



Osteopenia in anorexia nervosa: specific mechanisms of bone loss

Claudia Lennkh^{a,*}, Martina de Zwaan^a, Ursula Bailer^a, Alexandra Strnad^a,
Christine Nagy^a, Nadia El-Giamal^a, Stephan Wiesnagrotzki^a, Elisabeth Vytiska^b,
Johannes Huber^b, Siegfried Kasper^a

^aDepartment of General Psychiatry, University Hospital of Psychiatry, Währinger Gürtel 18–20, 1090 Vienna, Austria

^bUniversity Hospital of Gynaecology, Vienna, Austria

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Abstract

Osteopenia is a well recognized medical complication of anorexia nervosa (AN). The mechanism of bone loss is not fully understood and there is uncertainty about its management. New markers of bone turnover have been developed. C-terminal type 1 propeptide (PICP) is a measure of bone formation and urinary pyridinolines such as deoxypyridinoline (DPYRX) and serum carboxyterminal crosslinked telopeptide (ICTP) are markers of bone resorption. The aim of this study was to examine these bone markers in patients with AN.

Twenty female patients with AN and 12 healthy controls were included in the study. Bone mineral density (BMD) of AN patients was measured by dual energy X-ray absorptiometry (DEXA). Lumbar bone density was significantly reduced in the AN group compared to standardised values of thirty year old adults (*t*-score 83.2%, S.D. 12.1). Femoral neck bone density showed an even greater reduction (*t*-score 79.4%, S.D. 13.5). We found a significant negative correlation between femoral BMD and the duration of the illness. Femoral BMD correlated significantly with minimal body weight ($r(16) = 0.504$, $p = 0.033$).

The markers of bone resorption were significantly higher in the patients with AN compared to the values of the control group (ICTP $t(30) = -2.15$, $p = 0.04$, DPYRX $t(25) = -2.26$, $p = 0.033$), whereas the markers of bone formation did not differ significantly between the groups.

AN appears to be a low turn over state associated with increased bone resorption without concomitant bone formation. This pattern differs from osteopenia in menopausal women and should, therefore, lead to the development of specific therapeutic strategies in AN associated osteopenia. Hormone replacement therapy as well as calcium and vitamin D-supplementation are so far discussed controversially. Long-term treatment studies are warranted. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Anorexia nervosa; Osteopenia; PICP; ICTP; DEXA

1. Introduction

Anorexia nervosa (AN) is a common chronic disorder with an estimated prevalence of 1% in female adolescents and young women (APA, 1993). The restrictive eating pattern is associated with profound metabolic complications, including prolonged amenorrhea. Long-term studies up to 10 years demonstrate that only 42–48% of patients recover to normal weight

and attain regular menstrual function (Herzog et al., 1997). Regarding the chronicity and severity of AN, it is crucial to study its putative long-term metabolic consequences.

A serious complication of AN is osteopenia, defined by a bone density of more than 2 standard deviations below the normal mean. Bone loss is often rapid (Rigotti et al., 1984; Biller et al., 1989; Bachrach et al., 1991) and affects adolescents, in whom there is a significant reduction in peak bone mass achieved during the critical years of bone formation (Ayers et al., 1984; Bachrach et al., 1990). Whether such deficiency is permanent or can be restored remains unanswered. As a

* Corresponding author. Tel.: +43-1-40400/3547; fax: +43-1-40400/3560.

Table 1

Baseline clinical data of patients with AN and healthy controls. BMI: body mass index; N/A: not applicable, * $p < 0.05$ (t -test), ** $p < 0.01$ (t -test)

Variables	AN, mean (SD)	Controls, mean (S.D.)
Sample size	20	12
Age (yr)	22.5 (5.8)	27.9 (4.3)*
BMI (kg/m ²)	15.7 (1.3)	20.5 (1.9)**
Minimal weight (kg)	38.9 (5.4)	N/A
Maximum weight (kg)	59.1 (10.5)	N/A
Duration of illness (yr)	3.9 (3.6)	N/A
Age at onset (yr)	18.7 (4.6)	N/A

consequence, young anorexic women are at risk of early osteoporosis, kyphosis, and spontaneous fractures at multiple sites (Brotman and Stern, 1985; Szmukler et al., 1985; Rigotti et al., 1991).

So far the exact mechanisms are not fully clarified. Several factors such as malnutrition, reduced body weight, amenorrhea, and hypercortisolaemia seem to be involved.

There are only few data available concerning bone turnover and mechanisms of osteopenia in this population. New markers of bone turnover have been developed. C-terminal type 1 propeptide (PICP) is a measure of bone formation and urinary pyridinolines such as deoxypyridinoline (DPYRX) and serum carboxyterminal crosslinked telopeptide (ICTP) are markers of bone resorption. The aim of this study was to investigate the specific mechanisms of anorexia associated bone loss by examining these bone markers in patients with AN.

2. Methods

2.1. Subjects

We investigated 20 women with AN diagnosed according to the criteria of the fourth version of the Diagnostic and Statistical Manual of Mental Disorders

Table 3

Markers of bone formation and bone resorption in patients with anorexia nervosa (AN) compared to controls. ICTP: carboxyterminal crosslinked telopeptide; DPYRX: deoxypyridinoline; PICP: C-terminal type 1 propeptide. * $p < 0.05$ (t -tests)

Variables	AN	Controls
<i>Bone resorption</i>		
ICTP (μ g/ml)	4.7 (2.5)	3.1 (0.7)*
DPYRX (nmol/mmol creat.)	7.7 (3.0)	5.3 (1.2)*
<i>Bone formation</i>		
Alkaline phosphatase (U/l)	84.8 (27.6)	98.3 (25.9)
Osteocalcin (ng/ml)	21.8 (9.1)	21.4 (7.9)
PICP (ng/ml)	100.3 (39.5)	112.8 (33.2)

(DSM IV, APA, 1994). Four patients were recruited from the Psychosomatic Ward and 16 patients from the Eating Disorder Clinic, Department of General Psychiatry at the University Hospital of Psychiatry in Vienna. Two patients from the inpatient ward had been tube fed, one of them for the last ten days prior to the examination and the second one three weeks ago for a period of two weeks. However, tube feeding is initiated when the patient has a BMI of less than 13 and the tube is removed when the patient reaches a BMI of 13. The mean age of the patients was 22.5 years (S.D. 5.8) and all had amenorrhea for at least 3 months prior to the examination. No patient had any other illness or was taking any medication known to affect bone density, including thyroid hormones, anti-seizure medication, or glucocorticoids.

The mean age of the 12 healthy controls was 27.9 years (S.D. 4.3). In clinical interviews all controls were carefully examined about their present and former eating habits. None of them had any current or past symptoms of eating disorders. There was no history of abnormal dietary practices and their weight had been stable for the last years. All of them had regular menses from menarche on up to present.

All patients and healthy controls gave written informed consent. The study was approved by the sub-

Table 2

Bone mineral density (BMD) of 20 patients with anorexia nervosa (AN), measured by DEXA (t -scores, %)

BMD (t -score)	Mean (S.D.) (%)	Minimum (%)	Maximum (%)
Lumbal total	83.2 (12.10)	63	109
L1	83.75 (13.07)	58	102
L2	83.5 (12.31)	64	107
L3	80.00 (10.89)	63	100
L4	81.15 (11.83)	63	103
Hip total	83.60 (13.129)	53	102
Hip neck	79.40 (13.52)	54	111
Intertrochanter	81.12 (14.33)	50	105
Trochanter	87.63 (12.90)	62	105

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