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Assessment of Sex Differences in Body Composition Among Adolescents With Anorexia Nervosa

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Abstract

Purpose—To compare deficits in fat mass (FM) and lean body mass (LM) among male and female adolescents with anorexia nervosa (AN) and to identify other covariates associated with body composition.

Methods—We retrospectively reviewed electronic medical records of all subjects aged 9–20 years with a Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition diagnosis of AN and dual-energy x-ray absorptiometry scans after initial evaluation at Stanford between March 1997 and February 2011. From the dual-energy x-ray absorptiometry scans, LM and FM results were converted to age-, height-, sex-, and race-specific Z-scores for age using the National Health and Nutrition Examination Survey reference data.

Results—A total of 16 boys and 119 girls with AN met eligibility criteria. The FM Z-score in girls with AN (−3.24 ± 1.50) was significantly lower than that in boys with AN (−2.41 ± .96) in unadjusted models ($p = .007$). LM was reduced in both girls and boys with AN, but there was no significant sex difference in LM Z-scores. In multivariate models, lower percentage median body mass index was significantly associated with lower FM Z-scores ($\beta = .08$, $p < .0001$) and lower LM Z-score ($\beta = .03$, $p = .0002$), whereas lower whole body bone mineral content Z-score was significantly associated with lower LM Z-score ($\beta = .21$, $p = .0006$).

Conclusions—FM deficits in girls were significantly greater than those in boys with AN in unadjusted models; however, the degree of malnutrition appeared to be the primary factor

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accounting for this difference. There were no significant sex differences in FM or LM in adjusted models.

Keywords

Anorexia nervosa; Eating disorders; Dual-energy x-ray absorptiometry; Body composition; Sex differences; Males; Females

Anorexia nervosa (AN) is a condition characterized by self-directed weight loss, severe body image distortion, and a profound fear of weight gain [1]. Adolescence is the most typical period of onset in AN, where eating disorders rank as the third leading cause of chronic illness in adolescents [2]. As such, much clinical and empirical work has been oriented toward eating disorders in adolescence, where treatment prognosis is more favorable than in adult presentations [3]. However, to date, a disproportionately sparse amount of clinical and research efforts have focused on male presentations of AN [2]. Reflecting this, although AN is increasing in prevalence among males in both community and clinical samples, less than 1% of empirical research relating to AN has focused on males [4,5]. The 2013 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria eliminated specific body weight and amenorrhea requirements for the diagnosis of AN [1]; therefore, the prevalence of AN is expected to rise even further [6].

A crucial component in the treatment of AN lies in managing the array of concomitant medical complications associated with AN, which include electrolyte disturbances, gastrointestinal manifestations including pancreatitis and elevated liver enzymes, low bone mineral density (BMD), and increased fracture risk [7–18]. Importantly, relatively few studies have assessed body composition in males with AN, and to our knowledge, there are no current studies comparing sex differences in body composition in AN [8,9]. In the general population, girls gain more fat mass (FM) than boys through adolescence; whereas boys have greater lean body mass (LM) than girls [19]. Prior studies in female adolescents with AN have shown striking reductions in FM and significant but less severe reductions in LM [10,14,20–22]. This is particularly salient in light of findings showing that LM is a reliable determinant of low BMD and impaired bone structure in adolescents and adults with AN [10,14,20–22]. The few studies in adolescent males with AN have similarly shown that LM is an important determinant of BMD [8,9], and with empirical findings noting a greater propensity for risk of osteoporosis in male patients [23], further research is warranted in male populations.

To our knowledge, no studies have examined sex differences in body composition in adolescents with AN. Previous studies on body composition in AN used older DSM-IV diagnostic criteria and were published before the availability of robust sex-, race-, and age-specific body composition reference data from the National Health and Nutrition Examination Survey (NHANES) [19]. The objective of this study was therefore to compare body composition in males and females with AN, as well as to identify correlates of body composition among male and female adolescents with AN using DSM-V criteria and robust NHANES reference curves.

Methods

Study population

We retrospectively reviewed the electronic medical record (EMR) of all patients presenting for an initial evaluation to the Eating Disorders Program at Lucile Packard Children's Hospital, Stanford, between March 1997 and February 2011 who were aged 9–20 years. Although patients were initially diagnosed using DSM-IV criteria, we reviewed their clinical and psychosocial characteristics and recategorized them using DSM-V criteria.

Inclusion criteria included age 9–20 years, DSM-V diagnosis of AN, and availability of body composition results via dual-energy x-ray absorptiometry (DXA) obtained using a Hologic bone densitometer. We excluded girls with DXA scans performed after 3 months of presentation because of the potential for the change in height (measured at presentation) to affect NHANES Z-scores. Males with DXA scans performed after 3 months of presentation were not excluded given the imbalance of girls compared with boys and the importance of increasing the power and sample size in boys. We excluded patients with a DSM-V diagnosis of bulimia nervosa, binge eating disorder, avoidant/restrictive food intake disorder, other specified feeding or eating disorder (including atypical AN), or unspecified feeding or eating disorder.

Study design

We collected demographics, anthropometry, and disease characteristics documented in the EMR for this retrospective cross-sectional study. Clinic and hospital staff in the Stanford Eating Disorders Program completed assessments for the purposes of medical care. We then retrospectively reviewed their clinical assessments in the EMR and entered them into a database. The duration of illness documented in the EMR was based on self-report of time of onset of symptoms. Body mass index (BMI, kg/m^2) was calculated, and median BMI was defined as the 50th percentile BMI for age using the Centers for Disease Control and Prevention growth curves [24]. Percentage median BMI (%mBMI) on admission was defined as the patient's BMI on admission divided by the median BMI multiplied by 100 [25].

FM, LM, and whole body bone mineral content (BMC) were obtained by DXA (Hologic 4500; Hologic, Waltham, MA). All bone density assessments were performed on the same Hologic 4500 densitometer using similar software. We excluded DXAs (n = 8) that were performed on different scanners. The coefficient of variation is .28% for Hologic DXA scans at Stanford. Height-normalized FM index and LM index were converted to sex-, race-, and age-specific Z-scores using reference values from the NHANES [19]. Whole body BMC measurements were converted to sex-, race-, and age-specific Z-scores using reference curves generated with the Lambda-Mu-Sigma method [26] by the Bone Mineral Density in Childhood Study (BMDCS) [27]. The Z-scores were further adjusted for height Z-score using the method developed by BMDCS investigators [28].

The study was approved by the Committee on Human Research (IRB) at Stanford University.

Statistical analysis

Data were analyzed using Stata (StataCorp LP, College Station, TX). Unadjusted differences between boys and girls in demographic characteristics, %mBMI, duration of illness, FM Z-score, and LM Z-score were calculated using independent samples *t*-tests or Fisher's exact tests. Median and interquartile range were reported for age and duration of illness, and differences were analyzed using the rank-sum test. Linear regression analyses were used to identify risk factors for low FM and LM Z-scores, including sex, age, %mBMI, and duration of illness. The duration of illness variable was log transformed in the regression analysis due to skewness of the original variable. Previous literature has demonstrated that LM but not FM was associated with BMD [8]. Preliminary univariate linear regression analysis in our data found an association with whole body BMC and LM ($\beta = .21$, $R^2 = .28$, $p = .0006$) but not FM ($\beta = -.26$, $R^2 = .19$, $p = .09$); therefore, whole body BMC was included in the multivariate regression for LM but not FM. $p < .05$ was considered significant. Given a sample size of adolescent girls (N = 119) and boys (N = 16) with AN, and using an estimated mean FM and LM Z-score standard deviation of 1.0, our study had statistical power (alpha = .05, 2 sided) of 80% to detect a difference in Z-score of .75 or greater [29].

Results

Clinical characteristics

A total of 16 boys and 119 girls with AN met eligibility criteria. Median age was 14.96 years (Table 1). Boys had younger age at presentation than girls (median 13.53 vs. 15.04, $p = .03$). There were no significant sex differences in median duration of illness or mean BMI. Median duration of illness was 8 months, and mean BMI was 15.73 ± 1.61 kg/m^2.

Body composition measurements

Body composition results in total and divided by sex are shown in Table 1. FM Z-score in girls with AN (-3.24 ± 1.50) was significantly lower than the FM Z-score in boys with AN ($-2.41 \pm .96$) in unadjusted models ($p = .007$). LM was reduced in both girls and boys with AN, but there was no significant sex difference in LM Z-scores. For both boys and girls, there were significant deficits in Z-scores compared with zero for FM ($p = .00015$ for boys, $p < .0001$ for girls) and LM ($p = .01$ for boys, $p < .0001$ for girls).

Correlates of body composition

The multivariate regression models are summarized in Table 2. Lower %mBMI was significantly associated with deficits in FM Z-score ($\beta = .08$, $p < .0001$) and LM Z-score ($\beta = .03$, $p < .0001$) when controlling for sex, age, and duration of illness (and whole body BMC Z-score for LM only). Whole body BMC Z-score was associated with LM Z-score ($\beta = .21$, $p = .0006$), when controlling for sex, age, %mBMI, and duration of illness. Sex was not significantly associated with FM Z-score in multivariate models when controlling for %mBMI, age, and duration of illness. Sex was not significantly associated with LM Z-score in multivariate models when controlling for %mBMI, age, duration of illness, and whole body BMC Z-score.

Discussion

This is the first study to assess sex differences in body composition among adolescent boys and girls with AN finding significant deficits in FM and LM Z-scores in both boys and girls. FM deficits in girls were significantly greater than those in boys with AN in unadjusted models; however, the degree of malnutrition appeared to be the primary factor accounting for this difference. There were no significant differences between sexes in LM Z-scores. LM was significantly associated with whole body BMC.

We report significant deficits in FM and LM Z-scores among both boys and girls with AN, consistent with previous reports of body composition in male [8,9,30] and female adolescents with AN [10,14,20–22]. Prior studies in female adolescents with AN have shown greater reductions in FM than LM [10,14,20–22], which is supported by our data in both males and females with AN. Previously reported deficits in LM in boys with AN were 14% lower than healthy controls. [30]. One study in girls with AN showed LM deficits 5% lower than healthy controls [31]. Prior studies have not directly compared sex differences in body composition in adolescents with AN. Although boys had greater deficits in LM Z-score than girls in our sample, the difference was not statistically significant. With increased statistical power, one might expect to find significantly greater LM deficits in male patients. Previous studies have demonstrated that LM but not FM is a determinant of low BMD and impaired bone structure in adolescents boys with AN [8,9]. Our results similarly demonstrate a significant association between whole body BMC and LM but not FM.

Furthermore, previous studies have found that boys with AN had lower percentage extremity fat but higher percentage trunk fat than male control subjects after adjusting for weight [30]. This was thought to be mediated by lower testosterone levels in boys with AN since testosterone is an important determinant of muscle mass and studies in hypogonadal adults have demonstrated an increase in LM after testosterone replacement [32,33]. However, males with AN frequently endorse muscularity-oriented body concerns, relating particularly to upper body regions (i.e., biceps) [2], which may lead to differences in body composition such as increased muscle mass but decreased FM in the extremities [4]. As such, site-specific differences in body composition may be more likely in males, reflecting subtle nuances in AN psychopathology in males [34], and may cloud the accuracy of clinical measurements.

Greater degree of malnutrition was a significant predictor of both lower FM Z-score and lower LM Z-score. Prior studies using DXA have similarly found that degree of malnutrition significantly predicted low whole body BMC and BMD at the lumbar spine, total hip, and femoral neck [17,18]. In addition, LM but not FM has been shown to be a determinant of low BMD and impaired bone structure in adolescents boys with AN [8,9]. Our data similarly demonstrates a significant association between whole body BMC and LM but not FM. One study found that LM was the only independent predictor of hip structural analysis measures after controlling for age, height, gonadal steroids, and insulin-like growth factor 1 levels [9]. LM may influence bone density through the effects of muscle pull and mechanical loading on bone [35]. In addition, lower testosterone levels in boys with AN may contribute to lower

LM and subsequent impaired bone structure and strength. Testosterone may lead to increase muscle mass and has antiresorptive and bone-anabolic effects [36].

Also of note in the present study was the age of illness onset in boys with AN. The onset of AN is typically thought to occur later in males than in females, with existing data reporting an age of onset for male AN in mid-late adolescence [37]. Notwithstanding the relatively small sample size in the present study, these data suggest that the onset of male AN may be shifting toward earlier adolescence. This is consistent with empirical data suggesting that male body objectification, and a definite preference for “desirable” body types, may be observable during preadolescence [38]. Reflecting this, our data suggest that these concerns may reach pathological extremes during early adolescence. Alternately, and perhaps equally important, these data may also reflect an improved accuracy of early illness detection in male patients, who typically report first diagnosis later into their illness trajectory, after frequent misdiagnoses among health professionals [39].

Research on the physiology and body composition among males with AN is critical given the rising prevalence of AN in the male population [5] and the fact that observations from female patients may not necessarily be extrapolated to males [4]. Three previous studies compared body composition in boys with AN to healthy male controls but not to females with the disorder [8,9,30]. These studies used DSM-IV criteria for AN and did not report sex-, height-, race-, and age-specific Z-scores. The paucity of studies of body composition in males with AN may reflect decreased recognition of eating disorders in males, delays in diagnosis in part given the lack of amenorrhea which may alert clinicians to the diagnosis of AN in females [9], and challenges of recruiting large numbers of male participants.

Notwithstanding, several limitations apply to the present study, including its retrospective nature, retrospectively assessed DSM-V criteria, and cross-sectional design which precludes causal inferences. We lacked data on sex hormones, growth factors, and physical activity. Selection bias is a possible limitation because we only included participants with body composition data from DXA scans; however, there were no significant differences in demographic or anthropometric data between the total sample of patients with AN and the study sample of participants who were included (Table 3). We did not include healthy controls. We also note the imbalance in the smaller number of boys compared with girls in this sample; however, the proportion of boys in our study (12% male) is consistent with overall sex differences in AN prevalence nationally (5%–15% male) [40]. We excluded girls with DXA scans performed after 3 months of presentation because of a sufficiently large sample size and the potential for the change in height (measured at presentation) to affect BMDCS Z-scores; however, we did not exclude boys based on this criterion, given the importance of increasing the power and sample size in boys, and the imbalance of girls compared with boys. It is possible that boys with DXA scans performed after 3 months of presentation may have increased height since their last evaluation and therefore their height adjustments may not be accurate. In addition, we did not have data regarding the regional distribution of body composition (such as breakdown of trunk vs. extremity).

Strengths of this study include the evaluation by a specialized eating disorders team with systematic data collection. We included males with AN who are an understudied population

[4,5]. Furthermore, FM and LM Z-scores were calculated using the NHANES reference curves which are the most robust reference values for body composition in the pediatric population. The NHANES reference curves were generated from observations of 8,961 participants with Hologic DXA scans throughout the United States [19]. Prior studies did not include Z-scores for body composition. Finally, this study is the first to use new DSM-V criteria for the diagnosis of AN, as previous studies on body composition in AN collected data using DSM-IV criteria.

The Society for Adolescent Health and Medicine recommends obtaining DXA scans in females with AN when amenorrhea is present for six months or more [25]. However, to our knowledge, there are no published guidelines regarding when to obtain DXA scans in males with AN, who will not present with amenorrhea. Because degree of malnutrition is a significant predictor of body composition as well as bone density, clinicians may consider obtaining a DXA scan to evaluate FM, LM, BMD, BMC, and increased fracture risk in the most severely malnourished patients with AN. This study shows that degree of malnutrition may be a particularly important consideration to guide clinicians in deciding when to order a DXA scan in males with AN.

To our knowledge, this is the first study to assess sex differences in body composition among adolescents with AN. We found deficits in FM and LM for both adolescent boys and girls. FM deficits in girls were significantly greater than FM deficits in boys with AN in unadjusted models; however, the degree of malnutrition appeared to be the primary factor accounting for this difference as there were no significant sex differences in FM in adjusted models. The degree of malnutrition was significantly associated with FM and LM. BMC was significantly associated with LM but not FM. Future research should evaluate FM and LM longitudinally to determine the impact of recovery and changing weight in adolescents with AN.

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IMPLICATIONS AND CONTRIBUTION

This study evaluates sex differences in body composition among adolescents with anorexia nervosa, using DSM-5 criteria and robust National Health and Nutrition Examination Survey reference data. Fat mass deficits in girls were greater than those in boys in unadjusted models; however, the degree of malnutrition appeared to be the primary factor accounting for this difference as there were no significant sex differences in fat or lean body mass in adjusted models.

Table 1

Demographic and body composition characteristics of adolescents with anorexia nervosa by sex, unadjusted comparisons

	Total	Male	Female	*p* value
n	119	16	103	
Age, years[a]	14.96 (13.72–16.16)	13.53 (12.93–15.57)	15.04 (13.96–16.17)	.03
Height, cm	159.52 ± 9.94	161.43 ± 9.90	159.29 ± 9.96	.42
Height Z-score	−.12 ± 1.08	−.11 ± 1.02	−.12 ± 1.10	.99
BMI, kg/m^2	15.73 ± 1.61	15.59 ± 1.39	15.75 ± 1.65	.68
%mBMI	79.23 ±6.74	80.64 ± 5.07	79.02 ± 6.95	.29
Duration illness (months)[a]	8 (5–12)	8 (5–16.5)	8 (5–12)	.6
Whole body BMC Z-score	−.58 ± .95	−.67 ± .94	−.56 ± .96	.67
Fat mass index Z-score	−3.13 ± 1.47	−2.41 ± .96	−3.24 ± 1.50	.007
Lean body mass Z-score	−.31 ± .62	−.47 ± .63	−.28 ± .62	.29

BMC = bone mineral content; %mBMI = percentage median body mass index.

[a]Median and interquartile range reported, rank-sum test.

Table 2

Linear regression analysis of covariates associated with increased body composition Z-scores, adjusted models

	β (95% CI)	*p* value	R^2
Fat mass Z-score			
Female (vs. male)	−.65 (−1.39 to .09)	.09	.16
Age	−.05 (−.19 to .09)	.47	
%mBMI	.08 (.04 to .12)	<.0001	
Duration of illness[a]	−.09 (−.42 to .24)	.61	
Lean body mass Z-score			
Female (vs. male)	.21 (−.08 to .50)	.16	.28
Age	−.01 (−.07 to .05)	.75	
%mBMI	.03 (.01 to .05)	.0001	
Duration of illness[a]	−.07 (−.20 to .06)	.26	
Whole body BMC Z-score	.21 (.09 to .33)	.0006	

BMC = bone mineral content; CI = confidence interval; %mBMI = percentage median body mass index.

[a]Duration has been log transformed due to the skewness of the original data.

Table 3

Comparison of characteristics of adolescents with anorexia nervosa with and without body composition data via dual-energy x-ray absorptiometry (DXA)

	Total		
	All AN (excluded)	Study sample[a]	*p* value
n	1,016	119	
Age, years[b]	15.62 (13.87–17.14)	14.96 (13.72–16.16)	.0033
BMI, kg/m^2	15.79 ± 1.74	15.73 ± 1.61	.67
%mBMI	78.57 ± 7.90	79.23 ± 6.74	.33
Duration illness (months)[b]	9 (5–18)	8 (5–12)	.05

AN = anorexia nervosa; %mBMI = percentage median body mass index.

[a]Patients with AN who met study inclusion criteria, i.e., had body composition data via DXA on Hologic scanner within 3 months of presentation.

[b]Median and interquartile range reported, rank-sum test.