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Bone mineralization and densitometric evaluation of vertebral fractures in women 6–21 years after the onset of anorexia nervosa symptoms

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Summary

Objectives: We attempted to assess bone mineralization and the frequency of fractures occurrence in women with a history of treatment of anorexia nervosa (AN) in adolescence.

Material and methods: 47 women (age 20–36.8 years) were re-examined 6.33–21.2 years after the onset of AN symptoms. Bone mineral density (BMD) of total body, lumbar spine, femoral neck, total hip (DXA) and densitometric Vertebral Fracture Assessment (VFA) were performed on 46 of women and BAP, P1NP, CTX, estradiol, testosterone, cortisol, IGF-1, leptin, DHEA-S on 45 of women entered for the current study. Current BMD results were compared with available baseline results from the time of hospitalization.

Results: Currently BMD Z-score <-1 examined at any location occurred in 28 from 46 women (including Z-score <-2 in 5 women). In 11 from 12 women with reduced BMD at the time of hospitalization current total body BMD was within the normal range. Lumbar spine BMD was normalized or improved respectively in 5 and 6 from 15 women. Currently increased levels/activity of bone formation markers: P1NP in 27 (60%) and BAP in 28 women (62.2%) were observed. In 7 women (15.6%) increased values of bone formation markers with increased marker of bone resorption (CTX) occurred. Osteoporotic fractures and fractures in the spine in VFA were not observed during the observation period.

Conclusions: Despite early treatment of adolescent-onset AN and good outcomes of the treatment, decreased BMD was currently present in 60.9% of women. During follow-up normalization or significant improvement in BMD results (total body, lumbar spine) were observed in majority of cases.

Key words: anorexia nervosa, osteoporosis, densitometric vertebral fracture assessment

Introduction

Anorexia nervosa (AN) usually begins in adolescence and early adulthood – crucial periods to achieve peak bone mass. During adolescence in women a range of 40 to 60% bone mass increase occurs. In healthy women 90% of peak bone mass is achieved at age about 15 and the final bone mineral density (BMD) at the age of 25 or even 30 [1, 2]. AN often has a chronic or recurrent course [3] with tendency to long-term amenorrhea even with normal body weight achieved [4]. During AN course many abnormalities in hormone secretion which affect bone metabolism are observed [1, 5–7]. All above, starvation and low body weight, are related to high risk of osteoporosis secondary to AN.

The values of BMD matching the osteopenia or osteoporosis criteria were observed respectively in 35–92% and 13–50% of AN patients [8]. BMD at the border or below the threshold of bone fragility in the lumbar spine and femoral neck in chronic course of AN occurred even in 45% and 75% of women, respectively [9].

Prospective studies of BMD changes in AN give inconsistent results. Some studies show improvement of BMD associated with the restoration of normal body weight up to the normal range for age [10, 11]. Others show maintenance of the low BMD despite recovery [12–16].

Retrospective studies indicate an increased risk of bone fractures in AN. According to Lucas et al. [17], standardized risk of fractures in AN (number of fractures in comparison to those expected from the general population) was 2.9, and 40 years after diagnosis of AN spine, femur and distal radius fractures were observed in 57% of women. In another study almost doubled fracture risk was observed (for spine almost 3.5-times higher) [18].

Due to inconsistent results regarding BMD changes in women who suffered from AN we have attempted to assess bone mineralization and the frequency of spine fractures occurrence using densitometric Vertebral Fracture Assessment (VFA) [19] in women with the onset of AN during adolescence and relatively short period of AN symptoms before treatment.

Material

47 women were examined 11.6±3.2 years (range from 5.91 to 18.33) after the hospitalization due to adolescent-onset AN (according to ICD-10 criteria [20]). These

women have entered for the study following a mail invitation to 154 former female patients. 47 of them agreed to participate in the study personally. We received information that 3 women died (in 2 cases the reason of death were complication of AN). 17 women phoned informing about the absence of fractures after hospitalization. The remaining were not available due to a change of address or a lack of response to the invitation.

The study was approved by the Bioethical Committee of Medical University of Warsaw. Participants gave their informed consent to the participation in the study.

Methods

Structured interview about the course of illness, assessment of nutritional status and examination of total body and lumbar spine BMD (respectively in 128 and 120 of patients) were performed in all cases at the beginning of the hospitalization that took place in adolescence.

Currently, a structured interview about the course of illness after discharge from hospital, and other factors having potential impact on BMD was performed (recurrence of AN, menstrual history, contraceptives and hormones receiving, dietary restrictions, the occurrence of episodes of binge eating, purging, laxatives abuse, age of being cured for AN – defined as the restoration of normal patterns of eating and body weight, physical activity, smoking, alcohol abuse, chronic use of medication, chronic illnesses), the incidence of fractures after AN onset and about current state of health was conducted. Patients were weighed and measured. An interview regarding occurrence of osteoporosis in family was conducted.

Densitometry

During hospitalization in adolescence BMD measurements of total skeleton and lumbar spine BMD (L2-L4) were performed using DXA method (dual-energy X-ray absorptiometry) with Lunar DPX-L densitometer. Due to the age of the patients during hospitalization (under 20 years) results were presented as a Z-score and in g/cm^2.

Currently total body, lumbar spine (L1-L4), femoral neck and proximal end of the femur BMD were examined in 46 women with the Discovery A densitometer (Hologic). Due to the fact that in young adults (over 20 years of age), T-scores values $\leq$-2.5 may suggest the presence of secondary osteoporosis, the results should be analyzed in conjunction with the values of Z-score, which is the amount of standard deviations compared to the mean for age and sex (limit value of Z-score for osteoporosis is – 2), the current results of BMD were shown in T-score (the number of standard deviations from the peak BMD), Z-score and in g/cm^2. Baseline BMD measurements (from the time of hospitalization) of the total body and lumbar spine were available respectively in 37 and 35 of women who currently entered for the study.

Unfortunately, due to changes in the densitometers, associated with the necessity of their replacement during the period of observation, it is impossible to compare BMD values expressed in g/cm^2, which would only be possible using the same densitometer. The dynamics of BMD was evaluated by comparing Z-scores

Asymptomatic vertebral fractures were assessed in examined women with VFA method [19].

Biochemical tests

Biochemical tests were performed in 45 from 47 women. Fasting blood samples were collected between 7:30 and 9:30 a.m. Samples for biochemical determinations were routinely centrifuged and serum was kept frozen at –70ºC until quantitative assay. The concentrations of estradiol, testosterone, cortisol, dehydroepiandrosterone sulfate (DHEA-S), C-terminal cross-linked telopeptide of collagen type 1 (CTX) and procollagen type 1 amino-terminal propeptide (P1NP) were measured using the Roche diagnostics tests (http://e-labdoc.roche.com) dedicated to Hitachi High-Technologies Corporation (Tokyo, Japan) Elecsys 2010 automatic analyzer.

The concentrations of other analytes – leptin, insulin-like growth factor 1 (IGF-1), bone alkaline phosphatase (BAP) activity – in serum were measured by following manual immunoassays according to manufacturer's protocol: Human Leptin ELISA Clinical Range Cat No RD 191001100 BioVendor (Brno, Czech Republic), IGF-1-EASIA Cat No KAP1581, DiAsource ImmnunoAssays S.A (Louvain-la-Neuve, Belgium), BAP EIA kit Quidel Corp, (San Diego, USA). The color intensity of individual wells was measured using ELISA Multiscan Ex (Thermo Labsystems; Finland) at 450 nm wavelength. Ascent Software Version 2.6 (Thermo Labsystems; Finland) was used to analyze the results.

Statistical analysis

Statistical analysis was performed using Statistica 10.0 (Statsoft, Tulsa, OK, USA). Continuous data were presented as mean, standard deviation and range. Normality of distribution was tested using the Shapiro-Wilk test. Continuous variables that deviated from normality were logarithmically transformed before analysis. Categorical variables were analyzed with the χ^2 test or Fisher exact test. For comparisons between two groups Student's t-test was performed. Intra-group changes were evaluated by paired sample Student's t-tests. Correlations were evaluated using the Pearson's correlation coefficient. A p value of <0.05 was considered as statistically significant.

Results

Clinical data

The characteristics of the study group including clinical data from the hospitalization and BMD results are shown in Table1. Twelve girls were premenarcheal. Atypical AN was diagnosed in 3 patients (they did not meet the criterion of weight deficiency).

Table 1. **Characteristics of the study group and baseline results of densitometry (during hospitalization in adolescence)**

Clinical variable	Mean	SD	Minimum	Maximum
Age of hospitalization (years)	14.6	2.0	11.4	22.3
Onset of AN (years)	13.7	1.6	10.3	17.0
Age of menarche onset (years)	12.4	1.2	10.0	14.5
Age of menstrual period stop (years)	14.3	1.6	11.1	17.8
Period of the AN before hospitalization (months)	10.1	12.0	3.0	84.0
Period of secondary amenorrhea before hospitalization (months)	8.4	10.5	2.0	60.0
Body weight (kg)	36.6	5.8	28.5	49.9
Height (cm)	160.0	6.9	145.0	176.0
%IBW (% of ideal body weight)	72.9	9.8	49.1	92.5
Weight loss relative to weight before illness (%)	28.0	10.0	12.0	59.5
BMI (kg/m^2)	14.3	1.7	10.9	18.4
sdBMI	-1.59	0.69	-3.68	-0.11
BMD – total body (g/cm^2)	1.01	0.10	0.85	1.21
BMD – total body(Z-score)	-0.48	1.17	-2.80	2.59
BMD L2-L4 (g/cm^2)	0.99	0.16	0.71	1.35
BMD L2-L4 (Z-score)	-0.66	1.59	-3.20	3.08

Patients with BMD Z-score <-1 in baseline examination were recommended to take 500 IU of Vit. D_3 and 600 mg elemental calcium daily.

There were no statistical differences in terms of clinical data and the results of BMD at the time of former hospitalization in the group of women who entered for the current study compared with those who did not come forward.

Actual health status of women (at follow-up) is presented in Table 2. Descriptive statistics of current clinical data are presented in Table 3.

Table 2. **Actual health status (follow-up)**

	Without symptoms of AN*or BN**	AN	BN	BMI (kg/m^2)			Menstruation		
				18.5–24.99	<18.5***	≥25	Spontaneous menstruation	Contraceptives or hormonal therapy	Breast-feeding
Number of women	34	5	8	34	8	5	29****	16	2
%	72	11	17	72	17	11	62	34	4

* AN – anorexia nervosa; ** BN – bulimia nervosa; *** In the group of women with BMI below normal range (BMI <18.5 kg/m^2): 6 (12.8%) were underweight (BMI 17–18.49 kg/m^2), 2 were emaciated (16–16.99 BMI kg/m^2). BMI <16 kg/m^2 was not found in any case. **** Including 5 menstruating irregularly

Table 3. **Clinical data at the time of follow-up**

Clinical variable	Mean	SD	Minimum	Maximum
Age (years)	26.12	3.82	20.00	36.83
Period of time since hospitalization (years)	11.55	3.20	5.91	18.33
Period of time since the onset of AN (years)	12.69	3.62	6.33	21.20
Body weight (kg)	56.54	8.50	42.50	81.00
Height (cm)	164.81	6.35	152	182
BMI (kg/m^2)	20.83	2.67	16.13	27.80
Age of recovery from AN (years), n = 39	18.01	2.93	12.50	25.00
Period of time from the onset of AN to recovery (years)	4.61	3.48	0.83	17.00
Age in which menstruation returned or age of menarche (years)	16.75	2.63	12.50	26.00
Maintenance time of secondary amenorrhea (years), n = 29	2.86	2.02	0.67	9.50

Most of the women were currently under 30 years of age (43 women). Menarche occurred in all patients who were premenarcheal at the time of hospitalization (including one after hormonal treatment). In group with secondary amenorrhea at the time of hospitalization, in 17 cases there was a spontaneous return of menses while in 18 after hormonal treatment.

Seventeen women smoked cigarettes, 8 abused alcohol. One woman suffered from ulcerative colitis (treated with sulfasalazine). Other women did not take chronically drugs which could affect BMD.

Densitometry and biochemistry results (at the time of follow-up)

Descriptive statistics on the current densitometry results, hormonal results and markers of bone metabolism are presented in Table 4.

Table 4. **Results of densitometry, markers of bone metabolism and hormonal tests at the time of follow-up**

Result	Mean	SD	Minimum	Maximum
BMD – total body (g/cm^2)	1.14	0.08	1.01	1.42
BMD – total body (T-score)	0.39	0.93	-1.1	3.7
BMD L1-L4 (g/cm^2)	0.95	0.11	0.77	1.27
BMD L1-L4 (T-score)	-0.85	0.98	-2.5	2.1
BMD proximal end of the femur (g/cm^2)	0.85	0.1	0.64	1.14
BMD proximal end of the femur (T-score)	-0.77	0.81	-2.5	1.6
BMD femoral neck (g/cm^2)	0.76	0.1	0.58	1.1
BMD femoral neck (T-score)	-0.83	0.86	-2.4	2.3
Osteocalcin (ng/ml)	24.22	9.53	6.54	55.39
P1NP (ng/ml)	79.82	49.07	19.25	228.7
BAP (U/l)	36.37	16.87	15.66	94.78
CTX (pg/ml)	398.42	199.78	124.6	919.3
Estradiol (pg/ml)	86.76	87.48	<5	443.7
Testosterone (ng/ml)	0.28	0.16	0.06	0.66
DHEA-S (ug/dl)	224.25	91.66	70.26	504.5
Cortisol in serum (ug/dl)	19.32	8.98	8.73	46.89
Leptin (ng/ml)	9.4	9.64	0.99	41.95
IGF-1 (ng/ml)	224.93	94.91	120.5	493.3

Current results of densitometry (in accordance to BMD in T-score ranges, i.e., an amount of standard deviations compared to the peak bone mass) are shown in Table 5.

Table 5. **Current results of bone mineral density (T-score range); N = 46**

Localization	T-score ≥-1 (norm)	T-score <-1 and >-2.5 osteopenia	T-score ≤ – 2.5 osteoporosis
Lumbar spine	23 patients 50%	22 patients 47.8%	1 patient
Femoral neck	27 patients 58.7%	19 patients 41.3%	0

table continued on the next page

Proximal end of the femur	32 patients 69.6%	13 patients 28.3%	1 patient
Total body	45 patients 97.8%	1 patient	0
Any of tested locations	18 patients 39.1%	26 patients 56.5%	2 patients 4.4%

Table 6 presents the actual results of the densitometry according to Z-score ranges (the amount of standard deviations from the mean BMD for age and sex). In both cases in the current study, decrease in BMD in T-score corresponding to values for osteoporosis (T-score of ≤-2.5) was accompanied by a decrease in BMD expressed as Z-score (Z-score <-2). Z-score <-2 was found in 3 additional women (T-score > – 2.5).

Table 6. **Current results of bone mineral density – Z-score range; N = 46**

Localization	Z-score ≥-1 (norm)	Z-score <-1 a ≥-2 (slightly lowered)	Z-score <-2 (greatly lowered)
Lumbar spine	25 women 54.3%	18 women 39.1%	3 women 6.5%
Femoral neck	28women 60.9%	16 women 34.8%	2 women 4.3%
Proximal end of the femur	32 women 69.6%	12 women 26.1%	2 women 4.3%
Total body	46 women 100%	0	0
Any of tested locations	20 women 43.5%	21 women 45.7%	5 women 10.9%

Markers of bone formation (P1NP, BAP) were within normal limits,, in 18 (40%) and 17 of women (37.8%), respectively. Higher than normal concentrations were found respectively in 27 (60%) and 28 patients (62.2%). Indicator of bone resorption (CTX) was elevated in seven patients (15.6%) and in others it was within normal range. All woman with an elevated CTX also had elevated levels/activity of P1NP and BAP.

Total skeleton BMD was performed in 37 women twice (during hospitalization and currently), whereas lumbar spine BMD in 35. During hospitalization in adolescence decreased BMD (Z-score <-1) in terms of the total skeleton was found in 12 cases (32.4%) and in the lumbar spine in 15 patients (42.9%).

Figures 1 and 2 show the comparisons of current results of BMD (Z-score) to results from the period of the hospitalization in adolescence (in women who had reduced BMD Z-score <-1 during previous hospitalization). In 11 out of 12 women with reduced total skeleton BMD (Z-score <-1) at the time of hospitalization, current results

were within the normal range (Z-score ≥-1). In one patient BMD remained decreased (Z-score currently amounting to – 1.1 vs. – 1.3 in the first study). In terms of lumbar spine the overall normalization (change in the Z-score value in the first study from the range between <-1 and > – 2.5 to Z-score ≥-1) was observed in 5 patients, and results improved (change in the value of Z-score from ≤-2.5 to Z-score >-2) in 6 out of 15 women. In three women the maintenance of BMD Z-score in the range of <-1 and ≥ 2 was found. In one case there was a decrease of Z-score from – 1.6 to – 2.3.

Comparison of the results in the Z-score indicates a favorable dynamic change in BMD in the period of observation (Figures 1 and 2).

Total body BMD and lumbar spine BMD (Z-score) in present study closely correlated with the results of BMD from the period of hospitalization (for total skeleton BMD $r = 0.66$, $p < 0.001$; for lumbar spine BMD $r = 0.67$, $p < 0.001$). Analysis of variance showed significantly lower results in lumbar spine BMD (T-score of – 1.9 vs. – 0.72; $F = 3.58$, $p < 0.04$), femoral neck (T-score – 1.64 vs. – 0.65; $F = 3.65$, $p < 0.03$) and proximal end of the femur (T-score – 1.58 vs. 0.58; $F = 4.45$, $p < 0.02$) in the groups that currently meet the criteria for AN or bulimia nervosa (BN) compared with women who do not meet these criteria. Such differences were not found for total

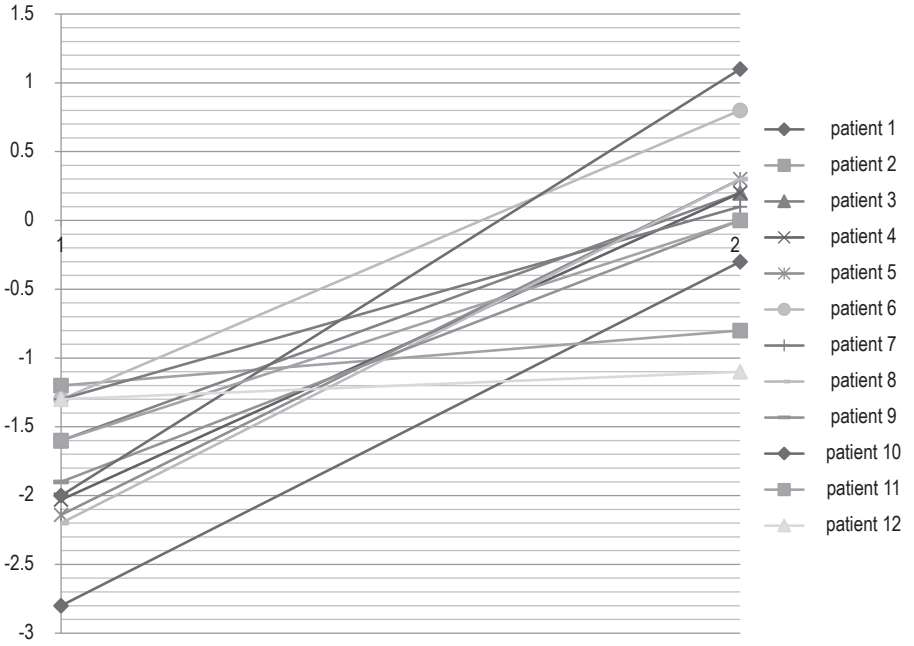

Figure 1. **Comparison of BMD total body (Z-score) results at the time of follow-up to results from the hospitalization in patients with primarily decreased BMD**

BMD – total body (Z-score)

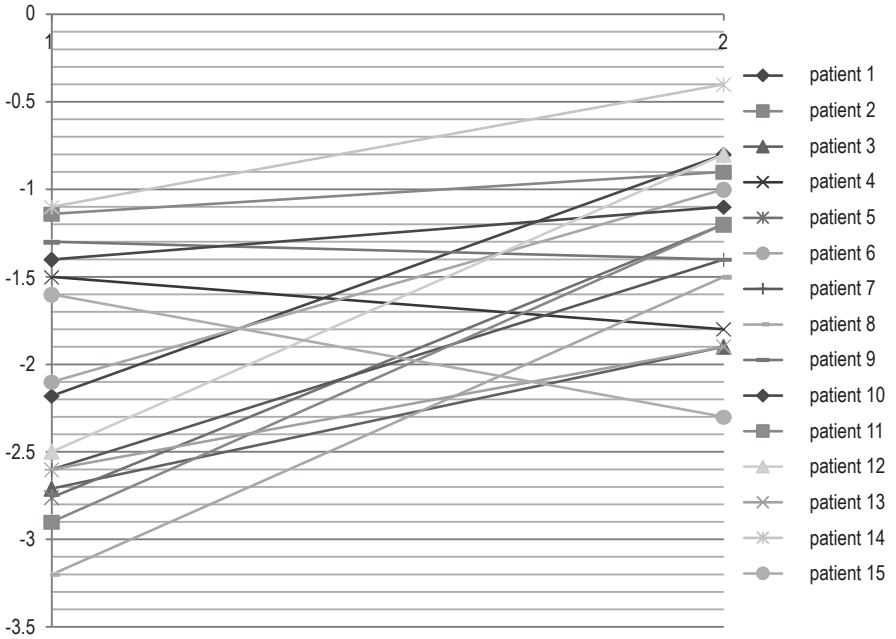

Figure 2. **Comparison of BMD lumbar spine (Z-score) results at the time of follow-up to results from the hospitalization in patients with primarily decreased BMD**

BMD – lumbar spine (Z-score)

skeleton BMD. There were no statistical differences in current BMD (T-scores) at any of the examined locations in groups of smokers, alcohol abusers, those with history of osteoporosis in the family compared with those without these problems. There were also no statistical differences in BMD in groups divided due to the level of physical activity (in 22 women activity less than 3 hours, in 12 – 3–6 hours and in 13 over 6 hours of exercise per week) and in groups divided due to levels of cortisol and P1NP, BAP, CTX (within and above the normal range), estradiol and DHEA-S (levels in the normal range compared to the group with concentrations below the norm).

No correlation between BMD (T-scores) and the concentration of hormones associated with the current level of nutrition (leptin, IGF-1), estradiol, testosterone, cortisol and markers of bone metabolism were found. No differences between groups divided due to BMD within (T-score ≥-1) and below the normal range (T-score <-1) in terms of bone metabolism markers and tested hormones concentration were found.

Fractures occurred in seven women (radial bone – 3 cases, metatarsal – 2, rib – 1, thumb – 1). In 6 cases, the fractures resulted from injuries. As far as fractures of radial bone are concerned they were results of injuries during sports. In one female features of fracture of the first degree according to VTA of the 4th lumbar vertebra was suspected.

The radiological examination did not confirm presence of a fracture. Deformation was caused by malformation of the spine (lack of fusion of posterior arch of L5 and S1).

Seventeen (36.2%) women reported a family history of osteoporosis (in each case referred to women, mostly grandmothers).

Discussion

Previous prospective studies of bone mineralization in patients with AN are mostly short-term and show decrease of BMD in the initial period of AN treatment or lack of expected increases of BMD during adolescence. The increase of BMD is observed after improvement in body weight and return of menstruation [9, 21–29]. Several studies with long-term observation indicate the possibility of BMD normalization [10, 11, 30] or the persistence of low BMD many years after initial diagnosis and beginning of AN treatment [12–15].

Our study covers long period of observation from the implementation of treatment (11.6±3.2 years) and involves relatively homogeneous group in terms of duration of AN and amenorrhea before hospitalization. The observed group in the final point of observation was mostly in the age at which BMD increase is still possible (43 persons aged between 20th and 30th year of life). In addition, the impact of age in the observed group of women could be strengthened by the fact that in AN in adolescence maturation of bone might be delayed (which is reflected in delayed bone age).

Our study demonstrated possibility to normalize BMD in women who were treated due to AN during adolescence. Comparison of results of total skeleton and lumbar spine BMD from the period of previous hospitalization with current results indicates that in majority of cases with reduced BMD (Z-score) at the time of hospitalization occurred normalization or significant improvement in BMD. Advantageous changes over the observation period can be associated with short periods of illness and secondary amenorrhea before the beginning of treatment in the study group, a long period of observation and good outcomes of treatment. Overestimation of the proportion of patients with decreased BMD during hospitalization cannot be excluded due to the fact that Z-score was calculated using chronological age and not a bone age [25, 31, 32]. The results of our study are consistent with other studies that have shown the ability to increase BMD to normal range after restoration of normal body weight [10, 11].

Currently, decrease in BMD (T-score <-1 to >-2.5) in any location corresponding to the value for osteopenia was found in 56.5% of women. There were only 2 women (4.4%) with BMD values typical for osteoporosis (T-score ≤-2.5). Z-score <-2 was found in five (10.9%) cases (including 2 cases with T score ≤-2.5 at the same time).

In other studies densitometry values for osteoporosis were observed in 21–44% [26, 29, 33–36] and BMD values for osteopenia in 48–92% of women with AN [26, 29, 33–37]. After an average of 11.4 years from initial diagnosis of AN Brooks et al. [12] observed BMD values in the lumbar spine, femoral neck and proximal end of

the femur corresponding with osteopenia in 50% and with osteoporosis in 35% of women. Worse results of BMD in this study can be explained by a longer amenorrhea period prior to treatment than in women from our study (2.1±2.5 vs. 0.7±0.88 years). The heterogeneity of the group regarding age of respondents, among whom 19% were before the age of 19 may have implication on results. In another study, which was conducted on average of 6 years after recovery [15] osteopenia was found in 12 out of 18 subjects in the lumbar spine and femur, and values for osteoporosis were found in 2 examined women. In that study BMD correlated with the period of amenorrhea and the ratio of the period from being cured and duration of illness. Reduced BMD in lumbar spine, total skeleton and proximal end of the femur was also observed by Wentz et al. [16, 38] 11 years after initial diagnosis of AN. After another 4 years of follow-up there was an increase in total skeleton and lumbar spine BMD and the upward trend in the proximal end of the femur. In 8 out of 11 subjects reduced BMD was found, however, values for osteoporosis have not been reported in any case. In another study [8] osteoporosis was found only in 8% of women with good results of treatment for AN with onset in adolescence.

In this study no fractures were found in spine using VFA method. In contrast to our study Di Vasta et al. [39] found the presence of asymptomatic fractures in spine in 2 women (2.5% of respondents) at baseline and then 10 fractures in 9 women (12.5%) during the 18-month observation of young women (mean age at baseline 18.1±2.7 years). It is not known whether fractures were confirmed radiographically. Average Z-score of the lumbar spine in this study was lower than in our study group.

In our study group 14.9% of women reported fractures, however, only one appeared without a significant injury. About 11 years after the onset of the illness, Wentz et al. [38], in a group comparable in terms of age and observation period, found that women reported fractures as often as in the control group. After another 4 years of follow-up, there was no further fractures in women with low BMD [16]. In contrast Maugars et al. [24] found low-energy fractures in 22% of women with AN during 30 months of observation. Women examined by them were very heterogeneous in terms of duration of illness (0.5 to 22 years), had a significantly longer mean duration of illness and duration of amenorrhea as well as significantly lower BMD than observed by us. In large group of women recruited from the entire population (50% never treated) researchers [36] found the presence of fractures in 30% of examined patients, but these women had longer period of AN and amenorrhea and had lower BMI during the study compared to our group. 34% of these patients had BMD values that met the criteria for osteoporosis in densitometry.

A current state of the patients (persistence of the symptoms of AN and bulimia nervosa) had the negative impact on the BMD results. In many recent studies the major importance of weight gain and recovery as the factors related to the improvement of bone mineralization were also indicated [9, 21, 22–29].

The majority of patients had increased levels of markers of bone formation and in others concentrations were within the normal limits. In 15.6% of women occurred increased values of bone formation markers with increased concentration of bone resorption marker. Our results may indicate an increased rate of bone formation and, in some cases, increased bone turnover. These results are consistent with the results of a study by Hotta et al. [23], in which remission of changes in markers of bone metabolism typical for adult women with AN (decrease in the concentrations of markers of bone formation and increased bone resorption markers) was observed in women with BMI >16.4 kg/m^2. Other authors [10, 28] also found an increase in markers concentration of bone formation after the restoration of normal body weight. In contrast to other studies [28, 35] we did not found differences in the concentrations/activity of markers of bone resorption and formation in women with densitometric BMD values corresponding to values for osteopenia compared to those with normal BMD results, which can be associated with a relatively good nutritional status of the examined women and the fact that most of them no longer met the diagnostic criteria of AN during follow-up.

Limitations of the study

The major limitation of our study is relatively low ratio of re-examined patients (30.5% of invited patients). However, as mentioned above, there were no statistical differences in terms of clinical data and the results of BMD at the hospitalization in the group of women who entered for the current study compared with those who did not come forward.

Another issue is use of different densitometers at baseline and in the current study. Due to this fact we did not have the possibility to compare changes in BMD in g/cm^2. Comparison of the Z-score, although closer to the truth, may also be subject to some error. L2-L4 BMD was determined at baseline, whereas in the current study L1-L4 BMD, thus comparisons of changes of lumbar spine BMD during the observation period should be made with caution.

Conclusions

The study shows that early implementation of effective treatment of adolescent-onset anorexia nervosa may prevent from osteoporosis and osteoporotic fracture in the future. However, an episode of anorexia nervosa in adolescence is associated with the presence of lower bone mineral density in substantial percentage of women. Current symptoms of anorexia nervosa or bulimia nervosa in women with history of hospitalization due to anorexia nervosa in adolescence are associated with the presence of lower bone mineral density.

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