	68.4 ± 15.6 ^b	<0.0001 ^c	<0.0001 ^c	0.08
Trabecular Stiffness (kN/mm)	16.9 ± 9.3	14.6 ± 8.6 ^b	7.2 ± 6.9	8.7 ± 6.2	<0.0001 ^c	<0.0001 ^c	0.11
Tibia							
Whole bone stiffness (kN/mm)	249.5 ± 45.0	231.3 ± 42.4 ^{a,b}	207.4 ± 32.0	206.3 ± 39.0	<0.0001 ^c	0.001 ^c	0.16
Trabecular stiffness (kN/mm)	90.6 ± 29.4	82.5 ± 29.9 ^b	75.1 ± 26.1	82.3 ± 31.4	0.03	0.96	0.09

Values represent unadjusted mean±SD;

^a p<0.05 between race within menopausal status;

^b p<0.05 between race within menopausal status after adjustment for height, weight and age;

^c p<0.05 between pre- vs. postmenopausal women within race after adjustment for height and weight