Hip Structural Analysis in Adolescent Boys With Anorexia Nervosa and Controls

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Context: We have reported lower hip bone mineral density (BMD) in adolescent boys with anorexia nervosa (AN) compared with controls. Although studies have described bone structure in girls with AN, these data are not available for boys. Hip structural analysis (HSA) using dual-energy x-ray absorptiometry is a validated technique to assess hip geometry and strength while avoiding radiation associated with quantitative computed tomography.

Objective: We hypothesized that boys with AN would have impaired hip structure/strength (assessed by HSA) compared with controls.

Design and Setting: We conducted a cross-sectional study at a clinical research center.

Subjects and Intervention: We used HSA techniques on hip dual-energy x-ray absorptiometry scans in 31 previously enrolled boys, 15 with AN and 16 normal-weight controls, 12 to 19 years old.

Results: AN boys had lower body mass index SD score ($P < .0001$), testosterone ($P = .0005$), and estradiol ($P = .006$) than controls. A larger proportion of AN boys had BMD Z-scores <-1 at the femoral neck (60% vs 12.5%, $P = 0008$). Using HSA, at the narrow neck and trochanter region, boys with AN had lower cross-sectional area ($P = .03$, 0.02) and cortical thickness ($P = .02$, 0.03). Buckling ratio at the trochanter region was higher in AN ($P = .008$). After controlling for age and height, subperiosteal width at the femoral shaft, cross-sectional moment of inertia (narrow neck and femoral shaft), and section modulus (all sites) were lower in AN. The strongest associations of HSA measures were observed with lean mass, testosterone, and estradiol. On multivariate analysis, lean mass remained associated with most HSA measures.

Conclusions: Boys with AN have impaired hip geometric parameters, associated with lower lean mass. (***J Clin Endocrinol Metab*** **98: 2952–2958, 2013)**

Anorexia nervosa (AN), a condition characterized by very low weight and an impaired body image, affects 0.2% to 1% of adolescent girls and is associated with marked reductions in bone density and decreased bone accrual rates (1–5). Importantly, although 5% to 15% of all people affected by AN are males, there are very limited data regarding the impact of this disorder on bone biology in males. This limitation is seen most strikingly in understanding the impact of AN during adolescence, a time when bone mass is maximized in normal children. We have previously reported that adolescent boys with AN (similar to girls) have markedly lower bone density measures compared with controls (6). Interestingly, boys differ from girls in the bone sites most severely affected. Bone density is most affected at the lumbar spine (a site of mostly trabecular bone) in girls with AN (4), whereas for boys

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Abbreviations: aBMD, areal bone mineral density; AN, anorexia nervosa; BMI, body mass index; CT, computed tomography; DXA, dual-energy x-ray absorptiometry; HSA, hip structural analysis; QCT, quantitative CT; SDS, SD score.

with AN, low Z-scores are more common at the hip, femoral neck, and trochanteric and intertrochanteric regions (sites of primarily cortical bone) than at the spine (6), raising long-term concerns for hip fractures.

For fracture risk assessment, bone structure and geometry provide information beyond that provided by areal bone mineral density (aBMD) (using dual-energy x-ray absorptiometry [DXA]) (7–9). In girls with AN, we have reported impaired bone trabecular parameters using flat-panel ultra–high-resolution peripheral quantitative computed tomography (CT) (10). This impairment was noted even when aBMD did not differ from controls, indicating that microarchitectural abnormalities may precede abnormal DXA readings. In contrast, there are no data regarding bone structure and geometry in boys with AN. Given that the hip is more affected than the spine in boys, we sought to examine hip structure and geometry in a previously recruited cohort of boys with AN and controls. Quantitative CT (QCT) of the hip is associated with significant radiation exposure, limiting its use in children. We thus used hip structural analysis (HSA) in this study.

HSA derives strength parameters for the hip using properties of DXA images (11). This validated technique allows assessment of hip bone geometry while avoiding radiation associated with QCT at this site. HSA has been shown to correlate very strongly with hip QCT for measures such as cross-sectional area, cross-sectional moment of inertia, and section modulus (12) and to predict hip fractures (13–15). This technique has also been effectively used in large and longitudinal studies in children (16, 17).

We therefore used HSA to define bone geometry at the hip (at the narrow neck, trochanteric region, and femoral shaft) in adolescent boys with AN and normal-weight controls. We hypothesized that boys with AN would have impaired hip geometry and strength estimates compared with controls.

Subjects and Methods

Subject selection

Subjects were enrolled at Massachusetts General Hospital (MGH), Boston, Massachusetts, and the Hospital for Sick Children (SickKids), Toronto, Ontario, Canada. We included 31 subjects (15 boys with AN and 16 normal-weight controls) from 12 to 19 years old in this study. Clinical characteristics of these boys (but not HSA data) have been previously reported (6). Hip scans for 3 subjects included in the original study were not available for HSA. The diagnosis of AN was based on Diagnostic and Statistical Manual of Mental Disorders (DSM IV) criteria. Normal-weight controls were required to have a body mass index (BMI) between the 10th and 90th percentiles, and none of the controls had a present or past history of an eating disorder. Exclusion criteria included other medical conditions that may cause weight loss or impact bone health and use of medications that may affect weight or bone density (except use of calcium and vitamin D supplements). Boys with AN were recruited through referrals from eating disorder providers. Normal-weight controls were recruited through advertisements in pediatricians' offices and local newspapers. The protocol was approved by the Partners HealthCare Institutional Review Board and the Research Ethics Board of SickKids, Toronto. At MGH, informed consent was obtained from boys ≥18 years old and from parents of boys <18 years old. Informed assent was obtained from boys <18 years of age. At SickKids, parental consent was obtained as well as either participant consent or assent based on the subject's capacity to consent, per SickKids Research Ethics Board guidelines.

Experimental protocol

After a screening history and physical examination (including Tanner staging), height was measured on a wall-mounted stadiometer as the average of 3 measurements, and weight was measured on an electronic scale. BMI was calculated according to the following formula: weight in kilograms/(height in meters)^2. A fasting blood sample was drawn for testosterone, estradiol, and IGF-I. The specifics of assays used for these tests have been previously reported (10). IGF-I SD score (SDS) was calculated using normative data for gender and Tanner stage provided by the MGH Core Laboratory that ran the assays. An x-ray of the left wrist and hand was used to assess bone age using the methods of Greulich and Pyle (18). DXA was used to assess body composition (fat mass, lean mass, and percent body fat), aBMD at the total hip, femoral neck, and trochanteric and intertrochanteric regions, and to perform HSA (Hologic QDR-Discovery A, Apex software version 13.3; Hologic Inc, Waltham, Massachusetts). The coefficients of variation for fat mass, lean mass, and total hip BMD measurements are 2.1%, 1%, and 0.8% to 1.1%, respectively, for our institution. Based on a comparison of phantom scans (n = 10 at each site) evaluated for performance across a range of densities for consistency between the MGH and SickKids sites, no adjustments were deemed necessary across sites.

The HSA program analyzes 3 femoral sites and averages information from 5 parallel lines 1 pixel apart across the cross-section of these sites: 1) narrow neck (the narrowest point of the femoral neck), 2) trochanteric region (along the bisector of the angle of the axes of the neck and femoral shaft), and 3) femoral shaft (across the shaft 1.5 cm from the minimum neck width distal to the intersection of the neck and shaft axes). This program provides the following measurements at each site: 1) subperiosteal (outer) diameter, 2) endosteal (inner) diameter, 3) cross-sectional area excluding soft spaces in the marrow and pores (an index of resistance to axial forces), 4) estimated cortical thickness, 5) cross-sectional moment of inertia (estimate of resistance to bending forces in a cross-section), 6) section modulus (index of strength of bending), 7) buckling ratio (index of susceptibility to local cortical buckling under compressive loads, 8) neck shaft angle, and 9) hip axis length (19).

Statistical analysis

We used the JMP program (version 10; SAS Institute, Inc, Cary, North Carolina) for all analyses and report means ± SDs. The Student's *t* test was used to compare means when data were normally distributed, and the Wilcoxon rank-sum test was used to compare data not normally distributed or when a simple transformation did not result in a normal distribution. The Fisher's exact test was used to compare proportions. Associations of HSA parameters with body composition and hormones were tested using Pearson's correlation, and multivariate analysis was used

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Table 1. Clinical Characteristics of Adolescent Boys with AN and Normal-Weight Controls[a]

	AN	Controls	*P* Value
n	15	16	
Age, y	16.01 ± 1.96	15.66 ± 1.86	NS
Bone age, y	16.18 ± 1.57	16.17 ± 2.28	NS
Bone age/chronological age	1.02 ± 0.11	1.03 ± 0.06	NS
Age at diagnosis of anorexia nervosa, y	15.2 ± 1.8		
Duration since diagnosis, months	9.3 ± 14.2		
Testicular size, mL	10.5 ± 6.1	18.7 ± 5.9	**.002**
Tanner stage for pubic hair	4.0 ± 1.5	4.5 ± 0.8	NS
Weight, kg	50.66 ± 9.81	61.99 ± 9.31	**.002**
Weight SDS	−1.02 ± 0.20	0.13 ± 0.19	**.0002**
Height, cm	170.23 ± 10.39	170.56 ± 7.25	NS
Height SDS	−0.14 ± 1.14	0.14 ± 1.25	NS
BMI, kg/m^2	17.27 ± 1.69	21.27 ± 2.71	**<.0001**
BMI SDS	−1.16 ± 0.42	0.09 ± 0.76	**<.0001**
Fat mass, kg	6.95 ± 2.30	9.98 ± 3.49	**.008**
Lean body mass, kg	43.65 ± 8.48	51.27 ± 7.83	**.01**
Percent body fat	13.2 ± 3.6	15.6 ± 4.1	.09
Hip BMD, g/cm^3	0.86 ± 0.14	1.0 ± 0.13	**.006**
Hip BMD Z-score	−1.11 ± 1.00	0.03 ± 0.75	**.001**
Hip BMD Z-score < −1, %	53.3	18.8	**.05**
Femoral Neck BMD, g/cm^3	0.78 ± 0.11	0.90 ± 0.13	**.01**
Femoral Neck BMD Z-score	−1.11 ± 0.84	−0.12 ± 0.86	**.003**
Femoral neck BMD Z-score <−1, %	60.0	12.5	**.009**
Trochanteric BMD, g/cm^3	0.67 ± 0.11	0.79 ± 0.07	**.0007**
Trochanteric BMD Z-score	−1.15 ± 0.83	−0.02 ± 0.60	**.0001**
Trochanteric BMD Z-score <−1, %	66.7	0	**<.0001**
Intertrochanteric BMD, g/cm^3	0.98 ± 0.17	1.15 ± 0.17	**.01**
Intertrochanteric BMD Z-Score	−0.99 ± 1.17	0.16 ± 0.82	**.003**
Intertrochanteric BMD Z-score <−1, %	53.3	12.5	**.02**
Testosterone, ng/dL	172.5 ± 142.1	445.0 ± 201.2	**.0005**
Estradiol, pg/mL	11.6 ± 4.5	18.6 ± 7.2	**.006**
IGF-I, ng/mL	456.7 ± 264.6	567.5 ± 244.3	NS

Abbreviation: NS, not significant.

[a] Results are shown as mean ± SD or percent. *P* values < .1 are shown, and significant *P* values are in bold.

to determine independent associations after controlling for potential confounders. A *P* value < .05 was considered significant.

Results

Clinical characteristics

Clinical characteristics of our subjects are shown in Table 1 and have been previously reported (6). Boys with AN did not differ from normal-weight controls for chronological age, bone age, or height SDS. Per study design, weight SDS and BMI SDS were significantly lower in boys with AN than in controls. Similarly, boys with AN had lower fat mass and lean mass, and percent body fat trended lower compared with controls. Testosterone and estradiol levels were lower in boys with AN, whereas IGF-I levels did not differ from controls. Free testosterone levels (calculated by the law of mass action) were lower in boys with AN and are not reported. One boy with AN was prepubertal, whereas all controls were in puberty. All measures of BMD and BMD Z-scores (total hip, femoral neck, trochanter, and intertrochanter) were lower in boys with AN. A larger proportion of boys with AN than controls had Z-scores of <−1 at the total hip and the femoral neck.

HSA parameters

Boys with AN had lower cross-sectional area and cortical thickness of the narrow neck and trochanteric region compared with controls (Table 2). In addition, buckling ratio at the trochanteric region was higher in AN than controls and trended higher in AN at the narrow neck. Subperiosteal and endocortical width, cross-sectional moment of inertia and section modulus did not differ between groups. However, after controlling for age and height, we noted significantly lower subperiosteal width at the femoral shaft, cross-sectional moment of inertia (at the narrow neck and femoral shaft), and section modulus (all sites) in boys with AN compared with controls. Differences between groups for cross-sectional area at all sites and cortical thickness became stronger after controlling for age and height. The neck shaft angle was lower in AN than controls.

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Table 2. HSA Parameters in Adolescent Boys with AN and Normal-Weight Controls[a]

	AN	Normal-Weight Controls	*P*	*P*[b]
n	15	16		
Cross-sectional area, cm^2				
Narrow neck	2.89 ± 0.64	3.44 ± 0.66	**.03**	**.007**
Trochanter	4.88 ± 1.08	5.78 ± 0.90	**.02**	**.003**
Femoral shaft	3.77 ± 0.92	4.29 ± 0.75	.09	**.02**
CSMI, cm^4				
Narrow neck	2.61 ± 1.03	3.19 ± 1.11	NS	**.04**
Trochanter	13.21 ± 4.84	15.16 ± 4.21	NS	.08
Femoral shaft	3.11 ± 1.18	3.83 ± 1.05	.08	**.02**
Section modulus, cm^3				
Narrow neck	1.47 ± 0.51	1.78 ± 0.50	NS	**.03**
Trochanter	4.10 ± 1.22	4.89 ± 1.05	.06	**.02**
Femoral shaft	2.00 ± 0.62	2.37 ± 0.51	.08	**.01**
Cortical thickness, cm				
Narrow neck	0.18 ± 0.03	0.21 ± 0.04	**.02**	**.009**
Trochanter	0.41 ± 0.07	0.46 ± 0.06	**.03**	**.01**
Femoral shaft	0.51 ± 0.11	0.55 ± 0.10	NS	NS
Subperiosteal width, cm				
Narrow neck	3.29 ± 0.28	3.35 ± 0.37	NS	NS
Trochanter	5.53 ± 0.76	5.52 ± 0.41	NS	NS
Femoral shaft	2.87 ± 0.30	3.03 ± 0.19	.09	**.02**
Endocortical width, cm				
Narrow neck	2.93 ± 0.09	2.93 ± 0.39	NS	NS
Trochanter	4.72 ± 0.71	4.60 ± 0.37	NS	NS
Femoral shaft	1.86 ± 0.28	1.93 ± 0.21	NS	NS
Buckling ratio				
Narrow neck	10.33 ± 2.64	8.78 ± 2.37	.09	.08
Trochanter	7.90 ± 1.45	6.70 ± 0.83	**.008**	**.006**
Femoral shaft	3.15 ± 0.73	2.96 ± 0.48	NS	NS
Neck shaft angle, degrees	129.4 ± 4.4	132.4 ± 3.7	**.05**	**.05**
Hip axis length	112.7 ± 8.8	115.8 ± 7.2	NS	NS

Abbreviations: CSMI, cross-sectional moment of inertia; NS, not significant.

[a] Results are shown as mean ± SD. *P* values < .1 are shown, and significant *P* values are in bold.

[b] *P* values adjusted for age and height.

Determinants of HSA parameters

There were strong associations of HSA parameters with BMI SDS, lean mass, testosterone, and estradiol levels for the group as a whole (Table 3). Associations of free testosterone with HSA parameters were similar to those of total testosterone, and only total testosterone levels and associations are reported. Associations of lean mass and testosterone levels (but not estradiol) with HSA parameters held when AN and control groups were analyzed separately. In addition, BMI SDS was a determinant of cross-sectional area, cross-sectional moment of inertia, and section modulus in the AN group but not the control group.

IGF-I levels correlated positively with subperiosteal and endocortical width at the femoral shaft but not with other measures (Table 3). When we assessed correlations of IGF-I SDS with HSA parameters, IGF-I SDS correlated positively with endocortical width ($r = 0.53$, $P = .006$) and buckling ratio ($r = 0.41$, $P = .04$) at the femoral shaft for the group as a whole. In addition, lean mass was positively associated with testosterone and estradiol ($r = 0.76$ and 0.63, $P < .0001$ and .0006, respectively), and testosterone was positively associated with estradiol and IGF-I ($r = 0.62$ and 0.46, $P = .0006$ and .02, respectively).

On multivariate analysis, with age, height, and lean mass entered into the model (model 1), lean mass was an independent positive predictor of subperiosteal width at the femoral shaft ($P = .0006$), cross-sectional area at all sites ($P < .0001$ for all), cross-sectional moment of inertia at all sites ($P \leq .0006$), section modulus at all sites ($P \leq .0003$), cortical thickness at all sites ($P \leq .002$), and an inverse predictor of buckling ratio at all sites ($P \leq .04$). We next performed multivariate analysis with lean mass, testosterone, and estradiol entered into the model (model 2), and lean mass remained a significant predictor of most measures of HSA (data not shown), whereas testosterone and estradiol were no longer significant. When IGF-I was added to this model (model 3), associations of lean mass with most bone parameters persisted. In addition, IGF-I

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Table 3. Associations of HSA Measures With Body Composition Parameters, Total Testosterone, Estradiol, and IGF-I[a]

	BMI SDS		Lean Mass		Testosterone		Estradiol		IGF-I	
	r	*P*	*r*	*P*	*r*	*p*	*r*	*P*	*r*	*P*
Cross-sectional area										
Narrow neck	0.50	**.004**	0.76	**<.0001**	0.65	**.0003**	0.52	**.007**	0.14	NS
Trochanter	0.56	**.001**	0.83	**<.0001**	0.70	**<.0001**	0.50	**.009**	0.24	NS
Femoral shaft	0.51	**.004**	0.86	**<.0001**	0.62	**.0007**	0.44	**.02**	0.13	NS
CSMI										
Narrow neck	0.36	**.05**	0.82	**<.0001**	0.64	**.0004**	0.49	**.01**	0.15	NS
Trochanter	0.40	**.02**	0.87	**<.0001**	0.69	**.0001**	0.43	**.03**	0.35	.08
Femoral shaft	0.54	**.002**	0.86	**<.0001**	0.66	**.0002**	0.51	**.007**	0.28	NS
Section modulus										
Narrow neck	0.40	**.03**	0.79	**<.0001**	0.65	**.0004**	0.48	**.01**	0.15	NS
Trochanter	0.52	**.003**	0.87	**<.0001**	0.73	**<.0001**	0.45	**.02**	0.37	.06
Femoral shaft	0.57	**.0009**	0.87	**<.0001**	0.65	**.0004**	0.49	**.01**	0.23	NS
Cortical thickness										
Narrow neck	0.52	**.003**	0.54	**.002**	0.52	**.006**	0.46	**.02**	0.10	NS
Trochanter	0.47	**.008**	0.64	**<.0001**	0.55	**.004**	0.37	.07	0.06	NS
Femoral shaft	0.37	**.04**	0.69	**<.0001**	0.43	**.03**	0.26	NS	−0.10	NS
Subperiosteal width										
Narrow neck	0.16	NS	0.67	**<.0001**	0.51	**.008**	0.37	0.06	0.15	NS
Trochanter	0.17	NS	0.69	**<.0001**	0.45	**.02**	0.29	NS	0.35	.08
Femoral shaft	0.50	**.004**	0.81	**<.0001**	0.64	**.0004**	0.51	**.008**	0.45	**.02**
Endocortical width										
Narrow neck	0.04	NS	0.54	**.002**	0.40	**.04**	0.28	NS	0.13	NS
Trochanter	0.06	NS	0.57	**.0009**	0.35	.08	0.22	NS	0.34	.08
Femoral shaft	0.20	NS	0.26	NS	0.32	NS	0.32	NS	0.56	**.003**
Buckling ratio										
Narrow neck	−0.38	**.03**	−0.33	.07	−0.26	NS	−0.25	NS	−0.07	NS
Trochanter	−0.41	**.02**	−0.20	NS	−0.25	NS	−0.16	NS	0.10	NS
Femoral shaft	−0.28	NS	−0.49	**.005**	−0.25	NS	−0.15	NS	0.19	NS
Neck shaft angle	0.46	**.009**	0.23	NS	0.46	**.02**	0.17	NS	0.32	NS
Hip axis length	0.34	.06	0.74	**<.0001**	0.61	**.0009**	0.47	**.02**	0.39	**.05**

Abbreviations: CSMI, cross-sectional moment of inertia; NS, not significant.

[a] *P* values < .10 are shown, and significant *P* values are in bold.

was a positive and independent predictor of endocortical width at the femoral shaft ($P = .01$).

Discussion

We demonstrate for the first time that adolescent boys with AN had impaired hip structure and strength compared with normal-weight controls. Specifically, after controlling for age and height, cross-sectional area, cortical thickness, cross-sectional moment of inertia, section modulus, and buckling ratio were impaired in boys with AN, which may predispose them to a higher risk of hip fractures in the long term. In this study, the decrease in cross-sectional area and cortical thickness and the increase in the buckling ratio were associated mostly with decreases in lean mass.

Although data regarding fractures are limited in adolescent boys and adult men with AN, it is well known that females with AN are at an increased risk for fractures (20, 21). Studies in males are few (6, 22) and have been limited by difficulties in recruiting large numbers of subjects given delays in diagnosis or even a failure to recognize the condition by the patient, his family, and healthcare providers. This is mostly because an important clue to the disorder in females, namely amenorrhea, is not available as a diagnostic tool in males. In recent years, there has been a growing awareness of AN in males, and this underscores the need to better understand the impact of this eating disorder on bone health and fracture risk in males. Whether or not data from studies in females can be extrapolated to males with AN is not clear. We have reported significantly lower aBMD in adolescent boys with AN compared with controls (6), and the only other study in boys also reported a high prevalence of low aBMD in AN (22). Moreover, our study suggested that sites of primarily cortical bone (such as the hip) are affected most in males (6), as opposed to sites of primarily trabecular bone (such as the lumbar spine) in girls (1–5). These gender-specific effects of AN on aBMD suggest that not all data from females can be extrapolated to males.

We have previously reported using flat-panel ultra–high-resolution peripheral quantitative CT that girls with AN have a decrease in trabecular number and bone tra-

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becular volume (a measure of trabecular volumetric bone density), and an increase in trabecular separation (10). We have also reported a decrease in failure load and stiffness (measures of bone strength) using finite element analysis in adult women with AN (23). Because the hip is the site most affected in boys with AN, we sought to examine hip structure, geometry, and strength measures using HSA in this study. Our data indicate that adolescent boys with AN have a decrease in cross-sectional area and cortical thickness at the narrow neck and trochanteric region and an increase in buckling ratio at the trochanteric region. Cross-sectional area is an index of resistance to axial forces, whereas the buckling ratio indicates susceptibility to local cortical buckling with compressive loads. Thus, boys with AN have a decreased resistance to axial forces at the hip and an increased susceptibility to local cortical bending after compressive loads. Both these changes increase the risk for fractures, as indicated by studies in postmenopausal women. In one study of over 7000 women, cases with fracture (compared with those without fracture) had greater buckling ratios, neck-shaft angles, and subperiosteal and endosteal diameters and lower hip aBMD, cortical thickness, cross-sectional area, cross-sectional moment of inertia, and section modulus (15). Similarly, another large study of postmenopausal women reported that buckling ratio was an independent predictor of fracture risk even after controlling for age, body size, clinical risk factors, and aBMD (24).

When assessing hip structural parameters in teenage boys, who are still growing, it is important to adjust for age and size simultaneously to avoid bias, especially during the years surrounding the adolescent growth spurt (25, 26). This is because bones get wider as they get longer, and this normal and expected dimensional change affects most HSA outcomes. Interestingly, when we adjusted for age and height in our analysis, we noted that the groups also differed for subperiosteal width at the femoral shaft, cross-sectional moment of inertia (at the narrow neck and femoral shaft), and section modulus (all sites); in addition, other differences became more significant. Cross-sectional moment of inertia provides an estimate of resistance to bending forces in a cross-section, whereas section modulus is an index of strength of bending. Both parameters when impaired are associated with increased fracture risk (15) and were impaired in boys with AN compared with controls after controlling for age and height.

HSA measures were associated with BMI, lean mass, testosterone, estradiol, and to a lesser extent, IGF-I levels. On multivariate analysis, lean mass emerged as the only independent predictor of most measures after controlling for 1) age and height, 2) gonadal steroids, and 3) gonadal steroids and IGF-I levels. IGF-I was an independent predictor of endocortical width at the femoral shaft. The association of lean mass with HSA measures is consistent with the beneficial effects of muscle pull and mechanical loading on bone (27). Testosterone has the potential to increase muscle mass and also has antiresorptive and bone-anabolic effects (28). In growing boys, the increase in circumference and thickness of long bones is attributed to rising levels of sex steroids, GH, and IGF-I (28). In this study, however, despite lower testosterone levels in boys with AN, testosterone was not an independent determinant of hip structure and geometry. Lower testosterone levels in boys with AN likely contribute to lower lean mass, which in turn leads to impaired bone structure and strength. However, it is also possible that our study was not equipped to detect independent contributions of low testosterone levels to bone parameters, given the strong positive associations of testosterone levels with lean mass.

Limitations of this study include its cross-sectional nature and those inherent to HSA. HSA makes assumptions of shape and the proportion of measured bone in the cortex, whereas these typically vary from one individual to another (24). Reassuringly, despite these assumptions, HSA measures are usually effective in predicting hip fracture risk (13–15). Measures obtained through this technique also provide a mechanical explanation for why low hip BMD is concerning for fracture risk.

To conclude, our data indicate that adolescent boys with AN, in addition to having lower aBMD at the hip, have impaired bone structure and geometry (as assessed by HSA) compared with normal-weight controls, and this is mostly associated with lower lean mass. Longitudinal studies are necessary to determine the impact of recovery or persistent low weight on HSA parameters. This is particularly important in an adolescent population, because adolescence is a critical time for optimizing bone accrual and peak bone mass.

Acknowledgments

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