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Relationships Among Blood Leptin and Adiponectin Levels, Fat Mass, and Bone Mineral Density in Japanese Pre- and Postmenopausal Women

Tadayuki IIDA[1,*], Tokio DOMOTO[2], Atsushi TAKIGAWA[2], Satoru NAKAMURA[2], Yoji KATO[2], Masanori TOGO[2], Chiho CHIKAMURA[3], Toshihide HARADA[2], Fumiko ISHIZAKI[2] and Yuichiro ONO[1]

1) Department of Public Health, Fujita Health University School of Medicine, Toyoake, Aichi 470-1192, Japan
2) Faculty of Health and Welfare, Prefectural University of Hiroshima, 1-1 Gakuen-cho, Mihara, Hiroshima 723-0053, Japan
3) Attached Clinic, Prefectural University of Hiroshima, 1-1 Gakuen-cho, Mihara, Hiroshima 723-0053, Japan

ABSTRACT

We conducted a survey of 111 healthy middle-aged and older women, aged 40 to 80 years, to elucidate the relationships between blood leptin and adiponectin levels and bone mineral density (BMD) in September 2008. We examined the associations between the blood levels of these adipocytokines and the lumbar spine (L2-L4), left femoral, and distal forearm BMD after adjustment for the age and body fat percentage. No correlation was observed between leptin and the BMD. This is presumably due to the fact that the influence of menopause, age, duration of postmenopausal period, and body fat percentage on the BMD is greater than that of leptin levels in healthy women. The adiponectin levels were significantly correlated negatively with the lumbar spine and femoral BMD in premenopausal women, and with forearm BMD in postmenopausal women, regardless of adjustment for age and body fat percentage. It seems likely that adiponectin influences the BMD at different skeletal sites in pre- and postmenopausal women.

Key words: *Leptin, Adiponectin, BMD, Women*

It is well-known that obesity or body weight gain results in an increase in the bone mineral density (BMD). It has been speculated that an increase in body weight elevates the mechanical load on bone tissue, resulting in an increase in the BMD[14,29]. Furthermore, the increase in body fat mass in obesity may also have an influence on the BMD[10]. The fat stores would exert different effects on bone mass at different skeletal sites. The percentage of body fat correlated negatively with BMD at the ribs and both arms, which are non-weight-bearing bone[30]. Fat mass is known to influence bone metabolism and BMD through adipocytokines such as leptin and adiponectin, which are secreted from adipocytes[16]. It has been reported that leptin and adiponectin act not only on carbohydrate and lipid metabolism, but also on bone metabolism[19].

The relationship between blood leptin level and BMD is still unclear. Several authors have reported a positive correlation between blood leptin levels and BMD[2,24,27]. However, a negative correlation between leptin and BMD was also noted[1,2,17,18,21,23,24]. The relationship between serum adiponectin level and BMD is also still controversial. Several studies documented a significant positive relationship between adiponectin and bone formation[9,20]. Richards et al[22] studied 1,735 adult females (mean age, 50 years), and reported that there was a negative correlation between blood adiponectin levels and the BMD in the femoral, forearm bones and vertebrae, even if the influence of the amount of body fat was eliminated. However, Jürimäe et al[9] and Kotogianni et al[15] noted that blood adiponectin levels were correlated negatively with the BMD of the femoral, total body, and lumbar vertebrae in premenopausal women, but that the involvement of adiponectin in

* Correspondence: Tadayuki Iida, R.T. Ph.D
Department of Public Health, Fujita Health University School of Medicine,
1-98 Dengakugakubo, Kutsukakecho, Toyoake, Aichi 470-1192, Japan
Tel: +81-562-93-2453, Fax: +81-562-93-3079, E-mail: iida@fujita-hu.ac.jp (T. Iida)

the total body BMD was lost after adjustment for the amount of body fat[9,15].

As mentioned above, on the associations of adipocytokines and BMD, adjustment for confounding factors (such as age and body fat) in combination led to different results, and no definite views have been achieved. In this study, we examined the associations between blood adipocytokine levels and the lumbar spine, femoral, and distal forearm BMD after adjustment for age and body fat percentage separately by cross-sectional study. Very recently, a positive correlation between total serum cholesterol levels and BMD has been reported[6]. In this study, the contribution of cholesterol levels to BMD is also considered.

MATERIALS AND METHODS

SUBJECTS

In September 2008, we conducted a survey of 118 healthy middle-aged and older women aged, 40 to 80, who gave their consent to participate in the survey and resided on islands in the eastern part of Hiroshima Prefecture. Of these 118 women, those in whom oophorectomy- or hysterectomy-induced menopause or diseases affecting bone metabolism had been confirmed were excluded, and 111 who underwent measurement of their physical characteristics, BMD, and biochemical and serological parameters were included in the study, which was performed with the approval of the Ethics Committee of the Prefectural University of Hiroshima in accordance with the Declaration of Helsinki (recognized on 5th Aug. 2008 : N08-0011).

METHODS

The measurement of physical characteristics, the BMD, and biochemical and serological parameters was performed. The body height and weight were measured. The body mass index (BMI) in kg/m^2 was calculated from the values of body height and weight, and the body fat percentage was determined with a BC-118D Body Composition Analyzer (Tanita Corp., Tokyo, Japan). Using a QDR X-ray Bone Densitometer (Hologic Inc., MA, USA), the BMD (g/cm^2) of the lumbar vertebrae (L2-L4), left femur (femoral), and distal end of the forearm bone were measured. Biochemical and serological tests were performed to measure the levels of HDL-cholesterol (HDL-cho), LDL-cholesterol (LDL-cho), and adipocytokines (leptin and adiponectin) in serum samples obtained by centrifuging collected blood at 1,500 g for 10 min. These serum samples were sent to a privately owned clinical laboratory for biochemical and serological testing with commercially available kits. HDL-cho, LDL-cho, leptin, and adiponectin were measured using a liquid THO II kit (Toyo Co., Ltd., Fukui, Japan), MetaboLead HDL-C (Kyowa Medex Co., Ltd., Tokyo, Japan), Determiner LDL-C Reagent (Kyowa Medex Co., Ltd., Tokyo, Japan), Human Leptin RIA kit (Cosmic Corporation, Tokyo, Japan), and Human Adiponectin Latex (Mitsubishi Chemical Medience Corporation, Tokyo, Japan), respectively. The normal ranges of HDL-cho and LDL-cho are 40-96 mg/dl and 70-139 mg/dl, respectively.

DATA ANALYSIS

All data are expressed as the mean ± standard deviation and range. The data of physical characteristics were compared between pre- and postmenopausal women using Student's t-test. The correlations between the age, duration of the postmenopausal period, physical characteristics, HDL-cho, LDL-cho and leptin, adiponectin, L2-L4 BMD, femoral BMD, and distal forearm BMD were tested using Pearson's correlation coefficient. The relationship between the body fat and leptin or adiponectin was tested by partial correlation analysis after adjustment for the duration of the postmenopausal period and/or BMI. The relationship between the BMI and leptin or adiponectin was tested by partial correlation analysis after adjustment for the age (or the duration of the postmenopausal period in postmenopausal women) and/or body fat percentage. Multiple regression analysis was performed using the lumbar, femoral, and forearm BMD as dependent variables. The explanatory variables were selected if the p-value of the correlation coefficient between them and leptin or adiponectin was less than 0.25. The body height, LDL-cho, leptin, and adiponectin were used as independent variables. All statistical analyses were performed using SPSS 16.0 J (SPSS Japan Inc., Tokyo, Japan), and $p < 0.05$ was considered as significant.

RESULTS

Comparison of physical characteristics, leptin and adiponectin levels, and BMD in pre- and postmenopausal women

The physical characteristics of groups of pre- and postmenopausal women are shown in Table 1. Significant differences were observed in the age, body height, weight, and lumbar spine, femoral, and forearm BMD between the two groups. No significant differences were noted in the BMI, body fat percentage, HDL-cho, LDL-cho, leptin, and adiponectin between the two groups.

Correlations between BMD and physical characteristics, blood biochemical parameters, leptin, and adiponectin

Table 2 shows correlations between the BMD, leptin, adiponectin and age, duration of the

postmenopausal period, physical characteristics, HDL-cho and LDL-cho in pre- and postmenopausal women. In premenopausal women, leptin was positively correlated with the body fat percentage, but this relation disappeared after adjustment for age and BMI(partial correlation coefficient:0.193, p:0.509). Adiponectin was positively correlated with HDL-cho. On the other hand, the forearm BMD was significantly positively correlated with the body weight, BMI, and body fat percentage. In postmenopausal women, leptin was significantly positively correlated with the body weight, BMI, body fat percentage and LDL-cho. The positive correlation of leptin with body

Table 1. Physical characteristics of the subjects

	premenopausal (n=16)				postmenopausal (n=95)				p value
	mean	SD	min	max	mean	SD	min	max	
Age (yr)	47.6	3.8	40.0	54.0	61.3	6.6	49.0	80.0	<0.001
postmenopausal period (yr)	-	-	-	-	11.9	8.0	0.3	37.0	
Height (cm)	157.0	3.9	151.0	165.2	152.2	5.7	140.2	168.5	0.002
Weight (kg)	60.1	8.2	48.7	81.8	53.5	7.4	39.9	74.6	0.001
Body Mass Index	24.4	3.2	21.3	34.3	23.1	2.9	15.1	31.3	0.103
Body fat % (%)	35.3	4.9	29.1	48.6	33.6	5.9	18.0	45.5	0.278
HDL cholesterol (mg/dl)	65.8	14.6	40.0	94.0	60.4	15.9	27.0	118.0	0.206
LDL cholesterol (mg/dl)	126.1	31.2	78.0	209.0	128.7	28.4	64.0	201.0	0.733
Leptin (ng/ml)	5.09	2.37	0.81	8.23	4.26	2.27	0.23	11.74	0.181
Adiponectin (μg /ml)	8.01	4.43	3.25	15.50	11.00	6.42	1.67	31.50	0.076
lumbar spine BMD (g/cm^2)	1.10	0.13	0.92	1.33	0.86	0.15	0.58	1.45	<0.001
femoral BMD (g/cm^2)	0.99	0.10	0.83	1.19	0.83	0.13	0.59	1.21	<0.001
distal forearm BMD (g/cm^2)	0.56	0.06	0.49	0.66	0.46	0.06	0.29	0.67	<0.001

Table 2. Relationship between physical characteristics adipocytokines and the BMD in pre- and postmenopausal women

premenopausal (n=16)

	Leptin (ng/ml)		Adiponectin (μg/ml)		lumbar spine BMD (g/cm^2)		femoral BMD (g/cm^2)		distal forearm BMD (g/cm^2)	
	r	p value	r	p value	r	p value	r	p value	r	p value
Age (yr)	0.642	0.007	-0.160	0.555	0.001	0.997	-0.235	0.380	-0.111	0.681
postmenopausal period (yr)	-	-	-	-	-	-	-	-	-	-
Height (cm)	-0.021	0.938	-0.025	0.926	-0.030	0.912	0.152	0.575	0.183	0.498
Weight (kg)	0.452	0.079	-0.446	0.083	0.113	0.676	0.474	0.063	0.755	0.001
Body Mass Index	0.488	0.055	-0.443	0.086	0.115	0.671	0.431	0.096	0.726	0.001
Body fat % (%)	0.522	0.038	-0.467	0.068	0.126	0.641	0.468	0.068	0.747	0.001
HDL cholesterol (mg/dl)	-0.254	0.342	0.564	0.023	-0.386	0.140	-0.405	0.120	-0.284	0.287
LDL cholesterol (mg/dl)	0.261	0.329	-0.347	0.188	0.174	0.520	0.218	0.418	0.341	0.196

postmenopausal (n=95)

	Leptin (ng/ml)		Adiponectin (μg/ml)		lumbar spine BMD (g/cm^2)		femoral BMD (g/cm^2)		distal forearm BMD (g/cm^2)	
	r	p value	r	p value	r	p value	r	p value	r	p value
Age (yr)	-0.014	0.892	0.105	0.312	-0.382	<0.001	-0.240	0.020	-0.517	<0.001
postmenopausal period (yr)	-0.062	0.548	0.206	0.047	-0.429	<0.001	-0.321	0.002	-0.485	<0.001
Height (cm)	-0.074	0.475	-0.047	0.652	0.265	0.010	0.162	0.119	0.196	0.056
Weight (kg)	0.581	<0.001	-0.392	<0.001	0.350	0.001	0.431	<0.001	0.327	0.001
Body Mass Index	0.678	<0.001	-0.405	<0.001	0.222	0.031	0.371	<0.001	0.226	0.027
Body fat % (%)	0.690	<0.001	-0.370	<0.001	0.113	0.273	0.289	0.005	0.093	0.370
HDL cholesterol (mg/dl)	-0.069	0.507	0.296	0.004	0.001	0.995	-0.104	0.321	-0.047	0.654
LDL cholesterol (mg/dl)	0.204	0.047	-0.020	0.845	0.033	0.754	0.032	0.762	0.026	0.805

fat percentage was verified even after adjustment for the age and BMI (partial correlation coefficient:0.272, p:0.009). Adiponectin was significantly positively correlated with the postmenopausal period and HDL-cho, and significantly negatively correlated with the body weight, BMI, and body fat percentage. But the negative correlation of adiponectin with body fat percentage was not observed after adjustment for age and BMI (partial correlation coefficient:-0.034, p:0.748). The BMD at the three skeletal sites was significantly negatively correlated with age and the duration of the postmenopausal period, and significantly positively correlated with the body weight and BMI. In addition, the femoral BMD was significantly positively correlated with the body fat percentage. There was no relationship between BMD and HDL-cholesterol nor LDL-cholesterol.

Correlations between BMD and leptin and adiponectin in pre- and postmenopausal women

Table 3 shows the relationships between the BMD and leptin and adiponectin levels in pre- and postmenopausal women in consideration of age and body fat percentage. In premenopausal women, no significant difference was observed in the correlation coefficient between blood leptin levels except in the age-adjusted forearm BMD. A significant negative correlation between blood adiponectin levels and the lumbar spine and femoral BMD were verified even after adjustment for age and/or body fat percentage. For the forearm, a significant negative correlation between blood adiponectin levels and BMD disappeared after adjustment for the body fat percentage. In postmenopausal women, the correlation coefficient and age-adjusted partial correlation coefficient showed a significant positive correlation between blood leptin levels and the femoral BMD alone. However, this relation disappeared after adjustment for the body fat percentage. Adiponectin levels were significantly negatively correlated with the femoral BMD. This significant correlation remained after adjustment for the duration of the postmenopausal period or body fat percentage, but disappeared after adjustment for both the duration of the postmenopausal period and body fat percentage. The correlation coefficient and all partial correlation coefficients indicated a significant correlation between adiponectin levels and the forearm BMD.

Multiple regression analysis of factors influencing BMD in pre- and postmenopausal women

Table 4 shows the results of multiple regression analysis using the lumbar spine, femoral and forearm BMD as dependent variables and body height, LDL-cho, leptin and adiponectin as independent variables in premenopausal women. Adiponectin was identified as a significant factor associated with the unadjusted lumbar spine and

Table 3. Relationship between adipocytokines and the BMD in pre- and postmenopausal women

premenopausal

	unadjusted		Age adjusted		Body fat %, adjusted		Age and Body fat %, adjusted	
	correlation coefficient	p value	partial correlation coefficient	p value	partial correlation coefficient	p value	partial correlation coefficient	p value
lumbar spine								
Leptin	0.123	0.649	0.160	0.569	0.068	0.810	0.111	0.705
Adiponectin	-0.661	0.005	-0.669	0.006	-0.686	0.005	-0.689	0.006
femoral								
Leptin	0.129	0.635	0.375	0.168	-0.153	0.586	0.141	0.631
Adiponectin	-0.724	0.002	-0.793	0.000	-0.646	0.009	-0.733	0.003
distal forearm								
Leptin	0.377	0.150	0.588	0.021	-0.022	0.939	0.376	0.185
Adiponectin	-0.496	0.051	-0.524	0.045	-0.251	0.367	-0.309	0.282

postmenopausal

	unadjusted		postmenopausal period adjusted		Body fat %, adjusted		postmenopausal period and Body fat %, adjusted	
	correlation coefficient	p value	partial correlation coefficient	p value	partial correlation coefficient	p value	partial correlation coefficient	p value
lumbar spine								
Leptin	0.136	0.190	0.114	0.280	0.068	0.522	-0.033	0.755
Adiponectin	-0.186	0.073	-0.104	0.324	-0.148	0.160	-0.026	0.803
femoral								
Leptin	0.298	0.004	0.287	0.005	0.131	0.215	0.054	0.609
Adiponectin	-0.325	0.001	-0.279	0.007	-0.242	0.020	-0.154	0.145
distal forearm								
Leptin	0.161	0.120	0.145	0.167	0.132	0.209	0.031	0.774
Adiponectin	-0.420	<0.001	-0.377	<0.001	-0.420	<0.001	-0.339	0.001

Table 4. Multiple regression analysis of factors influencing the BMD in premenopausal women

unadjusted

		ß coefficient	p value	R^2	p value*
lumbar spine					
	Height (cm)	-0.028	0.914	0.509	0.050
	LDL cholesterol (mg/dl)	-0.044	0.876		
	Leptin (ng/ml)	-0.025	0.919		
	Adiponectin (μg/ml)	-0.683	0.018		
femoral					
	Height (cm)	0.189	0.428	0.554	0.048
	LDL cholesterol (mg/dl)	-0.128	0.617		
	Leptin (ng/ml)	-0.013	0.953		
	Adiponectin (μg/ml)	-0.766	0.005		
distal forearm					
	Height (cm)	0.151	0.596	0.353	0.269
	LDL cholesterol (mg/dl)	0.063	0.837		
	Leptin (ng/ml)	0.269	0.318		
	Adiponectin (μg/ml)	-0.408	0.151		

Age and Body fat %, adjusted

		ß coefficient	p value	R^2	p value*
lumbar spine					
	Height (cm)	-0.056	0.844	0.512	0.049
	LDL cholesterol (mg/dl)	0.027	0.930		
	Leptin (ng/ml)	0.229	0.529		
	Adiponectin (μg/ml)	-0.776	0.020		
femoral					
	Height (cm)	0.040	0.854	0.722	0.034
	LDL cholesterol (mg/dl)	-0.023	0.920		
	Leptin (ng/ml)	0.220	0.425		
	Adiponectin (μg/ml)	-0.686	0.009		
distal forearm					
	Height (cm)	-0.044	0.830	0.751	0.022
	LDL cholesterol (mg/dl)	0.146	0.512		
	Leptin (ng/ml)	0.353	0.191		
	Adiponectin (μg/ml)	-0.188	0.361		

*:analysis of variance

Table 5. Multiple regression analysis of factors influencing the BMD in postmenopausal women

unadjusted

		ß coefficient	p value	R^2	p value*
lumbar spine					
	Height (cm)	0.276	0.007	0.116	0.025
	LDL cholesterol (mg/dl)	-0.022	0.827		
	Leptin (ng/ml)	0.116	0.278		
	Adiponectin (μg/ml)	-0.142	0.175		
femoral					
	Height (cm)	0.183	0.063	0.185	0.001
	LDL cholesterol (mg/dl)	-0.047	0.634		
	Leptin (ng/ml)	0.246	0.019		
	Adiponectin (μg/ml)	-0.251	0.014		
distal forearm					
	Hight (cm)	0.186	0.053	0.212	<0.001
	LDL cholesterol (mg/dl)	-0.013	0.891		
	Leptin (ng/ml)	0.068	0.498		
	Adiponectin (μg/ml)	-0.393	<0.001		

postmenopausal period and Body fat %, adjusted

		ß coefficient	p value	R^2	p value*
lumbar spine					
	Height (cm)	0.154	0.129	0.241	<0.001
	LDL cholesterol (mg/dl)	-0.021	0.828		
	Leptin (ng/ml)	-0.015	0.909		
	Adiponectin (μg/ml)	-0.034	0.745		
femoral					
	Hight (cm)	0.103	0.308	0.254	<0.001
	LDL cholesterol (mg/dl)	-0.048	0.614		
	Leptin (ng/ml)	0.095	0.480		
	Adiponectin (μg/ml)	-0.153	0.149		
distal forearm					
	Hight (cm)	0.049	0.598	0.349	<0.001
	LDL cholesterol (mg/dl)	-0.008	0.932		
	Leptin (ng/ml)	0.058	0.643		
	Adiponectin (μg/ml)	-0.324	0.001		

*:analysis of variance

femoral BMD. Adiponectin alone showed a significant negative correlation with the lumbar spine and femoral BMD after adjustment for age and body fat percentage. Table 5 shows the results of multiple regression analysis in postmenopausal women. Leptin and adiponectin were identified as significant factors associated with the unadjusted femoral BMD, and adiponectin as a significant factor associated with the unadjusted forearm BMD. Adiponectin alone showed a significant correlation with the forearm BMD after adjustment for the duration of the postmenopausal period and body fat percentage.

DISCUSSION

Although some studies documented a significant positive relationship between adiponectin and bone formation[11,20], several authors reported a negative correlation between blood adiponectin levels and the BMD. Richards et al[22] reported that there was a negative correlation between blood adiponectin levels and the BMD in the femoral, forearm bones, and vertebrae, and these negative relations were intensified in postmenopausal women. Jürimäe et al[9] and Kotogianni et al[15] noted that blood adiponectin levels were correlated negatively with the BMD of the femoral, total body, and lumbar vertebrae in premenopausal women, but that the involvement of adiponectin in the total body BMD was lost after adjustment for the amount of body fat[9,15]. On the other hand, Huang et al[7] reported that plasma adiponectin concentrations were not related to the total-body BMD independent of the age and BMI, or to fat mass in nondiabetic female adolescents, although they were highly correlated in simple correlation analyses. In studies recruiting type 2 diabetic patients, the relationship between serum adiponectin level and BMD is still controversial[12,13]. However, in our study in healthy subjects, blood adiponectin levels were negatively correlated with the BMD.

Cell biology evidence showed the possibility that adiponectin gene expression in adipocytes would be regulated by the proteins (mainly OST-PTP: osteotesticular protein tyrosine phosphatase) derived from osteoblasts[16]. On the other hand, osteocalcin(OS) derived from osteoblasts functions as a hormone regulating glucose metabolism and fat mass[4]. Fat mass is known to influence bone metabolism through adipocytokines including adiponectin and leptin[16]. The baseline serum adiponectin level is associated with changes in bone markers including osteocalcin during glycemic control in type 2 diabetes mellitus[12]. Adiponectin might be included in such a reciprocal regulation of bone and energy metabolism[16].

Shinoda et al[25] reported that the addition of recombinant adiponectin to cultured osteoprogenitor cells suppressed osteogenesis, and this suppression was blunted by the enhancement of insulin signaling. Thus, we speculate that endogenous adiponectin is involved in promoting bone formation in a complex manner: circulating adiponectin directly suppresses bone formation, but indirectly promotes osteogenesis by enhancing the effect of insulin through its signaling pathway, thereby regulating the bone mass[20].

Our present study indicated that the association between leptin and BMD was restricted to the age-adjusted forearm and femoral BMD in the pre- and postmenopausal women, respectively. However, the correlation disappeared after adjustment for the body fat percentage. Taken together, these findings suggest that the correlation between blood leptin levels and the BMD, particularly of the forearm, is influenced by the body fat percentage. This is also supported by the correlation between the body fat percentage and forearm BMD shown in Table 2.

There are conflicting results in earlier reports regarding the association of leptin with BMD[1,2,17,18,21,23,24,27]. These conflicting results may be due to differences between studies in the skeletal regions measured, and /or differences in the age and menopausal status of the subjects studied. In premenopausal women, leptin had a significant positive association with femoral neck and lumbar spine BMD, but these associations do not exist any more when adjusted for body fat mass[10]. Kontogianni et al[15] reported that serum leptin levels were negatively correlated, and this relation was observed only when serum insulin levels were included as an independent variable. Huang et al[7] reported that plasma leptin concentrations were not related to the total-body BMD independent of the age, BMI, or fat mass in nondiabetic female adolescents, although they were highly correlated in simple correlation analyses. From studies in mice, it has been speculated that leptin regulates the bone mass via a balance between an indirect action through the nervous system[3,26] and a direct action on osteoclasts[25]. In our study, the association between leptin and BMD was restricted to the age-adjusted forearm and femoral BMD in the pre- and postmenopausal women, respectively. This is presumably due to the fact that, in healthy women, the influence of menopause, age, duration of the postmenopausal period, and body fat percentage on the BMD is greater than that of leptin levels.

Recently, Jeon et al[8] reported the association of the components of metabolic syndrome with BMD in pre- and postmenopausal women. They found that metabolic syndrome had negative correlations with the BMD of the lumbar spine and femoral neck in the postmenopausal group and with the BMD of the lumbar spine in the premenopausal group[8]. They proposed that inflammation might

have a more important role in BMD than obesity. Furthermore, Hernández et al[6] reported that a more unfavorable lipid profile (mainly higher LDL-cholesterol level) was associated with higher BMD at the lumbar spine and hip in men. In our results, LDL-cholesterol level had no association with BMD at the three sites examined, although serum adiponectin level correlated negatively with HDL-cholesterol level and serum leptin level correlated positively with LDL-cholesterol level. As shown in our multiple regression analysis, adiponectin seems to affect BMD independently. It seems likely that the effects of metabolic syndrome on BMD depends on the blood adipocyokine (mainly adiponectin) level.

Therefore, according to the results of this study, it is possible that, in clinical practice, leptin and adiponectin could be used as one of the indices of a lifestyle disease involving increasing body fat. In addition, the serum adiponectin level is associated with changes in bone markers including osteocalcin during glycemic control in type 2 diabetes mellitus[12]. However, it is suggested in this study that the serum adiponectin level is important as an indicator of lifestyle diseases, including loss of BMD even in healthy persons.

The physiques of the subjects were close to the age-matched means[5] in other surveys in Japan as well as those in subjects excluded from this survey, suggesting that the findings are valid for application to young women in general. The limitations of this study are that the subjects were female volunteers, who participated in a health survey including BMD measurement, and therefore might be biased toward those who were in good health or had marked health awareness. Furthermore, this study has limitations in that the number of premenopausal subjects was small, and some variables showed no significant differences between groups despite strong tendencies. A large-scale study is particularly necessary to examine the correlation between adipocytokines and the BMD in pre- and postmenopausal women.

CONCLUSIONS

Our study indicated that adiponectin was a significant factor associated with the lumbar spine and femoral BMD in premenopausal women, and with the forearm BMD in postmenopausal women. Adiponectin might be included in a reciprocal regulation of bone and fat metabolism. The association between blood leptin level and the BMD was restricted to the age-adjusted forearm and femoral BMD in the pre- and postmenopausal women, and the association of leptin with BMD might be affected strongly by age and body fat percentage.

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