Association between Lumbar Bone Mineral Density and Carotid Intima-Media Thickness in Korean Adults: a Cross-sectional Study of Healthy Twin Study

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INTRODUCTION

Low bone mineral density (BMD) and atherosclerosis are degenerative changes commonly accompanying aging. Low BMD increases the risk of osteoporotic fracture for the elderly, which results in functional decline and increased mortality (1,2). Atherosclerosis occurs in the subendothelial space (i.e., the intima) of medium-sized arteries and is triggered by mechanotransduction and inflammatory processes in endothelial cells (3).

A growing body of evidence indicates that BMD is associated with atherosclerosis. This association has been proposed to be explained by a number of biological mechanisms including similar processes of bone and vascular mineralization (4), osteoblastic differentiation by lipid oxidation (5), and shared risk factors including lifestyle factors (6), estrogen deficiency (7), and vitamin D receptor polymorphisms (8,9).

Bone mineral density (BMD) has been suggested to be associated with atherosclerosis. In the present study, we evaluated the association between lumbar BMD and the segments of carotid intima-media thickness (CIMT), a surrogate marker of subclinical atherosclerosis, in Korean adults, with consideration of sex and menopause status. Among 1,679 Korean adults who enrolled in a Healthy Twin Study, 723 men, 690 premenopausal women, and 266 postmenopausal women measured the CIMT at the common carotid artery intima-media thickness (CCA-IMT), carotid bifurcation intima-media thickness (BIF-IMT), internal carotid artery intima-media thickness (ICA-IMT) using B-mode ultrasound and lumbar BMD using dual-energy X-ray absorptiometry. The composite CIMT was calculated as the mean value of three CIMTs. The association was evaluated using linear mixed models. In premenopausal women, lumbar BMD was positively associated with composite CIMT and with CCA-IMT (P = 0.008 and 0.002, respectively). However, no association was observed between BMD and CIMT in men or in postmenopausal women. Stratified analysis revealed the effect of body mass index (BMI) on the association between BMD and CIMT. The positive association in premenopausal women persisted only in low BMI (< 25 kg/m²) group, whereas a positive association appeared at high BMI (≥ 25 kg/m²) group. A high lumbar BMD may indicate an elevated risk of subclinical atherosclerosis in premenopausal women and men with high BMI.

Keywords: Bone Mineral Density; Carotid Arteries; Osteoporosis; Atherosclerosis

The association between BMD and carotid intima-media thickness (CIMT) as a surrogate marker of subclinical atherosclerosis has been evaluated in many studies (8,10-16). However, these studies have yielded inconsistent findings. Some studies found an inverse association (10,13), whereas others found a positive (12) or no association (11,14,16).

We thought that the association between BMD and CIMT may differ according to sex or menopausal status because the prevalence of atherosclerotic vascular disease and the distribution of BMD tend to differ according to these factors (17,18). In addition, the identification of segment-specific associations between intima-media thickness (IMT) and cardiovascular disease (19,20) suggests that the association between BMD and CIMT may vary according to carotid artery segment.
To resolve these discrepancies, we evaluated the association between BMD and segment-specific CIMT according to sex and menopausal status with adjustment for a wide range of cardiovascular risk factors.

MATERIALS AND METHODS

Subjects and study design
The study subjects consisted of 1,820 individuals (754 men, 734 premenopausal women, and 332 postmenopausal women) aged 18 to 83 years old. All subjects had undergone B-mode ultrasound for CIMT measurement, in addition to dual-energy X-ray absorptiometry for BMD measurement of the lumbar spine, between April 2009 and February 2012. All examinations took place at the same institution.

The study subjects were the participants in the Healthy Twin Study, a nationwide population-based cohort study that has been conducted as part of the Korean Genome Epidemiology Study since 2005. The participants are composed of twins and their first-degree family members who were voluntarily recruited through a nationwide media advertisement and mailing campaign. Details about the study design and methodology of the Healthy Twin Study have been previously published (21, 22).

Subjects with missing data (29 cases) and who had received osteoporosis treatment (51 cases) were excluded. In addition, subjects with a history of stroke (3 cases), myocardial infarction (21 cases), or cancer (37 cases) were also excluded. Finally, 1,679 subjects (723 men, 690 premenopausal women, and 266 postmenopausal women) were analyzed.

CIMT measurements
CIMT measurements were performed according to standardized protocols. Briefly, the CIMT was measured during the end-diastolic phase between the P and Q waves from the electrocardiogram trace using an automated IMT package using an automated IMT package of a high-resolution B-mode ultrasound machine (VIVID; General Electric, Horten, Norway) and an EKO 7 system (Samsung Medison Co., Ltd., Cypress, CA, USA) equipped with a seven-MHz linear transducer. CIMT scanning was performed on the far walls of the following three segments: 10-20 mm proximal to the tip of the flow divider into the common carotid artery (CCA), the carotid bifurcation (BIF) beginning at the tip of the flow divider and extending 10 mm proximal to the flow divider tip, and the proximal 10 mm of the internal carotid artery (ICA). The composite CIMT was calculated as the mean value of the three carotid artery segment CIMTs from both sides. Since two different machines (Vivid, General Electric; and EKO 7, Samsung Medison, Co., Ltd.) were used for CIMT measurement, reproducibility of the IMT measurement was assessed in 14 randomly chosen subjects. The intra-class correlation coefficients between the repeatedly measured IMT were 0.93, 0.86, and 0.90 for CCA, BIF, and ICA, respectively.

Measurements of BMD and covariates
Area (cm²), bone mineral concentration (g) of the lumbar spine, and lean mass (g) were measured using whole body dual-energy X-ray absorptiometry on a Delphi W system (Hologic, Boston, MA, USA). All measurements were recorded by a well-trained technician. For measurements of lumbar BMD, the lumbar spine region was defined superiorly by the transverse line between the twelfth thoracic vertebra (T12) and the first lumbar vertebra (L1). The lumbar spine region was defined inferiorly by the horizontal line at the iliac crest. Calibration of the dual-energy X-ray absorptiometer was conducted using a phantom according to standard quality control procedures recommended by the manufacturer. All coefficients of variation for the BMD measurements were ≤ 1.0% for the machine. Lumbar BMD was calculated by dividing the bone mineral concentration by the area of the lumbar spine region.

Blood pressure was measured manually using a standardized mercury sphygmomanometer. Weight (kg) and height (cm) were measured using standardized scales and stadiometers while wearing light clothing. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m²). All physical measurements were taken twice and analyses were performed on average values. After overnight fasting (> 12 hours), serum glucose and lipid levels were measured. All biochemical analyses were conducted in one central laboratory that is accredited by the Korea Association of Quality Assurance for Clinical Laboratory.

Demographic characteristics, smoking status, physical exercise habits, and medical histories of hypertension and diabetes were obtained using a self-administered standardized questionnaire. Incomplete or ambiguous responses were clarified in face-to-face interviews. Postmenopausal status was defined as having no menstrual periods for the preceding year and fulfilling at least one of the following conditions: natural menopause, use of estrogen replacement therapy, or 55 years of age or older. Study subjects were categorized into two groups (never smoker and ever smoker) according to smoking status. If the study subject reported performing physical exercise at least once a week, the subject was considered to be involved in regular physical exercise. Hypertension was defined as current treatment with antihypertensive medication or blood pressure exceeding 140 (systolic) or 90 (diastolic) mmHg. Diabetes mellitus was defined as current treatment with glucose-lowering medication, high serum glucose (≥ 6.99 mM/L), or a high level of hemoglobin A1C (≥ 6.5%).

Statistical analysis
We compared the characteristics of men, premenopausal women, and postmenopausal women using the t-test for continuous
variables and the chi-square test for categorical variables. Variations in CIMTs, cardiovascular risk factors, and lifestyle factors were analyzed according to composite IMT tertile using linear regression or by the Mantel-Haenszel $\chi^2$ test.

To evaluate the extent of association between BMD and CIMT, the percent difference of CIMT per increase (in 1 g/cm$^2$) of BMD of the lumbar spine were assessed using linear mixed models. Since all study subjects were recruited for a twin/family study, correlations were considered within the context of family relationships by adjusting for each family unit and each twin unit as random effects in the linear mixed model. Age, height, hypertension status, diabetes status, thyroid stimulating hormone level, low-density lipoprotein (LDL) cholesterol level, high-density lipoprotein (HDL) cholesterol level, triglyceride (TG) level, BMI, lipid-lowering medication status, smoking status, regular exercise habits, calcium supplementation status, and estrogen replacement therapy status (for postmenopausal women) were adjusted as fixed effects. Prior to this analysis, CIMT values were log transformed to approximate a normal distribution.

We also examined the association between CIMT and lumbar BMD according to BMI. High BMI was defined as a BMI $\geq$ 25 kg/m$^2$; low BMI was defined as a BMI $<$ 25 kg/m$^2$. We also evaluated whether BMI influences the association between BMD and CIMT by including an interaction term (BMI $\times$ lumbar BMD) in the analytic model. All statistical analyses were conducted using PASW Statistics 18 software (SPSS Inc., Chicago, IL, USA).

**Ethics statement**
Written informed consent was obtained from each participant. All study procedures were approved by the Institutional Review Board of Samsung Medical Center (2005-08-113).

**RESULTS**

The study variables for men, premenopausal women, and postmenopausal women were compared in Supplementary Table 1. The lumbar BMD, CCA-IMT, BIF-IMT, LDL-cholesterol level, HDL-cholesterol level, triglyceride (TG) level, BMI, lipid-lowering medication status, smoking status, regular exercise habits, calcium supplementation status, and estrogen replacement therapy status (for postmenopausal women) were adjusted as fixed effects. Prior to this analysis, CIMT values were log transformed to approximate a normal distribution.

| Table 1. Clinical characteristics and metabolic parameters according to tertiles of composite intima-media thickness |
|---------------------------------------------------------------|
| **Characteristics**                                           | **Men (n = 723)** | **Premenopausal women (n = 690)** | **Postmenopausal women (n = 630)** |
| **Age, yr**                                                   | 52.0 (10.9)       | 54.5 (11.8)                      | 56.5 (11.2)                        |
| **Height, cm**                                                | 167.8 (8.1)       | 162.0 (7.8)                      | 163.8 (7.9)                        |
| **BMI, kg/m$^2$**                                             | 25.9 (3.4)        | 24.6 (3.7)                       | 24.9 (3.8)                         |
| **TSH, IU/L**                                                 | 1.58 (0.94)       | 1.20 (0.86)                      | 1.54 (0.91)                        |
| **Total cholesterol, mM/L**                                  | 4.70 (0.93)       | 4.29 (0.93)                      | 4.57 (0.95)                        |
| **LDL cholesterol, mM/L**                                    | 2.77 (0.62)       | 2.12 (0.60)                      | 2.42 (0.65)                        |
| **HDL cholesterol, mM/L**                                    | 1.22 (0.29)       | 1.15 (0.29)                      | 1.15 (0.29)                        |
| **Triglyceride, mM/L**                                        | 2.71 (1.06)       | 1.98 (1.07)                      | 2.40 (1.12)                        |
| **Lipid lowering medication, %**                             | 1.57 (1.74)       | 1.59 (1.80)                      | 1.50 (1.76)                        |
| **Dietary fat, %**                                            | 0.4 (0.0)         | 0.4 (0.0)                        | 0.4 (0.0)                          |
| **Dietary protein, %**                                        | 0.4 (0.0)         | 0.4 (0.0)                        | 0.4 (0.0)                          |
| **Dietary carbohydrate, %**                                  | 0.4 (0.0)         | 0.4 (0.0)                        | 0.4 (0.0)                          |
| **Physical activity, %**                                      | 0.4 (0.0)         | 0.4 (0.0)                        | 0.4 (0.0)                          |
| **Comorbidities**                                             | 0.4 (0.0)         | 0.4 (0.0)                        | 0.4 (0.0)                          |

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**RESULTS**

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exercise status did not differ between men and postmenopausal women. The prevalence of thyroid disease did not significantly differ between premenopausal women and postmenopausal women. Similarly, the level of thyroid-stimulating hormone and the prevalence of lipid-lowering medication were not significantly different between men and premenopausal women.

The study variable relationships for men, premenopausal women, and postmenopausal women with respect to composite CIMT tertile distribution are shown in Table 1. In all three groups, subjects with a higher composite CIMT tended to be older. With increasing composite CIMT, the lumbar BMD gradually increased in premenopausal women (P for trend = 0.026), whereas no specific trend was observed in postmenopausal women or in men. As the composite CIMT increased, height decreased in all three groups, whereas BMI increased only in premenopausal women. Moreover, as the composite CIMT increased, total cholesterol and LDL-cholesterol levels increased in both men and premenopausal women, while the HDL-cholesterol level decreased in both men and postmenopausal women. The prevalence of hypertension gradually increased as composite CIMT increased in all three groups. The prevalence of diabetes increased as composite CIMT increased; however, this trend was observed only in men. In premenopausal women, calcium supplementation was more prevalent among women with higher composite CIMT.

The relationship between lumbar BMD and CIMT is shown in Table 2. After adjusting for age, positive associations were observed between BMD and composite IMT and CCA-IMT in men and between BMD and composite CIMT, CCA-IMT, and ICA-IMT in premenopausal women. After adjusting for covariates, this significant association persisted for composite CIMT and CCA-IMT. Borderline significant associations were also observed between lumbar BMD and BIF-IMT and between lumbar BMD and ICA-IMT in premenopausal women. However, the association in men between CIMT and lumbar BMD did not persist after this adjustment. In postmenopausal women, no association was observed between CIMT and BMD. We repeated the multivariable adjusted analysis after stratifying male subjects into two groups by the age cut-off level (≥ 50 years, < 50 years) and found no difference in the association between BMD

### Table 2. Association* between CIMT and BMD at lumbar spine

| Variables          | Men (n = 723) | Premenopausal women (n = 690) | Postmenopausal women (n = 266) |
|--------------------|--------------|-------------------------------|--------------------------------|
|                    | Percent difference (95% CI) | P value | Percent difference (95% CI) | P value | Percent difference (95% CI) | P value |
| Age adjusted       |              |                                |                                |          |                                |          |
| Composite          | 12.0 (0.3–25.0) | 0.0396                         | 15.4 (5.3–26.6) | 0.005 | −3.1 (−10.9–5.3) | 0.704 |
| Common carotid     | 13.3 (4.1–26.6) | < 0.001                        | 18.0 (7.9–29.1) | 0.002 | −0.8 (−8.8–7.8) | 0.991 |
| Carotid bifurcation| 12.6 (−29.7–31.2) | 0.194                           | 11.1 (−2.1–26.1) | 0.084 | −3.4 (−14.5–9.1) | 0.720 |
| Internal carotid   | 8.3 (−44.1–24.3) | 0.190                           | 14.2 (−4.1–29.0) | < 0.001 | −6.5 (−16.5–4.7) | 0.396 |
| Multivariable adjusted* |          |                                |                                |          |                                |          |
| Composite          | 9.7 (−3.9–25.2) | 0.170                           | 14.0 (6.1–25.7) | 0.008 | −2.2 (−10.3–6.5) | 0.614 |
| Common carotid     | 8.3 (−5.6–24.1) | 0.255                           | 16.1 (5.7–27.6) | 0.002 | −1.4 (−9.5–7.4) | 0.751 |
| Carotid bifurcation| 10.7 (−7.7–32.8) | 0.273                           | 13.0 (1.3–29.3) | 0.071 | −2.3 (−13.9–10.9) | 0.724 |
| Internal carotid   | 6.6 (−9.5–25.6) | 0.443                           | 11.9 (−1.2–26.7) | 0.006 | −5.5 (−15.9–6.1) | 0.200 |

CIMT = carotid intima-media thickness, BMD = bone mineral density, CI = confidence interval, BMI = body mass index.

*P coefficients (95% CI) for log-transformed carotid intima media thickness per 1 g/cm² increase in BMD were assessed by linear mixed model. Then, percent difference of carotid intima media thickness was calculated by multiplying 100 to the value of (exponentiated β coefficient − 1). In all analytic models, household and twin pair was adjusted as the random effects; †In the multivariable-adjusted model, age, BMI, hypertension, diabetes, thyroid stimulating hormone, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, lipid lowering medication, smoking habit, physical exercise, calcium supplement and estrogen replacement therapy (for postmenopausal women) were additionally adjusted as fixed effects.

### Table 3. Percent difference (95% CI)* of CIMT according to BMI

| Sites of IMT measure | Men | Premenopausal women | Postmenopausal women |
|---------------------|-----|---------------------|----------------------|
|                     | Low BMI (n = 361) | High BMI (n = 362) | interaction |
|                     | Low BMI (n = 536) | High BMI (n = 154) | interaction |
|                     | Low BMI (n = 141) | High BMI (n = 125) | interaction |
| Composite           | −9.6 (−25.6–9.9) | 24.5 (5.2–47.9)† | 0.014 | 14.5 (2.7–27.7)† | 16.1 (4.9–41.6) | 0.976 | −4.2 (−18.2–12.2) | 6.3 (−9.2–24.5) | 0.437 |
| Common carotid      | −5.7 (−23.8–16.6) | 24.1 (4.1–48.0)† | 0.062 | 13.5 (2.9–25.8)† | 30.0 (4.6–61.4) | 0.233 | −1.4 (−5.0–14.2) | 4.4 (10.7–21.9) | 0.794 |
| Carotid bifurcation | −14.7 (−34.6–11.3) | 24.0 (−2.3–57.4)  | 0.007 | 12.5 (−3.0–30.9) | 8.1 (−18.1–42.6) | 0.812 | −8.5 (−28.6–17.4) | 13.5 (−9.4–42.2) | 0.246 |
| Internal carotid    | −13.5 (−31.7–9.4) | 12.0 (−0.9–37.7)  | 0.047 | 13.8 (−0.5–30.2) | 15.5 (12.0–51.4) | 0.948 | −1.5 (−22.7–25.4) | −0.8 (−16.9–16.5) | 0.986 |

CI = confidence interval, CIMT = carotid intima-media thickness, BMI = body mass index.

*P coefficients (95% CI) for log-transformed carotid intima media thickness per 1 g/cm² increase in lumbar BMD were assessed by linear mixed model. Then, percent difference of carotid intima media thickness was calculated by multiplying 100 to the value of (exponentiated β coefficient − 1). In the model, household and twin pair was adjusted as the random effects. Age, height, hypertension, diabetes, thyroid stimulating hormone, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, lipid lowering medication, smoking habit, physical exercise, calcium replacement therapy and estrogen replacement therapy (for postmenopausal women) were additionally adjusted as fixed effects; †BMI was divided as two-group ( < 25 or ≥ 25 kg/m²)
and CIMT depending on the age level in men (data not shown).

The findings from stratified analysis regarding the association between lumbar BMD and CIMT according to the BMI level are shown in Table 3. In premenopausal women, a positive association was observed, while statistically significant positive association with BMD was confirmed only with composite CIMT and CCA-IMT in low BMI women. In premenopausal women, no significant association was observed between BMI and lumbar BMD. Lumbar BMD tended to be positively associated with CIMT in men with high BMI, while an inverse but statistically insignificant relationship was observed in men with low BMI. The interaction between BMI and lumbar BMD on the association with CIMT was statistically significant in men. In postmenopausal women, no association between BMD and CIMT was observed at any site, regardless of BMI level.

DISCUSSION

In this Korean study, we observed a positive association between lumbar BMD and CIMT, although this association was restricted to premenopausal women and obese men, and mainly to composite CIMT and CCA-IMT. The positive associations between lumbar BMD, composite CIMT, and CCA-IMT in premenopausal women are consistent with the findings of a previous study in Mexican American young women (mean age = 26.7 years) in which the BMDs at the hip, radius, and spine were found to be positively associated with CCA-IMT (8). Cecelja et al. (12) also observed positive associations between hip and lumbar BMD and CIMT in British women (mean age 57.7 years, standard deviation 8.9 years). However, these associations were not evaluated according to menopausal status in the British study.

Estrogen may play a role in the positive association between BMD and atherosclerosis observed in premenopausal women, given the biological relationships that have been described between BMD and CIMT. Specifically, both BMD and CIMT have been shown to be regulated by estrogen receptor-alpha gene polymorphisms (23,24); mitogen-activated protein (MAP) kinase, a serine/threonine kinase that mediates tumor necrosis factor-α signaling, and various interleukins that are associated positively with CIMT have been shown to be regulated by estrogen (25,26); single nucleotide polymorphism variants of the estrogen receptor have been reported to be associated with CIMT in Taiwanese women, but not in men (24); and the vitamin D receptor polymorphism was reported to affect BMD by combining the estrogen receptor polymorphism (27). These biological mechanisms may underlie the association between BMD and CIMT and strongly suggest that future studies on BMD and atherosclerosis in women should consider menopausal status.

Estrogen levels are known to decrease after menopause, which results in reduced estrogen-mediated protection against atherosclerosis and osteoporosis in postmenopausal women (7). Postmenopausal women also experience changes in their body composition such as increased fat distribution and decreased lean mass (28) that are associated with both BMD and atherosclerosis (29,30). Moreover, increasing calcium supplementation during the menopausal period may accelerate vascular atherosclerosis (31). Therefore, an inverse association between BMD and atherosclerosis seems plausible in postmenopausal women. Some studies found an inverse association between BMD and CIMT (8,13,32). However, other studies in Morocco, the USA, Finland, China, Japan, and Korea (including the present study) did not find any association between lumbar BMD and CIMT, or any other surrogate marker of atherosclerosis, in postmenopausal women (10,11,14,16,20).

These discrepancies have a number of potential explanations. Variation regarding the site of BMD measurement is one possible reason. In support of this explanation, one study found that femur BMD was inversely associated with CIMT, whereas lumbar BMD was not (10). However, since even the findings regarding the association of lumbar spine BMD with CIMT vary between studies (10,11,32), variation regarding the site of BMD measurement cannot fully explain the discrepancies between these studies. Second, different age distributions between studies may have resulted in these discrepancies. The age distribution of postmenopausal women in our study (mean age = 59.5 years) was somewhat younger than that in another study that found an inverse association (mean age = 69.2 years) (8). However, another study of older women (mean age = 73.6 years) did not find any association, which is consistent with our findings. To clarify this issue, the association needs to be studied according to age or time after menopause. Third, study-to-study variation of covariates such as osteoporosis treatment and hormonal replacement therapy may also explain the different findings. However, we did not observe any significant influence by covariates after adjustment in the present study. Forth, differences in ethnicity/race might be another reason (13,20). Finally, the association between BMD and CIMT might not be shown distinctly due to the effect modification by other factors such as BMI level on the association. In our study, stratified analysis by BMI level in postmenopausal women has revealed that BMD may be associated with CIMT inversely in lower BMI group but positively in higher BMI group. Although the estimates lacked statistical significance, this finding seems compatible with the findings observed in men. In our study the sample size of postmenopausal women may not be enough to do a subgroup analysis to examine the effect modifying role of BMI. We think further study with larger sample size of postmenopausal women would be needed to clarify this issue.

Few studies have been conducted in men regarding the relationship between BMD and CIMT compared with women. Although two studies in Chinese population did not identify significant association (16,33), the direction was consistent with
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our study. However, another study in multiethnic population reported an inverse association (20). In our study, age-adjusted analysis revealed a positive relationship between lumbar BMD and CIMT, but this relationship did not persist after adjusting for covariates. All other studies also considered known confounding variables such as smoking status, BMI, lipid level, hypertension status, and diabetes status. Thus, these discrepancies do not seem to be due to different covariate adjustments.

Obesity is known to be positively associated with BMD, since a high BMI can increase the mechanical load on the bones (29, 34). Moreover, a high BMI increases the risk of atherosclerosis through mechanisms related to chronic inflammation and insulin resistance (35). The known relationships between obesity and both BMD and atherosclerosis prompted us to carefully investigate the effects of BMI via stratified analysis. Although our results need to be confirmed in future studies, interestingly, we found that BMD was positively associated with CIMT in men with high BMI but not in men with low BMI. This finding seems to suggest an effect modification by BMI in men. We assume that obesity related factors such as increased mechanical load, chronic inflammation and insulin resistance may explain the effect modifying role of BMI on the association between CIMT and BMD. However, we were unable to examine the biological mechanism. Further study is needed to investigate and to explain the association between BMD and CIMT in men.

The present study has a number of strengths. First, a large number of subjects were included, which allowed us to consider both sex and menopausal status. Second, a wide range of covariates including thyroid-stimulating hormone status, estrogen replacement therapy status, and calcium supplementation status could be considered. Therefore, we believe that the influence of most confounding factors on our results was minimized.

However, the present study has some limitations. First, we measured lumbar BMD using whole body dual-energy X-ray absorptiometry, which does not provide BMD at each segment of the lumbar spine. Thus, measurement error could have affected our results. Second, we could not take into consideration of the probable influence by aortic calcification or osteophytes of spine on the measurement of lumbar BMD because we could not obtain those information. Third, we were unable to evaluate the extent of association of CIMT with femoral BMD, which was a measurement that is commonly used in the clinical setting along with lumbar BMD, because whole body dual-energy X-ray absorptiometry does not provide femoral BMD information. Fourth, the sample size of postmenopausal women might be relatively limited to disclose the association between CIMT and BMD with enough power.

We found that lumbar BMD has a positive association with CIMT in premenopausal women and men with high BMI. This finding suggests that the association between lumbar BMD and subclinical atherosclerosis may differ according to sex and menopausal status.

DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Participating in the conception and design: Sung J. Analysis and interpretation of data: Shin J, Park JH, Song YM, Lee K, Sung J. Drafting the article or critically revising: Shin J, Park JH, Song YM, Lee K, Sung J. Approving the final version submitted: all authors.

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