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Original Research Article

Prevalence of breast arterial calcification and its relationship with cardiovascular disease risk factors: insights from a cross-sectional study in South India

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ABSTRACT

Background: Cardiovascular risk prediction algorithms often underestimate risk in women, resulting in underuse of preventive therapies and lifestyle interventions. Female-specific strategies may more accurately identify those at risk. As many women undergo routine mammography, identifying an association between breast arterial calcification (BAC) and cardiovascular disease (CVD) could improve risk stratification without added cost or radiation exposure. Mammography also offers an opportunity for counseling, given the shared lifestyle risk factors between breast cancer and CVD. Due to limited data on BAC prevalence and its relationship with CVD risk factors in Indian women, this study aims to bridge that gap.
Methods: A cross-sectional study was conducted using retrospective hospital data from 286 women over 40 years who underwent routine mammograms at a tertiary care hospital. Data were analyzed using SPSS version 29. Appropriate statistical tests were applied based on data distribution.
Results: The median age of participants was 54 years (IQR 48-60). BAC was present in 25% of women. Its prevalence was higher among those with cardiovascular risk factors such as high BMI, elevated triglycerides, low HDL, elevated blood pressure, increased HbA1c, and elevated fasting blood sugar. However, only the association with elevated fasting blood glucose was statistically significant.
Conclusion: BAC may serve as a useful surrogate marker for identifying women at increased risk for CVD during routine mammography. Further large-scale, prospective studies are needed to establish its role in early detection and prevention strategies.

Keywords: Breast arterial calcification, Cardiovascular disease, Women

INTRODUCTION

Cardiovascular disease (CVD) when spoken about is equated to "men" with poor lifestyle habits and risk factors. But women are also equally at risk, with CVD being the leading cause of mortality globally and in developed countries. According to the Global burden of disease report 2017, in developing countries like India too CVD tops the list. Women have a disadvantage with regard to early diagnosis and treatment of CVD due to factors that could be personal- patient's knowledge and behavior-prioritizing men's health before theirs, delayed health seeking or professional- delays in diagnosis and treatment and difference in risk factors and presentation of symptoms between both sexes.

On the other hand, breast cancer seems to be a commonly thought of health problem among middle aged women.[1] Global as well as Indian statistics reveal that breast cancer is the leading cause of all cancers among women. According to the Globocon 2020 data, breast cancer accounted for 13.5% of all cancers and 10% of all deaths.[2] With the availability of mammogram as a sensitive screening tool and with increasing awareness, more women seek the health care system for screening.

BAC expressed as Monckeberg's calcification is the medial thickening found in the arteries is a frequent incidental finding in mammogram that is not routinely reported.[3,4] A systematic review by Henricks et al revealed a pooled BAC prevalence of 12.7% among women who underwent screening for breast cancer.[5] There is increasing evidence gathering on the association of non coronary artery calcification (CAC) such as BAC with CVD risk. Yeonyee et al concluded from a study of 2100 asymptomatic women that presence and severity of BAC is significantly associated with subclinical atherosclerosis.[6] A retrospective imaging study by Chadashvili et al revealed a strong correlation between coronary artery calcium and BAC.[7] Other studies in different countries also revealed a strong correlation between BAC and Coronary artery calcium.[8,9]

Increasing age, parity and diabetes were associated with higher prevalence of BAC. Other CVD risk factors like hypertension, obesity and dyslipidemia did not have significant association. Though not associated with the traditional risk factors for CVD, BAC was significantly associated with CVD events.[5] While there is growing evidence of the role of BAC in assessing CVD risk across many countries there is limited data regarding BAC prevalence and its association with CVD risk in India.

With the growing burden and more women in younger age groups being affected, the role of screening programs using mammography becomes more evident and so its dual role in screening for breast cancer and the CVD risk.[2]

There is also an opportunistic role for providing counseling for risk modification as both breast cancer and CVD have similar lifestyle risk factors. Owing to the paucity of literature regarding the prevalence of BAC and its association with other CVD risk factors in India, the current study is undertaken as an initiative to bridge gap.

Objectives

Objectives were to assess the association between BAC and CVD risk factors such as diabetes, hypertension, obesity and dyslipidemia, to explore the role of routine mammography in the dual screening of breast cancer and CVD risk and to highlight the need for female-specific strategies in the early detection and prevention of the CVD.

METHODS

Design

This was a cross-sectional study using retrospective data of women who had undergone mammogram as part of the routine health checkup program at our tertiary care hospital during 2018-21.

Sample

Reddy et al in their cross sectional study among women from diverse ethnicities inferred that 7.1% women had BAC.[10] Considering this prevalence, with allowable alpha error of 5% at 95% confidence interval the minimum sample size required was 102. We had records of 286 women above 40 years who had attended the routine health checkup during the study period. Data of all the women who had no known history of CVD were included for the study except women whose mammogram showed dense breast and hence visualizing BAC was difficult.

Data collection

Demographic information and data on CVD risk factors were obtained from the subject's records. BMI≥23 kg/m^2 was considered to be overweight, ≥25 kg/m^2 to be obese class I and ≥30 kg/m^2 obese class II; LDL level above 100 mg/dl, HDL<50 mg/dl and total cholesterol above 200 mg/dl were considered as abnormal; glycosylated hemoglobin ≥6.5 or fasting blood glucose >100 mg/dl or postprandial blood sugar >200 mg/dl or a known diabetic on treatment were considered for type 2 diabetes mellitus; known hypertensive on treatment or a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or both were considered for hypertension.[11,12]

Two radiologists independently reviewed each mammogram on a picture archiving and communication system (PACS) to grade the BAC. To obtain a BAC score, the number, length, and density of BAC were evaluated. If more than six vessels in both breasts are involved a score of six is given. The longest length of calcified vessel is scored using a 4-step scale (0, none; 1, less than 1/3; 2, between 1/3 and 2/3; and 3, more than 2/3). The calcification density of the vessel in the densest segment is scored using 4-step scale (0, none; 1, vessel wall calcification with clear visualization of the lumen and/or single wall calcification; 2, vessel wall calcification with clouding of the lumen; and 3, dense vessel wall calcification without visualization of the lumen). To evaluate the severity of BAC, radiologists sum these three scores for each woman, and total BAC score was divided into 3 grades: none (0), mild (1 to 6), and severe (7 to 12).[9]

Analytic approach

Data were entered and analyzed using Statistical package for social sciences (SPSS) version 28, IBM corporation.

Categorical variables are presented in percentages and continuous variables as mean and standard deviation or median and interquartile range based on distribution of data. Univariate analysis was done to find out the association between BAC and various CVD risk factors and results were interpreted with odds ratio and 95% confidence interval.

***Ethical considerations*:** This study was approved by the institutional human ethics committee (21/027) and was carried out according to the rules of the Declaration of Helsinki.

RESULTS

This cross sectional study using retrospective data was conducted among women above the age of 40 years who had undergone screening mammography as a part of routine master health check-up. Of the 286 women who participated in the study, the majority (67.8%) were above >50 years with the median age being 54 years (IQR 48-60 years). Table.1 displays the age distribution of the women as well as some of the CVD risk factors.

Table 1: Age distribution and risk factors for CVD.

Variables	Percentage (%)
Age (n=286) (in years)	
≤50	32.2
≥51	67.8
BMI (kg/m^2) (n=286)	
<23	13.3
23-24.9	11.9
25-29.9	39.2
≥30	30.8
Systemic hypertension (n=286)	11.9
Lipid profile (n=286)	
High total cholesterol	32.5
High LDL	78.3
Low HDL	68.5
High TGL	29.0
HbA1C (n=273)	
<5.7	22.3
5.7 to 6.4	42.3
≥ 6.5	34.4
Family history of CVD (n=286)	36.3

BAC and its association with CVD risk factors

Among our study subjects around 24.1% of women had BAC. Among them the median BAC score was 6 with interquartile range of 5 to 7.

Table 2 depicts the distribution of BAC based on severity among women who had BAC.

Table 2: Distribution of BAC based on severity, (n=69).

BAC	Percentage (%)
Mild	62.9
Severe	37.1

A univariate analysis revealed an absence of association between BAC and other CVD risk factors which is depicted in table3. Older age was significantly associated with presence of BAC. Around 40% of women above 50 years had severe calcifications whereas none had it below 50 years. Among the women who were positive for BAC, we analyzed the association of severity of BAC with the risk factors for CVD, but could not find a significant association.

Table 3: Association between BAC and select CVD risk factors.

Variables	BAC (%)	Unadjusted OR (95%CI)
Age (in years)		
<50	5.4	1.41 (1.2-1.5)*
>50	32.9	
BMI (kg/m^2)		
<23	23.1	1.10 (0.86-1.20)
>23	24.3	
Family history of CVD		
Yes	22.1	1.19 (0.67-2.10)
No	25.2	
Diabetes mellitus		
Yes	34.1	1.17 (0.93-1.48)
No	22.4	
Systemic hypertension		
Yes	35.2	0.53 (0.25-1.14)
No	22.6	
Total cholesterol		
Normal	23.8	1.12 (0.58- 2.28)
Abnormal	28.5	
LDL		
Normal	27.4	1.25 (0.66-2.36)
Abnormal	23.2	
HDL		
Normal	27.7	0.75 (0.42-1.33)
Low	22.4	

*Statistically significant

DISCUSSION

This cross sectional study done among women above 40 years revealed BAC prevalence of 24.1%, with women older than 50 years having a higher prevalence (33%). BAC score was obtained based on 12 point scoring system calculated by measuring the number, length and severity of calcifications. This 12 point scoring system was proved to have good inter-observer correlation by many investigators.[6,9] A wide variation in BAC has been

observed across the globe varying from 9-45% the highest observed among Saudi women.[5,6,8,9] The prevalence seems to be higher in Asian population compared to women from other ethnicities which is quite contrasting to the findings of Reddy et al study done among multiethnic population, where the prevalence of BAC was only 9 percent among women of Asian origin.[10] A systematic review by Hendriks et al revealed a pooled prevalence of BAC to be 12.4%.[5] The current study showed a relatively higher prevalence of BAC. In addition, the study also revealed that one third of the women positive for BAC had high scores (>7). This finding is important as a number of studies have shown a correlation of severe BAC with coronary artery lesions.[9,13]

In the present study we also analyzed the association of BAC with other conventional risk factors for CVD. Age was the only significant factor associated with presence of BAC. Diabetics had a higher prevalence of BAC compared to non-diabetics, but the association was not statistically significant. Chadashvili et al in their retrospective study incurred similar results with age and diabetes being the only significant factors associated with BAC. Hypertension, dyslipidemia, smoking and family history did not show any significant association.[7] Hendriks et al in their systemic review also proved that age, diabetes and null parity were significantly associated with BAC.[5] This negative association becomes very important as several longitudinal studies with follow up periods varying from 5 to 20 years have established the role of BAC as an independent risk factor for CVD.[14-18] The controversy surrounding the utility of BAC is that the calcification here is in the media termed as Monckeberg's calcification which has a different pathogenic pathway compared to intimal calcification that causes coronary disease. The medial thickening causes stiffening of vessels whereas intimal thickening is associated with atheromatous disease. The medial artery thickening is related to aging, diabetes and chronic conditions like renal disease.[5,13,19] which explains the association of age and diabetes with BAC in the present study. Recent evidence is gaining ground on the inability of traditional tests like exercise ECG and coronary angiography to detect CAD among women compared to men, probably due to late manifestation of luminal stenosis among women. Mostafavi et al have shown a higher strength of association of BAC with CVD morbidity and mortality compared to CAD probably since microvascular and functional changes in blood vessels occur much earlier than luminal stenosis. Risk scoring systems like Framingham risk score (FRS) and pooled cohort equation (PCE) have less significance in Indian population. Hence BAC could be a better predictor of CVD risk much earlier even in the absence of other risk factors or other risk prediction scores.[9,13,20,21] Another argument favoring BAC is that, though the pathways through which calcification occur in breast cancer and CVD differ, the risk factors that trigger calcification are the same.[19] Hence there is huge place for opportunistic counseling for CVD prevention when women come for mammogram without additional radiation exposure.

CONCLUSION

While this study had limitations, including a small sample size and the use of retrospective data, it successfully highlighted the prevalence of BAC and its relationship with traditional CVD risk factors. The inability to establish a statistical association between diabetes and BAC or to examine the correlation with CAC or other atherosclerotic markers warrants further investigation. To better understand BAC as an independent predictor of CVD, future longitudinal studies are essential. Given the increasing incidence of both breast cancer and CVD among women in India, incorporating mammography as a dual-purpose screening tool-detecting both breast cancer and assessing CVD risk-could be a cost-effective strategy. Radiologists should consider routinely reporting vascular calcifications alongside parenchymal calcifications during mammograms to help identify women at increased cardiovascular risk.

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