Original Article

Relationship between breast arterial calcification on mammography with CT Calcium scoring and coronary CT angiography results

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Abstract

Background: Mammography as a non invasive method has been suggested to be helpful in predicting coronary artery disease. This study aimed to investigate whether presence and severity of breast artery calcification (BAC) on mammograms is associated with computed tomography coronary angiography (CTCA) finding such as coronary artery calcium (CAC) score and the severity of coronary artery stenosis.

Materials and Methods: This cross-sectional study was performed on 150 women aged >40 years who were referred for CTCA. Women who had undergone screening mammography during the first year after CTCA entered the study. CAC score was determined and the severity of coronary artery stenosis was classified into normal, non-significant stenosis, or significant stenosis. Based on the severity of BAC, patients were also grouped into normal, mild, moderate, or severe groups. Then, the correlation between BAC severity and CAC score was determined. Patients with different BAC severity were also compared regarding the relative frequency of different grades of coronary artery stenosis.

Results: Mean age of subjects with BAC (*n*: 35) was significantly higher than patients without BAC (*n*: 115) (68.03 ± 6.16 versus 54.36 ± 7.63 years, $P < 0.0001$). Although the relative frequency of different grades of coronary artery stenosis was significantly higher in women with BAC ($P < 0.0001$), after controlling for age, there was no significant difference between patients with different severity of BAC in the mean of CAC score (*P*: 0.09). In addition, the correlation between BAC severity and CAC score was not statistically significant (*R*: 0.09, *P*: 0.26).

Conclusion: We concluded that presence and severity of BAC have no significant correlation with CAC score on CTCA.

Key Words: Breast arterial calcification, calcium scoring, coronary CT Angiography, mammography

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INTRODUCTION

The leading cause of mortality in developed countries is atherosclerotic cardiovascular disease that results from systemic arterial diseases.[1-3] Calcium deposition in the vascular wall is a common feature of degenerative atherosclerotic disease.[1-4] Modern imaging techniques have been used to detect arterial

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calcification as a marker of the presence of subclinical atherosclerosis in the arteries to predict future cardiovascular events.[2-7]

For this reason, several studies have used multi-slice computed tomography (MSCT) coronary CT angiography (CTCA) as a non-invasive imaging method to estimate coronary artery calcification.[1] It was reported moderate increased risk of cardiac events for asymptomatic patients with high calcification of coronary arteries.[8] In order to evaluate the severity of atherosclerosis by CT-scan, coronary artery calcium (CAC) score has been used as an indicator of subclinical atherosclerosis.[9]

Since atherosclerosis affects not only the coronary arteries, but also blood vessels throughout the entire body,[10] calcium deposits could be found in other parts of the vascular tree as a sign of subclinical atherosclerosis.[11] Therefore, vascular calcification other than in the coronary arteries has also been investigated to determine whether they can predict the risk of cardiac events or not.[1]

Breast arterial calcification (BAC) is a common mammographic finding that is frequently observed among elderly women;[12,13] however, it is a medial arterial calcification, which is different from intimal calcification.[14]

Several investigations have suggested BAC as a marker of arterial disease that could be associated with increased risk of cardiac events or cardiovascular risk factors such as diabetes or hypertension.[13.15-19] On the other hand, other studies have reported no significant association between BAC and cardiovascular diseases.[20-22]

Based on these inconsistent reports, the clinical significance of BAC and its association with cardiovascular disease is still controversial.[11]

In the light of above considerations, this study was aimed to determine the relation between CTCA findings and BAC detected on mammography.

MATERIALS AND METHODS

After approval of the study by the ethic committee of Isfahan University of Medical Sciences, this cross sectional study was performed on women of more than 40 years of age who were referred for CTCA to the MSCT scan unit of Al-Zahra hospital, Isfahan, Iran, between February 2011 and March 2012.

All women were referred for screening mammography if they had not undergone the screening mammography within one year prior to CTCA.[23]

Subjects were excluded if they had a previous history of cardiac surgery, coronary artery stenting, breast surgery or breast trauma.

A convenience sample of 168 patients was initially included in the study. Eighteen women were excluded due to exclusion criteria, and a total of 150 women who met all study criteria were entered in this study.

All CTCA studies were performed using a single multi-detector 64-slice CT scanner (Sensation 64, Siemens Medical Solutions, Forchheim, Germany). CAC score and the severity of coronary artery stenosis were determined for each participant.

Quantification of CAC was performed using software for calcium scoring (Heartbeat-CS, EBW, Philips Medical Systems, Best, Netherlands). All regions with a density over 130 Hounsfield units were considered as potential calcifications.[11]

According to the severity of coronary artery stenosis, patients were classified into the following three groups: normal (no stenosis), non-significant stenosis (less than 50% of luminal narrowing), or significant stenosis (equal or more than 50% of luminal narrowing).[24]

All mammograms were analyzed by a single experienced breast-imaging radiologist who was blinded to the results of CTCA.

Patients were considered to have BAC if they had the classical 'railroad track' pattern-linear and parallel calcified lines with amorphous calcification between them-on their mammograms of one or two breasts (either mediolateral oblique view (MLO) or craniocaudal view (CC)).

According to the severity of calcification, patients were also grouped into four categories of normal (no calcification of the breast artery), mild BAC (slightly calcified breast artery), moderate BAC (distinctly calcified breast artery), or severe BAC (solid calcification of the breast artery).[23]

Finally, the relative frequency of different grades of coronary artery stenosis in women with and without BAC was determined; the mean of CAC score was compared between women with different severity of BAC; and the correlation between BAC severity and CAC sore was checked.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 20.0 (SPSS Inc., Chicago, IL, USA). One-way ANCOVA, Post-Hoc, Spearman correlation test and Chi-square were

used when appropriate. *P*-values less than 0.05 were considered statistically significant.

RESULTS

Total of 168 women were participated, eighteen women were excluded because of exclusion criteria, and 150 women who met all study critera were entered. The mean time between mammography and CTCA was 9.83 ± 2.43 months. Thirty-five women (23%) had positive results for BAC, while 115 women (77%) had no evidence of BAC on mammograms. Mean age of subjects who had BAC on mammogram was significantly higher than patients without BAC (68.03 ± 6.16 years versus 54.36 ± 7.63 years, $P < 0.0001$).

Although the relative frequency of different grades of coronary artery stenosis was significantly different between women with and without BAC, after controlling for age as a covariate, there was no significant difference between patients with different severity of BAC in the mean of CAC score [Table 1]. Similar result was found regarding the correlation between BAC severity and CAC score. Despite the strong positive correlation between BAC severity and CAC score (*r*: 0.20, *P*: 0.01), the correlation was not statistically significant after controlling for age as a covariate (*r*: 0.09, *P*: 0.26).

DISCUSSION

Screening mammography has been widely used for early detection of breast cancer. BAC is a common benign finding on mammograms particularly in those who are elderly.[17,25] It has been suggested that this incidental finding could be an indicator of generalized vascular disease.[26,27] For this reason, a large number of research studies have been conducted to investigate the association of BAC with cardiovascular disease, its markers and potential risk factors.[28,29]

This cross-sectional study was performed to evaluate the association between BAC and CTCA findings. Our results do not support a significant association between BAC and CAC score.

Although we found significantly higher prevalence of BAC in patients with more severe coronary artery stenosis, this finding could be attributed to the effects of age as a covariate. It means that both BAC and the presence of more significant coronary artery stenosis could be independently correlated with age; and therefore, older women are more susceptible to have both BAC and coronary artery stenosis. In our study, the patients with BAC were significantly older than the other group. Further analyses after controlling for age as a covariate confirmed the role of age in the correlation of BAC and CTCA findings.

Although it is believed that a systemic vascular process may have been occurring in the patients with more BAC, we did not find any statistically significant correlation between CAC score and presence of BAC as well as the severity of BAC.

Several previous studies that have investigated the correlation between BAC and cardiac events, marker or risk factors confirm our findings.

Zgheib and coworkers performed a study on 172 women who underwent coronary catheterization, and investigated their mammographic findings. They did not observe a correlation between BAC and coronary angiography–detected coronary artery disease (CAD), even when CAD severity was considered.[22]

Another study by Penugonda *et al.,* recruited 94 patients who underwent mammography and cardiac catheterization. They reviewed cardiac catheterization films and mammograms for the presence of CAD and BAC, respectively. Cardiovascular risk factors, history of revascularization, and history of myocardial infarction were compared between women with and without BAC. Penugonda and colleagues demonstrated that BAC was not positively associated with cardiovascular risk factors, documented CAD, or acute cardiovascular events.

They suggested that the presence of BAC on mammogram is not a useful predictor of CAD in intermediate- to high-risk patients.[21]

In contrast, Pecchi *et al,* and Maas *et al.,* have reported significant association between BAC and CTCA findings.

Table 1: Comparison of CAC score and severity of coronary artery stenosis in patients with different BAC severity

		CAC score	Coronary artery stenosis severity		
			Normal (*n*: 98)	Non-significant (*n*: 38)	Significant (*n*: 14)
BAC severity	Normal (*n*: 115)	106.24±285±80	85 (74%)	24 (21%)	6 (5%)
	Mild (*n*: 27)	150.85±201±38	10 (37%)	12 (44%)	5 (19%)
	Moderate (*n*: 8)	406.62±404.40	3 (37.5%)	2 (25%)	3 (37.5%)
P		0.09		<0.0001	

Data are presented as mean±SD or number(%); CAC score: Coronary artery calcium score; BAC: Breast arterial calcification; *n*: Number of patients

Pecchi *et al.,* studied 74 post-menopausal women aged less than 65 years who had undergone mammography, and determined their CAC score. They graded mammograms according to severity and extension, and observed a strong correlation between presence and severity of BAC with coronary calcifications.[30]

Maas *et al.,* studied 499 women aged 49-70 years to determine whether BAC is associated with (CAC) after 9 years follow-up. They found that calcifications in the breast arteries are related to the development of calcifications in the coronary arteries. However, they suggested that because of differences in etiology of BAC and CAC, mammograms may be not a useful tool in CAD risk assessment in women.[11]

Various factors might have contributed to such inconsistent findings. Different study design could be the leading cause of these different findings. Influence of cardiovascular risk factors on the coronary arteries is another important factor that should never be ignored. Most of cardiovascular risk factors are strongly associated with age, and BAC is also associated with age. Therefore, age is a significant factor that may have an impact on the correlation of BAC and CAD.

In addition to age, BAC varies significantly by race/ethnicity.[31] Therefore, these factors should be taken into consideration when the association of BAC with CAD or CAD-related factors are investigated.

Moreover, lack of a clear correlation between BAC and CAD markers may reflect differences in the pathogenic nature of calcium deposition in breast arteries versus coronary arteries.[21]

In contrast to the coronary arteries in which calcium is located in the intima and contributes to arterial narrowing, BAC is usually localized in the media. Hence, calcification of the breast artery is considered as a benign entity not associated with inflammation or plaque instability.[32]

According to our findings, it could be concluded that presence and severity of BAC have no significant correlation with CAC score on CTCA. The higher relative frequency of BAC in women with significant coronary artery stenosis could be due to the effects of age on BAC and CAD. However, there are several factors that limit our findings.

The relatively small number of participants is one of the limitations of this study. In addition, we recruited subjects who were referred for CTCA. Therefore, we have investigated only women who were at intermediate to high risk for CAD. Besides, there was no long-term follow-up as well as no tight control for other cardiovascular risk factors. Hence, further investigations are recommended to achieve more accurate results.

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