Relationship of Body Composition and Circulatory Adiponectin to Bone Mineral Density in Young Premenopausal Women

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Objective: *Adiponectin is a recently discovered hormone secreted by adipocytes. Adiponectin plays an important role in the regulation of insulin sensitivity as well as the propensity to inflammation and atherosclerosis. In the present study, the authors explore the relationship between adiponectin and bone mass in premenopausal women. The relationship of fat mass compared to lean body mass to bone mass was also investigated.*
Material and Method: *Two hundred premenopausal women aged between 20 and 40 years were studied. Bone mineral density (BMD) was measured at L2-4 and femoral neck by dual-energy X-ray absorptiometry (DEXA). Serum adiponectin concentrations were measured by radioimmunoassay.*
Results: *At the lumbar spines, factors associated with BMD were age ($p < 0.01$) and lean body mass ($p < 0.001$). No independent association with fat mass was demonstrated. Likewise, at the femoral neck, only lean body mass was related to BMD ($p < 0.01$). In terms of the relation of serum adiponectin to BMD, no association of serum adiponectin to BMD at the lumbar spines or femoral neck was found.*
Conclusion: *Altogether, the present findings do not suggest the independent role of adiponectin in the accrual of bone mass in females, although such a role still cannot be excluded in men or postmenopausal women.*

Keywords: *Adiponectin, BMD, Premenopausal, Body composition*

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It is now well established that adipose tissue functions as an endocrine organ besides providing energy storage. A number of active substances are secreted from adipocytes. These include substrate such as free fatty acid, cytokines such as interleukin-6 and tumor necrosis factor alpha, hormones such as leptin, resistin, and adiponectin. Leptin plays roles in the regulation of energy homeostasis and modulation of food intake. Moreover, leptin has been shown to influence bone metabolism through a central pathway[1] and inhibit bone formation. The effect can be abolished by adrenergic antagonist suggesting that the effect of leptin on bone formation is likely to be indirect through peripheral adrenergic system.

Adiponectin is a recently discovered hormone secreted by adipocytes. Adiponectin plays an important role in the regulation of insulin sensitivity as well as the propensity to inflammation and atherosclerosis. Adiponectin is an abundant circulating protein in humans constituting 0.01% of the total circulating protein. To date, there has been only scarce information regarding the effect of adiponectin on bone[2-4]. To explore the issue, the authors investigated the relation between adiponectin and bone mass in premenopausal women. The relationship of fat mass compared to lean body mass to bone mass was also investigated to examine the possible role of fat mass as a determinant of bone mass.

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Material and Method

Two hundred premenopausal women aged between 20 and 40 years living in Bangkok Metropolitan area in Thailand were recruited by flyers and direct contact. All were healthy and ambulatory. None of the subjects was a smoker or consumed significant amounts of alcohol. Medical history-taking and complete physical examination were performed on the volunteers to assess their health status.

BMD and body composition were measured by dual-energy X-ray absorptiometry (DEXA) (Lunar Prodigy Lunar Corp., USA) at anteroposterior lumbar spine (L2-L4) and femoral neck in each subject. Measured body composition included fat mass, lean body mass and bone mass. Daily calibration and quality control were performed regularly according to the manufacturer's instructions. In vivo coefficient of variance (CV) for anteroposterior lumbar spine (L2-L4) and femoral neck was 1.2% and 1.6% respectively.

Fasting blood samples were obtained from subjects between 8.00 and 10.00 am. Samples were allowed to clot and after centrifugation, the serum was frozen at -20 C until measurement. Radioimmunoassay kits were used to determine serum adiponectin (Linco, USA).

Data were expressed as mean $\pm$ SD. The correlations among variables were determined by linear regression analyses. Stepwise multiple regression and ANOVA were used to determine the relative importance of various independent variables on BMD. Statistic significance was assigned at $p < 0.05$.

Results

Table 1 demonstrates the clinical characteristics, body composition and serum adiponectin levels of the subjects. Within the age range of the studied population, there was an increase in L2-4 BMD with advancing age ($p < 0.05$) while a decrease in femoral neck BMD was demonstrated ($p < 0.05$). Body weight was associated with increased BMD at both the lumbar spines ($p < 0.001$) and the femoral neck ($p < 0.001$).

To investigate the relative role of body compartments in the determination of bone mass, the association of body weight with bone mass was further analyzed in terms of lean and fat masses. As shown in Table 2, factors associated with BMD at the lumbar spines included age ($p < 0.01$) and lean body mass ($p < 0.001$). No independent association with fat mass was demonstrated. Likewise, at the femoral neck, only lean body mass was related to BMD ($p < 0.01$). No effect of age and fat mass was found.

With regard to serum adiponectin, there was negative correlation between serum adiponectin levels and body weight ($r = -0.16$, $p < 0.05$), BMI ($r = -0.16$, $p < 0.05$), fat mass ($r = -0.19$, $p < 0.01$) and percentage of body fat ($r = -0.19$, $p < 0.01$) as shown in Table 3. The degree of adiposity as measured by the percentage of body fat is the only parameter associated with serum adiponectin in a stepwise linear regression model with

Table 1. Clinical characteristics, body composition and serum adiponectin levels of the subjects

Age (yr)	29.4 $\pm$ 5.7
Body weight (kg)	51.0 $\pm$ 7.0
Height (cm)	156.8 $\pm$ 4.9
BMI (kg/m^2)	20.7 $\pm$ 2.8
Lean body mass (kg)	31.4 $\pm$ 3.1
Fat mass (kg)	16.0 $\pm$ 5.3
Percentage of body fat (%)	33.1 $\pm$ 6.3
L2-4 BMD (g/cm^2)	1.15 $\pm$ 0.14
Femoral neck BMD (g/cm^2)	0.97 $\pm$ 0.12
Adiponectin (g/ml)	9.4 $\pm$ 3.7

Values are mean $\pm$ SD
L2-L4 BMD: bone mineral density at anterorposterior lumbar spine

Table 2. Relations of BMD to age, lean body mass and fat mass at the lumbar spines and the femoral neck

Variable	L2-4 BMD		Femoral neck BMD	
	Standardized coefficient	p-value	Standardized coefficient	p-value
Age	0.26	<0.01	-	NS
Lean body mass	0.19	<0.001	0.21	<0.01
Fat mass	-	NS	-	NS

L2-L4 BMD: bone mineral density at anterorposterior lumbar spine
NS: not significance

Table 3. Correlation coefficients among serum adipnonectin, L2-4 BMD, femoral neck BMD and body composition

	Adiponectin	L2-4 BMD	Femoral neck BMD	Body weight	BMI	Lean body mass	Fat mass
L2-4 BMD	-0.04						
Femoral neck BMD	-0.10	0.56***					
Body weight	-0.16*	0.36***	0.22***				
BMI	-0.16*	0.29***	0.16*	0.89***			
Lean body mass	-0.06	0.30***	0.21**	0.75***	0.52***		
Fat mass	-0.19**	0.26***	0.10	0.92***	0.93***	0.45***	
Percentage body fat	-0.19**	0.20**	0.05	0.82***	0.82***	0.13	0.93***

BMI: body mass index
L2-L4 BMD: bone mineral density at anterorposterior lumbar spine
Difference among variables; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

body weight, BMI, fat mass and percentage of body fat as independent variables. In terms of the relation of serum adiponectin to BMD, no association of serum adiponectin to BMD at the lumbar spines or femoral neck was found. The non-association persisted after being corrected for other confounding variables including age, lean mass and fat mass.

Discussion

Body weight is a strong determinant of bone mass. However, the relative contribution of specific body compartment is less clear. A number of studies have demonstrated the relatively more importance of lean body mass compared to fat mass in the determination of bone mass in premenopausal women[5]. On the contrary, fat mass may have relatively more contribution in postmenopausal women[6] which is possibly related to bone-protective effect of residual endogenous estrogen[7,8] derived partly from adipose tissue. Most of the studies relating body composition to bone mass were performed on Caucasian populations. There is increasing evidence suggesting a difference in body composition, particularly fat mass, despite similar body mass indices between Asians and Caucasians. Nevertheless, a study in Chinese premenopausal women has also demonstrated the predominant association of lean body mass compared to fat mass with bone mass[5]. In keeping with the findings in premenopausal women, the present study in young premenopausal women confirmed the influence of lean body mass on bone mass such that only lean body mass was shown to be independently related to BMD at both the lumbar spine and the femoral neck regions. The underlying basis for such influence is unclear. Lean body mass may exert its influence through the mechanical stress the skeleton needs to sustain. In this regard, the attainment of peak lean body mass has been shown to precede the maximal accrual of bone mass in adolescents[9]. On the other hand, higher lean body mass may result from more physical activity which also exerts beneficial on bone mass. Moreover, both lean body mass and fat mass may be independently influenced by genetic factors. Nevertheless, the less apparent association of fat mass to bone mass may suggest the relatively minor role of various adipokines recently found to be secreted from adipose tissue.

Adipose tissue secretes a number of peptides such as leptin and adiponectin, which may be partly accountable for the apparent relation between body weight and bone mass. Leptin may affect bone directly since leptin receptors have been demonstrated in bone cells[10,11]. However, leptin has been suggested to possess indirect effects on bone through its action in the hypothalamus[1]. The relation between leptin and bone has been demonstrated in studies both in experimental animals[12,13] and in humans[14,15]. Unlike the suggested role of leptin on bone metabolism, fewer studies investigated the association of serum adiponectin with bone mineral density. Data regarding the effect of adiponectin on bone are scarce. Adipose tissue appears to be the sole source of adiponectin. Adiponectin exerts its effect through adiponectin receptors, which are abundantly expressed in skeletal muscle and liver tissues[16]. Adiponectin receptors have also been demonstrated in pancreatic beta cells[17], macrophages[18]. However, to date, there has been no report of the presence of adiponectin receptors in bone cells. With regard to clinical investigations, a number of studies have recently looked into the relationship between circulating adiponectin and bone to mass. No association was

found in a study of female adolescents[3], perimenopausal women[2].

In conclusion, the present study particularly addressed the issue in young premenopausal women. In keeping with most previous studies, no association of adiponectin has been found either in univariate or multivariate analysis adjusting for the confounding effect of age and body composition. Altogether, the findings do not suggest an independent role of adiponectin in the accrual of bone mass in females, although such a role still cannot be excluded in men or postmenopausal women.

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ความสัมพันธ์ระหว่างส่วนประกอบของร่างกายและระดับอะดิโปเนคตินในเลือดกับความหนาแน่นกระดูกในหญิงวัยก่อนหมดประจำเดือน

สุวรรณี ชั้นประเสริฐโยธิน, สุนีย์ แซ่ตั้ง, เพ็ญพรรณ พยัตติกุล, รัชตะ รัชตะนาวิน, บุญส่ง องค์พิพัฒนกุล

วัตถุประสงค์: *อะดิโปเนคตินเป็นฮอร์โมนที่ผลิตโดยเซลล์ไขมันซึ่งมีความสำคัญในการควบคุมความไวต่ออินซูลิน รวมทั้งมีผลต่อการเกิดการอักเสบและภาวะผนังเส้นโลหิตแดงหนาและมีความยืดหยุ่นน้อยลง ในการศึกษาครั้งนี้เพื่อดูความสัมพันธ์ระหว่างอะดิโปเนคตินและความหนาแน่นกระดูกในหญิงวัยก่อนหมดประจำเดือน ความสัมพันธ์ระหว่างมวลไขมันเปรียบเทียบกับมวลกล้ามเนื้อกับความหนาแน่นกระดูก*

วัสดุและวิธีการ: *หญิงวัยก่อนหมดประจำเดือนจำนวน 200 คน อายุระหว่าง 20 ถึง 40 ปี ได้รับการวัดความหนาแน่นกระดูกส่วน L2-4 lumbar spine และ femoral neck โดย dual-energy X-ray absorptiometry (DEXA) ระดับอะดิโปเนคติน วัดโดยวิธี radioimmunoassay*

ผลการศึกษา: *ในส่วน L2-4 lumbar spine พบว่า มีความสัมพันธ์ระหว่างความหนาแน่นกระดูกกับอายุ ($p < 0.01$), และมวลกล้ามเนื้อ ($p < 0.001$) แต่ไม่พบความสัมพันธ์กับมวลไขมัน ส่วน femoral neck พบว่ามีความสัมพันธ์ระหว่างความหนาแน่นกระดูกกับมวลกล้ามเนื้อเพียงอย่างเดียว ($p < 0.01$) ไม่พบความสัมพันธ์ระหว่างอะดิโปเนคตินกับความหนาแน่นกระดูกทั้งที่ L2-4 lumbar spine และ femoral neck*

สรุป: *จากการศึกษานี้แสดงให้เห็นว่าไม่มีความสัมพันธ์ระหว่างอะดิโปเนคตินกับความหนาแน่นกระดูกของหญิงวัยก่อนหมดประจำเดือน แต่ก็ยังไม่สามารถสรุปได้ในชายและหญิงวัยหลังหมดประจำเดือน*