Depression in Anorexia Nervosa: A Risk Factor for Osteoporosis

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Context: Both anorexia nervosa (AN) and depression are associated with osteoporosis. We hypothesized that adolescent girls with AN and depression will have lower bone mineral density (BMD) than anorexic girls without depression.

Objective: The objective of this study was to investigate whether depression is an independent risk factor for osteoporosis in anorexic adolescent girls.

Design: This study was cross-sectional.

Setting: This study was conducted at the University Children’s Hospital (Bialystok, Poland) from October 2002 through September 2003.

Participants: Forty-five Caucasian anorexic girls aged 13–23 yr, matched by age, Tanner stage, weight, height, calcium intake, and duration of AN, were studied, including 14 with comorbid depression (based on Hamilton Depression Rating Scale and Montgomery-Asberg Depression Rating Scale) and 31 anorexic girls without depression.

Depression is associated with weight loss, bone loss, and osteoporosis in adults (9–12). Depression is reported in 36% of adolescent girls with AN (13). Although it is not a core element in anorexic disorder, it may exacerbate the course and severity of AN (14–16). Both conditions occur during growth and puberty, but no published data exist regarding BMD and depression in anorexic adolescent girls.

The aim of the study was to investigate whether there is a link between depressive symptoms and low BMD in adolescent girls with AN. We hypothesized that adolescent girls with AN and depression have lower BMD than anorexic girls without depression.

Main Outcome Measures: Total body and lumbar spine (LS) BMD, fat mass, and lean mass assessed using dual-energy x-ray absorptiometry were compared between AN girls with and without depression.

Results: BMD was reduced in both groups, relative to reference data, but girls with AN and depression had lower BMD than those with AN alone (LS Z-scores, −2.6 ± 0.3 vs. −1.7 ± 0.3; P = 0.02) (mean ± SEM). Quantitative assessment of depression correlated independently with total body BMD (r = −0.4; P < 0.05) and LS BMD (r = −0.6; P < 0.001).

Conclusion: Anorexic girls with depression are at higher risk of osteoporosis than those without depression. The mechanisms responsible for decreased BMD in depression are not known. Independent treatment of the depressive disorder in AN may partly alleviate the bone fragility. (J Clin Endocrinol Metab 90: 5382–5385, 2005)

Patients and Methods

The study was conducted between October 2002 and September 2003 in the Outpatient Psychosomatic Clinic and the Pediatric Departments in the University Children’s Hospital “Dr. L. Zamenhof” at the Medical University of Bialystok (Bialystok, Poland). Girls suffering from AN for at least 6 months, being treated either as inpatients (96%) or outpatients, were recruited for this study. Written consent was obtained from participants and their parents or legal guardians. The study was approved by the Ethical Committee at the Medical University in Bialystok.

Forty-nine Caucasian adolescent females aged 12.8–23.1 yr (mean 16.6 ± 1.8 yr) who were diagnosed with AN according to both Diagnostic and Statistical Manual of Mental Disorders IV American Psychiatric Association (17) and International Classification of Diseases (ICD-10) (18) criteria, were enrolled into the study. All girls were undernourished (BMI below the third percentile of the reference range), presented with body image distortion based on psychiatric assessment (17, 18), and had either primary amenorrhoea or secondary amenorrhoea for more than 6 months during the study. Duration of AN ranged between 0.6 and 5.6 yr. Before inclusion to the study, patients were screened for the following conditions: primary kidney and liver diseases, juvenile rheumatoid arthritis and other connective tissue diseases, scoliosis, hyperthyroidism, malabsorption, celiac disease, and schizophrenia. Of the 49 patients screened, four were excluded because they failed to meet the criteria; two had schizophrenia, one had hyperthyroidism, and one had chronic hepatitis B. None of the girls had ever received hormone therapy, glucocorticosteroids, neuroleptics, or parenteral nutrition, and none had had spinal surgery.

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Abbreviations: AN, Anorexia nervosa; BMC, bone mineral content; BMD, bone mineral density; BMI, body mass index; FM, fat mass; HAM-D, Hamilton Depression Rating Scale; LM, lean mass; LS, lumbar spine; MADRS, Montgomery-Asberg Depression Rating Scale; TB, total body.

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Medical history and questionnaire were used to assess age of menarche, gynecological age (measured as a number of years since first menstruation), history of fractures, and current and past medication use. Dietary calcium intake was assessed by an interview-based 24-h recall (19, 20). All patients underwent clinical examination and anthropometric measurements. Weight was measured on an electronic scale (Seca, Hamburg, Germany) and height using a Martin anthropometer. The body mass index (BMI) was derived from the formula: BMI = weight (kilograms)/height² (square meters). Pubertal status was based on Tanner staging of breast development and ascertained by a physician (21).

Total body (TB) bone mineral content (BMC; grams), TB BMD (grams per centimeter squared), lumbar spine (LS) BMD (grams per centimeter squared), fat mass (FM; grams and percentage), and lean mass (LM; grams) were determined using dual-energy x-ray absorptiometry (DPX-L, Lunar Radiation Corp., Madison, WI; versions 1.3z and 1.5 h). LS BMD was compared with age-matched reference ranges and expressed as a Z-score. The estimated reproducibility error (coefficient of variation) was 1.14%, based on duplicate LS dual-energy x-ray absorptiometry examination performed within 3 d in 32 subjects. All participants were examined by a psychiatrist and screened for depressive symptoms. Anorexic subjects were divided into those with a depressive disorder and those without, based on the Hamilton Depression Rating Scale (HAMD-D) and the Montgomery-Asberg Depression Rating Scale (MADRS), which are used to indicate the intensity of depression (22, 23). The criteria for the presence of depression in HAM-D is more than or equal to eight scores, whereas the cut-off score for depression in MADRS is more than or equal to 13. These two methods have been validated as screening tools for depression in adolescents (23). Using multiple regression analyses, BMD was adjusted for body composition scores were assessed using the Pearson correlation coefficients. Differences were observed in age, Tanner stage, menarche, weight, height, and FM between the two groups. Of the six girls with primary amenorrhoea, five occurred in those with AN and depression. Two girls with AN and depression reported fractures (wrist and ankle), whereas no fractures were reported in those without depression. There was a tendency toward decreased BMI in depressed AN girls. Depressed anorexic girls had lower total and LS BMD and LM than nondepressed girls (Fig. 1). Depression scores were negatively associated with all bone parameters, BMI, and LM, but not FM (Table 2 and Fig. 2). After Bonferroni corrections, the significant differences between the depressed and nondepressed groups remained for all variables. After adjustment for LM and BMI, the association between depression and LS BMD remained significant (P = 0.05). However, TB BMD was no longer associated with depression after adjustment for BMI (P = 0.34) and LM (P = 0.26). The five depressed AN girls with primary amenorrhoea had significantly lower spine BMD than those with depression who had menstruated (Z-score, -3.6 ± 0.04 vs. -2.1 ± 0.3; P = 0.02). However, when girls with primary amenorrhoea were excluded from the analysis, there was a tendency for BMD to be lower in depressed (n = 9) compared with nondepressed (n = 30) anorexic girls.

Results

Fourteen of the 45 anorexic girls had moderate to severe depression (HAMD-D ≥ 13 and MADRS ≥ 20) (Table 1). No differences were observed in age, Tanner stage, menarche, gynecological age, duration of AN, calcium intake, body weight, height, and FM between the two groups. Of the six girls with primary amenorrhoea, five occurred in those with AN and depression. Two girls with AN and depression reported fractures (wrist and ankle), whereas no fractures were reported in those without depression. There was a tendency toward decreased BMI in depressed AN girls. Depressed anorexic girls had lower total and LS BMD and LM than nondepressed girls (Fig. 1). Depression scores were negatively associated with all bone parameters, BMI, and LM, but not FM (Table 2 and Fig. 2). After Bonferroni corrections, the significant differences between the depressed and nondepressed groups remained for all variables. After adjustment for LM and BMI, the association between depression and LS BMD remained significant (P = 0.05). However, TB BMD was no longer associated with depression after adjustment for BMI (P = 0.34) and LM (P = 0.26). The five depressed AN girls with primary amenorrhoea had significantly lower spine BMD than those with depression who had menstruated (Z-score, -3.6 ± 0.04 vs. -2.1 ± 0.3; P = 0.02). However, when girls with primary amenorrhoea were excluded from the analysis, there was a tendency for BMD to be lower in depressed (n = 9) compared with nondepressed (n = 30) anorexic girls.

Discussion

In this cross-sectional study, anorexic adolescent girls with depression had greater deficits in BMD than those without depression. A negative relationship was observed between BMD and the depression score. LM and BMI were also negatively associated with depression score. Girls with depression and primary amenorrhoea had an additional reduction in BMD compared with those who had menstruated. We confirmed low BMD is common in girls with AN (1, 4, 5, 8) and extend this observation by reporting that depression in this condition is associated with more severe deficits in BMD. A coincidence of depression and AN has been reported in adolescent girls and women (13, 16). Ivansson et al. (24) reported that depression was a common comorbid problem in anorexic females, and AN may trigger the first episode of
TABLE 2. Correlations between BMI, bone mass measures, body composition and depression scores using two different tools in 45 anorexic adolescent girls

<table>
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<tr>
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<th>HAM-D</th>
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<tr>
<td></td>
<td>r</td>
<td>P</td>
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<tr>
<td>BMI</td>
<td>-0.32</td>
<td>0.03</td>
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<tr>
<td>Total BMC</td>
<td>-0.39</td>
<td>0.009</td>
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<tr>
<td>Total body BMD</td>
<td>-0.4</td>
<td>0.006</td>
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<tr>
<td>Spine BMD</td>
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<td>0.0001</td>
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<tr>
<td>Z-score spine BMD</td>
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<td>0.0005</td>
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<tr>
<td>Fat mass (%)</td>
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<td>0.34</td>
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<tr>
<td>Lean mass</td>
<td>-0.32</td>
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FIG. 2. Relationship between the depression scores (MADRS) and LS BMD in 45 adolescent girls with AN (r = −0.56; P = 0.0001).

depression in adolescents. Bizeul et al. (16) reported that the severity of depression influenced the eating disorder's inventory in young anorexic women. Depression concomitant with adolescent AN has been considered mainly secondary to the features of AN, but the underlying relationships remain unclear (25).

To our knowledge, this is the first demonstration of a quantitative association between BMD and depression in anorexic adolescent girls. Depression may modify the course of AN and is associated with the severity of the disease in adolescence (26, 27). In this study, more severe deficits in BMD and LM occurred in depressed girls, whereas other variables, including FM, did not differ. Yazici et al. (28) found decreased BMD in women with major depressive disorder but did not confirm an association between BMD and the severity of depression.

Depression may be an independent risk factor for osteoporosis in AN, although the causal pathway for lower BMD in depressed anorexic girls is unclear. An association between depression and reduced bone mass in middle-aged or older population has been found in several studies (9, 11, 12). Osteoporosis has been considered a consequence of depression in adults (29, 30), although results varied by sex and age. Depressive disorders have been reported to increase a risk of osteoporosis in men (31–34) and women (11, 28). Depression-induced neuroendocrine alterations may contribute to low BMD in conjunction with caloric deficiency, inadequate dietary calcium intake, and malnutrition in anorexic girls. BMI and body composition, reflecting nutritional status, correlate positively with BMD; thus, the deficits in BMD may partly result from malnutrition, reduced LM, and mechanical implications associated therewith. It is also possible that depressed individuals in this study had lower BMI, LM, and lower BMD independent of the AN. Furthermore, a cross-sectional study is not able to reveal if reduced BMD occurred before the development of depression. However, this does not detract from the likelihood that the risk of fracture is higher in these patients than in girls with AN alone.

Insight into the differing associations may offer alternatives to treatment. Thus, antidepressants may be a part of the management of anorexic girls with depression. Randomized double-blind placebo-controlled trials will be needed in this group to investigate the effect of such a therapy on BMD.

We conclude that anorexic girls with depression are at higher risk of low BMD than those without depression. Further studies are needed to identify factors associated with the deficits in BMD and whether antidepressants may alleviate the deficit in BMD.

Acknowledgments

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