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How weight gain change bone turnover with women in Anorexia nervosa

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Introduction / Objectifs

Osteoporosis is one of the principal complications of anorexia nervosa (AN). We already know that body weight gain and menstrual recovery ameliorate their bone mineral density (BMD). However it is often difficult to improve BMD especially in severe AN patients.
Objective; We investigated the process of bone metabolism change during the treatment including body weight gain in patients with AN.

Patients et méthodes

36 patients of severe AN (female, mean age ±SEM, 30 ±11.3 years, BMI 12.1±1.2kg/m^2) treated with the inpatients CBT program were enrolled in this retrospective research at one hospital. Prior to and after treatment, their BMD of the spine and whole body by dual-energy x-ray absorptiometry, serum intact N-terminal propeptide of type 1 procollagen (P1NP), tartrate-resistant acid phosphatase-5b (TRACP-5b) and sclerostin levels were measured. All statistical analyses were performed using *JMP pro* version 11.0. The significant difference value was set as $P < 0.05$.

Résultats

Table1

	At admission	Endopoint (292±29 days)	Change	*P* value
Age (years)	29.8 ±1.9	-	-	-
Amenorrhea duration(year)	6.7±1.1	-	-	-
Height (cm)	155 ±1.0	-	-	-
Body weight (kg)	29.4±0.6	38.1±0.6	8.6±0.5	<0.0001
BMI (kg/m2)	12.2±0.2	15.7±0.2	3.5±0.2	<0.0001
L2-4 BMD (g/cm2)	0.76±0.02	0.74±0.02	-2.8±1.3(%)	0.008
L2-4 BMD Z-score (SD)	-2.1 ±0.2	-2.4 ± 0.2	-0.24±0.09	0.005
Whole body BMD (g/cm2)	0.96±0.02	0.94±0.02	-1.5±0.6(%)	0.0056
Bone mass (g)	1544±38	1422±36	-121.9±12.3	<0.0001
Body fat percentage (%)	10.9±0.5	20.4±0.8	9.5±0.8	<0.0001
Osteoporosis (%)	47.2	52.8	-	<0.0001
Sclerostin (pmmol/l)	46.3±1.1	45.2±0.8	-1.1±1.1	0.36
intact P1NP (μg/L)	65.0±10.7	175.2±15.9	110.2±17.5	<0.0001
TRACP-5b (mU/dL)	428.3±53.9	293.4±24.0	-134.9±45.6	0.02
Phosphorus (mg/dl)	3.8±0.1	4.0±0.1	0.17±0.13	0.16
Calcium (mg/dl)	9.4±0.1	9.5±0.1	0.05±0.06	0.19
Alkaline phosphatase (IU/L)	223.1±23.9	325.4±24.9	102.0±16.2	<0.0001
Oestradiol (pg/ml)	15.8±2.0	21.6±2.5	5.9±2.6	0.006
Lutenizing hormone (mIU/mL)	0.5±0.1	3.7±0.6	3.2±0.6	<0.0001
Follicle-stimulating hormone(mIU/mL)	3.8±0.6	10.1±1.7	6.3±1.8	0.001

n=36, mean±SEM, Wilcoxon signed-rank test

Table1 Baseline characteristics of the study participants, and changes in physical and biological markers during the treatment.
Despite body weight increased significantly (All remained amenorrhea), bone mass and BMD significantly decreased. Serum ALP, LH, FSH, E2 and P1NP levels increased. TRACP-5b levels decreased, whereas sclerostin levels were invariant in this treatment protocol.

Table2 Correlations between sclerostin and bone markers in women with AN.
The relationship among them was disrupted. We found that the negative relationship between sclerostin and change in whole body BMD.

Table3 Correlation coefficients for the changes during the treatment among bone turnover marker and BMI.
Change in BMD positively correlated with change in BMI and sclerostin. In fact, there is a significant correlation between sclerostin and change in sclerostin (*R*=-0.773, *P*<.0001), so which may be confounding factor. Other biological markers have no correlation with change in BMD(data not shown).

Table2

Correlations	Sclerostin	intact P1NP	TRACP-5b	ΔBMD L2-4	ΔBMD Whole body
Sclerostin	1			-0.284	**-0.524**
				P=.093	**P=.001**
intact P1NP	-0.123	1		**0.348**	0.179
	P=.440			**P=.038**	P=.297
TRACP-5b	-0.086	0.094	1	0.031	-0.085
	P=.598	P=.587		P=.858	P=.624

n=36

Table3

Correlations	ΔSclerostin	ΔP1NP	ΔTRACP-5b	ΔBMI	ΔBMD L2-4	ΔBMD Whole body
ΔSclerostin	1				**0.441**	0.266
					P=.006	P=.115
ΔP1NP	-0.248	1			-0.074	0.083
	P=.165				P=.667	P=.632
ΔTRACP-5b	0.042	0.059	1		0.023	0.186
	P=.816	P=.733			P=.893	P=.278
ΔBMI	-0.03	0.236	-0.01	1	**0.369**	**0.508**
	P=.0.869	P=.172	0.948		**P=.029**	**P=0.002**

n=36

Discussion

■**High sclerostin levels in women with AN**
■**Negative correlation between sclerostin and change in BMD whole body**

Two studies reported that sclerostin levels were higher in women with AN compared with normal weight controls and had no correlations with other bone turnover markers.[1)2)] High expression of AMPK, glucocorticoid, weak mechanical load and low body fat increase the expression of sclerostin, which might explain high sclerostin level in patients with AN.
High sclerostin and low P1NP represent depression of osteoblast activity.
Our data demonstrate that sclerostin and P1NP levels are key factors for amelioration of BMD. It therefore suggests that **recovery of bone formation is essential for treatment of osteoporosis in women with AN.**

Conclusion

This study demonstrates that weight gain induces bone formation and reduces bone resorption in severe case of AN without BMD recovery. Sclerostin at baseline could be a good predictor of reaction of BMD.

Références
1) Faje AT, Fazeli PK, Katzman DK, et al. *Bone*. 2012;51:474–479.
2) **Maïmoun L, Guillaume S, Lefebvre P, et al.** *JCEM*. 2014;99:E582-E590

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