Original Article

Bone Density in Postmenopausal Women with or without Breast Arterial Calcification

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Abstract

Background: Identification of osteoporosis in women in order to prevent its related morbidity and mortality is considered a priority. Routine mammography is performed on all menopausal women as a screening tool. Determination of the relation between breast arterial calcification (BAC) on mammography and the bone density of this high-risk population could help us to determine those with osteoporosis. The aim of this study was to investigate the mentioned probable relation between BAC and osteoporosis. **Materials and Methods:** In this cross-sectional study, menopausal women referred for annual screening mammography were enrolled. According to the results of mammography, they were classified into two groups: menopausal women with and without calcification of breast arteries. The selected women were referred for bone mineral density (BMD) evaluation by dual-energy x-ray absorptiometry (DXA). The results of BMD were compared between the two studied groups. **Results:** In this study, BMD was measured in 43 and 45 menopausal women with and without BAC, respectively. After age adjustment the difference between BMD measurements were not statistically significantly different ($P > 0.05$). There was a significant negative correlation between age and lumbar ($P = 0.002$, $r = -0.42$) and hip bone ($P = 0.000$, $r = -0.67$) density in menopausal women with BAC. **Conclusion:** The results of the current study indicated that there was no significant relationship between BAC and BMD in our studied population, but it seems that increasing age has an important role in both developing BAC and reducing BMD. For obtaining more conclusive results, further studies with larger sample sizes and considering the severity of BAC is recommended.

Keywords: *Bone densitometry, bone density, breast arterial calcification, mammography, post menopause*

Introduction

Menopause is one of the most striking events occurring during a women's life that holds intrinsic clinical and public health interest due to its related complications. It is considered an important marker of aging and health in women.[1,2]

Increasing life expectancy results in an increase in postmenopausal women population worldwide. It is estimated that the mentioned population is expected to increase to 1200 million by 2030. Of this population 76% will be from developing countries.[3]

Postmenopausal women are at risk from many chronic disorders including cardiovascular disease (CVD), osteoporosis, and consequently higher rates of morbidity and mortality.[4]

Osteoporosis is a common, asymptomatic postmenopausal disease that has a substantial impact on the quality of life of older women and is defined as bone mineral density (BMD) 2.5 standard deviations (SD) below the young healthy adult mean (T-score $\leq$ -2.5). According to a World Health Organization (WHO) report, 30% of all postmenopausal women suffered from osteoporosis.[5]

Osteoporosis-related fractures are one of the causes of disability among the elderly population.[6]

In addition, the association between decreased BMD or osteoporosis with CVD and subclinical vascular disease has been documented in many studies.[7-9]

The calcium transport hypothesis could explain the pathogenesis of the mentioned association. According to this hypothesis, calcium loss from bone leads to calcium deposition into the arterial wall, that is, arterial wall calcification and, consequently, arterial stiffness that results in CVD.[10]

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The deposition of calcium within the media of breast tissue arteries is defined as breast arterial calcification (BAC).[11]

Several studies have indicated that women with BAC are at increased risk of CVD.[12,13] The relationship between BAC and osteoporosis has also been reported in some research.[14,15]

The process of osteoporosis in women develops from the perimenopause period and is established during the postmenopausal period. It is asymptomatic in most cases and not frequently detected until a fracture occurs. So the identification of women with osteoporosis in order to prevent its related morbidity and mortality should be considered a priority.

With regard to the fact that routine mammography is performed in all menopausal women as a screening tool, the determination of the relationship between BAC and bone density of this high risk population could also help us to determine those with osteoporosis. The early diagnosis and treatment of this group of patients will consequently reduce its related complications and improve public health. The importance of the issue would become more prominent by understanding the fact that the elderly population of our community is growing and that it is estimated that in the coming 20 years the elderly population will be increasing three times.[16] The aim of this study was to investigate the mentioned probable relationship between BAC and osteoporosis in postmenopausal women.

Materials and Methods

In this cross-sectional study, menopausal women referred to the Radiology department of Seyed Al-Shohada hospital affiliated to the Isfahan University of Medical Sciences, for annual screening mammographies were enrolled.

The inclusion criteria were: Age >45 years, body mass index (BMI) 19.8-30, normal process of menopause, not using hormone replacement therapy during the past 6 months, nonhypertensive, and having a history of normal dietary habits.

The protocol of study was approved by the Regional Bioethics Committee of Isfahan University of Medical Sciences. Written informed consent was obtained from all selected patients.

Those with any history of liver, cardiac, renal, pulmonary, thyroid (hypothyroid or hyperthyroid or levothyroxine use), parathyroid disease, diabetes, chronic inflammatory bowel disease, malabsorption disorders, inflammatory disorders (infectious or noninfectious), sedentary lifestyle for more than 3 months, any chronic disorders that affect the quality of life, premature ovarian failure, radiotherapy, diagnosed osteoporosis before menopause, suspicious malignant breast lesions in mammography, smoking, alcohol or drug use, history of glucocorticoid use, history of bilateral salpingo-oophorectomy before menopause, and otherwise history of use of any drugs known to have effects on BMD such as thyroid drugs, glucocorticoids, metotrexate, heparin, warfarin, antiepileptic agents, alendronate, calcitonin, raloxifene, or vitamin D, and those with inappropriate cooperation were excluded.

The mammography results of selected patients were reviewed by two radiologists (Adibi and Rabani).They classified them into two groups of menopausal women with and without calcification of breast arteries. The selected women were referred for BMD evaluation by dual-energy x-ray absorptiometry (DXA). The results of BMD were compared between the two studied groups.

Mammography

Mammograms were conducted according to breast cancer screening protocols, that is, by using a standard two-view protocol of craniocaudal and mediolateral oblique for each breast.[17] BAC was judged to be present if detected with the unaided eye under standard mammogram viewing conditions. Calcifications were determined using the standardized methods described previously.[18] If calcifications were present on the right, left, or both projections of the breast, the mammogram was categorized as BAC-positive.

Bone mineral density measurements

Bone density was measured according to osteoporosis screening guidelines and assessed in the lumbar spine (L1-L4) and total hip by the DXA method, using a Lunar DPX Alpha machine (DPX-MD, Lunar Radiation, Madison, WI, USA). The BMD results were categorized into three groups as normal (*T*-score > -1.0 SD), osteopenia or low bone mass (-1.0 > *T*-score > -2.50 SD), and osteoporosis (*T*-score < -2.5 SD), according to the WHO's criteria for diagnosing osteoporosis.[19]

Statistical analysis

The obtained data were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL, USA) software and independent *t*-test, a chi square test, and a logistic regression test.

Results

In this study, bone density was measured in 43 and 45 menopausal women with and without BAC, respectively.

Mean +/- SD of age and bone density findings are presented in Table 1.

The frequency of risk of fracture according to hip and lumbar bone density in menopausal women with and without BAC is presented in Figure 1.

The frequency of osteopenia and osteoporosis according to lumbar and hip *T*-scores in menopausal women with and without BAC are presented in Figure 2.

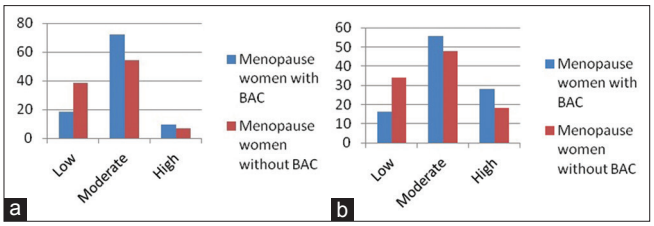

Figure 1: Frequency of risk of fracture according to hip and lumbar bone density in menopausal women with and without BAC (*P* = 0.057 for a and *P* = 0.065 for b)

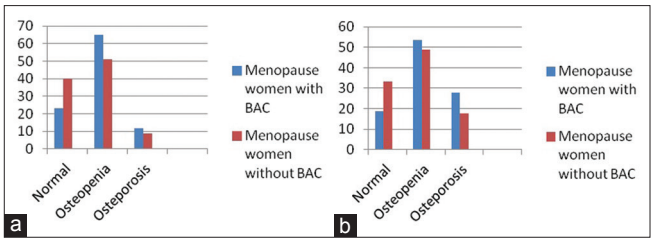

Figure 2: Frequency of osteopenia and osteoporosis according to lumbar and hip *T*-scores in menopausal women with and without BAC (*P* = 0.12 for a and *P* = 0.09 for b)

Table 1: Mean +/- SD of age and bone density findings in menopausal women with and without BAC

	Menopausal women with BAC *n*=43	Menopausal women without BAC *n*=45	*P*
Age (year)	61.13 10.59	52.48±8.13	0.000
Lumbar BMD	78.27 12.14	83.59 15.35	0.076
Hip BMD	76.79 12.18	80.08 13.92	0.030
Lumbar *T*-score	-1.47±0.82	-1.11±1.04	0.076
Hip *T*-score	-1.95±1.02	-1.40±1.24	0.026

After age adjustment, *P* values for comparing hip bone density and hip bone *T*-scores in the two studied groups were 0.75 and 0.48, respectively.

After age adjustment, *P* values for the frequency of lumbar and hip fracture in the two studied groups were 0.23 and 0.90, respectively.

After age adjustment, *P* values for the frequency of osteopenia and osteoporosis in two studied groups were 0.61 and 0.72, respectively.

There was a significant negative correlation between age and lumbar ($P = 0.002$, $r = -0.42$) and hip bone ($P = 0.000$, $r = -0.67$) density in menopausal women with BAC.

There was no significant correlation between age and lumbar and hip bone density in menopausal women without BAC.

Discussion

In this study we investigated the relationship between BAC and BMD among postmenopausal women in Isfahan. The findings indicated that BMD was not different among postmenopausal women with and without BAC.

There were several studies that sought to determine the association between both osteoporosis and reduced BMD and BAC with CVD.[7-9,12-15] The evidence from those studies could suggest the shared pathophysiology of the mentioned factors for CVD as well their association with each other. So this study was designed to evaluate the probable association. However, by determining the association, postmenopausal women at risk for osteoporosis would be diagnosed in the earlier phase of the disease during routine screening mammography.[15]

Evidence suggested that there is an association between loss of bone mass and increased arterial stiffness in postmenopausal women. Sumino *et al*. in Japan have in a retrospective study evaluated the correlation between carotid intima-media thickness (IMT) and lumbar spine BMD in 175 postmenopausal women. They showed that carotid atherosclerosis might be associated with lumbar spine bone mass in postmenopausal women.[20]

Fodor *et al*. in Romania investigated the relationship between IMT of the common carotid artery, the presence of calcified atherosclerotic plaques, and BMD in 100 postmenopausal women using DXA. Their study indicated that carotid IMT was higher in postmenopausal women with osteoporosis than in those with normal BMD or osteopenia. The association between BMD and IMT was independent of the site of BMD and IMT measurement.[21]

Though several studies reported the association between arterial calcification and BMD even after adjustment for age, and also the potential pathogenesis of the linkage of mentioned association has been suggested, the exact underlying mechanisms have not been clearly determined.[22-25]

There were a few studies that similarly evaluated the relationship between BAC and BMD. Though most of them reported a relationship between the mentioned factors but the results were not conclusive enough.

Reddy *et al*. in the US retrospectively investigated the association between reduced BMD and BAC among 228 menopausal women. According to their results, reduced BMD was more prevalent among women with BAC and osteoporosis was strongly associated with the presence of BAC. They concluded that BAC and reduced BMD are strongly and independently correlated and that women with BAC are at increased risk of osteoporosis as well as other vascular diseases.[15]

Wada *et al*. in Japan have shown that postmenopausal women with vertebral fractures had a significantly higher age, lower ultradistal BMD, and a higher number of BAC compared to those without vertebral fractures.[14]

The results of the current study indicated that hip and lumbar BMDs and their *T*-scores were not significantly

different in postmenopausal women with and without BAC after adjusting the data according to their age.

The findings could be explained by differences in population, methods, and anatomic sites that were selected for osteoporosis evaluation. The results of some studies like ours indicated that the association between BMD and arterial calcification was lost after age adjustment,[26,27] whereas in others the association was independent of age.[23,28]

Another explanation was ethnic differences. However, as reported by previous studies including Coronary Artery Risk Development in Young Adults (CARDIA)[29] and the Multi-Ethnic Study of Atherosclerosis (MESA),[30] the extent of vascular calcification is different in populations with different ethnic backgrounds. The prevalence of BAC was evaluated among women aged 32-92 years with different races and ethnicities in a large cohort study. The results of that study showed that the prevalence of BAC was the highest in Hispanic and the lowest in Asian women.[31]

There was a significant negative correlation between age and hip and lumbar BMD in women with BAC. It seems that age plays a crucial role in the development of BAC and in reduced BMD.

Recently, Loberant *et al*. have determined the prevalence and degree of BAC on mammography of 1786 women aged >40 years. They showed that both the prevalence and the higher degree of BAC increase with age and only 1% of women aged <60 years had graded 2-3 BAC.[32]

It is recommended to plan future studies of postmenopausal women aged >60-65 years. In the presence of a probable association between BAC and BMD, the presence of osteoporosis would be predicted by routine mammography without using DXA, which is considered a high-cost procedure.

The limitations of this study were its cross-sectional design and the small sample size of the studied population.

In sum, the results of the current study indicate that there was no significant relationship between BAC and BMD in our studied population, but it seems that increasing age plays an important role in both developing BAC and reducing BMD. For obtaining more conclusive results, further studies with larger sample sizes and considering the severity of BAC is recommended.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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