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Volumetric bone mineral density at the spine and hip in Chinese American and White women

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Abstract

Summary—This study evaluated racial differences in bone size and volumetric density at the spine and hip in pre- and postmenopausal Chinese American and White women. Compared with White women, Chinese American women have greater cortical volumetric bone density (vBMD) at the hip, congruent with the results at the peripheral skeleton.

Introduction—Chinese American women have lower rates of fracture than White women despite lower areal bone density. At the forearm and tibia, however, Chinese American women have higher cortical vBMD as well as greater trabecular and cortical thickness, but smaller bone area as measured by high-resolution peripheral quantitative computed tomography (HR-pQCT) compared with White women. Since HR-pQCT data are obtained at peripheral sites, it is unclear whether these differences are relevant to the clinically important lumbar spine and hip. This study assesses racial differences in bone size and vBMD at the spine and hip in Chinese American and White women.

Methods—QCT of the spine and hip was measured to assess racial differences in bone size, structure, and vBMD in pre- ($n=83$) and postmenopausal ($n=50$) Chinese American and White women. Data were adjusted for weight, height, physical activity, total calcium intake, parathyroid hormone, and 25-hydroxyvitamin D levels.

Results—Among premenopausal women, lumbar spine trabecular vBMD was 5.8% greater in Chinese American versus White women ($p=0.01$). At the hip, cortical vBMD was 3% greater at the femoral neck ($p=0.05$) and 3.6% greater at the total hip ($p=0.01$) in premenopausal Chinese American compared with White women. Among postmenopausal women, there was no difference in lumbar spine trabecular vBMD. Cortical vBMD was 4% greater at the total hip ($p=0.02$) and tended to be greater at the femoral neck ($p=0.058$) in Chinese American versus White women.

Conclusions—Consistent with earlier findings in the peripheral skeleton, cortical vBMD is greater at the hip in Chinese American versus White women.

Keywords

Central QCT; Chinese American; Race; Volumetric bone density; White

Introduction

Chinese American women have lower rates of hip and forearm fracture than White women despite lower areal bone density by dual X-ray absorptiometry (DXA) [1–7]. In contrast, vertebral fracture risk in Chinese American women is similar to that of White women [8]. These paradoxical findings have remained poorly understood. We and others recently reported that pre- and postmenopausal Chinese American women have smaller bone size than White women, but thicker, denser cortices and thicker trabeculae leading to greater mechanical competence at the radius and tibia as measured by high-resolution peripheral quantitative computed tomography (HR-pQCT) [9–12]. Premenopausal, but not postmenopausal, Chinese American women also have higher trabecular bone density compared with White women [9, 10]. These observations help to explain the low incidence of peripheral skeletal fractures in Chinese American women.

Recent work suggests that bone density and microarchitecture measured by HR-pQCT at the distal radius and tibia correlate with measurements at the central skeleton [13]. It is unclear, however, whether the specific advantages observed in skeletal structure at peripheral sites in Chinese American as compared with White women are relevant to the central sites such as the hip and spine, which cannot currently be measured with a noninvasive high-resolution methodology. Differences in volumetric BMD and bone size, as measured by central QCT (cQCT), could help to explain racial differences in fracture risk at the hip and spine, where the most serious osteoporotic fractures occur. The aim of this study was, therefore, to assess racial differences in bone size and volumetric density at the spine and hip measured by cQCT in pre- and postmenopausal Chinese American and White women in whom we had previously demonstrated differences by HR-pQCT.

Material and methods

Subjects

Fifty postmenopausal (24 White and 26 Chinese American) and 83 premenopausal women (47 White and 36 Chinese American) women were studied. Participants in the current report represent those included in our studies utilizing HR-pQCT who agreed to undergo cQCT of the hip and spine [9, 10, 12]. There were no differences in demographic, lifestyle, or biochemical factors between those who did and did not agree to have cQCT measurements ($n=20$). cQCT images from 16 participants were not of sufficiently high quality to be

included in the analysis (i.e., lacked part of phantom or participant ID or incorrect positioning). 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 American or White race/ethnicity [9, 10].

In this article, the term Chinese American defines a group having all four grandparents of Chinese descent and who reside in USA; the term White indicates White race/ non-Hispanic ethnicity (all four grandparents) with residence in USA. We excluded women of mixed race/ethnicity. Specific country of birth was not an inclusion/exclusion criterion and the cohort represents women born in USA, China, and other countries. Pre- and postmenopausal women were included in this analysis. 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 bone and mineral 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 comorbid conditions/medications would be 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 such as primary or secondary hyperparathyroidism, amenorrhea 6 months duration (other than menopause or while breastfeeding), 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). 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, which approved this study.

Clinical evaluation

Information regarding past medical history and medications was collected. Daily calcium intake, including supplement use, was assessed with a validated food frequency questionnaire [14]. Alcohol intake was assessed as number of drinks per day. Participants were considered alcohol users if they had 1 drink per day. Tobacco use was assessed as current use (yes/no). Physical activity was evaluated with the Modified Baecke Questionnaire [15]. Weight and height were measured by balance beam and a wall-mounted, calibrated Harpenden stadiometer, respectively (Holtain Ltd, Crymych, 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 (Quest Diagnostics, Nichols Institute, San Juan Capistrano, CA, USA) [16].

Volumetric bone density

Helical CT images (GE LightSpeed 64 VCT Scanner; GE Medical Systems, Milwaukee, WI, USA) were acquired at the L1 and L2 vertebrae and the hips as previously described (0.937×0.937-mm pixel size, 2.5-mm slice thickness, standard reconstruction algorithm)

[17–19] at Columbia University. Anonymized CT images were archived onto CD-ROM. Images were processed to extract measures of volumetric BMD and bone size using analysis techniques described previously [17–19]. The processing task included calibration of the CT images from the native scanner Hounsfield Units to equivalent concentration (in grams per cubic centimeter) of calcium hydroxyapatite. The following BMD and geometry measures were determined according to previously published methods [17–19]: L1–L2 vertebral cross-sectional area (CSA); average mid-vertebra (central 10 mm of the vertebra between the two endplates) integral and trabecular volumetric BMD; integral, trabecular, and cortical volumetric BMD at the femoral neck and total hip; minimum femoral neck cross-sectional area; and the ratio of tissue volume in the cortical region of the total hip and femoral neck to total tissue volume within the periosteal boundaries (C/I, the proportion of total bone volume that is cortical bone). The femoral neck region of interest was defined as the region bounded by the femoral neck cross section at minimum CSA medially and by a point 25% of the distance between the minimum CSA and maximum CSA (intertrochanteric plane) laterally. As previously described, within those bounds, the cortical component was obtained by shrinking the outer boundary by erosion and then applying a threshold of 350 mg/cm³ to all voxels in the region between the original and the eroded boundaries to capture the cortical bone from the mixture of cortical and trabecular bone between those two boundaries [20]. Precision values for QCT measures are 1.76–2.93% for lumbar spine density measures, 1.56–5.85% for femoral neck density measures, 0.72–1.36% for total hip density measures, and 1.44–2.41% for cross-sectional area.

Statistical analysis

Data are expressed as mean±standard deviation. Comparisons of group characteristics between the Chinese American and White groups were evaluated by independent two-sided *t* test. Criterion values were adjusted for unequal variances where appropriate. cQCT variables for each site were first compared between the two racial groups without adjustment using two-sided *t* tests and then compared again after adjustment for between-group differences in weight, height, physical activity, total calcium intake, serum 25-hydroxyvitamin D, and parathyroid hormone level using generalized linear models. Data were not adjusted for tobacco or alcohol use because only three participants were smokers or alcohol consumers in the premenopausal age range, and no postmenopausal Chinese American women consumed alcohol or smoked. Both unadjusted and adjusted *p* values are reported to show the influence of covariates on comparisons. Generalized linear mixed models were also used to assess whether the effect of race/ethnicity differed by age group. For all analyses, a two-tailed *p* 0.05 was considered to indicate statistical significance. Statistical analysis was performed using SAS, Version 9.2 (SAS Institute, Cary, NC, USA).

Results

This cohort included both women born in the USA and abroad: 89% of premenopausal Chinese women, 96% of postmenopausal Chinese women, 17% of premenopausal White women, and 8% of postmenopausal White women were born outside the USA. As shown in Table 1, Chinese American women weighed less and were shorter than White women. White premenopausal women were more physically active than their Chinese American counterparts. White postmenopausal women were more likely to consume alcohol. Total calcium intake from diet and supplements was lower in Chinese American women in both age groups compared with White women. There were no racial differences in the frequency of calcium supplement use in either age group. Mean serum 25-hydroxyvitamin D level was lower and PTH higher in premenopausal Chinese American compared to White women. A similar trend for 25-hydroxyvitamin D was apparent among postmenopausal women.

Among premenopausal women (Table 2; Fig. 1a), there were no differences in average vertebral cross-sectional area, lumbar spine trabecular vBMD, or integral vBMD before adjustment for covariates. At the hip, femoral neck CSA was 6.5% lower ($p=0.02$) in premenopausal Chinese American compared with White women. Cortical vBMD was 3.6% greater at the total hip in premenopausal Chinese American versus White women, but there was no difference in cortical vBMD at the femoral neck. There were no differences in integral or trabecular vBMD or C/I at any hip site among premenopausal women before adjustment for covariates. Adjustment for between-group differences in weight, height, physical activity, total calcium intake, PTH, and 25-hydroxyvitamin D tended to accentuate differences in bone density such that premenopausal Chinese American women additionally had greater trabecular vBMD at the lumbar spine, greater integral as well as cortical vBMD at the femoral neck, and greater integral vBMD at the total hip compared with White women. The difference in vertebral cross-sectional area was accentuated such that Chinese American women had greater vertebral cross-sectional area after adjustment for covariates. In contrast, the difference in femoral neck bone size (CSA) was attenuated after adjustment and was no longer significantly different.

Among postmenopausal women (Table 3; Fig. 1b), lumbar spine cross-sectional area was 8.8% lower in Chinese American compared with White women before adjustment for covariates. There were no differences in integral or trabecular vBMD at the lumbar spine. At the hip, femoral neck CSA was 8.2% lower and cortical vBMD was 4% higher in postmenopausal Chinese American versus White women. There were no differences in integral or trabecular BMD or C/I at the femoral neck. At the total hip, cortical vBMD was 4% greater in Chinese American postmenopausal women compared with White women, but there were no differences in integral or trabecular vBMD or C/I. Cortical vBMD remained greater at the total hip after adjustment for weight, height, physical activity, total calcium intake, PTH, and 25-hydroxyvitamin D, while differences in vertebral and femoral neck CSA and cortical vBMD at the femoral neck were no longer significant.

Covariates responsible for differences between unadjusted and adjusted results differed by bone site and QCT measure: vertebral cross-sectional area due to weight ($p<0.0001$), total calcium intake ($p=0.02$), height ($p<0.0001$), and 25-hydroxyvitamin D (25OHD) ($p=0.02$); lumbar spine trabecular vBMD due to weight ($p<0.01$) and height ($p=0.01$); femoral neck CSA due to weight ($p<0.0001$), height ($p<0.0001$), and 25OHD ($p=0.02$); femoral neck integral vBMD due to physical activity ($p=0.02$); femoral neck cortical vBMD due to weight ($p=0.008$); and total hip integral vBMD because of 25OHD ($p=0.02$). The effect of race/ethnicity did not differ by age group for any cQCT measure except for lumbar spine vertebral CSA ($p=0.03$ for interaction) in unadjusted models. This interaction was no longer significant ($p=0.11$) in adjusted models containing covariates weight, height, physical activity, total calcium intake, PTH, and 25OHD.

Discussion

This study was designed to determine whether the differences we observed between Chinese American versus White women in the peripheral skeleton by HR-pQCT could be substantiated by central QCT measurements of the spine and hip. Similar to our previous findings in the peripheral skeleton [9, 10, 12], we found that Chinese American pre- and postmenopausal women have greater cortical bone density at the hip compared with White women. Analogously, we demonstrated that Chinese women have smaller bone size at the femoral neck. While this association between femoral neck area and race did diminish with adjustment for covariates, we suspect that weight and height are causal for hip geometry differences rather than being unrelated correlates of race (confounders). The denser cortical compartment may provide greater bone strength and contribute to the lower risk of hip

fracture that has been observed in Chinese American women despite their smaller bone size. Future studies utilizing whole bone finite element analysis to assess bone strength from QCT measures will be important to confirm this hypothesis.

Racial differences in vertebral bone cross-sectional area differed by menopausal status. In postmenopausal women vertebral CSA was smaller in Chinese than White women but this difference was attenuated and no longer significant after adjustment for covariates. In premenopausal women, vertebral CSA became greater in Chinese women after adjustment for covariates. This could be due to greater interracial differences in height and weight in the postmenopausal than in the premenopausal groups. Duan et al. have previously reported smaller vertebral cross-sectional area in both pre- and postmenopausal Chinese American compared with White women using a DXA-based methodology [21]. Lower average weight and height in their premenopausal group compared to ours, or differences in methodology, may explain these discrepancies. Among postmenopausal women, volumetric bone density at the lumbar spine was not different, which is consistent with the observations of comparable vertebral fracture rates between older White and Chinese American women [8]. Osteoporosis risk factors (low weight, physical activity, total calcium intake, and 25-hydroxyvitamin D) tended to be more frequent in Chinese American women. After adjustment for covariates, trabecular BMD at the lumbar spine was greater in premenopausal, but not postmenopausal, Chinese American versus White women. This observation is consistent with our findings in the peripheral skeleton where premenopausal, but not postmenopausal Chinese American women had greater trabecular BMD at the tibia and radius. It is also congruent with results from Duan et al. utilizing a different methodology [21].

In contrast to our HR-pQCT studies of the forearm and tibia [8], we did not find greater C/I, a proxy for cortical thickness, at the hip in Chinese American compared with White women. This may reflect a true difference between the peripheral and central skeleton in Chinese American women and could be secondary to the effects of greater load-bearing at the hip versus the peripheral skeleton. Our prior study did indicate greater racial differences in cortical thickness at the radius (23% difference) versus the tibia (9% difference), which would support this concept [9]. Alternatively, this finding could be a result of the small size of our study in combination with the relatively thin hip cortex and limited spacial resolution of cQCT (voxel size 350 μm compared with 80 μm for HR-pQCT), which might limit our ability to detect differences at this site. Unfortunately, a noninvasive higher resolution methodology is not available to assess central sites.

Our investigation has several limitations. The sample size was relatively small and determined by ability to demonstrate between-group differences in HR-pQCT parameters, as this study represents the further characterization of our previously described cohort [9, 10]. We did have limited power to detect differences in C/I by cQCT. In order to detect the observed 0.33–0.45 standard deviation between-group differences in C/I, we would have needed 80 post-menopausal and 118 premenopausal women per group. Additionally, the study group represents a convenience sample of healthy volunteers who were carefully screened for multiple exclusion criteria. Thus, the results could have been influenced by selection bias (i.e., better bone density than those in a random community-based sample) and may not be generalizable. While we attempted to exclude women of mixed racial background or with conditions/medications known to influence bone quality, we cannot be certain that the observed differences or lack thereof are not due to the inclusion of some women with such factors. Additionally, we were unable to adjust for the effects of alcohol or tobacco use as too few participants were smokers or alcohol users. This study, however, provides valuable information as it represents the first data quantitating differences in

volumetric bone density and architecture by QCT at the hip and spine in White and Chinese American women who have been documented to have differences at other sites.

Our study was not designed to address several other issues that may be relevant in the context of assessing racial differences in bone density and fracture risk. Specific country of birth was not a criterion for study entry and the cohort represents a mixture of women born in USA, China, or other countries. While, there is some evidence that changes in environmental factors and acculturation after immigration influence bone health [22], the size of our study precludes a subgroup analysis based on the country of birth. Additionally, information on acculturation was not collected. Our study did not investigate the environmental (such as differences in nutrition other than calcium intake) or genetic reasons for differences in bone size, density, and structure between the racial groups (other than anthropometric measures) and did not examine non-skeletal factors that might influence differences in fracture rates between these groups. A number of other mechanisms to account for the discrepantly low hip fracture rates in Chinese American women have been proposed and were not specifically examined in our study. Information from other investigations suggests that shorter height [23], lower incidence, or severity of falls [24], shorter hip axis length, and greater trochanteric soft tissue thickness [25, 26] may be possible protective factors against fracture in various populations [27, 28].

Despite these limitations, this study has several notable strengths including the use of a cohort whose bone quality has been well characterized by multiple other methodologies, the inclusion of both pre- and postmenopausal women, as well as the careful exclusion of medical conditions that might influence bone density. The availability of data on total calcium intake and physical activity as well as biochemical markers of mineral homeostasis such as PTH and vitamin D are also important strengths. This study provides the first data-quantitating differences in volumetric bone density and architecture by QCT at the hip and spine in Chinese American and White women. In summary, measurements of the peripheral skeleton by HR-pQCT demonstrating smaller bone size and greater cortical bone density in Chinese American versus White women generally reflect observations at the central skeleton. Though larger studies using population-based sampling methods will be important to conduct, this work suggests that Chinese American women have greater cortical BMD at the hip compared with White women.

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Fig. 1.

Comparison of unadjusted percentage difference in QCT measurements between Chinese American and White premenopausal (a) and postmenopausal (b) women at the lumbar spine (black), femoral neck (gray), and total hip (white). * p 0.05 before adjustment for covariates; # p 0.05 after adjustment for weight, height, physical activity, calcium intake, serum parathyroid hormone, and 25-hydroxyvitamin D levels. CSA cross-sectional area; INT integral; vBMD volumetric bone density; Tb trabecular; Ct cortical; C/I the ratio of tissue volume in Ct regions to total tissue volume within the periosteal boundaries, an estimate of Ct thickness

Table 1

Anthropometric, lifestyle, and biochemical characteristics

	Pre-menopausal			Post-menopausal		
	Chinese American	White	p value	Chinese American	White	p value
	Mean±SD N=36	Mean±SD N=47		Mean±SD N=26	Mean±SD N=24	
Age (years)	35.0±3.9	33.9±3.8	0.18	61.2±2.3	62.2±2.7	0.17
Height (inches)	63.9±2.0	65.0±2.8	0.03	61.7±2.0	64.0±2.1	0.0003
Weight (pounds)	126.3±23	142.5±41	0.03	127.3±19.2	153.3±28.3	0.0004
BMI (kg/m ²)	21.7±3.6	23±5.8	0.08	23.4±2.8	26.4±5.3	0.02
Menopause age (years)	N/A	N/A	N/A	51.1±4.1	50.5±3.3	0.59
Current smoking (%)	5.6	2.1	0.44	0	4	0.33
Alcohol use (%)	2.8	4.3	0.72	0	16.7	0.04
Physical activity (Baecke Index)	1.03±0.6	1.53±0.7	0.002	1.21±0.7	1.35±0.6	0.45
Total calcium intake (mg/day)	868±534	1,376±1,592	0.05	923±559	1,463±634	0.003
PTH (pg/ml)	38±13	32±14	0.04	36±10	41±11	0.09
25-hydroxyvitamin D (ng/ml)	24±10	36±15	<0.0001	32±10	39±15	0.06

Table 2

Comparison of volumetric BMD by QCT in premenopausal women

	Chinese American Mean±SD N=36	White Mean±SD N=47	<i>p</i> value ^a	<i>p</i> value ^b
Lumbar spine (L1, L2)				
Cross-sectional area (cm ²)	8.22±0.94	8.19±1.04	0.91	0.02
Integral mid-vertebra BMD (g/cm ³)	0.263±0.03	0.261±0.03	0.74	0.17
Mid-vertebra trabecular BMD (g/cm ³)	0.183±0.03	0.173±0.03	0.14	0.04
Femoral neck				
Cross-sectional area (cm ²)	9.35±0.9	10.0±1.4	0.02	0.90
Integral BMD (g/cm ³)	0.330±0.04	0.325±0.04	0.50	0.03
Trabecular BMD (g/cm ³)	0.164±0.04	0.168±0.04	0.68	0.15
Cortical BMD (g/cm ³)	0.510±0.04	0.495±0.05	0.12	0.02
C/I	0.515±0.04	0.514±0.05	0.93	0.38
Total hip				
Integral BMD (g/cm ³)	0.306±0.03	0.299±0.03	0.39	0.02
Trabecular BMD (g/cm ³)	0.157±0.03	0.165±0.03	0.28	0.54
Cortical BMD (g/cm ³)	0.512±0.03	0.494±0.03	0.02	<0.01
C/I	0.419±0.03	0.408±0.04	0.12	0.08

^a Unadjusted^b Adjusted for weight, height, physical activity, total calcium intake, PTH, 25-hydroxyvitamin D

Table 3

Comparison of volumetric BMD by cQCT in postmenopausal women

	Chinese American Mean±SD N=26	White Mean±SD N=24	<i>p</i> value ^a	<i>p</i> value ^b
Lumbar spine (L1, L2)				
Cross-sectional area (cm ²)	7.63±0.94	8.37±1.03	0.01	0.97
Integral mid-vertebra BMD (g/cm ³)	0.208±0.03	0.215±0.03	0.41	0.88
Mid-vertebra trabecular BMD (g/cm ³)	0.119±0.03	0.116±0.03	0.75	0.63
Femoral neck				
Cross-sectional area (cm ²)	9.26±1.1	10.09±1.0	0.008	0.46
Integral BMD (g/cm ³)	0.282±0.03	0.267±0.024	0.09	0.051
Trabecular BMD (g/cm ³)	0.096±0.04	0.097±0.04	0.96	0.65
Cortical BMD (g/cm ³)	0.494±0.03	0.475±0.03	0.04	0.058
C/I	0.452±0.05	0.434±0.03	0.13	0.13
Total hip				
Integral BMD (g/cm ³)	0.265±0.03	0.258±0.03	0.36	0.21
Trabecular BMD (g/cm ³)	0.121±0.03	0.122±0.03	0.83	0.61
Cortical BMD (g/cm ³)	0.491±0.03	0.472±0.03	0.03	0.02
C/I	0.377±0.03	0.367±0.03	0.22	0.98

^a Unadjusted^b Adjusted for weight, height, physical activity, total calcium intake, PTH, 25-hydroxyvitamin D