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Bone Density, Microarchitecture and Strength Estimates in White versus African American Youth with Obesity

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Abstract

Background: African Americans (AA) have more favorable bone density and microarchitecture compared to Whites (W), which may explain their observed lower fracture rates. Obesity has deleterious effects on bone microarchitecture and strength estimates and is associated with an increase in fracture risk. Adolescence and young adulthood are periods of active bone accrual and also periods characterized by an increasing prevalence of obesity. The effect of obesity on the relationship between race and bone parameters remains unclear, particularly in youth.

Objective: To assess differences in BMD, bone microarchitecture and strength estimates in AA and W adolescents and young adults with moderate to severe obesity. We hypothesized that racial differences in bone endpoints in lean youth would also be noted in youth with moderate to severe obesity.

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CRediT author statement

Dr. Karen Campoverde Reyes and Dr. Fatima Cody Stanford contributed equally to all aspects of this manuscript and should be considered co-first authors. Dr. Campoverde Reyes contributed significantly to validation, formal analysis, Data Curation, Writing-Original Draft and writing-review editing. Dr. Stanford contributed to all aspects of conceptualization, investigation, resources, writing-Review & Editing, visualization and supervision. Dr. Singhal contributed to conceptualization, methodology, visualization, and investigation. Abisayo O. Animashaun, Amita Bose, and Elizabeth L. Gleeson contributed to investigation, data curation, and project administration. Dr. Madhusmita Misra and Dr. Miriam Bredella contributed equally to conceptualization, methodology, visualization, supervision, Writing-Review & Editing, and funding acquisition of this manuscript. Dr. Misra also contributed in Writing-Original draft and formal analysis. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Massachusetts General Hospital Executive Committee on Research or the National Institutes of Health. *Denotes First Author

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Methods: We evaluated 24 AA and 48 W adolescent and young adults with a mean age of 18.2±2.4 years and a median body mass index (BMI) of 44.8 (40.5–49.4) kg/m² who underwent dual energy X-ray absorptiometry (DXA), high resolution peripheral quantitative computed tomography (HRpQCT), extended cortical analysis (ECA) and micro-finite element analysis (FEA) to obtain measures of volumetric bone mineral density (vBMD), bone geometry, microarchitecture, and strength estimates at the distal radius and tibia.

Results: We found no differences between AA and W for total fat and lean mass, and areal BMD Z-scores (p>0.05 for all). At the distal radius, no significant differences were detected in vBMD, bone geometry or microarchitecture (p>0.05 for all); however, stiffness and failure load were higher in the AA group (p=0.031 and 0.047 respectively). At the distal tibia, cortical vBMD was higher in AA vs. W (p=0.012), while trabecular number was higher and trabecular separation lower in W vs. AA (p 0.028). Stiffness and failure load trended higher in AA vs. W (p=0.052 and p=0.048, respectively). Groups did not differ for any other bone parameter (p>0.05).

Conclusion: Racial differences in bone endpoints appear to be less marked in those with moderate to severe obesity, suggesting that effects of obesity may blunt the effect of race on bone endpoints.

Keywords

children; adolescents; young adults; overweight; obesity; bone density; microarchitecture; bone strength

1. Introduction

Obesity is a serious chronic disease which affects up to 26% of the pediatric population in the United States [1]. Adolescence and young adulthood are critical periods for bone growth and peak bone mass achievement [2], and multiple variables, such as sex, race/ethnicity, nutritional status, physical activity, and pubertal stage influence bone mineral density (BMD), bone microarchitecture and strength estimates in the pediatric population [3–7].

Race has an important influence on bone mass, microarchitecture and estimated strength [5–8]. Cumulative evidence suggests that African Americans have lower rates of fractures compared to Whites [6, 7]. Higher BMD along with more favorable bone microarchitecture may explain this observation. Our studies and those of others have demonstrated that normal-weight African Americans have higher cortical perimeter, cortical area and trabecular thickness, lower cortical porosity, and higher total and trabecular volumetric BMD (vBMD) compared to Whites at the distal radius and tibia. They also demonstrate greater estimated bone stiffness and failure load at the distal radius and tibia [6–8]. Most importantly, these differences appear to be established by adolescence and young adulthood [7], though differences at the distal radius appear to be impacted in adults [6, 8]. However, the effect of moderate to severe obesity on the relationship between race and BMD, bone microarchitecture and strength remains unclear, particularly in youth.

The objective of this study was to assess differences in BMD, bone microarchitecture and strength estimates in African American and White adolescents and young adults with

moderate to severe obesity. Our hypothesis was that reported racial differences in bone endpoints in lean adolescents would also be noted in youth with moderate to severe obesity.

2. Methods

In this cross-sectional analysis of 72 adolescents and young adults with obesity between the ages of 13-24 years with moderate to severe obesity, data were collected from the baseline visit an ongoing observational study at Massachusetts General Hospital (MGH) examining bone outcomes following bariatric surgery. Inclusion criteria thus included a body mass index of 35 kg/m^2 (moderate obesity) and at least one obesity related complication or a BMI 40 (severe obesity) kg/m² (per guidelines from the American Society of Metabolic and Bariatric Surgery). Exclusion criteria included pregnancy or breastfeeding in females and the use of medications that can affect bone metabolism such as glucocorticoids. Hormonal contraception and calcium and vitamin D supplements were permitted given their widespread use in this population to ensure that our sample was representative of youth with obesity in this age range. Participants were weighed in a hospital gown on a calibrated electronic scale by our Clinical Research Center dietitians. Height was measured in triplicate using the same wall mounted stadiometer each time. BMI was calculated using the formula: weight $(kg) / height^2 (m^2)$. All participants had a bone age, assessed by the methods of Greulich and Pyle, of at least 15 years if female or at least 17 years if male (thus growth was mostly complete). Data were collected for self-reported race, physical activity hours per week, and history of tobacco and alcohol use. The type of physical activity (aerobic vs resistance) was also self-reported at the initial clinical evaluation of the participants. The Institutional Review Board (IRB) of Partners HealthCare approved this study. Written informed consent was obtained from each participant when 18 years old, or the parent if the participant was younger than 18 years old, in which case informed assent was obtained from the participant. This study is Health Insurance Portability and Accountability Act (HIPAA) compliant.

2.1 Dual-energy-X-ray-absorptiometry (DXA)

DXA (Hologic 4500, Hologic Inc., Waltham, MA) was used to measure bone mineral content (BMC) and areal BMD (aBMD) at the hip, spine, femoral neck, as well as body composition (fat and lean mass), and Z-scores were generated from a race-specific normative database based on age and sex. The same scanner was used for all subjects.

2.2 High Resolution Peripheral Quantitative Computed Tomography (HRpQCT)

HRpQCT (XtremeCT; Scanco Medical AG, Basserdorf, Siwtzerland) produces images with an isotropic voxel size of 82 μ m [9], allowing for the measurement of volumetric BMD (vBMD), bone geometry and microstructure in cortical and trabecular compartments. This was performed at the distal radius and distal tibia; these fixed sites were selected because linear growth was mostly achieved in our study participants (girls had a bone age 15 and boys 17). The non-dominant wrist and leg were scanned, unless a positive fracture history was reported, in which case, the contralateral extremity was used. Extended cortical analysis was used to assess cortical pore characteristics. HRpQCT assessment was not available in 14 participants each at the distal radius and distal tibia, either because of non-availability of the

scanner on the day of the study, or image degradation from significant motion in the scanner or the size limitation of the scanner.

2.3 Micro-finite element analysis (µFEA)

 μ FEA estimates the biomechanical properties of bone in the setting of simulated axial compression. Finite element software (Scanco Medical AG) was used to estimate bone stiffness (kN/m) and failure load (kN).

2.4 Statistical Methods

JMP software (SAS institute, Carey, NC) was used for statistical analyses; data are reported as means \pm standard deviation when normally distributed, or as median and interquartile range (IQR) for non-normal distributions. The Shapiro-Wilk test for normality was performed for continuous variables. Categorical variables, such as race and gender, were summarized using percentages and compared using Pearson's chi-squared test (χ 2). For the unadjusted univariate analyses of clinical characteristics and bone parameters the Student ttest was performed. For data not normally distributed, the Wilcoxon test was used. All bone parameters were adjusted for height and sex in multivariable regression as these have a direct impact on DXA and HRpQCT measures (p values from this analysis are reported in the abstract and text).

3. Results

3.1 Clinical Characteristics

Data of 24 African American (20 females and 4 males) and 48 White (40 female and 8 males) adolescents and young adults with obesity were analyzed. A summary of their clinical characteristics is presented in Table 1. No significant differences were noted between the two racial groups in age, sex, height, weight, BMI, fat and lean mass, physical activity hours, the type of physical activity (aerobic or resistance), use of hormonal contraception, 25(OH) vitamin D levels, vitamin D and calcium intake, tobacco and alcohol use. Vitamin D and calcium supplementation was reported in 92% of African Americans and 81% of Whites.

3.2 Areal Bone Mineral Density

Table 2 shows aBMD measures for study participants. We found no difference between African Americans and Whites for BMD Z-scores of the femoral neck, total hip, lumbar spine and whole-body (p>0.05 for all), though whole-body BMD Z-score trended higher in African Americans (p=0.081). Our findings were overall similar for females alone (Supplemental Table 2).

3.3. Volumetric Bone Mineral Density, Bone Geometry, Microarchitecture and Strength Estimates

Table 3 shows data from HRpQCT, ECA and µFEA. At the non-weight bearing distal radius, no significant differences were detected in total, cortical and trabecular vBMD, cortical and trabecular cross-sectional area, cortical thickness, or any component of trabecular

microarchitecture (p>0.05 for all). African Americans had higher total area (p=0.049) and trended to have higher pore diameter than White participants (p=0.074). Stiffness and failure load were higher in the African American group (p=0.031 and 0.047 respectively). In females alone, overall findings were similar, except that trabecular area was higher in African Americans (0.02) (Supplemental Table 3).

At the weight-bearing distal tibia, cortical vBMD was higher in African Americans (p=0.012), with no difference in total and trabecular vBMD (p>0.05 for both). Groups did not differ for total, cortical or trabecular cross-sectional area, cortical thickness or porosity (p>0.05 for all). Whites had higher trabecular number and lower trabecular separation (p=0.028 and 0.027 respectively). Stiffness by μ FEA trended higher in African Americans (p=0.052); failure load was higher in African Americans (p=0.048). When females were considered alone, the only differences were that African Americans had higher total and trabecular area than Whites (0.018 and 0.028), and the difference for failure load across groups became a trend (p=0.061).

Within females, adjusting for use of hormonal contraception (in addition to height) did not change our results at the distal radius or tibia.

4. Discussion

We demonstrate that many differences in bone components that usually confer the lower risk of fracture observed in African Americans compared to Whites[6–8] are either no longer evident or are blunted in the context of moderate/severe obesity. Most bone geometry, microarchitecture and density parameters that are typically higher in African American adolescents and adults compared to Whites, such as cortical area, trabecular thickness, total and trabecular vBMD, as well as aBMD Z-scores [6, 7] did not significantly differ between African Americans and Whites in our participants with obesity.

On HRpQCT analyses, African Americans with obesity did have higher cortical vBMD at the distal tibia compared to Whites with obesity, but not at the distal radius. In fact, this was the only HRpQCT bone parameter noted to be more robust in African Americans than in Whites in the current study (other than total area, which was higher in African Americans than Whites at both sites). We speculate that higher cortical vBMD in African Americans at the distal tibia (but not the distal radius) likely reflects lower cortical porosity in African Americans at this site, which was not observed for the radius. The cause for this trend for lower cortical porosity at the distal tibia, but not the distal radius, in African Americans merits further investigation. In contrast, at the tibia, African Americans compared to Whites had lower trabecular number and higher trabecular separation; these findings were not observed at the distal radius.

Strength estimates are impacted by bone vBMD, geometry, and microarchitecture, and small differences between groups in these endpoints might together contribute to a significant impact on bone strength. Failure load was higher in African Americans than Whites at both the distal radius and the distal tibia, while bone stiffness was higher at the distal radius and trended higher at the distal tibia after controlling for height and sex. The fact that strength

estimates were higher in African Americans than Whites at the radius, but only trended higher at the tibia (particularly within females) may reflect (i) the lower trabecular number and higher trabecular separation at the tibia in African Americans than Whites contributing to less marked differences in bone strength estimates across groups at this site (despite higher cortical vBMD), or (ii) insufficient power to detect this difference at the tibia.

Overall, these data suggest that racial differences in bone endpoints are less marked in those with moderate to severe obesity, suggesting that effects of obesity may blunt the effect of race on bone endpoints. Whether this translates to a reduction in the assumed protection against fractures in African Americans vs. Whites with obesity compared to those without obesity remains to be determined.

Possible mediators of the effect of obesity on bone include fat mass and related hormones. A relationship between body fat, bone mass and microarchitecture has been described in the literature [10–12]. However, whether this relationship is beneficial or harmful in youth with obesity remains controversial [13–19]. Further, adipokines such as leptin and adiponectin, and gut peptides such as ghrelin, GLP-1, and peptide YY, all have effects on bone, and differ in those with obesity versus those with normal weight [20–22]. Studies are necessary to assess the impact of body fat stores, adipokines and gut peptides on bone density, geometry, microarchitecture and strength estimates in youth with obesity.

This study has limitations that include its cross-sectional nature and modest sample size. The overall number of males compared to females in our cohort was small, thus differences contributed by males may have been limited. While our observations are based primarily on a female cohort, results after adjustment for sex and evaluation of females only did not change our conclusions (See Supplemental Tables). Our data provide important information regarding minimal differences between races in bone geometry and microstructure in youth with moderate to severe obesity and present the opportunity for further research to elaborate on these findings.

Conclusions

In conclusion, our data suggest that the advantages in bone parameters that may contribute to reduced fracture risk in African Americans vs. Whites may be lost (or blunted) when they have moderate to severe obesity. The mechanism underlying this effect on bone parameters is unknown and further studies with larger numbers of participants will be required to evaluate bone density, microstructure and strength in adolescents and young adults with moderate to severe obesity to confirm our results.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Areal BMD Z-scores do not differ in African American vs. White youth with obesity
- At the distal radius, volumetric BMD (vBMD) and bone geometry do not differ between the two groups.
- At the distal radius, strength estimates are higher in an American vs. White youth with obesity.
- At the distal tibia, cortical vBMD and strength estimates are higher in African American vs. White youth with obesity.
- Moderate to severe obesity may attenuate the impact of race on bone outcomes in youth.

Table 1:

Clinical characteristics of African American and White adolescents and young adults with moderate to severe obesity

| Characteristics | African American N=24 | White N=48 | p-Value |
|--|-----------------------|--------------------|---------|
| Age (years) | 18.2±2.6 | 18.2±2.4 | 0.885 |
| Sex | | | |
| Male | 4 (16.7 %) | 8 (16.7%) | |
| Female | 20 (83.3%) | 40 (83.3%) | 1.00 |
| Height (cm) | 164.9±8.7 | 166.8±7.5 | 0.355 |
| Weight (kg) | 124.7±21.5 | 127.3±19.8 | 0.611 |
| BMI (kg/m ²) | 42.6 (40.4–49.8) * | 45.0 (40.8–49.2) * | 0.711 |
| Total fat mass (kg) | 55.6 (50.9–68.9) * | 62.5 (54.3–70.0) * | 0.282 |
| Total lean mass (kg) | 65.0±11.0 | 65.1±9.0 | 0.948 |
| Reported physical activity hours per week | 5.0 (0.1–7.2) * | 2.8 (0.8–5.1) * | 0.336 |
| Type of physical activity | | | 0.942 |
| Cardio (%) | 56.5 | 52.1 | |
| Resistance (%) | 8.7 | 6.3 | |
| Both (%) | 13.0 | 16.7 | |
| None (%) | 21.7 | 25.0 | |
| Hormonal contraception (for females only) | | | |
| Estrogen + Progesterone pills or patch (%) | 15.0 | 35.0 | 0.267 |
| Progesterone alone (%) | 15.0 | 12.5 | |
| None (%) | 70.0 | 52.5 | |
| 25(OH) vitamin D (ng/ml) | 23.3±13.0 | 25.4±10.0 | 0.444 |
| Intake of vitamin D/day (mcg) | 3.89±3.51 | 4.14±6.39 | 0.865 |
| Intake of calcium/day (mcg) | 747.8±474.1 | 779.9±459.3 | 0.797 |
| Tobacco use (%) | 8.3 | 6.4 | 0.761 |
| Alcohol use (%) | 25.0 | 31.2 | 0.582 |

Means ± SD;

* Median (interquartile range)

Student t-test was used to compare the two groups when normally distributed. Wilcoxon test was used when at least one of the groups was not normally distributed

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Table 2:

DXA characteristics of African American and White adolescents and young adults with moderate to severe obesity.

| DXA Measures | African American | White | Unadjusted p-value | P-value adjusted for height and sex |
|--|------------------|-----------------|--------------------|-------------------------------------|
| | N = 24 | N = 48 | | |
| Femoral neck aBMD (g/cm ²) | 1.09 ± 0.15 | 1.05 ± 0.10 | 0.147 | 0.059 |
| Femoral neck BMD Z-Score | 1.68 ± 1.53 | 1.58 ± 0.97 | 0.758 | 0.476 |
| Hip aBMD (g/cm ²) | 1.20 ± 0.16 | 1.14 ± 0.12 | 0.108 | 0.044 |
| Hip BMD Z-Score | $1.78{\pm}1.53$ | 1.57 ± 1.08 | 0.508 | 0.267 |
| Lumbar aBMD (g/cm ²) | 1.13 ± 0.11 | 1.13 ± 0.10 | 0.995 | 0.536 |
| Lumbar BMD Z-Score | 1.00 ± 1.15 | $1.20{\pm}0.87$ | 0.396 | 0.698 |
| Whole body aBMD (g/cm ²) | 1.11 ± 0.09 | 1.07 ± 0.07 | 0.029 | 0.008 |
| Whole body BMD Z-Score | $0.20{\pm}1.44$ | -0.16 ± 0.97 | 0.212 | 0.081 |
| Means + SD | | | | |

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Student t-test was used to compare the two groups for unadjusted analysis.

Multivariate regression analyses were used to compare the two groups after adjusting for height and sex

Table 3:

HRpQCT and Micro-FEA in African American and White adolescents and young adults with obesity.

| | African American | White | p-Value | p-Value adjusted for height and sex |
|--|-----------------------|-----------------------------|---------|-------------------------------------|
| Distal Radius | N=20 | N=38 | | |
| Volumetric BMD (vBMD) | | | | |
| Total vBMD (mg HA/cm ³) | 354.8±54.6 | 359.9±69.0 | 0.774 | 0.704 |
| Cortical vBMD (mg HA/cm ³) | 841.7 (804.3–886.9) * | 832.8 (790.4–890.1) * | 086.0 | 0.939 |
| Trabecular vBMD (mg HA/cm ³) | 200.1 ± 34.7 | 203.9±36.2 | 0.702 | 0.723 |
| Bone Geometry | | | | |
| Total area (mm ²) | 282.2±53.5 | 267.1±54.9 | 0.319 | 0.049 |
| Cortical area (mm ²) | 62.8 ± 14.5 | 59.1 ± 13.9 | 0.338 | 0.230 |
| Trabecular area (mm ²) | 219.4±54.6 | 208.0±59.6 | 0.480 | 0.175 |
| Cortical thickness (mm) | 1.05 ± 0.17 | 0.98 ± 0.21 | 0.196 | 0.760 |
| Bone Microarchitecture | | | | |
| Cortical pore volume (mm ³) | 9.01 (4.57–11.22) * | 7.05 (4.51–11.73) * | 0.556 | 0.181 |
| Cortical porosity (%) | 1.54 (0.79–1.95) * | 1.15 (0.94–1.79) * | 0.806 | 0.473 |
| Cortical pore diameter (mm) | 0.15 (0.14–0.16) * | $0.14\ (0.14{-}0.15)\ ^{*}$ | 0.022 | 0.074 |
| Trabecular number (1/mm) | 2.19 ± 0.29 | 2.26±0.27 | 0.375 | 0.356 |
| Trabecular thickness (mm) | 0.08 ± 0.01 | 0.08 ± 0.01 | 0.768 | 0.749 |
| Trabecular separation (mm) | 0.39 ± 0.06 | 0.37 ± 0.06 | 0.366 | 0.362 |
| Strength Estimates | | | | |
| Stiffness (kN/mm) | 94.5±17.8 | 87.1±16.1 | 0.116 | 0.031 |
| Failure load (kN) | $4.74{\pm}0.87$ | 4.42 ± 0.81 | 0.172 | 0.047 |
| | | | | |
| Distal Tibia | N=17 | N=41 | | |
| Volumetric BMD (vBMD) | | | | |
| Total vBMD (mg HA/cm ³) | 351.0 ± 39.8 | 356.5±55.3 | 0.712 | 0.669 |
| Cortical vBMD (mg HA/cm ³) | 888.3 (868.7–910.1) * | 875.9 (846.9–888.3) * | 0.028 | 0.012 |
| Trabecular vBMD (mg HA/cm ³) | 212.2±33.5 | 223.0±29.8 | 0.232 | 0.291 |

| one Geometry | | | | |
|---|-----------------------------|---------------------------|-------|-------|
| otal area (mm²) | 759.2 ± 110.4 | 727.7 ± 131.8 | 0.381 | 0.160 |
| Cortical Area (mm ²) | 152.2±29.3 | 143.9 ± 29.1 | 0.259 | 0.317 |
| Trabecular Area (mm ²) | 607.7 ± 108.1 | 583.8 ± 139.4 | 0.530 | 0.306 |
| Cortical thickness (mm) | 1.31 (1.17–1.59) * | 1.31 (1.05–1.48) * | 0.344 | 0.792 |
| one Microarchitecture | | | | |
| Cortical pore volume (mm ³) | 38.6 ± 31.1 | 42.5±27.6 | 0.637 | 0.597 |
| Cortical porosity (%) | $2.94{\pm}1.87$ | $3.57{\pm}1.95$ | 0.247 | 0.172 |
| Cortical pore diameter (mm) | 0.15 (0.14–0.16) * | 0.14 (0.14–0.15) | 0.116 | 0.273 |
| Trabecular Number (1/mm) | 2.52 (2.16–2.66) * | 2.60 (2.38–2.82) * | 0.064 | 0.028 |
| Trabecular Thickness (mm) | 0.07 (0.07–0.09) * | $0.07\ (0.07-0.08)\ ^{*}$ | 0.365 | 0.216 |
| Trabecular Separation (mm) | $0.33\ (0.31{-}0.39)\ ^{*}$ | 0.31 (0.29–0.36) * | 0.076 | 0.027 |
| trength Estimates | | | | |
| Stiffness (N/mm) | 264.2±39.9 | 248.8 ± 32.1 | 0.120 | 0.052 |
| Failure load (N) | 13.4 ± 2.0 | 12.6±1.6 | 0.132 | 0.048 |

Means \pm SD;

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* Median (interquartile range) For unadjusted analysis, the Student t-test was used to compare the two groups when data were normally distributed, and the Wilcoxon test was used when at least one of the groups was not normally distributed

Multivariate regression analyses were used to compare groups after adjusting for height and sex