High Risk of Osteoporosis in Male Patients with Eating Disorders

Philip S. Mehler, MD[1,2]*
Allison L. Sabel, MD, PhD, MPH[1,2]
Tureka Watson, MS[3]
Arnold E. Andersen, MD[3]

ABSTRACT

Objective: Osteoporosis has traditionally been considered a female problem. This study's purpose is to evaluate bone mineral density (BMD) in males with eating disorders.

Method: Charts of 70 consecutive males admitted to an eating disorder program were reviewed. Females admitted during the same time period were used for comparison. BMD was measured by dual-energy X-ray absorptiometry.

Results: Thirty-six percent (19/53) had osteopenia and 26% (14/53) had osteoporosis at the lumbar spine. A disproportionate number of males with anorexia restricting or binge/purge subtype (ANR/ANB) had osteoporosis, as well as those of older age, lower weights, and longer illness duration. BMD for ANR and ANB males was significantly lower than females ($p = .02$ and $p = .03$, respectively). In multivariate stepwise linear and logistic regression, lowest BMI and illness duration predicted lumbar *Z*-scores.

Conclusion: Males with ANR/ANB often have severe bone disease, which is worse than females, and is best predicted by a patient's lowest BMI and illness duration.

Keywords: male; osteoporosis; anorexia nervosa; osteopenia; bone density

(Int J Eat Disord 2008; 41:666–672)

Introduction

Osteoporosis is characterized by increased bone turnover and bone fragility due to progressive loss of bone mass. This leads to an increased fracture risk. Osteoporotic fractures are a common cause of disability. Up to one-third of individuals with osteoporosis who suffer a hip fracture, become totally dependent for assistance with basic activities of daily living.[1] In the United States, direct expenditures for osteoporotic fractures are estimated to be $18 billion annually.[2]

Although osteoporosis has traditionally been considered a disease of women, men also incur substantial bone loss with aging. Osteoporotic vertebral fractures experienced by men occur at approximately one-third the rate of women.[3] However, the pattern of bone loss in males is distinctly different from that seen in females. In females, bone mineral density (BMD) begins to decline slowly after the age of 40 until the age of 55, when the loss of bone density accelerates. However, the pattern among males is a slow decline after the age of 40 so that by age 60, their BMD decreases to levels almost equivalent to females of equal age.[4] Overall, osteoporosis occurs less frequently in men due to several factors including greater accumulation of skeletal bone mass during youth, greater bone size, the absence of a distinct equivalent of menopause, and a shorter average lifespan.[5]

There is a group of patients who are at particularly high risk of developing osteoporosis, namely, females with anorexia nervosa. Low bone density constitutes a rather common complication of anorexia nervosa with severe implications for morbidity, due to the risk of fractures. Notwithstanding the young age of most patients with anorexia nervosa, bone density is reduced at either the spine or hip by more than 2.5 SD (osteoporosis) in almost 40% of patients and by more than one standard deviation (osteopenia) in 92% of women with anorexia nervosa.[6] Many questions remain regarding the etiology and course of bone loss in patients with eating disorders, but the majority of the studies of bone loss have been carried out in females. The clinical risk factors for low bone density in women with an eating disorder are weight loss, length of ill-

Accepted 13 March 2008
*Correspondence to: Dr. Philip S. Mehler, Department of Internal Medicine, Denver Health Medical Center, 660 Bannock Street, MC0278, Denver, CO 80204. E-mail: pmehler@dhha.org
[1] Department of Internal Medicine, Denver Health Medical Center, Denver, Colorado
[2] Department of Preventive Medicine, University of Colorado Health Sciences Center, Denver, Colorado
[3] Department of Psychiatry, University of Iowa, Iowa City, Iowa
Published online 4 June 2008 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/eat.20554

ness, and duration of amenorrhea.[7–10] Since there are a paucity of studies addressing osteoporosis in males with eating disorders, the purposes of this study are as follows: (1) to investigate BMD in male patients with eating disorders and document their severity of bone loss, (2) compare BMD in male patients with eating disorder versus females, (3) and identify factors that contribute to BMD reduction in males.

Method

Our study sample of patients consisted of 70 males consecutively admitted to the inpatient eating disorder unit at the University of Iowa Hospitals and Clinics between 1998 and June 2003. Female patients admitted for the treatment of eating disorder during this time period were also reviewed and stratified according to diagnosis and bone density ($n = 522$). The medical record of these patients were retrospectively reviewed and data concerning demographics, personal history, illness history, BMD, psychopathology, and comorbidity were extracted from the detailed histories and mental status examinations of the physicians, nurses, psychologists, social workers, and dieticians who examined each patient. The information collected was written on a code sheet with no personal identification and double entered into an Access database with quality control features. The eating disorder diagnosis of each patient conformed to DSM-IV criteria for anorexia nervosa restricting subtype (ANR), anorexia nervosa binge-eating/purging subtype (ANB), or bulimia nervosa (BN). Patients with a diagnosis of eating disorder not otherwise specified (EDNOS) suffered from eating disorders not meeting strict DSM-IV criteria for anorexia or BN, but who were sufficiently ill to require inpatient treatment. In regard to a particular factor in the past history such as excessive exercise, the chart review only identified patients in whom this variable was explicitly stated to be present or absent. The variable was considered missing if it was not located in the chart. BMD was evaluated using a Hologic dual-energy X-ray absorptiometry (DEXA Scan) of the lumbar spine at the L1–L4 level. BMD measurements were expressed as grams per square centimeter. DEXA results for females admitted during this time frame were reviewed. IRB approval was obtained prior to initiation of the study.

Statistical Analysis

Because of BMD assessment not being a standard part of the eating disorder medical evaluation in the past, 24.3% (17/70) of the male study population and 20.1% (105/522) of the female comparison group were missing the lumbar spine measurements. Since almost half of the study populations were missing total hip measurements (30/70), no detailed analysis was performed for the hip. Because the continuous variables were highly skewed, we described our study population with medians and interquartile ranges. The median test was used to determine significant differences between the eating disorders.

We analyzed the bone density using *Z*-scores, which compares the bone density of a participant with that of a gender- and age-matched control, rather than the better known *T*-scores, which compare the bone density of a participant to the mean peak bone density of gender-matched young adults. Since the majority of the patients in our study have not yet attained peak bone mass, the *Z*-score is a more appropriate measure. BMD was normally distributed; thus means and standard deviations (SD) were used to describe the population, and the analysis of variance test determined significant differences between the eating disorders. The lumbar *Z*-score was divided into two groups, above −1 SD and −1 SD or below. This division was used to compare the ratios of the categorical risk factors (childhood obesity, physical abuse, sexual abuse, lifetime binge, lifetime purge, lifetime depression, alcohol abuse, or drug abuse) with Pearson's Chi square or Fisher's exact test. Multivariate stepwise linear regression was used to predict lumbar *Z*-score based on six known risk factors [body mass index (BMI) at admission, lowest BMI, BMI at disease onset, duration of illness, age at disease onset, and Eating Attitudes Test] during hospitalization. Multivariate logistic regression was run using the same predictors to determine significant risk factors for osteoporosis.

Results

Ninety-nine percent of the male study populations were Caucasian, 78.6% were single, and 52.2% had completed the 12th grade. **Table 1** describes the study population's past history of comorbid conditions. A slightly larger proportion of BN males had a history of childhood obesity and excessive exercise than the other diagnostic groups, whereas a slightly smaller proportion of ANR males had a history of physical, sexual and substance abuse, and depression when compared with the other subgroups. Binging, purging, and substance abuse occurred more frequently among ANB and BN males.

Regarding weight history (**Table 2**), ANB males were slightly older at onset of illness and closer to normal weight. BN and EDNOS males were considerably more obese when their illness started and attained considerably higher weights than the males with anorexia. ANB males were noticeably

TABLE 1. Comorbid history of inpatient males with eating disorders

	ANB ($N = 9$)		ANR ($N = 25$)		BN ($N = 22$)		EDNOS ($N = 14$)	
	N	%	*N*	%	*N*	%	*N*	%
Childhood obesity	2/6	33.3	7/21	33.3	8/17	47.1	3/13	23.1
Sexual abuse	2/8	25.0	0/23	0.0	2/22	9.1	1/12	8.3
Physical abuse	1/8	12.5	1/23	4.4	5/22	22.7	3/10	30.0
Lifetime excessive exercise	4/8	50.0	14/24	56.0	18/21	81.8	9/14	64.3
Outpatient treatment	7/7	100.0	15/23	65.2	17/20	85.0	12/14	85.7
Lifetime binge	8/9	88.9	1/25	4.0	21/22	95.5	1/14	7.1
Lifetime purge	9/9	100.0	4/25	16.0	21/22	95.5	3/14	21.4
Lifetime depression	5/9	55.6	7/25	28.0	11/22	50.0	6/14	42.9
Alcohol abuse	3/9	33.3	1/25	4.0	10/22	45.5	2/14	14.3
Drug abuse	3/9	33.3	1/25	4.0	13/22	59.1	2/14	14.3

TABLE 2. Weight history of inpatient males with eating disorders (median, interquartile range)

	ANB ($n = 9$)	ANR ($n = 25$)	BN ($n = 22$)	EDNOS ($n = 14$)	Median Test *p*-Value
Onset age	18 (17–19)	14 (13–16)	15 (14–17)	16 (13–20)	.11
Onset %MMPW[a]	101 (93–115)	109 (98–117)	136 (120–168)	127 (96–166)	.002
Onset BMI	21.4 (19.9–24.0)	20.7 (19.4–22.4)	27.5 (23.4–34.4)	25.9 (18.9–35.9)	<.001
Highest weight age	18 (18–23)	14 (13–17)	16 (14–17)	16 (13–26)	.05
Highest %MMPW[a]	105 (92–132)	109 (101–117)	136 (120–181)	129 (106–166)	.003
Highest BMI	22.8 (20.5–27.2)	20.7 (20.0–22.4)	28.3 (23.4–35.9)	25.9 (20.4–35.9)	<.001
Lowest weight age	27 (24–39)	16 (14–25)	17 (14–22)	17 (14–23)	.01
Lowest %MMPW[a]	61 (57–65)	71 (63–75)	92 (85–112)	90 (83–98)	<.001
Lowest BMI	13.8 (12.4–14.5)	13.8 (12.9–15.3)	18.8 (16.2–23.1)	17.3 (16.2–19.8)	<.001

[a] %MMPW is percentage of mean-matched population weight.

TABLE 3. Admission and discharge data for inpatient males with eating disorders (median, interquartile range)

	ANB ($n = 9$)	ANR ($n = 25$)	BN ($n = 22$)	EDNOS ($n = 14$)	Median Test *p*-Value
Years with eating disorder	9.0 (6–12)	1.8 (1–4)	2.8 (1–10)	1.0 (0.7–5)	.01
Previous hospitalizations	3 (1–5)	1 (0–2)	0 (0–1)	0 (0–1)	.03
Testosterone (normal = 280–800 ng/dL)	189 (109–348)	155 (62–257)	449 (310–509)	19 (12–78)	.06
Admission Age	27 (24–39)	17 (14–26)	19 (16–28)	18 (14–28)	.02
Admission %MMPW[a]	65.8 (60.9–66.5)	70.8 (68.3–78.2)	102.7 (95.9–117.1)	97.2 (87.0–101.7)	<.001
Admission BMI	14.5 (13.6–14.7)	14.7 (13.5–16.0)	21.6 (20.0–25.3)	19.2 (16.7–22.2)	<.001
Discharge %MMPW[a]	85.6 (79.8–93.8)	89.5 (81.9–98.3)	107.6 (100.2–117.3)	101.2 (96.7–106.5)	<.001
Discharge BMI	19.0 (17.9–20.6)	18.4 (17.2–20.2)	21.9 (21.2–25.6)	20.3 (18.6–21.7)	.002
Hospital Days	74 (19–140)	41 (31–69)	16 (8–25)	18 (8–24)	<.001

[a] %MMPW is percentage of mean-matched population weight.

older and more severely underweight even at their lowest weight than the other diagnostic groups. On admission to the eating disorder unit, (**Table 3**), ANB males also appeared to be more severely ill than the other males. ANB males were older, sicker considerably longer and thus had more previous hospitalizations for their disorder, and had the lowest admission weight as a percentage of norms. Median admission testosterone levels were below normal range for all diagnostic groups, except BN males whose median testosterone was 449 ng/dL (normal 280–800 ng/dL). Each diagnostic group's median discharge weight was greater than 85% of normal, although ANB males were only slightly above at 85.6%.

Males with EDNOS and BN had the smallest reduction in their lumbar spine BMD (**Table 4**); they were above −1 SD while the males with anorexia nervosa were below −1 SD. On average, ANB males were the most bone deficient in the lumbar spine (−2.25 SD). When the lumbar *Z*-score was divided into two groups, above −1 SD and −1 SD or below, the diagnostic group with the largest proportion of patients below −1 SD on lumbar spine was the ANR group with 78.3% of patients (18/23) followed closely by ANB with 75% (6/8). Half of the patients with BN (7/14) and a quarter of the EDNOS patients (2/8) had a lumbar spine *Z*-score below −1 SD. The median age of the patients above −1 SD was 16 (IQR 15–25 years) and for patients −1 SD or below it was 24 (IQR 16–32 years). When lumbar *Z*-score cutoff was −2.5 SD, ANB also had the largest proportion of patients with a lumbar spine *Z*-score below −2.5 SD.

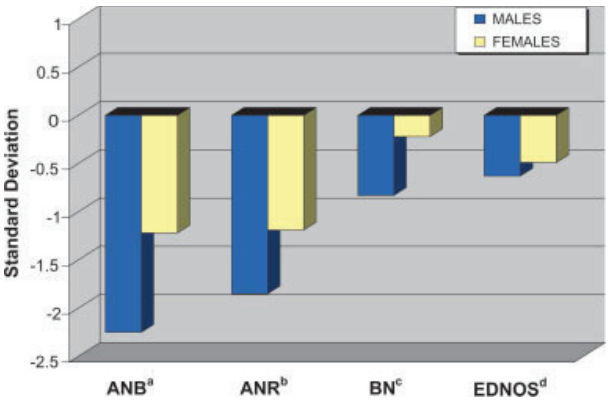
TABLE 4. Bone mineral density (BMD) of inpatient males and females with eating disorders

	ANB (n = 8)		ANR (n = 23)		BN (n = 14)		EDNOS (n = 8)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	ANOVA p-Value
Males									
Lumbar spine BMD (g/cm^2)	0.84	0.16	0.82	0.14	0.97	0.11	0.90	0.20	.02
Lumbar Z-score (SD)	−2.25	1.38	−1.85	1.36	−0.831	1.10	−0.634	1.93	.03
	ANB (n = 115)		ANR (n = 100)		BN (n = 93)		EDNOS (n = 120)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	ANOVA p-Value
Females									
Lumbar spine BMD (g/cm^2)	0.89	0.14	0.87	0.15	1.00	0.11	0.96	0.13	<.001
Lumbar Z-score (SD)	−1.22	1.27	−1.19	1.20	−0.219	1.06	−0.49	1.12	<.001

The females were not significantly different in admission age or BMI, length of stay for the admission, number of previous hospitalizations, or diagnosis category from the males (Median Test p = .29, p = .61, p = .46, p = .40; Pearson's Chi-square Test p = .22, respectively). Males did have a significantly shorter median duration of their eating disorder (males 4 years, females 2.8 years, Median test p = .04). The severity of bone loss in the male ANR and ANB patients was more pronounced than in females with the mentioned eating disorders, who were admitted as inpatients and measured during the same treatment period (p = .02 and p = .03, respectively) (see **Fig. 1**). However, bone deficiency in males with BN was only marginally worse than females with BN; there was essentially no gender difference in the EDNOS subgroups (p = .05 and p = .84, respectively).

There was also no significant difference in the proportion of childhood obesity, physical abuse, sexual abuse, lifetime binge, lifetime purge, lifetime depression, or alcohol abuse among the patients whose lumbar Z-score was above −1 SD and those patients whose lumbar Z-score was −1 SD or below. On multivariate linear regression analysis of lumbar Z-score, lowest BMI and longer duration of illness accounted for 46% of the variance at the lumbar spine. For every one unit increase in lowest BMI, the lumber Z-score increased by 0.2, and for every additional year of disease duration, the lumbar Z-score decreased by 0.12. Multivariate logistic regression, using the aforementioned six risk factors to predict osteoporosis, demonstrated a similar conclusion. BMI was protective for osteoporosis (odds ratio = 0.64, 95% CI = 0.41–0.99). Also, every additional year of disease duration increased the odds of developing osteoporosis by 57% (95% CI = 1.12–2.20). Spearman correlations were performed to determine if testosterone was highly correlated with other variables. Admission testosterone was not significantly correlated with any of the BMD measures or weight variables.

FIGURE 1. Lumbar spine Z-score of inpatient males and females with eating disorders. (a) Significant gender effect (t = 2.21, p = .03); (b) significant gender effect (t = 2.32, p = .02); (c) nonsignificant gender effect (t = 1.99, p = .05); (d) nonsignificant gender effect (t = 0.33, p = .84). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]



Discussion

Male osteoporosis is an under-recognized sequela among males with eating disorders despite the increasing concern about the prevalence of bone mineral loss in patients with anorexia nervosa.[11] Overall, male osteoporosis is a less commonly recognized condition when compared with osteoporosis in women.[12] Yet, fractures are increased in all patients with low bone density. Maximizing peak bone mass is critical to prevent the development of osteoporosis and its morbidities.[1] Bone mass increases throughout childhood, with the maximal bone mass accrual rate occurring in early to mid-puberty and slowing in late puberty. Peak bone mass is attained between the ages of 20 and 25 but

it occurs earlier in females than in males.[13] Bonjour et al., reported in females that most of the total gain in bone density, recorded between 9 and 18 years of age, is accumulated within the four-year period from 11 to 15 years of age.[14] In boys, bone mass accumulation is particularly pronounced between the ages of 13–17. Since eating disorders typically onset during adolescence, these patients will have low life-long peak bone mass if there are no diagnostic and therapeutic interventions. It is not surprising that anorexia nervosa, with its attendant failure to attain peak bone mass, is associated with a markedly overall increased long-term risk of nontraumatic fractures.[15,16] In our study, restricting male anorectics had a high prevalence of BMD loss. In addition, the BMD of the male patients with anorexia nervosa was more significantly reduced as compared with female patients with eating disorders from the same time period.

Testosterone plays an essential role in the maintenance of bone mass, and a low testosterone level is generally associated with osteoporosis in men.[17,18] The mechanisms that mediate testosterone's skeletal effects remain incompletely understood. However, in our study, we found no correlation between admission testosterone levels and bone density despite the fact that the older males had lower admission testosterone levels and more bone loss than the younger males. These older males predominantly had the diagnosis of ANB, and perhaps their protracted illness overshadowed the expected effect of testosterone on bone density. We found that the lowest body weights, as a percentage of norms, and duration of illness, explained 49% of the variance in BMD of the lumbar spine. Males with ANB had a history of lower weights and longer duration of illness, compared with the other males. Even in males from the general population, preserved BMD is associated with higher baseline body weight.[19]

The underlying mechanism of BMD loss in anorexia nervosa involves a state of increased bone resorption rate without concomitant increased bone formation.[20] This uncoupling of bone formation and resorption causes net loss of bone mass. Serum markers of bone resorption, such as *N*-telepeptide and deoxypyrdoline, are higher in patients with anorexia nervosa and markers of bone formation, such as osteocalcin, are not concomitantly elevated.[21] This is most closely analogous to steroid-induced osteoporosis. Indeed, female patients with anorexia nervosa, who had an average duration of illness of 5.8 years, were found to have a markedly elevated annual fracture rate, seven times greater than healthy women of the same age.[22] In our study population, bone loss in males with anorexia was significantly greater than in the females with anorexia even though males had a shorter duration of their eating disorder, which suggests that these male patients may be at even higher risk than females to suffer the adverse consequences of low bone mass. One standard deviation decrease in lumbar spine BMD is associated with a two fold increase in spine fracture risk.[1] This is notable since osteoporotic-induced vertebral and hip fracture rates in the general male population occur at approximately one-third the rate of women.[23] Further, studies suggest different fracture thresholds for males and females. Males may actually fracture at a higher bone density level as compared with females.[24]

Consistent with previous studies in females with eating disorders, males diagnosed with ANB in our study experienced the most bone loss among the different eating disorder subtypes. Herzog has reported that females with ANB were at an increased risk of developing osteoporosis independent of initial bone mass, weight history, and duration of illness.[9] Of note, similar to the BN females in the aforementioned study, the patients in our study with pure BN had lumbar spine BMD values within normal range. Males in our study with EDNOS also had normal bone density.

We found no association between bone density and lifestyle behavior such as binging, purging, substance abuse, and exercise. Although weight bearing exercise is known to help avert osteoporosis in the general population, there seems to be a varying relationship in anorexia nervosa. Several studies have reported that physical activity[25–27] increases bone density, while in other studies of patients with anorexia nervosa, exercise showed no protective capacity regarding BMD.[28,29] Our inability to find a relationship does not necessarily exclude the importance of this variable in influencing BMD; it may reflect that weight-bearing exercise is only protective if menstruation and the endocrinologic milieu has also been preserved. If on the other hand, excessive weight bearing exercise leads to hormonal disruption, it in fact may actually be deleterious and analogous to what has been observed in the female athletic triad.

Although not directly germane to these study results, it is worth briefly discussing treatment options. The cornerstone of treatment is weight restoration; normalized present weight is the best predictor of BMD in patients with eating disorders.[30] In addition, medicinally, all treatment begins with adequate calcium and vitamin D, 1200–1500 mg per day and 800 IU per day, respec-

tively. Of note, however, there is not good evidence from randomized-controlled trials that either calcium or vitamin D are major contributing factors to restitution of bone mineral content.[31] For osteopenia, calcium and vitamin D are also what is clinically indicated. However, for severe osteoporosis, bisphosphonates might be considered. Agents such as alendronate and risedronate, which are antiresorptive and are available as weekly oral preparations, have proven efficacy in both males and anorexia nervosa.[32,33] The unique ongoing concern regarding the usage of these agents in the female population of childbearing age does not seem to exist with respect to males and spermatogenesis. Although recent data suggest that 5 years of bisphosphonates treatment may be sufficient for postmenopausal osteoporosis, this likely does not apply to patients at high risk for fractures such as in anorexia nervosa.[34] Teriparatide, which is a human recombinant parathyroid hormone, is new and is the only available anabolic agent for the treatment of osteoporosis. It has no credible data as yet in anorexia nervosa, and requires a daily injection. Hormonally, dehyrdoepiandeosterone, and testosterone have not produced significant increases in BMD or markers of increased bone formation.[35,36]

Lastly, DEXA should be established as an important screening tool for all patients with moderate and severe anorexia nervosa, with a disease duration greater than 6–12 months. A repeat DEXA 2 years later is also recommended if there is ongoing weight loss, or the diagnosis of anorexia nervosa is still pertinent.[37] Calcaneous quantitative ultrasound measurements may emerge as a simpler test to predict fracture risk, but is not currently recommended.[38]

Limitations

A major limitation of this study is its retrospective design, which resulted in missing data about nutritional intake of calcium and vitamin D, testosterone levels, BMD measures, and personal history. The extent of missing data for personal history was not unexpected. For example, sexual abuse was missing for 7% and childhood obesity for 19%. The explanation for the low levels of testosterone in the EDNOS males is not known. The small sample size limited the analysis options, especially in the multivariate models. It was not possible to blind the data abstractor to the patient's type of eating disorder since it was present in the medical record. However, an independent statistician completed the analyses in order to avoid additional bias in the results. Furthermore, the study was carried out in a specialized setting for eating disorders, at a tertiary referral hospital, and perhaps resulted in a disproportionate number of severe cases referred for treatment. Another limitation is that this study consists of patients with heterogeneous eating disorders and a broad range of duration of illness. Lastly, the females were chosen using convenience sampling; thus, they were not a priori matched to the males. However, the female comparison group was similar to the males in respect to admission age and BMI, length of hospitalization, and number of previous admissions. The fact that the males had a shorter duration of illness than the females heightens our conclusion that the males with anorexia nervosa had more severe bone disease even though their eating disorders had a more recent onset.

Conclusion

The risk of osteoporosis in males with eating disorders remains an under-reported medical complication of eating disorders. Yet, our study indicates a high prevalence of low bone mass in male patients with eating disorders. Moreover, the severity of bone deficiency in these males is even greater than females with the same eating disorder, especially for those with anorexia nervosa and in those with a very low BMI and longer duration of illness. The results of our study should serve to heighten awareness about the clinical syndrome of osteoporosis in male patients with eating disorders. It should also encourage vigilance about the diagnostic and therapeutic implications of this robust and concerning association, particularly in those males with anorexia nervosa.

References

1. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. Lancet 2002;359:1761–1767.
2. Black DM, Delmas PD, Eastell R, Reid IR, Boonen S, Cauley JA, et al. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. N Engl J Med 2007;356:1809–1822.
3. Cummings SR, Black DM, Karpf DB, Harris F, Genant HK, Ensrud K, et al. Improvement in spine bone density and reduction in risk of vertebral fractures during treatment with antiresorptive drugs. Am J Med 2002;112:281–289.

4. Seeman E. Sexual dimorphism in skeletal size, density and strength. J Clin Endocrinol Metab 2001;86:4576–4584.
5. Ringe JD, Faber H, Dorst A. Alendronate treatment of established primary osteoporosis in men: Results of a 2-year prospective study. J Clin Endocrinol Metab 2001;86:5252–5255.
6. Grinspoon S, Thomas E, Pitts S, Gross E, Mickley D, Miller K, et al. Prevalence and predictive factors for regional osteopenia in women with anorexia nervosa. Ann Inten Med 2000;133: 790–794.
7. Hotta M, Shibasaki T, Sato K, Demura H. The importance of body weight history in the occurrence and recovery of osteoporosis in patients with anorexia nervosa: Evaluation by dual X-ray absorptiometry and bone metabolic markers. Eur J Endocrinol 1998;139:276–283.
8. Ward A, Brown N, Treasure J. Persistent osteopenia after recovery from anorexia nervosa. Int J Eat Disord 1997;22:71–75.
9. Herzog W, Minne H, Deter C, Leidig G, Schellberg D, Wüster C, et al. Outcome of bone mineral density in anorexia nervosa patients 11.7 years after first admission. J Bone Miner Res 1993;8:597–605.
10. McGee C. Secondary amenorrhea leading to osteoporosis: Incidence and prevention. Nurse Pract 1997;22:38, 41–45, 48.
11. Misra M, Aggarwal A, Miller KK, Almazan C, Worley M, Soyka LA, et al. Effects of anorexia nervosa on clinical, hematologic, biochemical, and bone density parameters in community-dwelling adolescent girls. Pediatrics 2004;114:1574–1583.
12. Gruntmanis U. Male osteoporosis: deadly, but ignored. Am J Med Sci 2007;333:85–92.
13. Nguyen TV, Maynard LM, Towne B, Roche AF, Wisemandle W, Li J, et al. Sex differences in bone mass acquisition during growth: The Fels Longitudinal Study. J Clin Densitom 2001;4: 147–157.
14. Bonjour JP, Theintz G, Buchs B, Slosman D, Rissoli R. Critical years and stages of puberty for spinal and femoral bone mass accumulation during adolescence. J Clin Endocrinol Metab 1991;73:555–563.
15. Rigotti NA, Neer RM, Skates SJ, Herzog DB, Nussbaum SR. The clinical course of osteoporosis in anorexia nervosa. A longitudinal study of cortical bone mass. JAMA 1991;265:1133–1138.
16. Castro J, Lazaro L, Pons F, Halperin I, Toro J. Adolescent anorexia nervosa the catch-up effect in bone mineral density after recovery. J Am Acad Child Adolesc Psychiatry 2001;40:1215–1221.
17. Winters SJ. Current status of testosterone replacement therapy in men. Arch Fam Med 1999;8:257–263.
18. Onpghiphadhanakul B, Rajatanavin R, Chanprasertyothin S, Piaseu N, Chailurkit L. Serum oestradiol and oestrogen-receptor gene polymorphism are associated with bone mineral density independently of serum testosterone in normal males. Clin Endocrinol 1998;49:803–809.
19. Kaptoge S, Reid DM, Scheidt-Nave C, Poor G, Pols HA, Khaw KT, et al. Geographic determinants of BMD change in European men and women at the hip and spine: A population-based study from the network in Europe for male osteoporsis (NEMO). Bone 2007;40:662–673.
20. Zipfel S, Seibel MJ, Lowe B, Beumont PJ, Kasperk C, Herzog W. Osteoporosis in eating disorders: A follow-up study of patients with anorexia and bulimia nervosa. J Clin Endocrinol Metab 2001;86:5227–5233.
21. Lennkh C, de Zwaan M, Bailer U, Strnad A, Nagy C, el-Giamal N, et al. Osteopenia in anorexia nervosa: Specific mechanisms of bone loss. J Psychiatr Res 1999;33:349–356.
22. Biller BM, Saxe V, Herzog DB, Rosenthal DI, Holzman S, Klibanski A. Mechanisms of osteoporosis in adult and adolescent women with anorexia nervosa. J Clin Endocrinol Metab 1989;68:548–554.
23. Scharla SH, Wolf S, Düll R, Lempert UG. Prevalence of low bone mass and endocrine disorders in hip fracture patients in Southern Germany. Exp Clin Endocrinol Diabetes 1999;107:547–554.
24. Lane JM, Serota AC, Raphael B. Osteoporosis: Differences and similarities in male and female patients. Orthop Clin North Am 2006;37:601–609.
25. Sagiv M, Vogelaere PP, Soudry M, Ehrsam R. Role of physical activity training in attenuation of height loss through aging. Gerontology 2000;46:266–270.
26. Taha W, Chin D, Silverberg AI, Lashiker L, Khateeb N, Anhalt H. Reduced spinal bone mineral density in adolescents of an ultra-orthodox Jewish community in Brooklyn. Pediatrics 2001;107:E79.
27. Thorsen K, Nordstrom P, Lorentzon R, Dahlen GH. The relation between bone mineral density, insulin-like growth factor 1, lipoprotein (a), body composition, and muscle strength in adolescent males. J Clin Endocrinol Metab 1999;84:3025–3029.
28. Castro J, Toro J, Lázaro L, Pons F, Halperin I. Bone mineral density in male adolescent with anorexia nervosa. J Am Acad Child Adolesc Psychiatry 2002;41:613–618.
29. Soyka LA, Grinspoon S, Levitsky LL, Herzog DB, Klibanski A. The effect of anorexia nervosa on bone metabolism in female adolsscents. J Clin Endocrinol Metab 1999;84:4489–4496.
30. Goebel G, Schweiger K, Kruger R, Fichter MM. Predictors of bone mineral density in patients with eating disorders. Int J Eat Disord 1999;25:143–150.
31. Grinspoon S, Thomas L, Miller K, Herzog D, Klibanski A. Effects of recombinant human IGF-I and oral contraceptive administration on bone density in anorexia nervosa. J Clin Endocrinol Metab 2002;87:2883–2891.
32. Miller KK, Grieco KA, Mulder J, Grinspoon S, Mickley D, Yehezkel R, et al. Effects of risedronate on bone density in anorexia nervosa. J Clin Endocrinol Metab 2004;89:3903–3906.
33. Ringe JD, Orwoll E, Daifotis A, Lombardi A. Treatment of male osteoporosis: Recent advances with alendronate. Osteoporos Int 2002;13:195–199.
34. Colon-Emeric CS. Ten versus five years of bisposphonate treatment for postmenopausal osteoporosis. JAMA 2006;296:2968–2969.
35. Gordon CM, Grace E, Emans SJ, Feldman HA, Goodman E, Becker KA, et al. Effects of oral dehydroepiandrosterone on bone density in young women with anorexia nervosa: A randomized trial. J Clin Endocrinol Metab 2002;87:4935–4941.
36. Miller KK, Grieco KA, Klibanski A. Testosterone administration in women with anorexia nervosa. J Clin Endocrinol Metab 2005;90:428–433.
37. Hillier TA, Stone KL, Bauer DC, Rizzo JH, Pedula KL, Cauley JA, et al. Evaluating the value of repeat bone mineral density measurement and prediction of fractures in older women: The study of osteoporotic fractures. Arch Intern Med 2007;167:155–160.
38. Meszaros S, Toth E, Ferencz V, Csupor E, Hosszu E, Horvath C. Calcaneous quantitative ultrasound measurements predicts vertebral fractures in male osteoporosis. Joint Bone Spine 2007;74:79–84.