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Males Have Larger Skeletal Size and Bone Mass Than Females, Despite Comparable Body Size

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ABSTRACT: Gender differences in fractures may be related to body size, bone size, geometry, or density. We studied this in 18-year-old males (n = 36) and females (n = 36) matched for height and weight. Despite comparable body size, males have greater BMC and BMD at the hip and distal tibia and greater tibial cortical thickness. This may confer greater skeletal integrity in males.

Introduction: Gender differences in fractures may be related to body size, bone size, geometry, or density. We studied this in males (n = 36) and females (n = 36; mean age = 18 years) pair-matched for height and weight.
Materials and Methods: BMC, bone area (BA), and BMD were measured in the spine and hip using DXA. Distal tibia was measured by pQCT.
Results and Conclusions: Males had a higher lean mass (92%) compared with females (79%). No gender differences were observed for vertebral BMC or vertebral height, although males had greater width and thus BA at the spine. Males had greater BMC and BA at the femoral neck and total femur ($p < 0.02$). Geometric variables of the hip including neck diameter and neck-axis length were also greater in males ($p < 0.02$). There was greater cross-sectional moment of inertia, safety factor, and fall index in males (all $p < 0.02$). Males had greater tibial BMC, volumetric BMD, and cortical area and thickness compared with females ($p < 0.01$), with both greater periosteal circumference ($p = 0.011$) and smaller endosteal circumference ($p = 0.058$). Statistically controlling for lean mass reduced gender differences, but males still had 8% higher hip BMD ($p = 0.24$) and 5.3% higher total tibial BMD ($p = 0.05$). A subset of males and females were matched (n = 14 pairs) for total hip BA. Males in this subset still had greater BMC and BMD at the total hip ($p < 0.05$) than females, despite similar BA. In summary, despite comparable body size, males have greater BMC and BMD than females at the hip and distal tibia but not at the spine. Differences in BMC and BMD were related to greater cortical thickness in the tibia. We conclude that differences in bone mass and geometry confer greater skeletal integrity in males, which may contribute to the lower incidence of stress and osteoporotic fractures in males.
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Key words: bone mass, bone size, gender, DXA, pQCT

INTRODUCTION

Stress fractures are far more common in female military cadets (3.4–21%) than in their male counterparts (0.9–5.2%).[1] Gender-related differences in osteoporosis-related fracture rates are also well known in older adults.[2–9] These differences in gender-related fracture rates have often been attributed to higher BMD in men than women.[9–10] Whereas it is plausible that differences in BMD may, in part, explain gender-related differences in fracture rates, it is also possible that differences in both BMD and fracture rates may be attributed to differences in body size, bone size, and bone geometry.[11–14] The geometry and structure of bone have been increasingly recognized as important risk factors for fracture. Women, with a naturally smaller skeleton, may also incur greater microarchitectural damage than men and adapt less effectively by periosteal apposition,[15] the latter contributing to gender differences in bone geometry.

The role of puberty in determining gender differences in bone size and mass is still being assessed. It is known that, before puberty in both sexes, the length and width of bone increase progressively. Because boys enter puberty about 2 years later than girls, they can acquire greater long bone length before puberty.[15,16] However, in prepubertal boys and girls, matched for age, height, and weight, cross-sectional area of the midshaft of the femur and cortical bone area measured by CT were similar.[17] Gender-related differences in bone width are more apparent after puberty. For example, periosteal growth, which enlarges bone diameter, accelerates at puberty in males. However, in females, periosteal growth is inhibited by estrogen at puberty, and thereafter, cortical thickness only changes by apposition of endocortical bone.[15,18] Long bone cross-sectional growth

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is also strongly driven by mechanical load associated with increased weight during growth.[19] Gender differences in proximal radius cortical thickness also seem to emerge after puberty (age > 15 years) based on pQCT, with cortical thickness in males exceeding that of females.[20]

Both hormones and nutrition influence the mechanical load on growing bone by acting on longitudinal bone growth and muscle mass. Hormones and nutrition may also alter the mechanostat set-point. When mechanical challenges exceed an acceptable level (the mechanostat set-point), bone tissue will be added to the location where it is mechanically needed,[21,22] and it is possible that these forces and the resulting effect on bone quality may be gender specific.

In an evaluation of the lumbar spine by QCT, females tended to have higher density values before puberty, with a cross-over to higher vertebral density in males in later decades.[23–25] Vertebral volumetric BMD, both trabecular and cortical, has been shown to be similar in younger males and females.[14,26,27] The greater vertebral bone strength measured in males may be a result of gender differences in vertebral width, area, and volume, not bone tissue density per se,[27,28] and vertebral size may be an important determinant of resistance to fracture in adults.[13,28–31]

In a recent analysis of NHANES data, it was found that body size had a major influence on the magnitude of gender differences in femur BMD and geometry.[32] In that analysis, statistical correction for differences in height and weight removed femur BMD differences but not geometric differences (subperiosteal width, section modulus, and cortical thickness) between the genders in young adults. However, in older adults from NHANES, the gender differences in BMD and bone geometry persisted even after statistical body size correction. Males tend to have larger bone volume and larger cross-sectional area than females, even after taking body size into account in some studies.[17,28] Several other studies have reported that, when both adults and children are matched for body size, many of the reported gender-related differences in bone mass disappear.[33–36] Body composition (percent lean mass and percent fat mass) rather than body size alone may also play a role in determining gender differences in bone mass, size, and geometry, although this may also have a genetic determinant.[37]

In this study, we sought to examine the gender-related differences in axial and appendicular bone mass, size, geometry, and biomechanical competence and their relationships with body composition in adolescent elite military cadets matched for body size.

MATERIALS AND METHODS

We studied a group of healthy, fit, adolescent white males ($n = 36$) and females ($n = 36$) with a mean age of 18 years recruited from the United States Military Academy, West Point, NY. The Keller Army Hospital Institutional Review Board approved this study, and all volunteers provided informed consent. These subjects are a subset of a larger cohort study of factors relating to peak bone mass and stress fracture risk in >850 military cadets. Each female cadet was pair-matched with a male cadet for height within 1 in and weight within 5 lb. Height and weight were determined at the time of the entry fitness test taken by each cadet. Subjects completed a baseline questionnaire including questions about exercise (number of hours per week) and glasses of milk consumed per day during the year before entry to the academy.

Axial measurements were performed by DXA using the Lunar DPX-IQ (GE-Lunar, Madison, WI, USA) in a mobile unit. Lumbar spine measurements included bone size in centimeters (vertebral height, width, and area), BMC (g), and areal BMD (aBMD; g/cm^2). Proximal femur measurements included bone size (area), BMD (g), and aBMD (g/cm^2) at the femoral neck, trochanter, shaft, and total proximal femur. Geometric parameters and strength indices were derived from these measurements using the methodology of Yoshikawa et al.[38] Variables of interest included distance (d_2) from the center of the femoral head to the neck axis–shaft axis intersection; distance from the center of mass to the superior neck margin (y); neck diameter; and neck cross-sectional area. The following hip strength parameters were also calculated: the cross-sectional moment of inertia (CSMI); the safety factor (a derived index of the strength of the femoral neck during walking); and the fall index, a derived index of the strength of the femoral neck during a fall.

The distal one-third of the tibia was determined by a manual measurement of tibial length between the base of the patella and the styloid process to the closest 0.5 centimeter. The tibia was chosen because it is a major site of stress fractures in military cadets. pQCT (Stratec XCT-2000) was used to image a single slice at the one-third distal tibia. The one-third site is located by the pQCT after placing the positioning light of the gantry above the styloid process. Bone area (mm^2), BMC (mg/1-mm slice of bone), BMD (mg/cm^3), cortical area (mm^2), cortical thickness (mm), and periosteal and endosteal circumferences (mm) were measured. Cortical bone was identified at a threshold >710 mg/cm^3. Cortical thickness was derived using the circular ring model, which calculates a mean cortical thickness from measures of total bone area and cortical bone area. Several geometric parameters relating to the cortical shell were calculated, including the axial moment of inertia of the cortical area, moment of resistance, polar moment of inertia of the cortical bone area, and the strength-strain index. Further analysis of pQCT data was performed to determine the total limb area and muscle area for the region of the distal one-third of the tibia.

Body composition was determined by bioelectrical impedance to determine lean mass (%) and fat mass (%) for the total body. In addition, percent fat and percent lean mass were determined by DXA for soft tissue overlying the spine and femur.

All data were analyzed with SAS software. Values of each bone parameter were compared in the males versus the females with paired *t*-tests. Measurements of total body lean and fat masses, as well as regional measurements of muscle, were correlated with bone parameters using Pearson correlation. Analysis of covariance was used to determine the influence of gender on bone size and geometry after controlling for lean mass.

TABLE 1. DEMOGRAPHIC VARIABLES FOR MALE AND FEMALE CADETS (MEAN ± SE AND RANGE)

	Females	*Males*
Age (years)	18 ± 0.14 (17–21)	18.5 ± 0.17 (17–21)
Height (cm)	173.6 ± 0.9 (160–188)	173.7 ± 1.0 (160–188)
Weight (kg)	69.0 ± 1.1 (56.2–83.9)	69.1 ± 1.1 (56.3–83.9)
BMI (kg/m^2)	22.9 ± 0.3 (19.4–25.8)	22.9 ± 0.3 (19.4–25.9)
Lean mass (%)	79.1 ± 0.5 (72.7–84.0)*	91.4 ± 0.5 (84–96.1)
Fat mass (%)	20.9 ± 0.5 (16.0–27.3)*	8.6 ± 0.5 (3.9–16.0)

* $p < 0.01$.

RESULTS

The males and females were closely matched for both height and weight (Table 1). The males were ~6 months older. The mean BMI was 22.9 kg/m^2 in both males and females, but the percent lean mass by bioelectric impedance was higher in males (Table 1). The average level of reported exercise (9 h/week) and the average milk intake (3 cups/day) over the year before this study were similar in both groups.

Vertebrae

Vertebral height was similar in the two groups; however, vertebral width, and therefore vertebral area, was greater in males than females (Table 2). BMC was similar in males and females; consequently, the females had a greater BMD at the spine than the males (1.323 ± 0.026 versus 1.266 ± 0.017 g/cm^2, $p < 0.06$), a difference that approached statistical significance.

Hip

At the hip, males had significantly greater bone area, BMC, and BMD in each region, including the femoral neck, trochanter, and total hip, as well as at the femoral shaft (Table 2). These differences all met or approached statistical significance. Results for the geometric variables are shown in Table 3. Males had a longer neck axis length (d_2), wider neck diameter, greater distance from the center of mass to the superior neck margin as measured for the section of minimum CSMI, and greater femoral neck cross-sectional area than the females (all $p < 0.02$). In addition, hip strength analyses based on the derived indices showed that the CSMI, safety factor, and fall index were all greater in males than females (Table 3). Even in women, however, safety factor and fall index were above average peak normal values (peak safety factor, 5.5; peak fall index, 1.5).

To determine whether hip BMD and strength index results were related to a true gender difference or simply a difference in bone size, 14 males and 14 females were further matched for total hip bone area (in addition to having been first matched for height and weight). Although the two groups were matched for total hip area, the gender differences in BMC, and thus BMD, persisted in the total hip (Fig. 1). Similar results were found at the femoral neck, trochanteric region, and femoral shaft, where males had significantly greater BMC and BMD at each of these hip regions compared with females matched for hip area (data not shown). In these 14 hip area–matched pairs, there was no significant differences in lumbar spine BMD, BMC, area, or vertebral height. Vertebral width was still greater in males compared with females, although the difference was no longer significant ($p = 0.30$).

TABLE 2. BMD OF THE LUMBAR SPINE AND HIP IN SIZE-MATCHED MALE AND FEMALE CADETS (MEAN ± SE)

Skeletal region	*Females*	*Males*	*Difference* (p *value*)
Lumbar spine (L_2–L_4)			
Vertebral height (cm)	10.51 ± 0.07	10.43 ± 0.08	0.41
Vertebral width (cm)	4.32 ± 0.05	4.51 ± 0.047	0.003
BMC (g)	59.56 ± 1.71	59.72 ± 1.35	0.93
Area (cm^2)	45.41 ± 0.71	47.09 ± 0.68	0.027
BMD (g/cm^2)	1.323 ± 0.026	1.266 ± 0.017	0.063
Femoral neck			
BMC (g)	5.70 ± 0.14	6.31 ± 0.14	0.001
Area (cm^2)	4.73 ± 0.05	4.94 ± 0.55	0.008
BMD (g/cm^2)	1.203 ± 0.023	1.279 ± 0.026	0.031
Femoral trochanter			
BMC (g)	12.77 ± 0.43	16.22 ± 0.50	0.001
Area (cm^2)	13.31 ± 0.29	15.01 ± 0.28	0.001
BMD (g/cm^2)	0.957 ± 0.020	1.075 ± 0.023	0.001
Femoral shaft			
BMC (g)	19.50 ± 0.41	21.43 ± 0.42	0.001
Area (cm^2)	14.17 ± 0.13	14.54 ± 0.18	0.078
BMD (g/cm^2)	1.377 ± 0.027	1.479 ± 0.029	0.019
Total proximal femur			
BMC (g)	37.97 ± 0.90	43.96 ± 0.97	0.001
Area (cm^2)	31.91 ± 0.46	34.53 ± 0.39	0.001
BMD (g/cm^2)	1.194 ± 0.026	1.273 ± 0.025	0.051

TABLE 3. GEOMETRIC VARIABLES OF THE HIP (MEAN ± SE)

	Female	*Male*	p *Value*
d_2	51.5 ± 0.72	53.8 ± 0.76	0.017
Neck diameter (mm)	33.1 ± 0.33	34.4 ± 0.38	0.002
y (mm)	16.2 ± 0.19	17.0 ± 0.26	0.001
Neck cross-sectional area (mm^2)	213.1 ± 5.00	235.6 ± 4.7	0.001
Cross-sectional moment of inertia (mm^4)	14892 ± 581	18032 ± 611	0.001
Safety factor	6.43 ± 0.31	7.48 ± 0.26	0.019
Fall index	1.89 ± 0.07	2.14 ± 0.06	0.011

d_2, distance from center of the femoral head to the neck axis–shaft axis intersection; *y*, distance from the center of mass to the superior neck margin for the section of minimum CSMI.

Tibia

Tibial length did not differ between males and females, as shown in Table 4; however, total bone area was greater in males compared with females ($p = 0.01$). Males also had significantly greater BMC and greater volumetric BMD than females. In addition, tibial cortical area, cortical BMC, and cortical thickness were significantly greater in males compared with females. This difference in the cortical thickness was reflected in the greater periosteal circumference ($p = 0.01$) and smaller endosteal circumference ($p =$

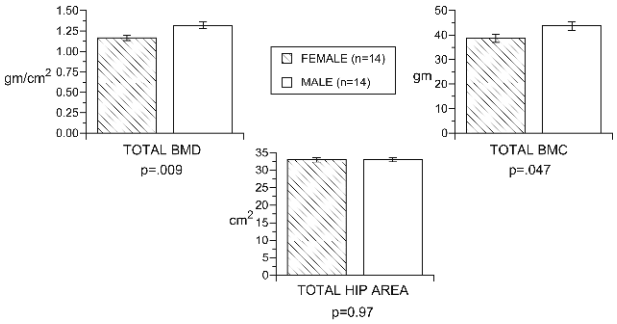

FIG. 1. Hip bone mass and BMD in a subset of male ($n = 14$) and female ($n = 14$) cadets matched for total hip area. Total BMD is shown in grams per centimeter squared, total BMC is shown in grams, and total hip area is shown in centimeters squared.

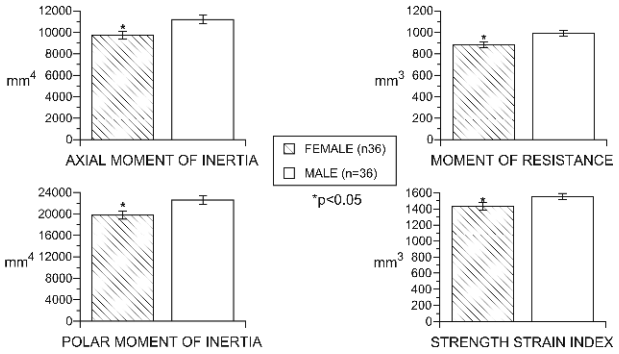

FIG. 2. Tibial strength analysis comparing males ($n = 36$) and females ($n = 36$) for axial moment of inertia (mm^4); polar moment of inertia (mm^4); moment of resistance (mm^3); and strength strain index (mm^3).

TABLE 4. PROXIMAL TIBIA ANALYSIS BY pQCT (MEAN ± SE)

	Female	*Male*	p *Value*
Length (mm)*	405.0 ± 4.1	401.9 ± 3.4	NS
BMC (mg/mm)	298.0 ± 6.26	336.6 ± 6.3	0.001
BMD (mg/cm^3)	794.3 ± 12.8	850.1 ± 14.1	0.004
Total bone area (mm^2)	377.1 ± 8.1	398.1 ± 7.3	0.011
Cortical area (mm^2)	237.1 ± 5.1	273.6 ± 5.3	0.001
Cortical content (mg)	273.8 ± 6.04	313.6 ± 6.29	0.001
Cortical thickness (mm)	4.32 ± 0.09	5.02 ± 0.11	0.001
Periosteal circumference (mm)	68.7 ± 0.75	70.6 ± 0.67	0.011
Endosteal circumference (mm)	41.6 ± 0.96	39.1 ± 1.00	0.058
Fat mass area (mm^2)	2311.4 ± 80.7	1546.5 ± 60.9	0.001
Muscle mass area (mm^2)	2487.5 ± 60.6	2896.1 ± 68.1	0.001
Percent fat (%)	44.5 ± 0.9	31.6 ± 0.9	0.001

* Measured by investigator.
NS, not significant.

0.058) in the males. As shown in Fig. 2, tibial strength analysis using pQCT results indicated that males have greater tibial strength than size-matched females. Gender-specific geometric differences resulted in greater axial moment of inertia, greater moment of resistance, greater polar moment of inertia, and a greater strength-strain index in the males than in the females (all $p < 0.05$).

Body composition

As shown in Table 1, total body lean mass was significantly greater in males than in females, and correspondingly, fat mass was greater in females. There were no significant correlations between total body lean mass and vertebral BMD, femoral neck BMD, or total hip BMD by gender in this population, perhaps related to the small sample size and limited range of lean and fat mass in this study.

Males had greater muscle mass ($p < 0.01$) and lower fat mass ($p < 0.01$) than females at the distal tibia site as well. Total body percent lean mass correlated with measurements of muscle area and bone area at the tibia as measured by pQCT. Furthermore, muscle area of the tibia was highly correlated with tibia BMC ($r = 0.67$, $p < 0.001$); total bone area ($r = 0.502$; $p < 0.001$); cortical content ($r = 0.664$, $p < 0.0001$), and cortical thickness ($r = 0.502$; $p < 0.001$) and was modestly correlated with total tibia density ($r = 0.280$, $p < 0.017$) and periosteal circumference ($r = 0.38$, $p < 0.001$).. After correction for tibia muscle area, gender differences in tibia BMD were still evident, with males having 5.3% greater total tibial BMD than females ($p = 0.05$).

The percent fat determination in the lumbar spine and total hip area from DXA was significantly greater in females compared with males, particularly in the hip region, where there was almost 3-fold greater hip fat in females. There was also greater variability in female (%) fat than in male (%) fat (vertebral fat: females = 6.64 ± 3.1%; males = 4.2 ± 0.6%; hip fat: females = 14.2 ± 3.1%; males = 5.2 ± 1.0%; $p < 0.001$). These regional measurements of percent fat and percent lean determined by DXA, however, were not correlated with the BMD at the corresponding skeletal site. There was still an 8% higher hip BMD in males compared with females, although the difference was no longer significant ($p = 0.24$) after controlling for regional lean mass.

DISCUSSION

We found that gender differences in skeletal size and BMD persist at most skeletal sites even after matching for body size. These differences seem to relate to differences in the width of bone, but not length of the long bones or height of the vertebrae, as expected in a height-matched population. In the vertebral bodies, although males had lower aBMD, the significantly greater vertebral width found in males might confer greater biomechanical competence. This larger cross-sectional area in male vertebral bodies has also been reported even after taking size into account.[17]

Males were reported to have 12–13% greater hip BMD than females in the NHANES data.[10] In a recent size-adjusted analysis of NHANES data, the femoral neck difference between makes and females was 3% after adjusting

for height and weight.[32] Similarly, in our size-matched population, total hip BMD was 6% higher and femoral neck BMD was 5% higher in males than females. In the NHANES study, geometric differences in young and older adults persisted after correction for height and weight.[32] This is similar to the geometric differences such as longer neck axis length and wider neck diameter noted in our size-matched young adult population. Bone volume differences could partially explain the greater hip BMD in males than females. However, after matching for total hip area, substantial gender differences in hip BMD and BMC were still found. This could be a result of differences in bone shape, resulting in failure to adequately assess volume when using DXA areal measurements. Another possible explanation is that males may have greater cortical thickness at the hip, although the only measurement available by DXA is a greater neck diameter in males than females. In fact, we did show greater cortical thickness in the tibia using pQCT, which can separate cortical bone from the medullary cavity. The same may be true for the hip, although it cannot be accurately assessed by DXA.

In the tibia, the thicker cortical shell result is evidenced by a larger periosteal circumference and smaller endosteal circumference in males. Tibial BMD and bone area were reported to be larger in males 20–39 years of age compared with females in an Italian study of 1205 people 20–102 years of age.[39] In our study population, gender differences persisted even after matching for height and weight. The difference in cortical thickness is of clinical importance, because the thickness of the cortex and total bone width are the primary determinants of bone strength. Several studies of hip fracture patients found than nonfractured controls had greater cortical thickness than the fracture patients.[40–45] A thicker cortical shell might also help explain the gender-related differences in stress fracture rates seen in military cadets,[46] especially tibial stress fractures. The derived indices of bone strength in our study, the higher safety and fall index of the hip, and the strength-strain index of the tibia in males also predict lower anticipated stress fracture and potentially osteoporotic fracture rates of males compared with females. In fact, stress fracture rates in the year after entry into the academy were approximately five times higher in the female cadets than in the male cadets in the military cohort from which this size-matched population was drawn.

In both appendicular sites of the skeleton (hip and tibia), males have greater BMC, BMD, and in the tibia, a greater cortical thickness. This may relate to the greater influence of muscle mass and mechanical stress placed on these skeletal sites compared with the axial site and the potential influence of this on the mechanostat.[22] The axial site measured showed no specific advantage to the male skeleton (lumbar spine BMC or BMD), except a greater vertebral width, although this could also contribute to strength.

It is important to consider the limitations of this study. Models for structure and geometric parameters using DXA are limited by its 2D acquisition plane (of a 3D structure) and inherent technical limitations of DXA, including edge detection resolution, influence of fat mass, and operator error. However, the use of the pQCT in this study enabled us to derive a true 3D measure of bone geometry for the tibia. Second, these data may not be generalizable to all gender differences because we matched larger women to smaller men, making this a select population. In addition, the gender-related differences and similarities noted here might not apply to an older population. Last, gender differences in the age at which peak bone mass is reached might influence these results. There may still be growth in bone occurring in males, whereas it is unlikely that females will still have changes in bone, so we might be comparing different stages in skeletal development, although chronological age was similar. However, in a population of this age, maximal height should have already been achieved in most males and females. Even if bone size has not yet reached a peak, particularly in the males, we are comparing BMD in males and females, who, at this time, are similar in body size and bone size. However, the lower vertebral BMD in men might change as the male cadets continue to achieve peak bone mass. Differences related to age at acquisition of peak bone mass may be clarified when these cadets reach age 22 (the completion of the longitudinal follow-up of this cohort). It is also possible that the greater contribution of the posterior vertebral arch to BMC in females[47,48] could lead to an apparently higher spine BMD in females versus males when measured in the anterior-posterior (AP) projection by DXA. It is also possible that there is a lower trabecular bone volume in males as a result of the larger vertebral size. Unfortunately, we do not have lateral spine measurements to clarify this issue.

Because gender-related BMD differences are only partially corrected when body size differences are eliminated, it is possible that the gender-related differences in both BMD and cortical size are related to the greater proportion of lean mass in males at each skeletal site compared with females, despite similar exercise levels. This is in agreement with several studies where differences in BMD between individuals are strongly related to the lean body mass components.[49–54] In this study, males had a greater percent lean mass in the total body as well as in each skeletal site. Body composition differences may explain some of the gender-related differences in bone mass. Because muscle mass may influence the mechanostat set-point leading to bone quality and size differences, we corrected for muscle area, and males still had a greater tibial density. Although correction for lean mass in this study removed some of the gender-related differences, higher bone density in males was still evident in the hip and tibial regions. Exercise is also known to influence lean mass, as well as bone size and strength.[55–57] The importance of lean mass on bone properties needs further study, as does the potential role of testosterone in causing higher lean mass in males performing at approximately the same level of exercise as the size-matched females.

Mechanical loading determines cortical periosteal and endosteal diameters and the resulting cortical thickness in various animal models.[58–63] Various investigators have shown that physical activity can increase bone circumference at the hip, tibia, and forearm,[64–67] and the type of force as well as other variables may determine the influence of exercise on cortical structure, including whether there is

a periosteal increase or endosteal circumference decease.[64,68–71] One study found that physical activity increased bone circumference, and when combined with higher calcium intake, there was an increase in cortical thickness, possibly because of less endosteal expansion.[64] It is possible that the gender-related differences in bone size are related, in part, to different types of physical activity, dietary forces, or muscle mass acting on bone geometry.

Gender differences in BMD seem to be skeletal site dependent, with appendicular skeletal sites that have a large proportion of cortical bone showing the greatest gender disparity. We conclude that gender-related differences in bone size and mass confer greater skeletal integrity in males, which may contribute to their lower gender-specific stress fracture incidence, and possibly, the lower adult fracture incidence in males. The causes of these gender-related differences in bone size and BMD in males and females of equivalent body size require further study.

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