

## Original Article

# Relationship between intima-media thickness and bone mineral density in postmenopausal women: a cross-sectional study

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**Abstract:** Background: Osteoporosis and atherosclerosis are two conditions that confer the major cause of mortality and morbidity in postmenopausal women. Several studies have suggested that these two conditions are negatively correlated by a common pathway. The aim of our study was to show a relationship between bone mineral density (BMD) and carotid intima media thickness (CIMT), as two factors that are directly related to osteoporosis and atherosclerosis respectively. Methods: The study group consisted of 136 postmenopausal women that presented at the Radiology Clinic of our hospital for BMD measurements. The CIMT was measured using High Resolution B mode Ultrasonography; BMD was measured at the lumbar spine and femoral neck using Dual-energy X-Ray Absorptiometry. Results: The mean IMT value in osteoporotic women ( $0.7\pm 0.1$  mm) was significantly higher compared to non-osteoporotic women ( $0.6\pm 0.1$  mm,  $P < 0.001$ ). A significant negative correlation was found between CIMT and the T score of lumbar spine ( $r=-0.35$ ;  $P < 0.001$ ) and femoral neck ( $r=-0.23$ ,  $P < 0.001$ ), as well as Z score of the lumbar spine ( $r=-0.27$ ,  $P=0.004$ ). No significant correlation was found between CIMT and Z score of the femoral neck. Conclusion: Our study shows that bone mineral density and carotid intima media thickness are negatively correlated, thus showing a possible relationship between osteoporosis and atherosclerosis. However, more research is necessary to determine the pathway that connects these two conditions.

**Keywords:** Bone mineral density, carotid intima media thickness, postmenopausal women, osteoporosis

## Introduction

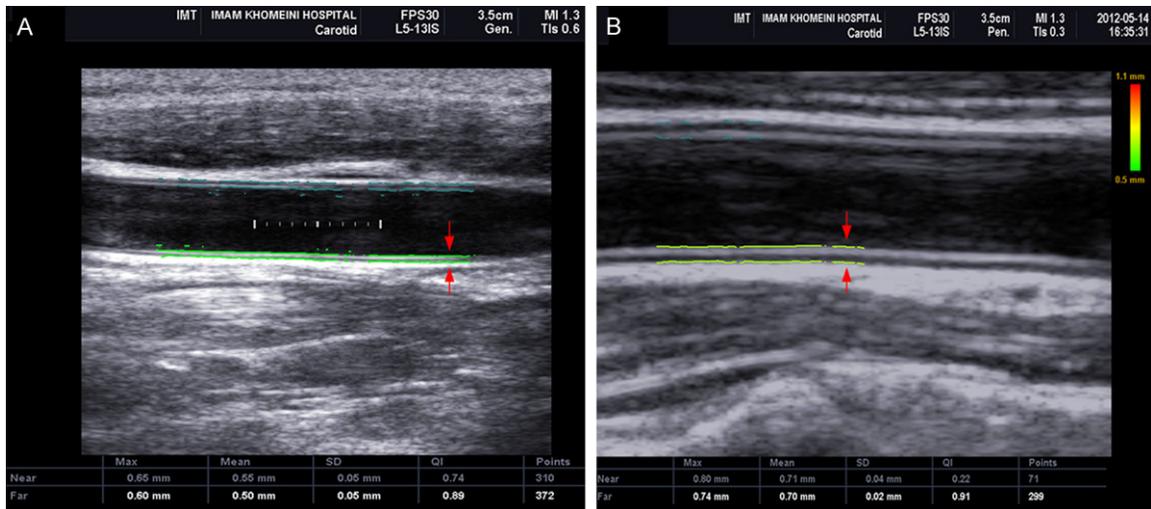
Osteoporosis and atherosclerosis are two conditions that seriously affect the health and lifestyle of a significant part of the female population, especially after menopause. The major causes of morbidity and mortality in postmenopausal women are osteoporosis and cardiovascular diseases [1]. These conditions could lead to bone fractures, myocardial infarction, as well as chances of stroke. The risk for osteoporosis and atherosclerosis is greatly elevated in postmenopausal women due to different factors, including the decline in estrogen production.

A possible relationship between osteoporosis and atherosclerosis has been suggested in the

past years. Currently, it has been shown that low bone mineral density (BMD) in postmenopausal women is associated with an increase in cardiovascular mortality [1]. A large number of studies have suggested that bone metabolism and vasculature may be affected by a common pathway negatively [2-5]. Despite the nature of the association between osteoporosis and atherosclerosis remains unclear, such a finding would have a great impact for the health of postmenopausal women, but also for the rest of the population.

Ultrasonographic measurement of carotid intima-media thickness (CIMT) is a noninvasive method for demonstrating subclinical athero-

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**Figure 1.** Longitudinal ultrasonograms show Auto Intima Media Thickness (AIMT) measurement at the near and far wall of the common carotid artery (as denoted by the red arrows). A. Normal Intima Media Thickness with mean thickness of 0.5 mm in a patient with normal BMD. B. Higher Intima Media Thickness with mean thickness of 0.70 mm in a patient with lower BMD.

**Table 1.** Characteristics of the study group (n=136)

Characteristic	Total subjects Mean $\pm$ SD	Two groups		P value
		Without osteoporosis	With osteoporosis	
Age (years)	50.54 $\pm$ 9.60	58.93 $\pm$ 9.19	56.52 $\pm$ 8.81	0.85
BMI	29.93 $\pm$ 7.46	30.41 $\pm$ 8.05	28.12 $\pm$ 4.24	0.07
Total cholesterol	109.31 $\pm$ 39.34	108.53 $\pm$ 39.05	112.21 $\pm$ 40.90	0.65
TG	130.92 $\pm$ 13.96	133.53 $\pm$ 51.96	121.21 $\pm$ 46.11	0.24
FBS	95.25 $\pm$ 13.96	94.90 $\pm$ 12.96	96.55 $\pm$ 17.41	0.90
SBP	118.97 $\pm$ 15.33	119.06 $\pm$ 15.40	118.62 $\pm$ 15.46	0.98
DBP	79.30 $\pm$ 7.51	79.67 $\pm$ 7.56	77.76 $\pm$ 7.30	0.24
IMT	0.62 $\pm$ 0.11	0.60 $\pm$ 0.19	0.70 $\pm$ 0.09	< 0.01

BMI, body mass index; TG, triglycerides; FBS, Fasting Blood Glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; IMT, intima media thickness.

sclerosis. Increased CIMT has a significant relationship with the presence and severity of coronary atherosclerosis, and has been proven to be a beneficial clinical index in the early recognition of general atherosclerosis [6]. Previous studies showed that women with echogenic plaques in comparison to women without plaques are at a higher risk of nonvertebral fractures [7]. In general, increased CIMT is correlated with future cardiovascular diseases [8, 9], thus it is an important clinical factor to be considered for research purposes.

The aims of the present study were to determine the relationship between BMD measured at different sites in postmenopausal women referred for routine bone density screening,

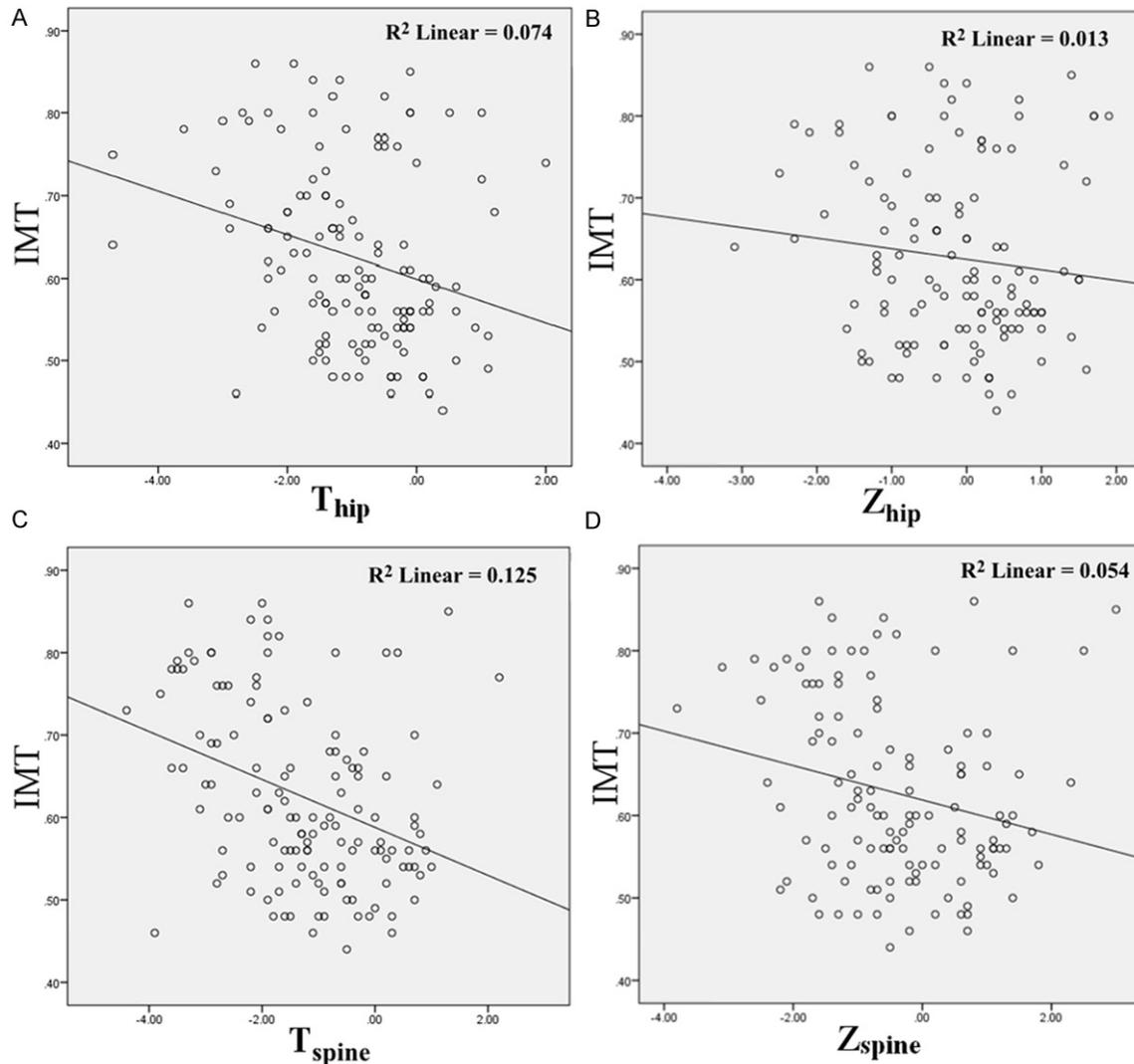
and IMT; as well as to establish whether there is any relationship between BMD and subclinical atherosclerosis.

### Methods

One hundred thirty six postmenopausal women (if menopause had occurred at least two years before) were enrolled in our study, from those patients presenting for BMD measurement at the Radiology clinic of our teaching hospital.

Subjects with a history of alcohol consumption, usage of hormone replacement therapy or medications affecting bone metabolism (corticosteroids, anticonvulsants or oral anticoagulants) were not enrolled in the study. Those sub-

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**Figure 2.** Correlation between IMT and: A. T score of femoral neck ( $T_{hip}$ ) ( $R^2=0.074$ ,  $P < 0.001$ ); B. Z score of femoral neck ( $Z_{hip}$ ) ( $R^2=0.013$ ,  $P=0.11$ ); C. T score of lumbar spine ( $T_{spine}$ ) ( $R^2=0.125$ ,  $P < 0.001$ ); D. Z score of lumbar spine ( $Z_{spine}$ ) ( $R^2=0.0054$ ,  $P=0.004$ ).

jects with conditions that interfere with bone metabolism or vasculature, such as thyroid disorders, malabsorption, chronic renal failure, diabetes mellitus, history of hypertension, hyperlipidemia, smoking and liver disorders were excluded from the study.

The study protocol was approved by the Ethics Committee of our University, and written informed consent was obtained from each subject prior to enrollment. Both carotid IMT and BMD were performed on the same day. Bone density was measured at the lumbar spine (L1- L4) and femoral neck by means of dual-energy X-ray absorptiometry (DXA), and the results were recor-

ded. The BMD measurements in all subjects were obtained by the same densitometer.

The results were expressed as T-scores, Z Scores and the standard deviation (SD) from the peak adult BMD. According to the World Health Organization's criteria for diagnosing osteoporosis, the women were classified into two groups: with osteoporosis, i.e. more than 2.5 SDs below the mean value for young adults with normal BMD; and without osteoporosis (normal or osteopenia: a BMD value that was 1-2.5 SDs below the mean value for young adults). All the measurements were made by one operator.

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High resolution B mode ultrasonography of the right common carotid artery was performed using an ultrasound machine (Medison, Accuvix V 20, Prestige, South Korea) equipped with a 10 MHz linear array transducer. Patients were examined in the supine position with the head tilted backwards. After the carotid arteries were located by transverse scans, the probe was rotated at 90° to obtain and record a longitudinal image of the common carotid arteries.

The maximum CIMT was measured at the far wall of the common carotid artery, 2 cm before the bifurcation, as the distance between the first and second echogenic lines on the anterior and posterior arterial walls. The measurement was performed using Auto IMT measurement software (**Figure 1**). The image was focused on the posterior wall of the common carotid artery, and gain settings were used to optimize image quality. The measurement was performed vertically to the arterial wall for accurate measurement of CIMT.

### Statistical analysis

The results were analyzed with SPSS software. The Pearson chi-square test and Fisher exact test (if the expected values of the cells of a contingency table were below 5) was applied to evaluate the association between IMT and osteoporosis. Independent sample t-test (Mann Whitney in non-normal distribution) was used to study the association between osteoporosis and numerical variables. To obtain the degree of correlation we used the Spearman's rank correlation coefficient measure as well as multiple regression analysis.

### Results

Statistical analysis was performed in one hundred thirty six postmenopausal women. The mean age of subjects was 55.5±5 years old. Thirty three subjects (24.2%) from one hundred thirty six postmenopausal women were osteoporotic. There were no statistically significant difference in BMI, fasting glucose level, triglyceride, total cholesterol, systolic and diastolic blood pressure, and age of subjects with and without osteoporosis. The results from the characteristics of the study groups are summarized in **Table 1**.

The mean ± SD value of IMT in osteoporotic women (0.7±0.1 mm) was significantly higher

than non-osteoporotic women (0.60±0.1 mm,  $P < 0.001$ ). The most significant negative correlation was found between carotid IMT and the T score of lumbar spine ( $r=-0.35$ ;  $P < 0.001$ ). A significant negative correlation was found between carotid IMT and the Z score of the lumbar spine ( $r=-0.23$ ,  $P=0.004$ ) and T score of the femoral neck ( $r=-0.27$ ,  $P < 0.001$ ). A negative correlation was found between carotid IMT and Z score of femoral neck as well, but this correlation was not statistically significant ( $r=-0.11$ ,  $P=0.11$ ). These statistical results are graphically represented in **Figure 2**.

### Discussion

The results of our study showed a negative correlation between IMT values and bone mineral density in different regions of the spine. The results were based on the T and Z scores of the lumbar spine and femoral neck. The only parameter that did not show significant differences was the Z score of the femoral neck. Osteoporotic patients (24.2%), as classified according to World's Health Organization criteria for diagnosing osteoporosis, showed higher IMT values than non-osteoporotic patients. Patients under hormone replacement therapy, corticosteroids and anticoagulants, as well as patients with thyroid disorders and diabetes were excluded from the study. All patients showed no differences in BMI, blood pressure, fat and glucose levels in the body. Considering the measures taken, the possibility that there is bias introduced in the study is very low.

The focus of the study was to show a possible relation between bone mineral density and atherosclerosis. The relationship between coronary heart diseases and osteoporosis has been long studied, and a negative correlation has been observed from several studies. This relationship has been proved mainly by studying the correlation between bone density and systemic calcified atherosclerosis [10], aortic calcification [11, 12], atherosclerosis of peripheral vessels [13] or arterial stiffness [14]. The goal of our study was to show a correlation between atherosclerosis and bone mineral density, by proving a possible relation between carotid intima-media thickness (CIMT) and bone mineral density.

Carotid intima-media thickness has been shown to be related to coronary heart diseases

and future cardiovascular events [9]. Studies have shown associations of CIMT with coronary heart disease risk factors [15]. Higher IMT has been seen in patients with incidence of heart failure, compared to those with no history of heart failure [16]. A more general study showed that patients with a history of coronary heart disease, as compared to those without, had a higher CIMT mean value [17]. Furthermore, CIMT measurements can be beneficial in lowering the risk of cardiovascular diseases, in particular for women [18]. The results from these studies have clearly shown the correlation between IMT and coronary heart diseases, including atherosclerosis. Based on these results, it can be reasoned that by showing a correlation between BMD and IMT, an association can be made between BMD and atherosclerosis.

With the exception of a few studies, there has not been previous research on the association between CIMT and BMD. The results from our study were confirmed from another study conducted in postmenopausal women, which showed a similar association between CIMT and BMD [19]. However, this study measured femoral neck and total body BMD, compared to our study, which studied femoral neck and lumbar spine. Other studies have observed drugs and genetic markers that show a possible relationship between BMD and atherosclerosis, however, without coming to a conclusion about their association [20, 21]. It seems important to assess the relationship between these two pathways in particular for postmenopausal women. Studies have shown that in women who performed a surgical menopause, the CIMT scores are higher and the BMD scores are lower as compared to women who went through natural menopause [22]. Despite the former study did not suggest a correlation between BMD and CIMT, its results are significant and should be considered for the health of postmenopausal women.

### Conclusion

The results of our study showed that IMT is negatively correlated to BMD levels. By showing the correlation between carotid intima-media thickness and bone mineral density, we suggest an association in the pathophysiology of bone and coronary disorders. Further research is necessary in establishing a more conclusive relationship between these two pathways. Considering the association of CIMT to future

cardiovascular disorders and the long term benefits CIMT follow-ups could have, it might be beneficial to assess carotid arteries in osteoporotic women.

### Disclosure of conflict of interest

None.

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