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Comparisons of Bone Density and Body Composition among Adolescents with Anorexia Nervosa and Atypical Anorexia Nervosa

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Abstract

Objective: To compare bone mineral density (BMD) and body composition among adolescents: 1) with atypical anorexia nervosa (AAN) versus anorexia nervosa (AN) and 2) those with and without a prior history of overweight.

Method: Electronic medical records of patients 9–20 years with AN or AAN who underwent dual-energy x-ray absorptiometry (DXA) scans were retrospectively reviewed and analyzed.

Results: A total of 286 adolescents with AN or AAN were included. In linear regression models, AAN was associated with greater Z-scores in whole body bone mineral content (BMC, B=0.88, p<0.001), lumbar spine BMD (B=0.79, p=0.002), femoral neck BMD (B=0.670, p=0.009); fat mass index (FMI, B=1.33, p=0.003), and lean body mass index (LBMI, B=1.10, p<0.001) compared to AN, adjusting for age, sex, and duration of illness. A prior overweight history was associated with greater Z-scores in whole body BMC; lumbar spine BMD, total hip BMD, femoral neck BMD, and LBMI.

Discussion: Adolescents with AAN had higher BMD Z-scores than adolescents with AN; adolescents with a prior overweight history had greater BMD Z-scores than adolescents without a prior overweight history. These findings may inform clinical guidelines for the medical management of AAN.

Keywords

anorexia nervosa; atypical anorexia nervosa; obesity; overweight; eating disorders; dual-energy x-ray absorptiometry; DXA; bone density; bone health; body composition

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Introduction

The Diagnostic and Statistical Manual, fifth Edition (DSM-5) introduced atypical anorexia nervosa (AAN) within the Other Specified Feeding or Eating Disorders (OSFED) diagnosis to describe individuals who meet psychological criteria for anorexia nervosa (AN), but whose weight is within or above the normal range (American Psychiatric Association, 2013). Much less is known about clinical features of AAN compared to AN; however, it is estimated that 70% of adolescents with AAN were previously overweight (Sawyer, Whitelaw, Le Grange, Yeo, & Hughes, 2016), and one large inpatient eating disorder (ED) unit has reported a fivefold increase in admissions of adolescents with AAN over a six-year period, representing nearly half of all inpatient admissions (Whitelaw, Gilbertson, Lee, & Sawyer, 2014). The severity of ED symptoms in AAN has been shown to be equal or greater to symptom severity in AN (Sawyer et al., 2016). Nearly a third of US adolescents considered overweight engage in ED behaviors (Nagata, Garber, Tabler, Murray, & Bibbins-Domingo, 2018; Neumark-Sztainer et al., 2007).

AN is associated with bone mineral density (BMD) deficits and increased fracture risk (Faje et al., 2014; Misra et al., 2004; Nagata, Golden, Leonard, Copelovitch, & Denburg, 2017; Solmi et al., 2016). Furthermore, adolescents with AN have striking reductions in fat mass and significant but less severe reductions in lean mass (Faje et al., 2013; Misra et al., 2004).

There is a paucity of data on bone health and body composition among adolescents with AAN. One recent study found higher mean BMD Z-scores at the spine, total hip, and total radius in AAN versus AN, but dual-energy x-ray absorptiometry (DXA) Z-scores were still lower than those of healthy controls; however, this study was limited to adult women (18–45 years) and did not include adolescents or males (Schorr et al., 2017). Little is known about the effect of prior overweight status on BMD in adolescents. Studying skeletal consequences of AAN and prior overweight history is important given the rising incidence of these disorders (Whitelaw et al., 2014).

The objectives of this study were to compare BMD, fat mass index, and lean body mass index among a sample of adolescents: 1) with AAN versus AN and 2) those with and without a prior history of overweight. We hypothesized that adolescents with AAN would have higher BMD, fat mass index, and lean body mass index Z-scores than adolescents with AN, and that those with a prior history of overweight would have higher BMD, fat mass index, and lean body mass index Z-scores than those without such a history.

Methods

Study Population

This cross-sectional study retrospectively reviewed the electronic medical record (EMR) of all patients, 9 to 20 years of age, presenting for an initial evaluation to the Eating Disorders Program at Lucile Packard Children’s Hospital, Stanford between March 1997 and February 2011. Inclusion criteria included DSM-5 diagnosis of AN or AAN, and availability of DXA results obtained using a Hologic 4500 bone densitometer within three months of presentation.

Measures

This retrospective cross-sectional study included demographics, anthropometry, DXA measures, and psychological and medical disease characteristics documented in the EMR. Assessments were completed by clinic and hospital staff for the purposes of medical care. These clinical assessments in the EMR were then retrospectively reviewed and entered into a database.

Clinical, psychological, and anthropometric characteristics of participants were reviewed and re-classified using DSM-5 criteria for this study as reported previously, given that participants were initially diagnosed using DSM-IV criteria (Nagata, Golden, Peebles, Long, Murray et al., 2017; Nagata, Golden, Peebles, Long, Leonard et al., 2017). Height and weight were measured at initial presentation. Highest premorbid weight was based on self-report. Body mass index (BMI, kg/m^2) was calculated, and mBMI defined as the 50th percentile BMI for age using the Centers for Disease Control and Prevention (CDC) growth curves (Centers for Disease Control, CDC, 2000). Percentage mBMI (%mBMI) on admission was (BMI/mBMI)*100 (Society for Adolescent Health and Medicine et al., 2015). Prior overweight denoted a BMI $>85^{th}$ percentile at self-reported highest weight using height at presentation (Centers for Disease Control, C D C, 2000). Duration of illness was time from self-reported onset of symptoms. Menstrual status was based on self-report.

All BMD and body composition assessments were obtained by DXA (Hologic 4500, Hologic, Waltham, MA). Whole body bone mineral content (BMC), and lumbar spine, total hip and femoral neck BMD measurements were converted to sex-, race-, and age-specific Z-scores using reference curves from healthy adolescents in the Bone Mineral Density in Childhood Study (Zemel et al., 2011). Z-scores were further adjusted for height Z-score per methods developed by BMDCS investigators (Zemel et al., 2010). DXA body composition height-normalized fat mass index (FMI, kg/m^2) and lean body mass index (LBMI, kg/m^2) were converted to sex-, race-, and age-specific Z-scores using reference values from healthy adolescents in the National Health and Nutrition Examination Surveys (NHANES) (Weber, Moore, Leonard, & Zemel, 2013).

Ethics

The study was approved by the Research Compliance Office (Institutional Review Board) at Stanford University.

Statistical Analysis

Data were analyzed using STATA 15.0 (StataCorp LP, College Station, TX). Unadjusted differences were calculated using independent samples t-tests, Pearson's chi square tests, or Fisher's exact tests. Because duration of illness was skewed, median and interquartile range were reported, the rank sum test was used for bivariate analyses, and log-transformation was performed for the regression analysis. Linear regression analyses were used with AAN or prior overweight history as the independent variable, DXA Z-scores as the dependent variable, adjusting for sex, age, and duration of illness. The Benjamini-Hochberg procedure was used to adjust for a false discovery rate given multiple statistical tests (Benjamini & Hochberg, 1995).

Results

Clinical Characteristics

Eligibility criteria narrowed the final sample to 286 participants (263 AN and 23 AAN, Appendix A). Clinical and DXA characteristics of the sample are shown in Table 1. Mean age was 15.3 years and 93% of participants were female. Forty-six participants reported a prior overweight history, of whom 19 also met criteria for AAN.

Adolescents with AN had greater deficits in Z-scores for whole body BMC, lumbar spine BMD, total hip BMD, femoral neck BMD, FMI, and LBMI than adolescents with AAN in unadjusted analyses (Table 1). Adolescents with no prior overweight history had greater deficits in Z-scores for whole body BMC, lumbar spine BMD, total hip BMD, femoral neck BMD, FMI, and LBMI than adolescents with a prior overweight history in unadjusted analyses (Table 1). Adolescents with AN and AAN, and those with or without a prior overweight history, all had significant deficits in FMI Z-score.

In linear regression models, AAN was associated with greater whole body BMC (B=0.88, p<0.001), lumbar spine BMD (B=0.79, p=0.002), femoral neck BMD (B=0.670, p=0.009), FMI (B=1.33, p=0.003), and LBMI (B=1.10, p<0.001), but not total hip (B=0.52, p=0.054) BMD Z-score compared to AN, adjusting for age, sex, and duration of illness (Table 2). In linear regression models, prior overweight history was significantly associated with greater whole body BMC (B=0.83, p<0.001), lumbar spine BMD (B=0.70, p=0.001), total hip BMD (B=0.53, p=0.009), femoral neck BMD (B=0.70, p<0.001), and LBMI (B=0.80, p<0.001), but not FMI (B=0.66, p=0.069) Z-score compared to no prior overweight history, adjusting for age, sex, and duration of illness.

Discussion

We found that adolescents with AAN had greater whole body BMC and BMD at the lumbar spine and femoral neck compared to those with AN. We also found that a prior history of overweight in these adolescents was associated with greater whole body BMC and BMD at all sites compared to no prior overweight history. FMI Z-scores were lower than expected in the AAN subgroup relative to their %mBMI. Given the dearth of knowledge on medical complications of AAN and the rising incidence of this clinical diagnosis, research on this topic is important to inform clinical guidelines.

Adolescents with AAN have been shown to have more severe ED symptoms including restraint, eating concerns, shape concerns, and weight concerns compared to adolescents with AN (Sawyer et al., 2016). Adolescents with AAN were also found to have equally severe binge-eating, vomiting, laxative misuse, and compulsive exercise as adolescents with AN (Sawyer et al., 2016). Despite significant ED symptoms at presentation in AAN, skeletal consequences to their BMD and lean mass may be relatively spared. One previous study in adult women found higher mean BMD Z-scores at the spine, total hip, and total radius in AAN versus AN (Schorr et al., 2017). Our study confirms these differences in an adolescent sample that includes males and females. However, adolescents with AAN had whole body, lumbar spine, and femoral neck Z-scores in the normal range (based on growth curves from

healthy controls (Zemel et al., 2011)), in contrast to the adults with AAN who demonstrated significant bone deficits (Schorr et al., 2017). Higher BMI is associated with greater BMC and BMD (Nagata et al., 2017), which may explain the BMC and BMD Z-score differences in AAN versus AN. In addition, we find that adolescents with a prior history of overweight may be protected from low BMD compared to those without a history of overweight.

It is well known that adolescents with AN have low fat mass (Faje et al., 2013; Misra et al., 2004). While we find that FMI Z-scores are lower in AN than AAN, adolescents with AAN nonetheless have FMI Z-scores lower than expected for age, race, and sex. These findings are consistent with the severe ED symptoms in AAN and the findings of fat mass deficits in adult women with AAN (Schorr et al., 2017). Adolescents with and without a history of prior overweight both had similarly severe deficits in FMI Z-scores in the context of AN or AAN. However, adolescents with AN had lower LBMI Z-score than adolescents with AAN, and adolescents without a prior history of overweight had lower LBMI Z-score than adolescents with a prior history of overweight. Deficits in lean mass may contribute to low BMD (Koşar, 2016). Adolescents with AAN and a prior history of overweight did not demonstrate significant deficits in LBMI Z-score. This contrasts the results in adult women with AAN which found significant deficits in lean body mass in AAN compared to healthy controls (Schorr et al., 2017). It is notable that a current higher weight does not fully protect against low FMI Z-score in the setting of AAN or a prior overweight history. These body composition findings are relevant to clinical practice because they demonstrate that despite less strict weight criteria, DSM-5 AAN still captures individuals with significantly low body fat.

Limitations of this study include its retrospective nature; the cross-sectional design precludes causal inferences. Selection bias is a possible limitation since we only included participants with DXA scans; however, there were no significant differences in demographic or anthropometric data between those who were included versus excluded (Appendix B) except than males were likely to be excluded, likely due to the lack of guidelines for obtaining DXA in males with EDs. Our AAN sample was small. We did not include healthy controls. We did not have individual BMI trajectories which could serve as guidance for target weight status. In addition, there are limitations to using DXA in assessing BMD, particularly in populations with abnormal body composition and fat distribution, such as in adolescents with AN (Wren, Liu, Pitukcheewanont, & Gilsanz, 2005).

Strengths of this study include evaluation by a specialized clinical ED team with systematic data collection. Bone and body composition Z-scores were calculated using robust reference curves (Weber et al., 2013; Zemel et al., 2011). This study used DSM-5 criteria for the diagnosis of AN and AAN.

Conclusion

To our knowledge, this is the first study to assess bone health and body composition among adolescents with AAN versus AN. We found higher whole body BMC, lumbar spine BMD, femoral neck BMD, and LBMI Z-score in AAN compared to AN. We found significant though less severe deficits in FMI Z-score in AAN compared to AN. Future research should

evaluate BMD trajectories longitudinally and evaluate fracture risk among adolescents with AAN.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic, anthropometric, bone, and body composition characteristics of adolescents with anorexia nervosa and atypical anorexia nervosa, by DSM-5 diagnosis and prior weight status

	n	Total	Anorexia nervosa	Atypical anorexia nervosa	p	No prior overweight history	Prior overweight history	p
n		286	263	23		179	46	
		Mean ± SD, median (IQR), or n (%)[a]	Mean ± SD, median (IQR), or n (%)[a]	Mean ± SD, median (IQR), or n (%)[a]		Mean ± SD, median (IQR), or n (%)[a]	Mean ± SD, median (IQR), or n (%)[a]	
Age, years	286	15.3 ± 2.0	15.4 ± 2.0	15.1 ± 1.8	0.475	15.3 ± 2.0	15.3 ± 1.9	0.875
Sex	286				0.065			**0.008**
Female		266 (93.0%)	247 (93.9%)	19 (82.6%)		**169 (94.4%)**	**38 (82.6%)**	
Male		20 (7.0%)	16 (6.1%)	4 (17.4%)		**10 (5.6%)**	**8 (17.4%)**	
Duration illness (months)	284	8.7 (5.0, 12.5)	8.0 (5.0, 12.0)	11.0 (4.0, 24.4)	0.174	**7.0 (5.0, 12.0)**	**11.5 (8, 18)**	**<0.001**
Menstrual status[b]	163				0.479			0.625
Normal periods		32 (19.6%)	28 (18.8%)	4 (28.6%)		27 (20.8%)	5 (15.2%)	
Amenorrhea or oligomenorrhea		131 (80.4%)	121 (81.2%)	10 (71.4%)		103 (79.2%)	28 (84.9%)	
BMI at presentation, kg/m^2	286	16.1 ± 1.9	**15.8 ± 1.5**	**19.8 ± 1.8**	**<0.001**	**15.7 ± 1.5**	**17.9 ± 2.4**	**<0.001**
%mBMI at presentation[c]	286	80.7 ± 8.7	**79.0 ± 6.5**	**99.7 ± 7.9**	**<0.001**	**78.6 ± 6.5**	**89.5 ± 11.8**	**<0.001**
BMI at highest premorbid weight, kg/m^2	174	21.1 ± 4.6	**20.3 ± 4.1**	**27.9 ± 3.4**	**<0.001**	**19.3 ±2.3**	**27.4 ± 5.1**	**<0.001**
Whole body BMC Z-score	273	−0.36 ± 0.95	**−0.43 ± 0.93**	**0.41 ± 0.89**	**<0.001**	**−0.49 ± 0.88**	**0.29 ± 0.91**	**<0.001**
Lumbar spine BMD Z-score	137	−0.40 ± 0.99	**−0.49 ± 0.96**	**0.34 ± 0.93**	**0.002**	**−0.54 ± 0.95**	**0.12 ± 0.89**	**0.002**
Total hip BMD Z-score	190	−0.88 ± 1.08	−0.93 ± 1.07	−0.39 ± 1.00	0.043	−0.97 ± 1.07	−0.48 ± 1.05	0.013
Femoral neck BMD Z-score	190	−0.71 ± 1.04	**−0.78 ± 1.03**	**−0.08 ± 0.90**	**0.007**	**−0.83 ± 1.00**	**−0.19 ± 0.93**	**<0.001**
Fat mass index Z-score	131	−3.02 ± 1.51	**−3.17 ± 1.45**	**−1.71 ± 1.50**	**<0.001**	−3.22 ± 1.53	−2.44 ± 1.59	0.028
Lean body mass index Z-score	131	−0.18 ± 0.70	**−0.29 ± 0.64**	**0.78 ± 0.13**	**<0.001**	**−0.29 ± 0.63**	**0.43 ± 0.64**	**<0.001**

Bold indicates statistical significance after Benjamini-Hochberg procedure

[a] SD = standard deviation, IQR = interquartile range

[b] among subset of sample who were postmenarchal females not taking hormonal contraceptives; secondary amenorrhea or oligomenorrhea was defined as absence of menses for >1 month

[c] %mBMI = percentage median body mass index

Table 2.

Multivariate linear regression analyses of atypical anorexia nervosa or prior overweight as the independent variables and dual-energy x-ray absorptiometry (DXA) Z-scores as the dependent variables, adjusting for covariates

	Atypical anorexia nervosa (vs anorexia nervosa)		Prior overweight history (vs no prior overweight history)	
	B (95% CI)	p	B (95% CI)	p
Whole body BMC Z-score[a]	**0.88 (0.48 to 1.29)**	**<0.001**	**0.83 (0.52 to 1.14)**	**<0.001**
Lumbar spine BMD Z-score[a]	**0.79 (0.29 to 1.29)**	**0.002**	**0.70 (0.32 to 1.08)**	**<0.001**
Total hip BMD Z-score[a]	0.52 (−0.01 to 1.04)	0.054	**0.53 (0.13 to 0.93)**	**0.009**
Femoral neck BMD Z-score[a]	**0.67 (0.17 to 1.18)**	**0.009**	**0.70 (0.33 to 1.07)**	**<0.001**
Fat mass index Z-score[a]	**1.33 (0.47 to 2.19)**	**0.003**	0.66 (−0.05 to 1.37)	0.069
Lean body mass index Z-score[a]	**1.10 (0.73 to 1.47)**	**<0.001**	**0.80 (0.51 to 1.09)**	**<0.001**

Bold indicates statistical significance after Benjamini-Hochberg procedure

B = beta coefficient; CI = confidence interval

[a]adjusted for age, sex, and duration of illness (log transformed)