Chinese Women in Both the United States and Hong Kong Have Cortical Microstructural Advantages and More Trabecular Plates Compared With White Women

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ABSTRACT
We cross-sectionally compared racial differences in bone quality between Chinese women in the United States (US) and Hong Kong (HK) with white women. A total of 514 women were included. We measured bone geometry, mass, microstructure, and stiffness by high-resolution peripheral quantitative computed tomography (HR-pQCT), individual trabecula segmentation (ITS), and microfinite element analysis (μFEA). After adjustment for age and body mass index (BMI), premenopausal Chinese women in the US and HK had smaller bone area but greater radial cortical (Ct.) thickness and Ct. and trabecular (Tb.) volumetric bone mineral density (vBMD) versus white women but did not differ from each other. At the radius, Tb. number was lower and spacing greater in Chinese women from HK and the US versus white women, whereas Chinese women did not differ from each other. Tb. thickness was highest in Chinese women from HK, intermediate in Chinese-Americans, and lowest in white women. Chinese women had more trabecular plates versus white women, leading to greater age- and BMI-adjusted stiffness for premenopausal Chinese women in HK and the US (both p < 0.05) versus white women. Tibial differences were similar in premenopausal women; analogous trends in microstructure were present in postmenopausal women at the tibia, although stiffness did not differ. In contrast, at the radius, cortical, plate-to-rod ratio, and stiffness were similar between postmenopausal HK and white women. Adjusting for age, weight, and height rather than age and BMI tended to reduce differences in bone size and Tb. parameters but accentuate cortical differences such that Chinese premenopausal women in both locations and postmenopausal women from HK had higher stiffness at both skeletal sites compared with white women. Compared with white women, Chinese women in the US and HK have vBMD and microstructural advantages leading to higher or similar mechanical competence in pre- and postmenopausal women, respectively, despite smaller bone size. © 2018 American Society for Bone and Mineral Research.

KEY WORDS: HR-PQCT; MICROARCHITECTURE; ITS; RACE; CHINESE; WHITE WOMEN; HONG KONG

Introduction
Asian women have lower areal bone mineral density (aBMD) as measured by dual-energy X-ray absorptiometry (DXA) when compared with white women and other racial groups.1–5 Despite lower aBMD, Asian women have a paradoxically lower nonvertebral fracture incidence than whites.6–8 Using high-resolution peripheral quantitative computed tomography (HR-pQCT), we and others recently reported that premenopausal and postmenopausal Chinese-American women have smaller bone size than white women in the US but thicker and denser cortices as well as thicker trabeculae at the radius and tibia.9–11 In addition, premenopausal, but not postmenopausal, Chinese-American women have higher trabecular bone density compared with white women.9,10

Using individual trabecula segmentation (ITS), a technique that further defines the trabecular architecture as either plates or rods from the HR-pQCT image, we have also shown that Chinese-American women have more plates versus rods in the trabecular compartment compared with white women.12,13 These cortical and trabecular microstructural features led to greater bone stiffness as measured by microfinite element analysis (μFEA).
analysis (µFEA) in premenopausal Chinese-American versus white women but similar strength in postmenopausal Chinese-American and white women. Recent work indicates that Asian men in the US share some similar microstructural features. We sought to determine if the skeletal microstructural features we identified in Chinese-American women were also present in women living in a different geographic location, namely Hong Kong (HK). In this analysis, we compared racial differences in bone microstructure by HR-pQCT, ITS, and µFEA in pre- and postmenopausal Chinese-American, HK Chinese, and white women.

Materials and Methods

A total of 514 women were included in this study. We studied 270 premenopausal women (46 Chinese-American, 175 HK Chinese, and 49 American white) and 244 postmenopausal women (29 Chinese-American, 186 HK Chinese, and 29 American white).

Study population

Recruitment and enrollment have been previously described for the US(9,10) and HK(15) cohorts and methods were similar. Briefly, both groups were recruited by advertisements. Additionally, the US cohort was recruited at primary care physician offices within the New York City region. All women were ambulatory. US inclusion criteria included self-reported Chinese or white ancestry (all four grandparents). Pre- and postmenopausal US women ages 29 to 40 years and 58 to 69 years were recruited. For the HK cohort, women ages 20 to 89 years were included. Menopause for both cohorts was defined as the absence of menses for >1 year.

Both cohorts excluded women with conditions (thyroid disease, parathyroid disorders, kidney dysfunction, liver dysfunction, malignancy, intestinal malabsorption, history of eating disorders, organ transplant) or medications (anticonvulsants, osteoporosis treatment, hormone replacement therapy, corticosteroids, etc.) known to affect bone metabolism. The US cohort additionally excluded those with amenorrhea for 6 months or more before menopause, current pregnancy or lactation, human immunodeficiency virus infection, or bilateral hip or spine hardware precluding assessment of bone density. The HK cohort additionally excluded those with fragility fracture or ophorectomy.

All patients gave written informed consent. This study was approved by the Institutional Review Boards of Columbia University Medical Center (CUMC) and the Chinese University of Hong Kong. In this article, the term “Chinese-American” defines a group having all four grandparents of Chinese descent and who reside in the US; the term “white” indicates white race/non-Hispanic ethnicity with residence in the US.

HR-pQCT

Participants were scanned with an XtremeCT I scanner (Scanco Medical, Brüttsielen, Switzerland) at each clinical site (New York, latitude 41°N, and Hong Kong, latitude 22°N) with daily phantom measurements. The nondominant distal radius and left distal tibia were scanned unless there was a previous fracture at the designated site, in which case we scanned the opposite limb. A highly trained operator at each site acquired and analyzed all scans according to the manufacturer’s standard in vivo protocol. Participants were scanned using 60 kVp effective energy, 900 µA current, and 100 ms integration time to acquire 110 slices at an 82 µm nominal isotropic resolution. We used the manufacturer’s standard method to filter and binarize the HR-pQCT images. We assessed standard HR-pQCT morphological microstructure outcomes, including total (D100), trabecular (Dtrab) and cortical (Dcort) volumetric BMD, cortical thickness (Ct.th), and trabecular number (Tb.N), thickness (Tb.Th), and separation (Tb.Sp). In vivo short-term reproducibility (CV) for HR-pQCT measures is <4.5%.(18,19)

Bone strength estimates

We estimated bone strength from the HR-pQCT images of both cohorts (US and HK) at CUMC using µFEA based on a voxel conversion approach.(20) We simulated uniaxial compression at the distal radius and tibia, which was separated from the whole bone based on an automatic segmentation technique.(12,13,21) The segmentation technique differs from our prior studies of this cohort.(12,13,21) 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, respectively), as well as plate and rod number densities (pTb.N and rTb.N, 1/mm, respectively). Plate to rod ratio (PR ratio), a summary 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, respectively). Detailed methods of the complete volumetric decomposition technique and ITS-based measurements can be found in our recent publications.(19,22,23)

Statistical analysis

Between-group differences in demographic and skeletal indices were evaluated with general linear models (GLM) with Scheffé’s adjustment for multiple comparisons. Adjusted analyses were controlled for age and body mass index (BMI) using GLM and were considered the primary analysis. We also explored adjusting for age, weight, and height rather than age and BMI. We calculated correlation coefficients between stiffness and trabecular parameters using Pearson’s correlation. Using the Fisher r-to-z transformation, we calculated the significance of the difference between the correlation coefficients in white and Chinese women. For all analyses, a two-tailed p value < 0.05 was considered to indicate statistical significance.

Results

Demographic factors

As shown in Table 1, Chinese women from HK, in both the pre- and postmenopausal age groups, were slightly older compared with white women and Chinese women from the US (both
Comparatively, postmenopausal Chinese women from HK were slightly shorter and weighed less compared with white women (all \( p < 0.0001 \)). Postmenopausal women in HK were also shorter than Chinese-American women (\( p = 0.02 \)). Chinese women in the US and HK did not differ in weight (\( p = 0.53 \)), but both weighed less compared with white women (both \( p < 0.0001 \)). Compared with white women, BMI was lower in postmenopausal Chinese women from HK (\( p = 0.008 \)) and a similar trend was apparent compared with Chinese-Americans (\( p = 0.06 \)).

### Table 1. Demographic Characteristics

| Variable     | Chinese-American | Hong Kong Chinese | White | \( p \) Value |
|--------------|------------------|-------------------|-------|---------------|
| **Premenopausal** |                  |                   |       |               |
| \( n \)       | 46               | 175               | 49    |               |
| Age (years)  | 35.8 ± 6.5\(^a\) | 40.0 ± 9.5        | 35.0 ± 3.9\(^a\) | 0.0001  |
| Height (cm)  | 161.9 ± 5.2\(^a\) | 157.8 ± 5.5       | 165.0 ± 6.9\(^a\) | <0.0001 |
| Weight (kg)  | 56.4 ± 9.8       | 54.7 ± 7.9        | 62.7 ± 17.2\(^{ab}\) | <0.0001 |
| BMI (kg/m\(^2\)) | 21.7 ± 3.5   | 22.0 ± 3.0        | 23.1 ± 5.5       | 0.13     |
| **Postmenopausal** |                  |                   |       |               |
| \( n \)       | 29               | 186               | 29    |               |
| Age (years)  | 61.1 ± 2.1\(^a\) | 66.4 ± 8.9        | 62.1 ± 2.6\(^a\) | 0.0003  |
| Height (cm)  | 156.7 ± 5.0\(^a\) | 153.4 ± 5.9       | 163.7 ± 4.6\(^{ab}\) | <0.0001 |
| Weight (kg)  | 57.6 ± 7.8       | 55.6 ± 8.3        | 68.6 ± 12.9\(^{ab}\) | <0.0001 |
| BMI (kg/m\(^2\)) | 23.6 ± 2.6   | 23.6 ± 3.5        | 25.9 ± 5.3\(^a\) | 0.008    |

*Values presented as mean ± SD.
\(^a\)\( p < 0.05 \) versus Hong Kong.
\(^b\)\( p < 0.05 \) versus Chinese-American.

Fig. 1. Age- and BMI-adjusted cortical thickness (A), cortical density (B), and PR ratio (C) in Chinese women compared with white women at the tibia. The error bars represent standard deviation.
At the radius, compared with white women, Chinese women in the US and HK had 8.7% \((p = 0.03)\) and 13.9% \((p < 0.0001)\) smaller bone size, respectively (Table 2). There were no bone size differences at the radius between Chinese women in the US versus HK \((p = 0.16)\). Radial Ct.th was 18% and 20% greater in Chinese women in the US and HK, respectively, versus white women \((\text{both} \ p < 0.0001)\), but Chinese women did not differ from each other \((p = 0.84)\). D100 was 20.1% higher in Chinese women from both the US and HK \((\text{both} \ p < 0.0001)\), whereas Dcort was 4.2% higher in both Chinese groups versus white women \((\text{both} \ p < 0.0001); \text{in contrast}, \text{Chinese women did not differ from each other in either D100 or Dcort (both} \ p = 1.0)\). Dtrab was 15.5% higher only between Chinese-Americans and white women \((p = 0.02)\); Chinese women in HK did not differ from either Chinese-Americans \((p = 0.20)\) or white women \((p = 0.21)\).

As shown in Table 2, Tb.N was lower in Chinese women from HK versus Chinese women from the US and white women \((\text{both} \ p < 0.0001)\), but the latter two groups did not differ from each other \((p = 0.62)\). Tb.Sp was 18% and 4% greater in Chinese women from HK versus both white \((p = 0.0003)\) and Chinese-American women \((p = 0.009)\), respectively, but the latter two groups did not differ from each other \((p = 0.77)\). Tb.Th was 7.9% and 28% greater in Chinese women from HK compared with both Chinese-Americans \((p = 0.02)\) and white \((p < 0.0001)\) women, respectively. Chinese-American women also had greater Tb.Th compared with white women \((p = 0.0001)\). Compared with white women, Chinese women in the US and HK had 53.7% \((p = 0.0006)\) and 50.7% higher \((p < 0.0001)\) PR ratio, respectively; Chinese women in the US and HK did not differ from each other \((p = 0.97)\). (Differences in other ITS parameters are shown in Supplemental Table S1.) These differences led to 8.0% \((p = 0.01)\) and 13.8% \((p = 0.0007)\) greater stiffness in Chinese women in the US versus Chinese women in HK and white women, respectively. Chinese women from Hong Kong did not differ from white women before adjustment for covariates \((p = 0.16)\).

As shown in Table 2, all between-group differences in radius area, Ct.th, D100, Dcort, Tb.N, Tb.Sp, and PR ratio remained significant after adjusting for age and BMI (Figure 1). Differences in Tb.Th were accentuated after adjustment such that Chinese women from HK had 8.3% to 24.6% higher Tb.Th compared with both Chinese women in the US \((p = 0.03)\) and white women \((p < 0.0001)\), respectively. Chinese women in the US had 15.2% greater Tb.Th compared with white women \((p = 0.002)\). There was also a trend toward higher Dtrab \((\text{overall} \ p = 0.04)\) in Chinese women in the US \((p = 0.06)\) and HK \((p = 0.09)\) compared with white women. After adjustment, stiffness was 10.2% greater in Chinese-American versus white women only \((p = 0.02)\).

Postmenopausal—radius

At the radius (Table 3), compared with white women, Chinese-American postmenopausal women had 11.5% smaller bone area compared with white women \((p = 0.03)\); there were no differences between Chinese women from HK versus either white women \((p = 0.35)\) or Chinese-Americans \((p = 0.13)\). Ct.th was 19.1% greater in Chinese women in the US versus HK \((p = 0.002)\) but did not differ between the other groups \((\text{HK versus} \ p = 0.74); \text{Chinese-American versus} \ p = 0.11)\). D100 was 18.5% higher in Chinese women in the US versus HK \((p = 0.002)\) but did not differ between the other groups \((\text{HK versus} \ p = 0.074); \text{Chinese-American versus} \ p = 0.25)\). Dcort was 9.6% and 5.9% higher in Chinese-American women versus both Chinese women in HK \((p < 0.0001)\) and white \((p = 0.05)\) women, respectively, but the latter two groups did not differ from each other \((p = 0.19)\). Dtrab was 25.7% higher in white women compared with Chinese women from HK \((p = 0.0007)\) but did not differ between the other groups \((\text{Chinese-American versus} \ p = 0.30); \text{Chinese-American versus} \ p = 0.18)\).

Tb.N was 16.9% to 24.9% lower in Chinese women from HK compared with Chinese \((p = 0.0003)\) and white \((p < 0.0001)\) women in the US, but the latter two groups did not differ from each other \((p = 0.13)\). Tb.Sp was 25.6% to 44.2% greater in Chinese women from HK versus Chinese women from the US \((p = 0.02)\) and white women \((p = 0.0001)\), respectively, but the
latter two groups did not differ from each other (p = 0.55). Tb.Th did not differ between the three groups (p = 0.14). There were no differences in the PR ratio (p = 0.34). Unadjusted stiffness was 12.7% to 14.6% lower in Chinese women from HK versus Chinese-Americans (p = 0.01) and white women (p = 0.002), respectively, but the latter two groups did not differ from each other (p = 0.91).

After adjusting for age and BMI, all between-group differences in radial area, Dcort, Dtrab, and Tb.N remained significant, whereas differences in D100 (p = 0.003) were attenuated and of borderline significance. After adjustment, Ct.th was 19.1% greater in Chinese-Americans versus whites (p = 0.01), but the other groups did not differ. After adjustment, Tb.Sp was 32.9% greater in Chinese women from HK versus white women (p = 0.003), whereas Chinese-Americans and HK no longer differed from each other (p = 0.15). There were no between-group differences in stiffness after adjustment for age and BMI (p = 0.09).

### Postmenopausal—tibia

At the tibia, total area was 11.7% and 12.1% higher in white women compared with Chinese women from HK (p = 0.001) and the US (p = 0.02), respectively, but Chinese women in the two different geographic locations did not differ from each other (p = 0.09). Neither Ct.th (p = 0.09), D100 (p = 0.12), nor Dcort (p = 0.05) differed between groups before adjustment. Dtrab was 12.3% to 23.4% lower in Chinese women from HK versus the US (p = 0.03) and white women (p < 0.0001), respectively, but the latter two groups did not differ (p = 0.06). Tb.N was lowest in Chinese women from HK, intermediate in Chinese-Americans, and highest in white women (p < 0.0001), whereas Tb.Sp had the opposite pattern (p < 0.0001). Tb.Th was 14.5% greater in Chinese women from HK versus white women (p = 0.01), but the other groups did not differ from each other. The PR ratio was 66.7% to 80.0% higher in Chinese women from HK and the US versus white women, but there were no differences between Chinese women (p = 0.59). Before adjustment, stiffness was 11.5% to 15.1% lower in Chinese women from HK compared with Chinese-Americans (p = 0.004) and white (p < 0.0001) women. White and Chinese-American women did not differ from each other (p = 0.65).

After adjustment for age and BMI, all between-group differences in tibial area, Tb.th, and PR ratio remained significant. Differences in Ct.th and Dcort were accentuated (Figure 1);
Table 3. HR-pQCT, ITS, and FEA Characteristics by Race in Postmenopausal Women

|                         | Chinese-American | Hong Kong Chinese | White | p Value  | Age- and BMI-adjusted p value | Age-, weight-, and height-adjusted p value |
|-------------------------|------------------|-------------------|-------|----------|-------------------------------|---------------------------------------------|
| **Radius**              |                  |                   |       |          |                               |                                             |
| Total area (mm²)        | 201 ± 33         | 216 ± 39          | 227 ± 38<sup>a</sup> | 0.03    | 0.045<sup>b</sup>             | 0.23                                         |
| D100 (mmHA/cm³)        | 340 ± 53<sup>a</sup> | 287 ± 74          | 308 ± 77 | 0.001  | 0.053                         | 0.02<sup>f</sup>                             |
| Dcort (mmHA/cm³)       | 916 ± 54<sup>a</sup> | 836 ± 82          | 865 ± 86<sup>a</sup> | <0.0001 | 0.006<sup>ag</sup>            | 0.007<sup>ef</sup>                           |
| Ct.th (mm)             | 0.862 ± 0.141<sup>a</sup> | 0.724 ± 0.200     | 0.754 ± 0.215 | 0.002  | 0.01<sup>d</sup>             | <0.001<sup>ef,g</sup>                       |
| Dtrab (mmHA/cm³)      | 118 ± 36         | 105 ± 34          | 132 ± 34<sup>a</sup> | 0.0003 | 0.03<sup>d</sup>             | 0.21                                         |
| Tb.N (1/mm)            | 1.60 ± 0.34<sup>a</sup> | 1.33 ± 0.32       | 1.77 ± 0.31<sup>c</sup> | <0.0001 | <0.0001<sup>fg</sup>        | 0.39                                         |
| Tb.Th (mm)             | 0.061 ± 0.013    | 0.066 ± 0.013     | 0.062 ± 0.012 | 0.14   | 0.02                          | 0.51                                         |
| Tb.Sp (mm)             | 0.597 ± 0.165<sup>a</sup> | 0.750 ± 0.295    | 0.520 ± 0.107<sup>e</sup> | <0.0001 | 0.001<sup>f</sup>            | 0.85                                         |
| PR ratio               | 0.608 ± 0.341    | 0.578 ± 0.275     | 0.502 ± 0.200 | 0.34   | 0.52                          | 0.72                                         |
| Stiffness (kN/mm)      | 71.6 ± 12.5<sup>a</sup> | 62.5 ± 14.7       | 73.2 ± 16.3<sup>a</sup> | <0.0001 | 0.09                          | 0.001<sup>e,g</sup>                         |
| **Tibia**              |                  |                   |       |          |                               |                                             |
| Total area (mm²)        | 613 ± 83         | 615 ± 99          | 687 ± 93<sup>sh</sup> | 0.001  | 0.002<sup>ef</sup>           | 0.05                                         |
| D100 (mmHA/cm³)        | 257 ± 42         | 238 ± 55          | 250 ± 39 | 0.12   | 0.61                          | 0.02<sup>g</sup>                             |
| Dcort (mmHA/cm³)       | 828 ± 57         | 796 ± 72          | 790 ± 59 | 0.05   | 0.005<sup>ef</sup>           | 0.007<sup>f</sup>                            |
| Ct.th (mm)             | 0.991 ± 0.201    | 0.935 ± 0.263     | 0.846 ± 0.229 | 0.09   | 0.0001<sup>ef</sup>         | <0.001<sup>ef,g</sup>                       |
| Dtrab (mmHA/cm³)       | 138 ± 29<sup>a</sup> | 121 ± 33          | 158 ± 25<sup>d</sup> | <0.0001 | <0.0001<sup>ef</sup>        | 0.13                                         |
| Tb.N (1/mm)            | 1.49 ± 0.25<sup>a</sup> | 1.28 ± 0.29       | 1.93 ± 0.35<sup>ad</sup> | <0.0001 | <0.0001<sup>ef</sup>        | <0.001<sup>e</sup>                          |
| Tb.Th (mm)             | 0.078 ± 0.015    | 0.079 ± 0.017     | 0.069 ± 0.011<sup>e</sup> | 0.01   | 0.009<sup>d</sup>            | 0.78                                         |
| Tb.Sp (mm)             | 0.612 ± 0.114<sup>a</sup> | 0.749 ± 0.228     | 0.466 ± 0.086<sup>h</sup> | <0.0001 | <0.0001<sup>ef</sup>        | 0.34                                         |
| PR ratio               | 1.35 ± 0.60      | 1.25 ± 0.52       | 0.75 ± 0.30<sup>ad</sup> | <0.0001 | <0.0001<sup>ef</sup>        | 0.01<sup>e</sup>                             |
| Stiffness (kN/mm)      | 207.5 ± 32.0<sup>a</sup> | 183.6 ± 36.3    | 216.2 ± 33.3<sup>c</sup> | <0.0001 | 0.02                          | <0.001<sup>ef</sup>                         |

HR-pQCT = high-resolution peripheral quantitative computed tomography; ITS = individual trabecula segmentation; FEA = finite element analysis; BMI = body mass index; D100 = total bone density; Ct.th = cortical thickness; Dcort = trabecular bone density; Tb. N = trabecular number; Tb.Th = trabecular thickness; Tb.Sp = trabecular spacing; PR ratio = plate to rod ratio.

Values presented as mean ± SD.

<sup>a</sup>p < 0.05 versus Hong Kong.
<sup>b</sup>p < 0.05 versus Chinese-American.
<sup>c</sup>p < 0.0001 versus Chinese-American.
<sup>d</sup>p < 0.0001 versus Hong Kong.
<sup>e</sup>p < 0.05 Chinese-American versus white.
<sup>f</sup>p < 0.05 Hong Kong versus white.
<sup>g</sup>p < 0.05 Chinese-American versus Hong Kong.
<sup>h</sup>p < 0.006 and Hong Kong (p = 0.0002) had 25.1% to 25.7% greater age- and BMI-adjusted Ct.th, respectively. Chinese women did not differ from each other (p = 0.99). Likewise, age- and BMI-adjusted Dcort was 4.7% to 5.8% greater in Chinese women from HK (p = 0.01) and the US (p = 0.02) versus white women, but Chinese women did not differ from each other (p = 0.79). In contrast, Dtrab was 14.5% to 22% higher in white women versus Chinese women from the US (p = 0.04) and Hong Kong (p < 0.001), respectively, but Chinese women did not differ from each other (p = 0.42). Higher Dcort but lower Dtrab in Chinese versus white women led to no between-group differences in D100 (p = 0.61) after adjustment. After adjustment, differences in Tb.N between Chinese women from HK and the US were attenuated (p = 0.06); only white women had higher Tb.N compared with Chinese women from the US and HK (both p < 0.0001). After adjustment, differences in Tb.Sp were attenuated between Chinese women (p = 0.14). Both Chinese women in the US (p = 0.02) and HK (p < 0.0001) had 28.8% to 43.6% greater Tb.Sp compared with white women. After adjustment, there was only borderline lower stiffness in Chinese women from HK versus white women (−7.4%, p = 0.051), but none of the other groups differed from each other.

**Adjustment for height**

To address possible limb length discrepancies between races and women in different geographic locations, we also explored adjusting for age, weight, and height, rather than age and BMI. By adjusting for age, weight, and height, some racial differences, particularly trabecular parameters and bone size, were attenuated and not significant. As shown in Table 2, among
premenopausal women after adjustment for age, weight, and height, differences in area, Tb.N, and Tb.Sp were not significant at either skeletal site. Among postmenopausal women (Table 3), differences in area, trabecular density, and trabecular microarchitecture were not significant at the radius after adjusting for age, weight, and height. At the tibia, area, Dtrab, Tb.Th, and Tb.Sp did not differ between postmenopausal groups.

Differences between the 3 groups, however, remained significant (overall p value) for all other parameters and the overall pattern of differences between groups was similar, but the significance of some pairwise comparisons changed, as shown in Tables 2 and 3. For example, as in the unadjusted and age- and BMI-adjusted analysis, radial D100, Dcort, and PR ratio were higher in premenopausal Chinese women from both locations compared with premenopausal white women, whereas Chinese women from the US and HK did not differ from each other; however differences in Ct.th were accentuated such that Ct.th was not only higher in both Chinese groups compared with white women but also 11.5% greater in Chinese women from HK versus the US (p = 0.03). After adjusting for age, weight, and height, Dtrab was only significantly higher in Chinese women from HK compared with white women in the US by 18.8% (p = 0.006), whereas Chinese women from HK did not differ from either group. Tb.th-adjusted values were still higher in Chinese women from both locations versus white women (20.3% to 26.6%, both p < 0.001), but Chinese women from different locations did not differ from each other (p = 0.44). Radial stiffness remained 23.6% and 36.9% higher in Chinese women from the US and HK, respectively, compared with white women, but Chinese women from HK and the US no longer differed from each other (p = 0.06).

At the tibia in premenopausal women (Table 2), adjustment for age, weight, and height tended to increase cortical density and microstructure values (D100, Dcomp, Ct.Th) of Chinese women from HK relative to the other groups, leading to accentuated differences in stiffness, such that stiffness differed between all groups (p < 0.001). Chinese women from HK had 30.3% higher stiffness compared with white women (p < 0.001) and 12.7% higher stiffness compared with Chinese women from the US (p = 0.03). Adjusted stiffness was 15.6% greater in Chinese women from the US compared with white women (p = 0.001). In contrast, Tb.N and Tb.Sp did not differ between groups (Table 2). PR ratio did not differ between Chinese women from HK and the other two groups, although PR ratio remained 64.4% higher in Chinese women from the US and white women, as shown in Table 2. Dtrab and Tb.th was higher in Chinese women from both locations compared with white women, but Chinese women from the US and HK did not differ from each other (p = 0.27).

Similar patterns were apparent among postmenopausal women at the radius. Adjusting for age, weight, and height tended to accentuate cortical differences between Chinese women from HK and white women, such that Chinese women from HK had 10.9%, 35.1%, and 74.0% higher Dcort, D100, and Ct.th, respectively, compared with white women (p < 0.05 for all). Chinese women from the US continued to have higher Dcort and Ct.th relative to white women (p < 0.05 for all). Chinese women did not differ from each other in cortical parameters except for Ct.th, which was 30.8% greater in women from HK (p = 0.02). Stiffness was 52.0% greater in Chinese women from HK compared with white women (p = 0.001) and 33.4% greater compared with Chinese women from the US (p = 0.002), but the latter two groups did not differ from each other (p = 0.21).

At the tibia, adjustment for age, weight, and height tended to increase Dcort and Ct.th among HK women relative to the other two groups. Dcort was 12.6% higher in Chinese women from HK compared with white women (p = 0.008). A similar trend was apparent compared with Chinese women from the US (7.1%, p = 0.07). Ct.th was 50.8% and 104% higher in Chinese women from HK compared with white women and Chinese women from the US, respectively. Chinese women from the US also had greater Ct.th than white women (p = 0.03). Differences in most trabecular parameters were attenuated, as shown in Table 3. PR ratio, however, remained higher only in Chinese women from the US versus white women (p = 0.03). In contrast, D100 became 24% higher in Chinese women in HK versus Chinese women from the US. Stiffness was 43.9% and 31.4% greater in Chinese women from HK versus white women and Chinese women from the US, respectively (both p < 0.001), but the latter two groups did not differ from each other (p = 0.30).

Correlations between trabecular parameters and stiffness

Almost all trabecular parameters at both skeletal sites correlated with stiffness at both skeletal sites in both races (R = 0.22–0.78, all p < 0.05). The only exception was for the correlation between PR ratio at the tibia and radial stiffness in white women (R = 0.11, p = 0.36). Several correlations were stronger in Chinese versus white women (tibial stiffness with: radius Dtrab R = 0.71 versus R = 0.49, p = 0.005; radius Tb.Th R = 0.50 versus R = 0.28, p = 0.04; tibial Tb.N R = 0.64 versus R = 0.34, p = 0.001; radial stiffness with: tibial Dtrab R = 0.69 versus R = 0.49, p = 0.01; tibial Tb.N R = 0.61 versus R = 0.33, p = 0.003; tibial Tb.Sp R = −0.57 versus R = −0.38, p = 0.05).

Discussion

Using HR-pQCT, we assessed whether Chinese women in HK have the cortical and trabecular microstructural advantages that we have described in Chinese-Americans compared with white women. To our knowledge, this is the first study to compare whether geographic location influences racial differences in skeletal microstructure. We found that Chinese women living in HK have similar age- and BMI-adjusted microstructural advantages to Chinese-American women. Specifically, Chinese women living in HK have greater age- and BMI-adjusted cortical thickness and density and more trabecular plates compared with white women.

There were, however, some age- and site-specific differences. For example, although the age- and BMI-adjusted trabecular and cortical advantages were present in premenopausal Chinese women from HK at both skeletal sites, they were only present in postmenopausal women at the tibia. Microstructural differences between Chinese women from HK and white women also generally tended to be less marked among postmenopausal women. In fact, microstructural differences led to higher age- and BMI-adjusted stiffness only among Chinese women in the premenopausal age group. Similar age- and BMI-adjusted stiffness among postmenopausal women, however, suggests that microstructural features such as greater cortical thickness and density as well as more platelike trabeculae may mechanically compensate for smaller bone size. Most of the trabecular parameters at both skeletal sites correlated with stiffness at both the radius and tibia in both races, suggesting that trabecular indices are indeed associated with mechanical...
competence. Some correlations were stronger in Chinese versus white women, further indicating that the relationship between microstructure and strength may vary between races.

The differences we have observed in microstructure and stiffness may, in part, underlie the lower risk of fracture in Chinese women. The reasons for the age- and site-specific differences are not clear and cannot be addressed by our study, but our findings suggest that some of the mechanical advantages observed in young Chinese women may, in part, dissipate with aging and/or menopause. Indeed, our prior published analyses do indicate race-menopause interactions for some variables.24 Longitudinal studies, however, would be needed to confirm these observations.

Although no other studies have formally compared whether geography influences racial differences in skeletal microstructure, our findings of greater cortical thickness, density, and trabecular thickness in Chinese women are also similar to results in Chinese women in Australia, whereby the finding of thicker cortices and trabeculae contained within a smaller bone was proposed to confer a lower fracture risk in Chinese women.19 A report in Canadian Asian adolescents also suggest similar cortical features.25 After adjusting for covariates, Asian adolescents and young adults had greater cortical bone density and thickness compared with their white counterparts. Our recent findings in Asian young men additionally indicate similar cortical characteristics and more platelike trabecular bone.14 As such, it is notable that premenopausal Chinese women in the current study did not differ from each other in age- or BMI-adj usted cortical parameters or PR ratio, whether from HK or the US.

The consistency of these vBMD and microstructural skeletal advantages among Asian individuals across sex and continents may very well suggest a genetic basis for them that persists, at least for a finite period of time despite geographical variability. Indeed, several recent studies support the hypothesis that HR-pQCT-derived bone microstructure is a heritable trait. Data suggest premenopausal daughters of women who sustained a fragility fracture had thinner cortices and impaired trabecular microarchitecture compared with premenopausal daughters of women without fracture.26 Another study examining HR-pQCT microstructure of monozygotic and dizygotic middle-aged white female twin pairs indicated that genetic factors accounted for 72% to 81% of the variance of microstructure, suggesting genetics plays a stronger role than environmental factors in bone microarchitecture.27 Furthermore, data from the Framingham Offspring cohort found high heritability of HR-pQCT traits ranging from 19.3% for radial trabecular number to 98.3% for tibial cortical cross-sectional area.28 Future studies are needed to assess the genes associated with these microstructural characteristics, as differences in allele frequencies between the white and Chinese populations in genes associated with microstructure may contribute to the microstructural skeletal advantages observed here among Asian individuals. Our current study does not allow us to assess this possibility, but we acknowledge that this is certainly an important area for further study.

In this study, unfortunately, information about environmental factors such as dietary intake, alcohol consumption, exercise, and smoking, were not acquired for all cohorts and is a limitation, as they may affect bone microstructure.29-34 Our prior work in premenopausal women suggests that Chinese-American women tend to have more lifestyle risk factors for poorer skeletal health, including lower calcium and vitamin D intake and exercise levels compared with white women,35 yet despite this, Chinese-Americans have more favorable microstructure. Adjustment for these covariates in our prior study tended to accentuate the more favorable microstructure in Chinese-Americans. Thus by not accounting for these factors in the current study, we may have biased ourselves against finding even more favorable microstructure in Chinese vs. white women.

On the other hand, Chinese-Americans may have some more favorable lifestyle factors due to acculturation (such as increased calcium and vitamin D intake) compared with HK Chinese women. Indeed, studies demonstrate Chinese individuals living in Western countries take on Western dietary patterns.35,36 Thus, we cannot exclude the possibility that we may have found more differences between Chinese-Americans and Chinese women in HK if we adjusted for such factors.

Our study has some additional limitations. The cohort studied was a convenience sample of women and results could be influenced by selection bias. For both the US and HK cohorts, the intent was to recruit "normal" ambulatory women without secondary causes of osteoporosis. Although the recruitment criteria overall were very similar, the exact criteria differed slightly with the US cohort having more specific exclusion criteria. The more "stringent" exclusion criteria in the US cohort could bias toward finding better microarchitecture in Chinese Americans and white women versus the Chinese women in HK. Because our results generally run counter to that expectation, we are reassured that this is not a major source of bias. Furthermore, the similar results between our findings and those of other Asian cohorts suggest the findings are likely to be generalizable.

Another limitation was the difference in sample size between the cohorts. Because statistical power is limited by the size of the smallest group, we cannot completely rule out that additional differences may have been found if we had a larger US sample. Differences in sample size could also lead to inequality of variances, but our analytic methods are robust for unbalanced designs. An additional limitation was that women in HK were slightly older. Despite this, Chinese women in HK (particularly premenopausal women) still had skeletal advantages; further, we adjusted for such differences in our analyses.

Another limitation derives from height differences between the groups. Differences in height and/or limb length could lead to acquisition of HR-pQCT images at slightly different regions of interest. Unfortunately, limb length was not measured in this study. To explore the effect of differences in height on results, we assessed the effect of adjusting for age, weight, and height rather than age and BMI. Adjusting for age, weight, and height tended to attenuate racial differences in bone size and some trabecular parameters. On the other hand, adjusting for age, weight, and height tended to increase cortical differences and stiffness particularly in Chinese women from HK, leading to greater stiffness in Chinese premenopausal women in both geographic locations as well as postmenopausal women from Hong Kong versus white women. A recent study compared HR-pQCT parameters using both a fixed region of interest (ROI) and a percent-based region of interest according to limb length.37 In Asian and white women, using a percent-based relative ROI did not change the significance or direction of density or microstructural differences between races.37 Whether a fixed region of interest or relative region of interest was used, Asian women had smaller bone size, lower cortical porosity, as well as higher
to elucidate the physiological or genetic basis of these microstructural advantages found in the Chinese population may pausal women, respectively, despite smaller bone size. The higher or similar mechanical competence in pre- and postmenopausal HK have vBMD and microstructural advantages that led to summary, compared with white women, Chinese women in the US and HK have vBMD and microstructural advantages that led to higher or similar mechanical competence in pre- and postmenopausal women, respectively, despite smaller bone size. The microstructural advantages found in the Chinese population may contribute to their favorable fracture risk. Future research is needed to elucidate the physiological or genetic basis of these findings.

Disclosures

All authors state that they have no conflicts of interest.

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