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RELATIONSHIP BETWEEN BONE MINERAL DENSITY AND CAROTID ARTERY INTIMAL MEDIAL THICKNESS IN POSTMENOPAUSAL WOMEN

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ABSTRACT

Background and objectives: Although most of the studies have indicated a negative correlation between bone mass density (BMD) and atherosclerosis in various sites of arterial system, some studies demonstrated no relation between these two conditions. This study was conducted to evaluate the possible relationship between bone mineral density (in femoral neck, hip and lumbar spine) and common carotid artery Intimal medial thickness in postmenopausal women.

Methods and Patients: Iranian Postmenopausal women that at least 1 year had passed since the last menstrual period were included. The BMD was evaluated at the lumbar spine (in the L2–L4) femoral neck and hip by dual-energy X-ray absorptiometry (DXA). The carotid arteries IMT was assessed bilaterally using an ultrasonography in the 4 points at 2 cm proximal to the bulb, the 4 points at 2 cm distal to the bulb and 2 points at the carotid bulb and averaged to obtain the mean IMT.

Results: Fifty eight subjects with the mean age of 58.76±5.51 years (range 50–74 years) were included in final analysis. Pearson correlation showed a significant negative correlation between MIT and BMD in femoral neck($r=0.717$, $P< 0.001$), hip($r=0.777$, $P< 0.001$), and spine($r=0.690$, $P< 0.001$). Similarly, spearman's correlation demonstrated a correlation between IMT and T scores in femoral neck($r=-0.340$, $P= 0.009$), hip($r=-0.533$, $P< 0.001$), and

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spine(r=-0.627, P< 0.001). IMT of normal group was significantly higher than osteoporosis and osteopenia groups regarding to the T score of hip and spine. According to the t score of femoral neck IMT in osteoporosis group was significantly lower than osteopenia and normal BMD groups.

Conclusion: The carotid atherosclerosis is negatively associated to BMD of spine, femoral neck and hip in postmenopausal women.

INTRODUCTION

Osteoporosis and atherosclerosis are two of the most prevalent diseases that are associated with significant morbidity and mortality in elderly people particularly in postmenopausal women. These two conditions are originally considered as independent diseases but have many points in common such as common risk factors, association to estrogen deficiency and involvement of calcification process in both conditions. In recent years, many studies have evaluated the association between osteoporosis and atherosclerosis at different sites of the vascular system and most of them have indicated a negative correlation between BMD and cardiovascular diseases (1;2).On the other hand decreased BMD is associated with non-traumatic mortality (3), including the mortality of cardiovascular diseases (4).

It has been reported that increased carotid intima-media thickness (IMT) [that is measured using B-mode ultrasonography] is associated with increased prevalence of cardiovascular diseases (5) stroke, and atherosclerosis elsewhere in the arterial system(6;7). A few studies have showed that BMD of the lumbar spine is negatively correlated with carotid IMT in postmenopausal women (8) and carotid atherosclerosis (and therefore atherosclerosis in other arteries) could be reversely associated to bone mass (9). But studies in this area are inconsistent. In Montalcini et al's study the prevalence of carotid atherosclerosis was not increased in women with low BMD (10) and they claimed that the result is consistent with the 2 previous clinical trials(10-12).

Therefore, the aim of the present study was to evaluate the possible relationship between bone mineral density (in femoral neck, hip and lumbar spine) and common carotid artery Intimal medial thickness in postmenopausal women.

METHODS AND PATIENTS

This study was conducted between November 2012 and November 2013 in Bone Densitometry Center of Isfahan Province and Radiology Department of Al-Zahra Hospital, Isfahan, Iran. The study protocol was approved by ethical committee of Isfahan University of Medical Sciences (project number: 392210) and written informed consent was obtained from participants.

Iranian Postmenopausal women that at least 1 year had passed since the last menstrual period were included Exclusion criteria included ; alcohol us(according to the history), problems interfered with the normal activities, hyperparathyroidism, diabetes mellitus, chronic kidney or liver dysfunction and history of taking drugs affecting the atherosclerosis or bone metabolism. The sample size was calculated using the comparison of two means formula with two-sided log-rank test, $\alpha = 0.05$, and 90% power ($\beta = 0.10$) for the absolute difference in IMT change between the groups exceeded 0.6.

The BMD for all participants was evaluated at the lumbar spine (in the L2–L4), femoral neck and hip by dual-energy X-ray absorptiometry (DXA) (QDR-1000W; Hologic, Waltham, USA), that reported as g/ cm2. The mean BMD of L2–L4 was considered as the patient's lumbar spine BMD. The same operator performed all measurements and all scans were analyzed by the same technician not otherwise involve with the study.

Thereafter, The participants were included in one of three following groups according to the BMD at the lumbar spine femoral neck and hip: normal density group (BMD< 1 SD below the mean value for young adults), the osteopenia group (BMD between 1 to 2.5 SD below the mean value for young adults), and the osteoporosis group (BMD > 2.5 SD below the mean value for young adults) based on World Health Organization (WHO) classification (13).

The carotid arteries IMT was assessed bilaterally using an ultrasonograph (Siemens, Sonoline G40, and Germany) equipped with a 7.5-MHz linear array type-B–mode transducer (GE-Yokogawa Logiq S6). Each participant has rested for a while in supine position, then her neck was slightly hyper extended and head was turned away from the monographer. The end-diastolic IMT of the far wall of the common carotid artery was measured in the 4 points at 2 cm proximal to the carotid bifurcation, internal carotid artery in the 4 points at 2 cm distal to the carotid bifurcation and 2 points at the carotid bulb and the average was calculated to obtain the patients mean IMT. Ultrasonography was performed by the same attending radiologist who was blinded to the

patients' clinical characteristics and BM densitometry results.

All statistical analyses were performed using the Statistical Package of Social Sciences (SPSS) version 19.0 (SPSS, Chicago, IL, USA). One-way analysis of variance (ANOVA) was used to compare the clinical characteristics among the three groups. The relationships between carotid IMT and the BMD in femoral neck, hip and spine and other variables were examined by using Pearson's correlation coefficient analyses. Spearman Correlation Coefficient were performed to assess the relationships between the values of carotid IMT and the T scores. P value less than 0.05 was considered statistically significant.

RESULT AND

Fifty eight subjects with the mean age of 58.76±5.51 years (range 50–74 years) were included in final analysis.

In all three regions that BMD was measured a significant deference was noted between normal BMD, osteopenia and osteoporosis group. In hip and spine the mean age of normal group was significantly lower than osteoporosis and osteopenia groups and in the femoral neck mean age of osteoporosis group was significantly higher. No other significant differences were noted. There was no significant difference between normal BMD, osteopenia and osteoporosis group in all three regions regarding to the BMI.

One way ANOVA test showed the significant difference in mean IMT between normal BMD, osteopenia and osteoporosis group in femoral neck, spine and hip. The post HOC analysis showed that the IMT of normal group was significantly higher than osteoporosis and osteopenia groups regarding to the T score measured for hip and spine. According to the t score report for femoral neck IMT in osteoporosis group was significantly lower than osteopenia and normal BMD groups. Other differences were not significant. To eliminate the confounding effect of age on, Analysis of Covariance (ANCOVA) was used to compare the mean IMT between normal BMD, osteopenia and osteoporosis group in each of three sites that the differences of IMT remain significant.

Pearson correlation showed a significant negative correlation between MIT and BMD in all three regions. Similarly, spearman's correlation demonstrated a correlation between IMT and T scores.

DISCUSSION

In this study we evaluated the relationship between MIT of carotid artery as an indicator of atherosclerosis and BMD in postmenopausal women. Our results showed a significant negative correlation between IMT and BMD.

Several studies were run on the relationship between BMD and atherosclerosis at different sites of arterial system. Hak et al. showed the associations between progressions of atherosclerotic calcification of aorta with increased bone lose in metacarpal bone during pregnancy in a population-based longitudinal study (14).

The association between BMD and carotid atherosclerosis has been shown in number of previous studies. Sumino et al. measured the IMT of common carotid artery (by ultrasonography) and BMD (by DEXA) of spine in 175 postmenopausal women. IMT in normal BMD group (0.71±0.17 mm) was significantly lower than in the osteoporosis (0.82±0.18 mm) and osteopenia (0.75±0.15) groups, and in osteopenia group was higher than osteoporosis group. The univariate linear regression analysis showed a significant negative correlation between carotid IMT and BMD(9). Uyama et all. used the plaque score to determine the carotid atherosclerosis and reported a significant relationship between plaque score and low BMD of lumbar spine in postmenopausal women (8). Jorgensen et al. showed that among the postmenopausal women and old aged men, the probability of visualizing echogenic calcified atherosclerotic carotid plaques on ultrasonography in subjects with a low forearm BMD was higher than in those with high BMD of the same bone (15) . Our results are in line with these studies; also we showed the negative relationship between carotid IMT and BMD of three different points in skeletal system and it is one of strengths of our study.

Why decreased BMD is associated with atherosclerosis is not clearly known. But the potential explanations are as follows: First, estrogen deficiency is a risk factor for both atherosclerosis and osteoporosis (16;17). Presence of estrogen receptors on the osteoblasts (18), osteoclasts (19), endothelial and vascular smooth muscle cells (20) demonstrated that the estrogen could have direct effect on these cells. Hormone replacement therapy (HRT) increases the BMD (21) and reduces the atherosclerosis (22) in postmenopausal women. Mucowski et al Reported that rate of IM thickening and bone mass loss in postmenopausal women with intact ovary was slower than those with prior oophorectomy (23). In Sumino et al 's study the serum estradiol level(although not statistically significant) tended to negatively correlated

with carotid IMT(9). Second, Oxidized lipids and hyperlipidemia promote atherogenesis (24) and inhibit bone mineralization and differentiation of bone cells (25). But, Sumino et al 's study showed that serum LDL cholesterol concentrations were positively correlated with carotid IMT, and were not associated to BMD of the lumbar spine (9). Third, common genes may influence the BMD and atherosclerosis (26). Vitamin D receptors are demonstrated on endothelial and vascular smooth muscle cells and is involve in both bone metabolism and development of atherosclerotic (27). The role of vitamin K epoxide reductase gene (VKORC1) 1173C>T polymorphism in osteoporosis and development of calcified plaques in the carotid artery has been reported too. Vitamin K is involved in bone metabolism and vascular health (28).

Although the data seems convincing about the relation between BM and atherosclerosis (including in carotid), but Montalcini et al didn't reported the same relationship. No significant differences were noted between patients with low and normal BMD regarding to the prevalence of carotid atherosclerosis (47% and 39% respectively). No clear explanation was presented to this discrepancy. Among women with low BMD the prevalence of carotid atheroscleros in subjects with osteocalcine levelshigher than median, was significantly more than subjects with osteocalcine levels below the median (10).

One of the limitations in this study was that we could not eliminate or control all the factors affect the BMD or IMT as confounding factors.

CONCLUSION

We conclude that the carotid atherosclerosis is negatively associated to BMD of spine, femoral neck and hip in postmenopausal women.

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