Bone 103 (2017) 200–208

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Bone mass, microarchitecture and strength are influenced by race/ethnicity in young adult men and women

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ARTICLE INFO

Article history:
Received 29 March 2017
Revised 18 June 2017
Accepted 12 July 2017
Available online 13 July 2017

Keywords:
High resolution peripheral quantitative computed tomography (HR-pQCT)
Bone mineral density (BMD)
Sex
Gender
Fracture risk
Stress fracture risk

ABSTRACT

Lower rates of fracture in both Blacks compared to Whites, and men compared to women are not completely explained by differences in bone mineral density (BMD). Prior evidence suggests that more favorable cortical bone microarchitecture may contribute to reduced fracture rates in older Black compared to White women, however it is not known whether these differences are established in young adulthood or develop during aging. Moreover, prior studies using high-resolution pQCT (HR-pQCT) have reported outcomes from a fixed-scan location, which may confound sex- and race/ethnicity-related differences in bone structure.

Purpose: We determined differences in bone mass, microarchitecture and strength between young adult Black and White men and women.

Methods: We enrolled 185 young adult (24.2 ± 3.4 yrs) women ($n = 51$ Black, $n = 50$ White) and men ($n = 34$ Black, $n = 50$ White) in this cross-sectional study. We used dual-energy X-ray absorptiometry (DXA) to determine areal BMD (aBMD) at the femoral neck (FN), total hip (TH) and lumbar spine (LS), as well as HR-pQCT to assess bone microarchitecture and failure load by micro-finite element analysis (μFEA) at the distal tibia (4% of tibial length). We used two-way ANOVA to compare bone outcomes, adjusted for age, height, weight and physical activity.

Results: The effect of race/ethnicity on bone outcomes did not differ by sex, and the effect of sex on bone outcomes did not differ by race/ethnicty. After adjusting for covariates, Blacks had significantly greater FN, TH and LS aBMD compared to Whites ($p < 0.05$ for all). Blacks also had greater cortical area, vBMD, and thickness, and lower cortical porosity, with greater trabecular thickness and total vBMD compared to Whites. μFEA-estimated FL was significantly higher among Blacks compared to Whites. Men had significantly greater total vBMD, trabecular thickness and cortical area and thickness, but greater cortical porosity than women, the net effects being a higher failure load in men than women.

Conclusion: These findings demonstrate that more favorable bone microarchitecture in Blacks compared to Whites and in men compared to women is established by young adulthood. Advantageous bone strength among Blacks and men likely contributes to their lower risk of fractures throughout life compared to their White and women counterparts.

Abbreviations: MrOS, Osteoporotic Fractures in Men Study; SWAN, Study of Women Across the Nation; FEA, finite element analysis; PA, posterior-anterior; FN, femoral neck; TH, total hip; Tt.Ar, total cross-sectional area; Tt.vBMD, total vBMD; Tb.vBMD, trabecular vBMD; Tb.N, trabecular number; Tb.Sp, trabecular separation; Tb.Th, Trabecular thickness; Ct.Ar, cortical area; Ct.Th, cortical thickness; Ct.vBMD, cortical vBMD; Ct.TMD, cortical tissue mineral density; Ct.Po, cortical porosity; Tb.Ar, trabecular area; Ct.Ar/Tt.Ar, cortical area fraction; μFEA, micro-finite-element-analysis; PTH, parathyroid hormone.

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http://dx.doi.org/10.1016/j.bone.2017.07.014
8756-3282/

1. Introduction

Worldwide, there are well-established differences in fracture rates by race and ethnic-origin [1–5]. In particular, Blacks/African-Americans have lower incidence of fractures in both youth and older adulthood than Whites/Caucasians residing in the US [3,6]. Black men and women also have a 2–3 fold lower incidence of stress fracture compared to their White counterparts [7,8]. Although Black individuals have higher areal bone mineral density (aBMD) than Whites/Caucasians at all ages [9–13], this higher aBMD does not entirely account for the lower fracture risk seen in Black compared to White individuals [14–16].

Therefore, it has been hypothesized that variation in bone morphology and microarchitecture due to racial background contributes to observed differences in fracture incidence [13,17–21]. Accordingly, as assessed by quantitative computed tomography (QCT), older Black men from the Osteoporotic Fractures in Men (MrOS) study had more favorable morphology at the proximal femur compared to White men [17]. Similarly, high-resolution peripheral quantitative computed tomography (HR-pQCT) scans of the distal radius and tibia revealed that postmenopausal Black women from the Study of Women Across the Nation (SWAN) cohort had greater trabecular volumetric BMD (vBMD), and cortical thickness compared to their White counterparts [13]. While studies comparing Asian compared to Caucasian women suggest that these differences in bone microarchitecture are evident in premenopausal women [18–20], there are few studies to indicate whether these race/ethnic advantages in bone microarchitecture among Black individuals are established during growth and development, or result from a different pattern of age-related changes in bone.

It is also well known that men have lower fracture risk than women at all ages. Many prior studies have reported higher aBMD and advantageous bone microarchitecture in adult men compared to women [22–25] [23,26]. However, to date, studies comparing bone microarchitecture by HR-pQCT in adults have used a fixed region-of-interest, starting 9.5 mm or 22.5 mm proximal to the distal endplate of the radius and tibia, respectively, regardless of body size. Therefore, results using this approach may be difficult to interpret in individuals of differing stature or limb length, as some bone microarchitecture outcomes vary significantly along the length of the limb in this metaphyseal region [27–29].

Thus, there is strong rationale to study the bone morphology and microstructural features that may explain race/ethnicity- and sex-based differences in both stress fracture risk in young adults and osteoporosis-related fracture risk later in life, particularly among young adult men and women of African ancestry. Therefore the, primary aim of this study was to determine differences in bone morphology, microarchitecture, and finite element analysis (FEA) derived bone strength of the distal tibia according to sex- and race/ethnic-origin in young Black and White adults. We located the region of interest relative to bone length to overcome potential confounding by differences in bone length and height among groups. We hypothesized that Black men and women will have more favorable bone microarchitecture parameters than White men and women, and that men of both races will have more favorable bone microarchitecture parameters than women.

2. Materials and methods

2.1. Subject characteristics

We enrolled young adult men and women between the ages of 18–30 yrs with a body mass index (BMI) between 18 and 30 kg/m^2. Subjects self-identified as White/Caucasian (50 women, 50 men) or Black/African-American (51 women, 34 men). For this study, we defined racial group identification as having at least three of four grandparents of the same race/ethnic background as the subjects' self-identified race/ethnicity. Women enrolled in this study were required to be currently eumenorrheic (>9 menses in the prior 12 months, including 1 menses in last 60 days). Exclusion criteria included underlying medical conditions or use of medications known to affect bone health, history of an eating disorder, and history of bilateral lower limb fractures. We screened 244 potential participants for this study: 59 screened subjects did not participate in the study, including 25 who did not meet BMI criteria, 15 who did not meet race criteria, 7 who were outside the age range, 2 who had a history of metabolic bone disorder, 2 who had an eating disorder, 2 who had a history of bilateral ankle fractures, 2 who were amenorrheic, 2 who had an endocrine disorder possibly affecting bone, 1 who was taking anti-seizure medication, and 1 who met more than one exclusion criteria. This study was approved by the Institutional Review Board of Partners Health Care and the Human Research Protection Office at the US Army Medical Research and Materiel Command. Informed written consent was obtained from each subject prior to participation in the study.

2.2. Clinical history and anthropometric measurements

We assessed socio-economic status, education, health history, fracture history, and physical activity history through questionnaires. For women, questionnaires also captured menstrual status and contraceptive use. Height (to the nearest millimeter) was obtained using a wall-mounted stadiometer. Body mass (to the nearest 0.1 kg) was measured on a calibrated electronic scale. BMI was calculated as mass (kg) divided by height squared (m^2). We measured tibia length from the medial tibial plateau to the distal edge of the medial malleolus to the nearest mm using an anthropometric tape. All measurements were taken twice, and the mean of two readings was used.

2.3. Areal bone mineral density

We used dual energy X-ray absorptiometry (DXA: QDR45000A; Hologic Inc., Bedford, MA, USA) to assess the posterior-anterior (PA) spine, femoral neck (FN), and total hip (TH) aBMD (g/cm^2). Quality control was maintained through daily measurements of a Hologic CXA anthropomorphic spine phantom and visual review of every scan image by an investigator experienced in bone densitometry.

2.4. Bone microarchitecture

We measured cortical and trabecular vBMD and microarchitecture at the distal tibia using HR-pQCT (XtremeCT, Scanco Medical AG, Basserdorf, Switzerland; isotropic voxel size of 82 μm). The scan region started at 4% of tibial length (distal) and extended proximally for 110 slices (9.02 mm). The non-dominant leg was scanned, unless there was a prior leg or ankle fracture, in which case the contralateral leg was scanned. Quality control was maintained with daily scanning of the manufacturer's phantom. All scans were reviewed immediately for motion artifact and were repeated up to two times if significant motion artifact was noted. Movement artifact was scored on a 5-point scale, with 1 = no movement and 5 = severe movement artifact [30].

Using Scanco analysis software version 5.11, total cross-sectional area (Tt.Ar mm^2), total and trabecular vBMD (Tt.vBMD, Tb.vBMD, mg HA/cm^3), and trabecular number (Tb.N, 1/mm) were measured directly. Trabecular separation (Tb.Sp, mm) and trabecular thickness (Tb.Th, mm) were then calculated from Tb.vBMD and Tb.N. We used a semiautomated technique [31,32] to measure cortical area (Ct.Ar, mm^2), cortical thickness (Ct.Th, mm), cortical vBMD (Ct.vBMD, mg HA/-cm^3), cortical tissue mineral density (Ct.TMD, mg HA/cm^3), cortical porosity (Ct.Po, %), and trabecular area (Tb.Ar, mm^2). Cortical area fraction (Ct.Ar/Tt.Ar,%) was then calculated. We also used 3D HR-pQCT images to perform linear micro-finite-element-analysis (μFEA) to estimate tibia metaphyseal stiffness and failure load under axial compression. In this method, each voxel in the HRpQCT image is converted to a linear