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Trabecular bone deficits among Vietnamese immigrants

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Abstract

Summary—Compared to white women, lower areal bone mineral density (aBMD) in middle-aged Vietnamese immigrants is due to reduced trabecular volumetric bone mineral density (vBMD), which in turn is associated with greater trabecular separation along with lower estrogen levels.

Introduction—The epidemiology of osteoporosis in Asian populations is still poorly known, but we previously found a deficit in lumbar spine aBMD among postmenopausal Southeast Asian women, compared to white women, that persisted after correction for bone size. This issue was revisited using more sophisticated imaging techniques.

Methods—Twenty Vietnamese immigrants (age, 44–79 years) were compared to 162 same-aged white women with respect to aBMD at the hip, spine and wrist, vBMD at the hip and spine by quantitative computed tomography and vBMD and bone microstructure at the ultradistal radius by high-resolution pQCT. Bone turnover and sex steroid levels were assessed in a subset (20 Vietnamese and 40 white women).

Results—The aBMD was lower at all sites among the Vietnamese women, but femoral neck vBMD did not differ from middle-aged white women. Significant differences in lumbar spine and ultradistal radius vBMD in the Vietnamese immigrants were due to lower trabecular vBMD,

which was associated with increased trabecular separation. Bone resorption was elevated and bone formation depressed among the Vietnamese immigrants, although trends were not statistically significant. Serum estradiol was positively associated with trabecular vBMD in the Vietnamese women, but their estrogen levels were dramatically lower compared to white women.

Conclusions—Although reported discrepancies in aBMD among Asian women are mainly an artifact of smaller bone size, we identified a specific deficit in the trabecular bone among a sample of Vietnamese immigrants that may be related to low estrogen levels and which needs further study.

Keywords

Bone mineral density; Bone structure; Bone turnover; Ethnic group; Southeast Asians

Introduction

Lower areal bone mineral density (aBMD) in Asian populations is generally considered an artifact of their smaller bone size, but their vertebral fracture risk may be comparable to white subjects [1, 2]. We previously reported that, compared to white women, immigrant women from Southeast Asia (Vietnam, Cambodia, Laos) had lower hip and spine aBMD [3], but they were almost four inches shorter. Adjusting for bone size by bone mineral apparent density (BMAD) eliminated race-specific differences at both hip and spine among premenopausal women and at the hip among postmenopausal women, but the deficit in bone density at the lumbar spine persisted. Since compartment-specific information might be relevant to the etiology of the low bone density observed, we recalled a subset of the Vietnamese women and assessed their cortical and trabecular volumetric bone density (vBMD) at the hip and spine by quantitative computed tomography (QCT), bone density and microstructure at the ultradistal radius using high-resolution peripheral quantitative computed tomography (HRpQCT), bone turnover with current biomarkers of bone formation and resorption, and serum estrogen levels by high-sensitivity mass spectroscopy [4]. Results were compared to a population-based sample of same-aged white women from the community.

Methods

Study subjects

As described in detail elsewhere [3], we previously attempted to enroll as many Rochester, MN residents ≥ 20 years of age of Southeast Asian heritage (Vietnamese, Cambodian, Laotian) as possible using last names common to each group as well as personal contacts with representatives of each community who acted as interpreters. Ultimately, 107 Vietnamese women provided informed consent and were included in that study, 46 of whom were postmenopausal [3]. Using seed money from Mayo's Center for Translational Science Activities (CTSA), we recalled a convenience sample of 20 middle-aged Vietnamese women. All steps of the recruitment process were approved in advance by the Mayo Clinic Institutional Review Board.

For comparison, we used data from an age-stratified random sample of Rochester women [5], 228 of whom were subsequently evaluated at a 6-year-follow-up visit. The comparison of bone density and structure was based on 162 white women (by self report) who were in the same age range as the Vietnamese immigrants (44 to 79 years) when they underwent the imaging studies described below. Because new measurements had to be made, the comparison of bone turnover and serum estrogen levels was restricted to 40 individually

age-matched (2:1) white women from the cohort using serum samples from their baseline visit.

Bone density and structure

Various aBMD (g/cm^2) measurements were made by DXA (Lunar Prodigy System, GE Healthcare, Madison, WI), while single energy QCT scans were made at the lumbar spine and left proximal femur with a high-speed helical CT scanner (Somatom Sensation 64, Siemens Healthcare, Forchheim, Germany). Bone density and microstructure measurements were obtained from the non-dominant wrist using the XtremeCT (Scanco Medical AG, Brüttisellen, Switzerland), as described in detail elsewhere [6].

Biochemical studies

Serum amino-terminal propeptide of type I collagen (PINP) was measured by radioimmunoassay (DiaSorin, Stillwater, MN; interassay CV <9%), while serum cross-linked C-telopeptide of type I collagen (CTX) was measured using an ELISA (Nordic Biosciences, Herlev, Denmark; interassay CV <10%). For the serum estrogen measurements, we used liquid chromatography-tandem mass spectrometry (LC-MS/MS) as described elsewhere [4]. Measurements were made simultaneously for the Vietnamese and white women.

Statistical analysis

The bone density and structure variables were summarized using means and standard deviations. Given similar age ranges and mean ages in the Vietnamese subjects and the white comparison group, the two-sample *t*-test was used to compare differences in means for the skeletal parameters. The biochemical results were not all normally distributed, and they were summarized by medians and interquartile ranges (IQR); differences were evaluated with rank sum tests. Spearman correlations were used to evaluate associations between serum CTX and E_2 measures and skeletal parameters. Biochemical data were ranked and linear regression then used to assess whether covariates eliminated race-specific differences. A *p*-value of 0.05 was considered significant, and all analyses were performed using SAS (SAS Institute Inc., Cary, NC).

Results

The mean age of the 20 women who had emigrated from Vietnam (15 postmenopausal) was 62.7 ± 10.1 years (range, 44 to 79 years) compared to 62.2 ± 9.8 years for the subset of 162 white women (133 postmenopausal). The median duration of United States residency for the Vietnamese women was 16 years (range, 12 to 33 years). They were considerably shorter than the white women (150.7 ± 5.2 versus 162.5 ± 5.9 cm; $p < 0.001$) and weighed less (52.4 ± 6.9 versus 75.3 ± 14.9 kg; $p < 0.001$). Forty percent of the Vietnamese immigrants and 49% of the white women (40% of the subset whose bone turnover and sex steroid levels were compared) were taking an osteoporosis-related drug (e.g., bisphosphonates, hormone therapy or selective estrogen receptor modulators).

Total body, femoral neck, lumbar spine and ultradistal radius aBMD were all significantly lower among the Vietnamese immigrants (Table 1). However, cross-sectional areas were less, and femoral neck total vBMD was actually slightly higher in the Vietnamese women as a consequence of significantly greater cortical vBMD at that site. vBMD of the mostly trabecular lumbar spine was lower in the Vietnamese women as was trabecular vBMD in the ultradistal radius; cortical vBMD in the radius did not differ. Bone microstructure in the ultra-distal radius (based on 19 Vietnamese immigrants) revealed much lower BV/TV and trabecular number among the Vietnamese immigrants but no difference in trabecular

thickness (Table 1). Instead, trabecular separation (Tb.Sp) was dramatically greater in the Vietnamese women, with much higher Tb.Sp.SD, a measure of trabecular heterogeneity. Conversely, connectivity density was greatly reduced in that group. The structure model index was greater among the Vietnamese immigrants indicating a shift from plate-like to more rod-like trabeculae. These differences were basically unchanged by focusing on the postmenopausal women alone or those not on treatment (data not shown).

In an exploratory analysis, we evaluated the bone turnover and sex steroid levels. As summarized in Table 2, bone resorption, assessed by serum CTx, was 12% greater among the 20 Vietnamese immigrants while bone formation, measured with PINP, was 19% lower than in the 40 age-matched white women. Neither trend was statistically significant given the limited sample size. Of note was the greater heterogeneity in biomarker values evident among the Vietnamese women as reflected in their larger IQR. By contrast, serum E_2 and E_1 levels were dramatically lower among the Vietnamese compared to the white women, and similar results were seen among the subset of postmenopausal women alone (E_2 , 2.8 versus 8.2 pg/mL and E_1 , 17.0 versus 41.0 pg/mL; both $p < 0.001$). Adjustment for body size (body mass index) or for the use of osteoporosis treatments did not eliminate the key race-specific differences in sex steroids and bone turnover (data not shown).

Among the Vietnamese women, serum E_2 was negatively correlated with CTx ($R = -0.19$; $p = 0.424$), although this was not statistically significant; and E_2 ($R = 0.56$; $p = 0.010$), but not CTx ($R = 0.13$; $p = 0.584$), was correlated with lumbar spine trabecular vBMD. Serum CTx ($R = 0.48$; $p = 0.038$) was correlated with connectivity density, but other correlations with bone microstructure were not statistically significant given the small number of subjects.

Discussion

Like others [1], we showed that 2-dimensional aBMD is lower in middle-aged Vietnamese than in middle-aged white women, but differences were generally less with 3-dimensional vBMD, which is not confounded by bone size. In particular, there was no significant difference in the femoral neck vBMD between the Vietnamese immigrants and the white women. Others have observed similar total vBMD values at the distal radius [7, 8] and lumbar spine [9] in Asian and white women. However, we found discrepancies in the vBMD at the wrist and spine among the Vietnamese women that were largely confined to the trabecular compartment of the bone.

In contrast to recent reports that distal radius vBMD, trabecular thickness, and trabecular separation are comparable in younger (mean age ~35 years) premenopausal Chinese and white women [10, 11], the trabecular bone deficit in these much older Vietnamese immigrants appeared to stem more from the trabecular separation than from the trabecular thinning. Disruption of the trabecular microstructure would be expected to have a significant negative impact on fracture risk in the spine [12]. Indeed, the risk of vertebral fractures may be as great among Asian women as in white women [1, 2], despite their generally lower risk of hip fracture. The basis for any exacerbated trabecular disruption is uncertain at present, although low sex steroid levels are associated with trabecular bone loss in peri- and postmenopausal white women [13]. Low sex steroid levels should lead to increased bone resorption [14], and the trend toward increased bone resorption relative to decreased bone formation seen here would be expected to enhance fracture risk [15]. However, there are few data comparing bone turnover in Asian and white populations [16].

This study has a number of strengths including the use of state-of-the-art assessments of bone microstructure by HRpQCT as well as serum estrogen measurements by high-sensitivity mass spectroscopy [4]. However, there are also important limitations especially

related to the small sample size. In addition, generalizability is limited since it was necessary to use a convenience sample of the minority subjects, whereas we were able to employ systematic sampling for the white population. Further study is needed to determine whether the deficits in trabecular bone observed in the Vietnamese immigrants represent a physiologic response to a smaller body size [16] or whether they are due instead to inadequate development of peak bone mass, possibly because of early and frequent childbearing [17] or cultural differences in calcium intake [3, 16], or to excessive subsequent bone loss, perhaps related to estrogen metabolism. This issue must be resolved because Asian-Americans are one of the fastest growing racial groups in the United States. Osteoporosis treatment appears to be generally effective in Asian women [18] but is greatly underutilized [19]. This might be improved by better definition of high-risk subsets of the population [20].

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Table 1
Comparison of bone density and structure measurements among 162 middle-aged white women and 20 Vietnamese immigrants of similar age (44–79 years) in Rochester, MN

Variable (units)	White $\bar{x} \pm SD$	Vietnamese $\bar{x} \pm SD$	Difference %
Bone density (aBMD, g/cm ²)			
Total body	1.15±0.11	1.01±0.10	−12 [*]
Femoral neck	0.90±0.15	0.78±0.15	−13 ^{**}
Lumbar spine	1.15±0.19	0.97±0.14	−16 [*]
Ultradistal radius	0.43±0.09	0.35±0.06	−19 [*]
Femoral neck (vBMD, mg/cm ³)			
Total	325±68.8	339±86.3	5
Trabecular	198±55.9	178±62.7	−10
Cortical	603±84.9	647±75.4	7 ^{***}
Lumbar spine (vBMD, mg/cm ³)			
Total	186±46.4	156±45.0	−16 ^{**}
Trabecular	148±39.2	122±41.2	−17 ^{**}
Ultradistal radius (vBMD, mg/cm ³)			
Total	343±83.4	302±91.8	−12 ^{***}
Trabecular	139±43.1	85.5±38.0	−39 [*]
Cortical	899±71.1	876±79.9	−3
Bone macrostructure			
Femoral neck			
Cross-sectional area (cm ²)	6.90±0.97	5.42±0.69	−21 [*]
Endocortical area (cm ²)	4.77±0.88	3.58±0.69	−25 [*]
Cortical thickness (mm)	2.89±0.48	2.83±0.42	−2
Lumbar spine			
Cross-sectional area (cm ²)	10.3±1.24	9.88±1.20	−4
Endocortical area (cm ²)	8.60±1.19	8.39±1.15	−2
Apparent cortical thickness (mm)	1.59±0.31	1.43±0.26	−10 ^{***}
Ultradistal radius			
Cross-sectional area (cm ²)	2.28±0.38	1.95±0.45	−14 ^{**}
Endocortical area (cm ²)	1.69±0.39	1.45±0.48	−14 ^{***}
Cortical thickness (mm)	0.88±0.22	0.80±0.22	−9
Bone microstructure			
Ultradistal radius			
Bone volume/total volume	0.12±0.04	0.07±0.03	−42 [*]
Trabecular number (1/mm)	1.61±0.36	1.04±0.41	−35 [*]
Trabecular thickness (mm)	0.07±0.01	0.07±0.01	0

Variable (units)	White $\bar{x} \pm SD$	Vietnamese $\bar{x} \pm SD$	Difference %
Trabecular separation (Tb.Sp, mm)	0.60±0.26	1.08±0.56	80 [*]
SD of Tb.Sp (mm)	0.31±0.22	0.72±0.49	132 [*]
Connectivity density (1/mm ³)	3.00±1.05	1.74±0.85	-42 [*]
Structure model index	2.31±0.43	2.60±0.30	13 ^{**}

^{*}
 $p < 0.001$,

^{**}
 $p < 0.01$,

^{***}
 $p < 0.05$ from two-sample *t*-test

Table 2
Comparison of bone resorption (CTx) and formation (PINP) markers and sex steroid levels among 40 middle-aged white women and 20 same age (44–79 years) Vietnamese immigrants in Rochester, MN

Variable (units)	White Median (IQR)	Vietnamese Median (IQR)	Difference %
Bone turnover			
Serum CTx (ng/mL)	0.34 (0.27–0.46)	0.38 (0.18–0.56)	12
Serum PINP (µg/L)	40.0 (28.8–49.3)	32.2 (19.0–71.8)	–19
Sex steroids			
Serum estradiol (pg/mL)	10.5 (5.2–28.5)	3.1 (2.0–7.4)	–70 *
Serum estrone (pg/mL)	50.0 (28.5–85.0)	17.0 (13.0–27.5)	–66 *

*
 $p < 0.001$ from rank sum test

CTx, cross-linked C-telopeptide of type I collagen

PINP, amino-terminal propeptide of Type I collagen