

# Prevalence and Predictive Factors for Regional Osteopenia in Women with Anorexia Nervosa

Steven Grinspoon, MD; Elizabeth Thomas, NP; Sarah Pitts, BA; Erin Gross, BA; Diane Mickley, MD; Karen Miller, MD; David Herzog, MD; and Anne Klibanski, MD

**Background:** Anorexia nervosa is highly prevalent among young women.

**Objective:** To determine prevalence and predictive factors for regional bone loss.

**Design:** Prospective cohort analysis.

**Setting:** University hospital.

**Patients:** 130 women with anorexia nervosa.

**Measurements:** Dual-energy x-ray absorptiometry.

**Results:** The prevalence of osteopenia ( $-1.0 \text{ SD} \geq \text{T-score} > -2.5 \text{ SD}$ ) and osteoporosis ( $\text{T-score} \leq -2.5 \text{ SD}$ ) was 50% and 13% for the anterior–posterior spine, 57% and 24% for the lateral spine, and 47% and 16% for the total hip, respectively. Bone

mineral density (BMD) was reduced by at least 1.0 SD at one or more skeletal sites in 92% of patients and by at least 2.5 SD in 38% of patients. Weight was the most consistent predictor of BMD at all skeletal sites. Twenty-three percent of patients were current estrogen users, and 58% were previous estrogen users. Bone mineral density did not differ by history of estrogen use at any site.

**Conclusions:** Bone mineral density is reduced at several skeletal sites in most women with anorexia nervosa. Weight, but not estrogen use, is a significant predictor of BMD in this population at all skeletal sites.

*Ann Intern Med.* 2000;133:790-794.

[www.annals.org](http://www.annals.org)

For author affiliations, current addresses, and contributions, see end of text.

See editorial comment on pp 828-830.

Anorexia nervosa is highly prevalent among U.S. women (1, 2) and is associated with substantial bone loss (3–6). Bone loss in women with this disorder is multifactorial; is related in part to estrogen deficiency and to direct effects of undernutrition (3, 4, 7); and is rapid, often occurring within 6 months of disease onset (4) and persisting to some degree after weight recovery (8). It is important to determine the prevalence of regional bone loss at different skeletal sites because it may predict site-specific fracture rates (9). We therefore measured bone mineral density (BMD) at several skeletal sites to determine the prevalence rates and predictive factors of regional osteopenia and osteoporosis in a large community-based sample of women with anorexia nervosa.

## METHODS

We studied 130 women with anorexia nervosa recruited through community advertisements and community physician referral. Telephone screening interviews were used to exclude patients who reported normal weight and menses; use of bisphosphonates, calcitonin, or glucocorticoids; or medical conditions other than anorexia nervosa that are known to affect BMD. Women who had regular uterine withdrawal bleeding while receiving estro-

gen therapy and women with concomitant bulimia nervosa were permitted to participate. Eligible patients underwent a 3-hour outpatient visit at the General Clinical Research Center of the Massachusetts General Hospital in Boston. Height, weight, age at menarche, time since last menstrual period, previous and current estrogen use, fracture history, and frame size were determined. Calcium and vitamin D intake were determined by diet history in a subset of 60 patients. The diagnosis of anorexia nervosa, according to criteria specified in *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, was confirmed in all patients (10). All patients gave written consent, as required by the Subcommittee on Human Studies.

Bone mineral density at the anterior–posterior lumbar spine (L1–L4), lateral spine, left total hip, femoral neck, and greater trochanter was determined with dual-energy x-ray absorptiometry using a Hologic 4500 densitometer (Hologic, Inc., Waltham, Massachusetts) (lumbar spine SD,  $0.01 \text{ g/cm}^2$ ) (11). At each skeletal site, patients were categorized as having normal BMD ( $\text{T-score} > -1.0 \text{ SD}$ ), osteopenia ( $-1.0 \text{ SD} \geq \text{T-score} > -2.5 \text{ SD}$ ), or osteoporosis ( $\text{T-score} \leq -2.5 \text{ SD}$ ), according to World Health Organization criteria. Data on BMD in a subset of 30 patients were published previously (7).

Wrist and frame size were determined (12, 13), and

**Table 1. Clinical Characteristics of Study Patients and Comparison by Estrogen Use and Menstrual History\***

Variable	All Patients (n = 130)	No Current Estrogen Use (n = 100)	Current Estrogen Use (n = 30)	P Value	No Previous Estrogen Use (n = 54)	Previous Estrogen Use (n = 74)	P Value	Primary Amenorrhea (n = 7)	Secondary Amenorrhea (n = 123)	P Value
Age, y	24.4 ± 0.5	24.9 ± 0.6	22.9 ± 1.0	0.110	23.5 ± 0.7	24.7 ± 0.7	>0.2	23.7 ± 2.5	24.4 ± 0.5	>0.2
Body mass index, kg/m <sup>2</sup>	17.1 ± 0.2	17.3 ± 0.2	16.6 ± 0.3	0.080	17.4 ± 0.2	16.9 ± 0.2	0.105	15.7 ± 0.7	17.2 ± 0.2	0.021
Duration of illness, mo	65.9 ± 6.1	71.5 ± 7.3	47.4 ± 9.1	0.096	70.7 ± 9.9	60.4 ± 7.5	>0.2	120.9 ± 25.3	62.3 ± 6.1	0.020
Age at menarche, y	13.5 ± 0.1	13.4 ± 0.2	13.9 ± 0.3	0.173	13.2 ± 0.2	13.7 ± 0.2	0.089	NA	13.5 ± 0.1	NA
Time since last menstrual period, mo	22.5 ± 2.9	24.8 ± 3.3	11.6 ± 5.5	0.081	24.0 ± 4.6	20.9 ± 3.8	>0.2	NA	21.6 ± 2.7	NA
Estrogen use, mo	13.0 ± 2.0	9.3 ± 1.9	25.3 ± 5.4	0.001	0.0 ± 0.0	23.9 ± 3.1	<0.001	12.7 ± 4.2	13.0 ± 2.1	>0.2
Wrist size, cm	14.5 ± 0.1	14.5 ± 0.1	14.5 ± 0.1	>0.2	14.5 ± 0.1	14.6 ± 0.1	>0.2	14.3 ± 0.4	14.5 ± 0.1	>0.2
History of fracture, %	26	30	13	0.096	26	26	>0.2	29	27	>0.2
BMD, g/cm <sup>2</sup>										
Anterior–posterior spine†	0.89 ± 0.01	0.89 ± 0.01	0.90 ± 0.02	>0.2	0.88 ± 0.01	0.90 ± 0.01	>0.2	0.77 ± 0.03	0.90 ± 0.01	0.001
Lateral spine‡	0.68 ± 0.01	0.68 ± 0.01	0.70 ± 0.02	>0.2	0.68 ± 0.01	0.68 ± 0.01	>0.2	0.58 ± 0.04	0.69 ± 0.01	0.003
Total hip§	0.81 ± 0.01	0.81 ± 0.01	0.83 ± 0.03	>0.2	0.81 ± 0.02	0.82 ± 0.02	>0.2	0.65 ± 0.03	0.82 ± 0.01	0.002
Femoral neck	0.74 ± 0.01	0.74 ± 0.01	0.75 ± 0.03	>0.2	0.75 ± 0.02	0.74 ± 0.02	>0.2	0.60 ± 0.03	0.75 ± 0.01	0.003
Trochanter¶	0.62 ± 0.01	0.61 ± 0.01	0.63 ± 0.03	>0.2	0.61 ± 0.02	0.62 ± 0.01	>0.2	0.51 ± 0.02	0.62 ± 0.01	0.016

\* Values given are the mean ± SE unless otherwise indicated. Data on previous estrogen use were unavailable for 2 patients. BMD = bone mineral density. NA = not applicable.

† -1.0 SD ≥ T-score ≥ -2.5 SD corresponds to 0.937 g/cm<sup>2</sup> ≥ BMD ≥ 0.772 g/cm<sup>2</sup>.

‡ -1.0 SD ≥ T-score ≥ -2.5 SD corresponds to 0.736 g/cm<sup>2</sup> ≥ BMD ≥ 0.610 g/cm<sup>2</sup>.

§ -1.0 SD ≥ T-score ≥ -2.5 SD corresponds to 0.855 g/cm<sup>2</sup> ≥ BMD ≥ 0.675 g/cm<sup>2</sup>.

|| -1.0 SD ≥ T-score ≥ -2.5 SD corresponds to 0.795 g/cm<sup>2</sup> ≥ BMD ≥ 0.645 g/cm<sup>2</sup>.

¶ -1.0 SD ≥ T-score ≥ -2.5 SD corresponds to 0.632 g/cm<sup>2</sup> ≥ BMD ≥ 0.497 g/cm<sup>2</sup>.

body mass index and percentage of ideal body weight were calculated (14). Age at menarche and time since last menstrual period were assessed for all patients. Whenever possible, total duration of amenorrhea since menarche was determined (*n* = 78). Current and previous lifetime estrogen use, including type of estrogen, was quantified and categorized for each patient.

We used the Mantel–Haenszel test to compare BMD at the anterior–posterior and lateral spine, stratifying on patients. Standard least-squares multivariate regression models were constructed for each skeletal site by using age, age at menarche, time since last menstrual period, weight, height, wrist size, and fracture history as covariates. Covariates were chosen in advance as important clinical variables affecting BMD. Adjusted regression coefficients and confidence intervals were determined for each covariate. Data are expressed as the mean ± SE.

The funding source had no role in the collection, analysis, or interpretation of the data or in the decision to submit the paper for publication.

## RESULTS

Clinical data and data on BMD are shown in Table 1. Ninety-eight percent of patients were white and 2% were Asian. Mean T-scores were  $-1.4 \pm 0.1$  SD for the anterior–posterior spine,  $-1.8 \pm 0.1$  SD for the lateral spine, and  $-1.4 \pm 0.1$  SD for the total hip. Twenty-six percent

of patients (*n* = 34) reported a history of fracture (foot or ankle [*n* = 6], hand or wrist [*n* = 7], leg [*n* = 1], arm or elbow [*n* = 4], stress fracture [*n* = 5], and other fracture [*n* = 11]).

Osteopenia and osteoporosis, respectively, were seen at the anterior–posterior spine in 50% and 13% of patients, at the lateral spine in 57% and 24% of patients, and at the total hip in 47% and 16% of patients. Normal BMD was seen at the anterior–posterior spine in only 37% of patients, at the lateral spine in 19% of patients, and at the total hip in 37% of patients. Results of lateral and anterior–posterior spinal tests of BMD were discordant in 36 patients, of whom 31 had normal BMD at the anterior–posterior spine (T-score > -1.0) but low BMD at the lateral spine (T-score ≤ -1.0) (*P* < 0.001). Bone mineral density was reduced by at least 1.0 SD at one or more skeletal sites in 92% of patients and by at least 2.5 SD in 38% of patients. No differences in BMD were observed between patients with anorexia nervosa alone and patients with anorexia nervosa and concomitant bulimia nervosa (*P* > 0.05 at all sites; data not shown).

Twenty-three percent of patients were current estrogen users (mean duration,  $25.3 \pm 5.4$  months) and 58% were previous estrogen users (mean duration,  $23.9 \pm 3.1$  months). Bone mineral density did not differ at any site according to current or previous estrogen use (Table 1). Age, body mass index, and age at menarche were similar in

Table 2. Univariate and Multivariate Regression Analyses\*

Variable†	Univariate Analysis		Multivariate Analysis‡	
	Regression Coefficient (95% CI)	P Value	Regression Coefficient (95% CI)	P Value
<b>Anterior–posterior spine BMD</b>				
Age	−0.0017 (−0.0049 to 0.0014)	>0.2	0.0006 (−0.0020 to 0.0033)	>0.2
Age at menarche	−0.0200 (−0.0325 to −0.0076)	0.002	−0.0158 (−0.0266 to −0.0049)	0.005
Time since last menstrual period	−0.0013 (−0.0019 to −0.0007)	<0.001	−0.0014 (0.0019 to −0.0008)	<0.001
Weight	0.0085 (0.0057 to 0.0113)	<0.001	0.0052 (0.0014 to 0.0091)	0.008
Height	0.0050 (0.0022 to 0.0078)	0.001	0.0020 (−0.0013 to 0.0051)	>0.2
Wrist size	0.0423 (0.0145 to 0.0700)	0.003	0.0135 (−0.0169 to 0.0439)	>0.2
History of fracture	0.0153 (−0.0276 to 0.0581)	>0.2	0.0127 (−0.0050 to 0.0304)	0.158
<b>Lateral spine BMD</b>				
Age	−0.0028 (−0.0055 to −0.0001)	0.042	−0.0008 (−0.0035 to 0.0020)	>0.2
Age at menarche	−0.0049 (−0.0158 to 0.0061)	>0.2	−0.0041 (−0.0150 to 0.0068)	>0.2
Time since last menstrual period	−0.0008 (−0.0013 to −0.0003)	0.005	−0.0007 (−0.0014 to −0.0001)	0.024
Weight	0.0065 (0.0038 to 0.0091)	<0.001	0.0049 (0.0009 to 0.0090)	0.018
Height	0.0026 (−0.00006 to 0.0051)	0.051	−0.0019 (−0.0054 to 0.0016)	>0.2
Wrist size	0.0384 (0.0136 to 0.0631)	0.003	0.0231 (−0.0111 to 0.0574)	0.182
History of fracture	0.0007 (−0.0371 to 0.0385)	>0.2	−0.0008 (−0.0194 to 0.0178)	>0.2
<b>Total hip BMD</b>				
Age	−0.008 (−0.0119 to −0.0041)	<0.001	−0.0060 (−0.0098 to −0.0023)	0.002
Age at menarche	−0.0134 (−0.0304 to 0.0037)	0.123	−0.0135 (−0.0281 to 0.0010)	0.067
Time since last menstrual period	−0.0016 (−0.0024 to −0.0008)	<0.001	−0.0006 (−0.0014 to 0.0002)	0.158
Weight	0.0115 (0.0076 to 0.0154)	<0.001	0.0108 (0.0055 to 0.0161)	<0.001
Height	0.0047 (0.0007 to 0.0087)	0.023	−0.000039 (−0.0046 to 0.0045)	>0.2
Wrist size	0.0161 (−0.0260 to 0.0582)	>0.2	−0.0287 (−0.0741 to 0.0166)	>0.2
History of fracture	0.0340 (−0.0245 to 0.0924)	>0.2	0.0192 (−0.0050 to 0.0434)	0.117
<b>Femoral neck BMD</b>				
Age	−0.0083 (−0.0117 to −0.0049)	<0.001	−0.0070 (−0.0103 to −0.0037)	<0.001
Age at menarche	−0.0073 (−0.0229 to 0.0084)	>0.2	−0.0087 (−0.0216 to 0.0042)	>0.2
Time since last menstrual period	−0.0013 (−0.0020 to −0.0006)	<0.001	−0.0003 (−0.0010 to 0.0004)	0.184
Weight	0.0091 (0.0055 to 0.0128)	<0.001	0.0097 (0.0049 to 0.0144)	<0.001
Height	0.0032 (−0.0004 to 0.0069)	0.084	−0.0013 (−0.0053 to 0.0028)	>0.2
Wrist size	0.0141 (−0.0233 to 0.0515)	>0.2	−0.0172 (−0.0576 to 0.0231)	>0.2
History of fracture	0.0131 (−0.0399 to 0.0662)	>0.2	0.0134 (−0.0081 to 0.0350)	>0.2
<b>Trochanter BMD</b>				
Age	−0.0070 (−0.0102 to −0.0039)	<0.001	−0.0054 (−0.0085 to −0.0023)	0.001
Age at menarche	−0.0062 (−0.0206 to 0.0082)	>0.2	−0.0083 (−0.0203 to 0.0037)	0.172
Time since last menstrual period	−0.0011 (−0.0018 to −0.0005)	0.001	−0.0003 (−0.0010 to 0.0004)	>0.2
Weight	0.0082 (0.0050 to 0.0113)	<0.001	0.0090 (0.0046 to 0.0134)	<0.001
Height	0.0031 (−0.0001 to 0.0063)	0.057	−0.0007 (−0.0044 to 0.0031)	>0.2
Wrist size	0.0088 (−0.0245 to 0.0422)	>0.2	−0.0267 (−0.0642 to 0.0108)	0.160
History of fracture	0.0189 (−0.0287 to 0.0665)	>0.2	0.0112 (−0.0088 to 0.0312)	>0.2

\* BMD = bone mineral density.

† History of fracture was recorded as a dichotomized variable, where yes = 1 and no = 0.

‡ In the multivariate analysis, the squared multiple correlation coefficient ( $R^2$ ) was 0.45 for the anterior–posterior spine, 0.25 for the lateral spine, 0.45 for the total hip, 0.45 for the femoral neck, and 0.42 for the trochanter.

the subgroup comparisons according to estrogen status. Oral contraceptives were used in all but 3 of the current estrogen users (10%) and all but 7 of the ever-estrogen users (10%); these 10 women received conjugated estrogen. Similar results were obtained in a subanalysis limited to the patients receiving oral contraceptives (data not shown). Total duration of estrogen use was not correlated with BMD at the anterior–posterior spine, lateral spine, femoral neck, total hip, trochanter, or total body ( $P > 0.10$  for all comparisons). Patients with primary amenorrhea ( $n = 7$ ) weighed less and had lower BMD at all sites

than patients with secondary amenorrhea ( $n = 123$ ) (Table 1), although sample size was small in the primary amenorrhea group. Total calcium intake was not correlated with BMD at any site ( $P > 0.1$  for all sites). Fifty-seven percent of patients were receiving calcium supplements, 53% were receiving a multivitamin containing 400 IU of vitamin D, and 43% were receiving both. Bone mineral density did not differ in patients receiving nutritional supplements (data not shown).

Weight was a significant independent predictor of BMD at all skeletal sites (Table 2). Patients with normal

BMD, osteopenia, and osteoporosis at the total hip weighed  $48.7 \pm 0.8$  kg,  $45.9 \pm 0.8$  kg, and  $39.0 \pm 0.7$  kg, respectively. Similar trends were seen at other skeletal sites (data not shown). Age at menarche was a significant independent predictor of BMD measured by anterior–posterior spinal densitometry. Time since last menstrual period was a significant predictor of BMD at the anterior–posterior and lateral spine. Our results were similar when we used multivariate regression models with total duration of amenorrhea instead of last menstrual period in patients for whom this information was available ( $n = 78$ ) (data not shown).

## DISCUSSION

Our data demonstrate the high prevalence and profound degree of site-specific bone loss in women with anorexia nervosa. Our study design had advantages: Patients were recruited from the community and were not preselected for bone loss, and we evaluated bone loss at several skeletal sites. Although weight was highly significant as a predictor of bone loss at all sites, time since last menstrual period and age at menarche were significant predictive factors for BMD at the anterior–posterior spine, suggesting a greater relative influence of estrogen deficiency at this site. Other mechanisms may also contribute to reduced BMD in patients with anorexia nervosa, such as failure to achieve peak BMD, hypercortisolemia, and reduced vitamin D intake (4). However, we did not see any association between calcium or vitamin D intake and BMD.

Increased risk for fracture is the major clinical implication of bone loss in women with anorexia nervosa. Fracture risk doubles with each decrease of 1 SD in BMD (9). Our data therefore suggest that patients with anorexia are at a markedly increased risk for fracture at many skeletal sites. A relatively high percentage of patients reported a previous history of fracture, but because radiologic confirmation was not obtained, relative risk for fracture was not determined. Bone mineral density was reduced by at least 1.0 SD at one or more skeletal sites in 97% of women with fractures, but fracture site was not correlated with the location of osteopenia.

Although our study was not designed to prospectively investigate the efficacy of estrogen use in women with anorexia nervosa, no effect of previous or current estrogen use on BMD was demonstrated at any skeletal sites. These retrospective data stand in partial contrast to cross-sectional

data from a previous study, which suggested an effect of estrogen exposure at the lumbar spine but not at other sites (15). The minimal effect of estrogen exposure on BMD in our study is consistent with that seen in a previous randomized study, which showed no effect of estrogen–progesterone replacement therapy on BMD in patients with anorexia nervosa (16).

The effectiveness of estrogen in increasing or preserving BMD in women with anorexia nervosa may be mitigated by continued undernutrition, which may act to uncouple bone formation and resorption. We have previously shown that women with anorexia nervosa exhibit low bone formation rates and increased resorption rates (3). Hotta and colleagues (17) have shown that low rates of bone formation in patients with anorexia nervosa increase with feeding, suggesting a mechanism whereby bone formation is reduced by undernutrition and is dissociated from increased resorption caused by estrogen deficiency. We have previously shown that bone loss is more severe in women with anorexia nervosa than in those with other estrogen-deficient conditions, such as hypothalamic amenorrhea (7). In adolescents with anorexia nervosa, Soyka and coworkers (18) recently found a striking reduction in bone formation that is closely correlated with weight. Similarly, our data strongly suggest that undernutrition has a primary role, independent of estrogen deficiency, in anorexia nervosa–related bone loss.

We found that lateral BMD was reduced to a greater extent than BMD at the anterior–posterior spine. Because spine radiographs were not available in our study, we do not know whether compression fractures or other changes in spinal morphometry may account for this difference. Although vertebral osteosclerosis would not be expected in young women, the potential usefulness of lateral BMD as a more sensitive test to determine the degree of bone loss in women with anorexia nervosa should receive additional study. We used the normative database provided by the manufacturer (Hologic, Inc.) to determine T-scores. Because normative reference ranges may differ among manufacturers, this may have affected quantification of bone loss.

More than 90% of the patients in this highly representative sample of young anorectic women demonstrated significant bone loss at one or more skeletal sites. Current weight is the best and most consistent predictor of BMD at several skeletal sites, independent of indices of estrogen deficiency. Furthermore, past or current prolonged use of

estrogen is not associated with increased BMD at any skeletal site. Our data suggest the importance of screening for bone loss and of counseling women with anorexia nervosa about the adverse effects of low weight on the skeleton.

From Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; and the Wilkins Center, Greenwich, Connecticut.

**Acknowledgments:** The authors thank the nursing and bionutrition staffs of the General Clinical Research Center and Caryn Coyle, NP, for dedicated patient care and Judy Krempin, BA, for assistance in patient recruitment.

**Grant Support:** In part by the National Institutes of Health (R01-DK52625, M01-RR01066, RO1-MH38333, and P32-DK07028), the Rubinstein Foundation, and the Harvard Eating Disorder Center.

**Requests for Single Reprints:** Steven Grinspoon, MD, Neuroendocrine Unit, Bulfinch 457b, Massachusetts General Hospital, Boston, MA 02114.

**Current Author Addresses:** Drs. Grinspoon, Miller, and Klibanski, Ms. Thomas, Ms. Pitts, and Ms. Gross: Neuroendocrine Unit, Bulfinch 457b, Massachusetts General Hospital, Boston, MA 02114.  
Dr. Mickley: Wilkins Center for Eating Disorders, 7 Riversville Road, Greenwich, CT 06831.  
Dr. Herzog: Eating Disorders Unit, Massachusetts General Hospital, Boston, MA 02114.

**Author Contributions:** Conception and design: S. Grinspoon, D. Herzog, A. Klibanski.  
Analysis and interpretation of the data: S. Grinspoon, E. Thomas, S. Pitts, E. Gross, K. Miller, D. Herzog, A. Klibanski.  
Drafting of the article: S. Grinspoon, E. Thomas, S. Pitts, E. Gross, D. Mickley, A. Klibanski.  
Critical revision of the article for important intellectual content: S. Grinspoon, E. Thomas, S. Pitts, E. Gross, K. Miller, D. Herzog, A. Klibanski.  
Final approval of the article: S. Grinspoon, E. Thomas, S. Pitts, E. Gross, K. Miller, D. Herzog, A. Klibanski.  
Provision of study materials or patients: S. Grinspoon, E. Thomas, S. Pitts, E. Gross, D. Mickley, K. Miller, D. Herzog, A. Klibanski.  
Statistical expertise: S. Grinspoon, S. Pitts, E. Gross.  
Obtaining of funding: S. Grinspoon, D. Herzog, A. Klibanski.  
Collection and assembly of data: S. Grinspoon, E. Thomas, S. Pitts, K. Miller, D. Herzog, A. Klibanski.

## References

1. Pope HG Jr, Hudson JI, Yurgelun-Todd D. Prevalence of anorexia nervosa and bulimia in three student populations. *Int J Eating Disord*. 1984;3:45-51.
2. Lucas AR, Beard CM, O'Fallon WM, Kurland LT. 50-year trends in the

incidence of anorexia nervosa in Rochester, Minn.: a population-based study. *Am J Psychiatry*. 1991;148:917-22.

3. Grinspoon S, Baum H, Lee K, Anderson E, Herzog D, Klibanski A. Effects of short-term recombinant human insulin-like growth factor I administration on bone turnover in osteopenic women with anorexia nervosa. *J Clin Endocrinol Metab*. 1996;81:3864-70.
4. 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;68:548-54.
5. Rigotti NA, Nussbaum SR, Herzog DB, Neer RM. Osteoporosis in women with anorexia nervosa. *N Engl J Med*. 1984;311:1601-6.
6. 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;265:1133-8.
7. Grinspoon S, Miller K, Coyle C, Krempin J, Armstrong C, Pitts S, et al. Severity of osteopenia in estrogen-deficient women with anorexia nervosa and hypothalamic amenorrhea. *J Clin Endocrinol Metab*. 1999;84:2049-55.
8. Herzog W, Minne H, Deter C, Leidig G, Schellberg D, Wuster 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.
9. Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet*. 1993;341:72-5.
10. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Assoc; 1994.
11. Finkelstein JS, Cleary RL, Butler JP, Antonelli R, Mitlak BH, Deraska DJ, et al. A comparison of lateral versus anterior-posterior spine dual energy x-ray absorptiometry for the diagnosis of osteopenia. *J Clin Endocrinol Metab*. 1994;78:724-30.
12. Frisanchi AR, Flegel PN. Elbow breadth as a measure of frame size for US males and females. *Am J Clin Nutr*. 1983;37:311-4.
13. Frisanchi AR. Anthropometric Standards for the Assessment of Growth and Nutritional Status. Ann Arbor, MI: Univ of Michigan Pr; 1990.
14. New weight standards for men and women. *Stat Bull Metropol Insur Co*. 1959;40:1.
15. Seeman E, Szmukler GI, Formica C, Tsalamandris C, Mestrovic R. Osteoporosis in anorexia nervosa: the influence of peak bone density, bone loss, oral contraceptive use, and exercise. *J Bone Miner Res*. 1992;12:1467-74.
16. Klibanski A, Biller BM, Schoenfeld DA, Herzog DB, Saxe VC. The effects of estrogen administration on trabecular bone loss in young women with anorexia nervosa. *J Clin Endocrinol Metab*. 1995;80:898-904.
17. Hotta M, Fukuda I, Sato K, Hizuka N, Shibasaki T, Takano K. The relationship between bone turnover and body weight, serum insulin-like growth factor (IGF) I, and serum IGF-binding protein levels in patients with anorexia nervosa. *J Clin Endocrinol Metab*. 2000;85:200-6.
18. Soyka L, Grinspoon S, Levitsky L, Herzog DB, Klibanski A. The effects of anorexia nervosa on bone metabolism in female adolescents. *J Clin Endocrinol Metab*. 1999;84:4489-96.

© 2000 American College of Physicians—American Society of Internal Medicine