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Breast Arterial Calcification on Mammography and Risk of Coronary Artery Disease

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Abstract **Original Research Article**

Background: Breast arterial calcification (BAC) is generally detected on screening mammography which shows medial calcification of the mammary arteries. On the other hand, CAD is an important cause of morbidity and mortality worldwide. BAC is associated with risk factors for cardiovascular disease specially in patients who underwent screening mammography. ***Methods:*** This study was a cross-sectional observational study that was conducted at Bangabandhu Sheik Mujib Medical University. Dhaka. Bangladesh during the period of January 2018-December 2022. The sample size for this study was 70. ***Result:*** The mean ±SD age of the respondents who underwent mammography was 58± 8 years where who had breast arterial calcification it was 62±7 years. Total cholesterol was 5.1±1.9 and 5.2±2.0, ASSIGN score was in 15±10.8 and 18.1±11.0, coronary artery calcium score was in 0(0,52) and 13 (0, 107), any coronary artery disease on CCTA was in 35(50%) and 7(58.3%), obstructive coronary artery disease on CCTA was in 10(14.3%) and 2(16.7%) cases. Coronary artery calcification 5 was found in TP, 14 was in TN, 3 was in FP, 14 was in FN, 2 was in sensitivity, 7 was in specificity, 6 was in PPV, 5 was in NPV and .545 was in AUC and followed by coronary artery calcification (>400 AU) was in 1, 27, 8, 1, 3, 6, 1, 9 and 0.554, any coronary artery disease on CCTA was in 5, 14, 3, 14, 2, 7, 6, 5 and 0.546, obstructive coronary artery disease on CCTA was in 2, 25, 7, 4, 3, 7, 2, 8 and 0.556. ***Conclusion:*** BAC on mammography is a potential woman-specific risk predictor for CAD and is also related to the growth of coronary atherosclerosis proven by CCTA having important clinical implications. BAC is also strongly associated with the development of CAC and CAP.

Keywords: Breast Arterial Calcification, Mammography, Coronary Artery Disease, Coronary Arterial Calcification, Cardiovascular Disease.

INTRODUCTION

Screening mammography is extensively used to detect early breast cancer with an acceptance of over 70% among eligible women who are aged between 50-70 years [1]. Breast arterial calcification (BAC) is generally detected on screening mammography which shows medial calcification of the mammary arteries. From an oncological perspective it is thought to be a benign and a frequent incidental finding but is not routinely reported. In other words, in 12.7% breast cancer screening programs, screening mammography can identify a frequency of BAC with a meta-analysis [2]. Contrasting the intimal calcification of coronary artery disease (CAD), BAC also signifies calcification of small mammary arteries or arterioles [3]. Besides, BAC has been emphasized as a women-specific risk indicator for cardiovascular disease [4, 5]. It is such a condition of coronary arterial calcification (CAC) that commonly happens during the absence of atherosclerosis and inflammation [6-8]. Along with the sex-specific risk factors for cardiovascular disease like menopause and pre-eclampsia there are some traditional risk factors such as hypertension, diabetes mellitus, and smoking which are more powerful indicators for

women than men [9]. Moreover, atypical presentations of chest pain are more common in women which has been associated to their reduced rate of diagnosis and treatment [9-12]. In broad sense, BAC is associated with risk factors for cardiovascular disease specially of patients who underwent screening mammography.2 Besides, there is an association between the presence of BAC along with cardiovascular disease and an increased risk of cardiovascular mortality [13-16]. On the other hand, CAD is an important cause of morbidity and mortality worldwide [17]. Hence, CAC is strongly related with an increased risk of CAD in patient's despite of having prior CAD events.18 Evidence from past studies had emphasized the associations between BAC presence and traditional cardiovascular risk factors, as well as an increased risk for adverse cardiac events in women with BAC [18, 19]. Although some recent studies have found the presence of BAC in relation with CAC and coronary atherosclerotic plaque (CAP) [20, 21]. But, there are less studies which had evaluated the association between BAC and computed tomography (CT) features of coronary artery disease. Hence, the aim of this study was to find the association between BAC with risk of CAD through screening mammography.

OBJECTIVE OF THE STUDY

To assess the prevalence of breast arterial calcification (BAC) in patients who also underwent routine surveillance mammography, and to determine the association with cardiovascular risk factors, coronary artery calcification, and coronary artery disease on coronary computed tomography angiography (CCTA).

MATERIALS AND METHODOLOGY

This study was a cross-sectional observational study which was conducted in Bangabandhu Sheik Mujib Medical University, Dhaka, Bangladesh during the period of January 2018- December 2022. The sample size for this study was 70.

Inclusion criteria:

- The adult female who had risk of coronary artery diseases related to breast arterial calcification.
- All female participants who had undergone CCTA and mammography for screening or symptomatic indications were included.
- The participants who were willing to give their consent after knowing the study purpose.

Exclusion criteria:

- The participants who had the risk of coronary artery disease other than breast arterial calcification.
- The patients who had the risk coronary artery disease associated with breast arterial calcification but hadn't underwent CCTA or mammography.
- The patients who were not willing to give consent after knowing the study purpose.

All the 70 patients were underwant mammography screening where BAC was found in 12 cases among them. Digital mammograms were assessed and reviewed by at least two of three trained radiologists using standard viewing parameters blind to the results of CCTA or any other clinical factors. Mediolateral oblique (MLO) and craniocaudal (CC) images were also combinedly evaluated for each breast. The existence of any calcification on mammography was recorded. The presence and severity of BAC was also recorded. A four-point scale was used to assess the severity of BAC (Table III). BAC severity was determined by evaluating the BAC score in each breast with a score of 0 as None, 1 as mild, 2 as moderate and 3 as severe. Coronary artery calcium score and CCTA CT was assessed using 64 or 320-multidetector scanners and non-contrast electrocardiogram-gated CT of the heart (Brilliance 64, Philips Medical Systems, Netherlands; Biograph mCT, Siemens Germany; Aquilion ONE, Toshiba Medical Systems, Japan) at three imaging sites. Agatston method using semi-automated software (V Score, Vital Images, Minnetonka, MN, USA or scanner console software) was used to assess CAC. CCTA images were evaluated by two trained observers. The overall results of the CCTA were marked as normal in <10% luminal cross-sectional area stenosis, non-obstructive in 10-70% stenosis, or obstructive CAD as a cross-sectional luminal stenosis of >70% in one or more major epicardial vessel or >50% in the left main stem.

RESULT

Table I: Baseline Characteristics

Baseline Characteristics	Who had mammography		Who had breast arterial calcification	
	N=70	(%)	N=12	(%)
Age (years)	58± 8		62±7a	
Body mass index (kg/m2)	29±6		29±6	
Atrial fibrillation	1	1.4	1	8.3
Previous coronary heart disease	3	4.3	3	25.0
Previous cerebrovascular disease	2	2.9	2	16.7
Previous peripheral vascular disease	1	1.4	1	8.3

Table I shows the baseline characteristics of respondents. The mean ±SD age of the respondents who underwent mammography was 58± 8 years where who had breast arterial calcification it was 62±7 years and followed by the mean ±SD of body mass index (kg/m2) was 29±6 in the both groups, Atrial fibrillation was found in 1(1.4%) cases of mammography group where 1(8.3%) in breast arterial calcification group and followed by previous coronary heart disease was found in 3(4.3%) and 3(25%), previous cerebrovascular disease was in 2(2.9%) and 2(16.7%) and previous peripheral vascular disease was in 1(1.4%) and 1(8.3%) cases.

Table II: Risk Factors and Computed Tomography (CT) Results for Participants Who Underwent Mammography and Coronary CT Angiography (CCTA)

Risk factors		**Who had mammography**		**Who had breast arterial calcification**	
		N=70	**(%)**	**N=12**	**(%)**
Smoking status	Current	14	20.0	0	0.0
	Ex-smoker	21	30.0	3	25.0
	Non-smoker	35	50.0	9	75.0
Hypertension		23	32.9	4	33.3
Diabetes		6	8.6	1	8.3
Total cholesterol		5.1±1.9		5.2±2.0	
ASSIGN score		15±10.8		18.1±11.0	
Coronary artery calcium score		0(0,52)		13 (0, 107)	
Any coronary artery disease on CCTA		35	50.0	7	58.3
Obstructive coronary artery disease on CCTA		10	14.3	2	16.7

Table II represents risk factors and computed tomography (CT) results for participants who underwent mammography and coronary CT angiography (CCTA). The current smoking status of mammography group was in 14(20%) but there were no such cases in breast arterial calcification group and followed by ex-smoker was in 21(30%) and 3(25%), non-smoker was in 35(50%) and 9(75%), hypertension was in 23(32.9%) and 4(33.3%), diabetes was in 6(8.6%) and 1(8.3%), total cholesterol was 5.1±1.9 and 5.2±2.0, ASSIGN score was in 15±10.8 and 18.1±11.0, coronary artery calcium score was in 0(0,52) and 13 (0, 107), any coronary artery disease on CCTA was in 35(50%) and 7(58.3%), obstructive coronary artery disease on CCTA was in 10(14.3%) and 2(16.7%) cases.

Table III: Risk Factors associated with different levels of severity of summed breast arterial calcification score

Risk factors		**Breast arterial calcification score**							
		None 0		**Mild (1)**		**Moderate (2)**		**Severe (>¼3)**	
		N=36	**(%)**	**N=12**	**(%)**	**N=12**	**(%)**	**N=10**	**(%)**
Smoking status	Current	2	5.6	0	0.0	0	0.0	0	0.0
	Ex-smoker	5	13.9	2	16.7	1	8.3	1	10.0
	Non-smoker	7	19.4	2	16.7	3	25.0	3	30.0
Hypertension		5	13.9	1	8.3	1	8.3	1	10.0
Diabetes		1	2.8	1	8.3	1	8.3	1	10.0
Total cholesterol		5±1.0		5.6±2.1		5.1±2.0		5±2.1	
ASSIGN score		15±10		14±8		19±12		21±12	
Coronary artery calcium score		0 (0,42)		3 (0, 127)		2 (0, 96)		10 (0, 55)	
Any coronary artery disease on CCTA		7	19.4	1	8.3	1	8.3	1	10.0
Obstructive coronary artery disease on CCTA		2	5.6	2	16.7	1	8.3	1	10.0
Family history		7	19.4		0.0	2	16.7	1	10.0

Table III illustrate the risk factors associated with different levels of severity of summed breast arterial calcification score. The current smoking status was 2(5.6%) in none group where no such cases was found in mild, moderate and severe were not found and followed by ex-smoker was in 5(13.9%), 2(16.7%), 1(8.3%) and 1(10%), non-smoker 7(19.4%), 2(16.7%), 3(25%) and 3(30%), hypertension was in 5(13.9%), 1(8.3%), 1(8.3%) and 1(10%), diabetes was in 1(2.8%), 1(8.3%), 1(8.3%) and 1(10%), total cholesterol was in 5±1.0, 5.6±2.1, 5.1±2.0 and 5±2.1, ASSIGN score was in 15±10, 14±8, 19±12 and 21±12, coronary artery calcium score was in 0(0,42), 3(0, 127), 2(0, 96) and 10(0, 55), any coronary artery disease on CCTA was in 7(19.4%), 1(8.3%), 1(8.3%) and 1(10%), obstructive coronary artery disease on CCTA was in 2(5.6%), 2(16.7%), 1(8.3%) and 1(10%), Family history was in 7(19.4%), 2(16.7%), and 1(10%) cases.

Table IV: Diagnostic Accuracy of Breast Arterial Calcification on Mammography to Predict the Presence of Coronary Artery Disease on Coronary Computed Tomography Angiography (CCTA)

Diagnostic accuracy of BAC on CCTA	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	AUC
Any coronary artery calcification	5	14	3	14	2	7	6	5	0.545
Coronary artery calcification (>400 AU)	1	27	8	1	3	6	1	9	0.554
Any coronary artery disease on CCTA	5	14	3	14	2	7	6	5	0.546
Obstructive coronary artery disease on CCTA	2	25	7	4	3	7	2	8	0.556

Table IV shows the diagnostic accuracy of breast arterial calcification on mammography to predict the presence of coronary artery disease on coronary computed tomography angiography (CCTA) where any coronary artery calcification 5 was found in TP, 14 was in TN, 3 was in FP, 14 was in FN, 2 was in sensitivity, 7 was in specificity, 6 was in PPV, 5 was in NPV and .545 was in AUC and followed by coronary artery calcification (>400 AU) was in 1, 27, 8, 1, 3, 6, 1, 9 and 0.554, any coronary artery disease on CCTA was in 5, 14, 3, 14, 2, 7, 6, 5 and 0.546, obstructive coronary artery disease on CCTA was in 2, 25, 7, 4, 3, 7, 2, 8 and 0.556.

DISCUSSION

The mean ±SD age of the respondents who underwent mammography was 58± 8 years where who had breast arterial calcification it was 62±7 years and followed by the mean ±SD of body mass index (kg/m2) was 29±6 in the both groups, Atrial fibrillation was found in 1.4% cases of mammography group where 8.3% in breast arterial calcification group and followed by previous coronary heart disease was found in 4.3% and 25%, previous cerebrovascular disease was in 2.9% and 16.7% and previous peripheral vascular disease was in 1.4% and 8.3% cases (Table I). Kataoka *et al*., in their study found the mean ±SD age of the respondents without BAC was 58± 8 years where who had breast arterial calcification it was 65.8 ±4.6 years and followed by the mean ±SD of body mass index (kg/m2) was 26.3±4.1 in the both groups, coronary heart disease was found in 1.2% and 3.1% [22]. Atrial fibrillation was found in 1% cases of mammography group where 1% in breast arterial calcification group and followed by previous cerebrovascular disease was in 3% and 2% and previous peripheral vascular disease was in 1% and 1% cases [23]. The current smoking status of mammography group was in 20% but there were no such cases in breast arterial calcification group and followed by ex-smoker was in 30% and 25%, non-smoker was in 50% and 75%, hypertension was in 32.9% and 33.3%, diabetes was in 8.6% and 8.3%, total cholesterol was 5.1±1.9 and 5.2±2.0, ASSIGN score was in 15±10.8 and 18.1±11.0, coronary artery calcium score was in 0(0,52) and 13 (0, 107), any coronary artery disease on CCTA was in 50% and 58.3%, obstructive coronary artery disease on CCTA was in 14.3% and 16.7% cases (Table II). Kataoka *et al*., in their study found the current smoking status of without BAC group was in 7.8% and in breast arterial calcification group 3.6% and followed by former smoker was in 30.7% and 28.5%, hypertension was in 11.7% and 10.4%, diabetes was in 1.9% and 2.4%, total cholesterol was 6.52±1.12 and 6.58±1.19 [22]. ASSIGN score was in 15.4±9.8 and 19.1±11.0, coronary artery calcium score was in 0(0,54), 1(0.58) and 14(0, 107), any coronary artery disease on CCTA was in 52% and 62%, obstructive coronary artery disease on CCTA was in 14% and 20% cases [23]. In assessing the risk factors associated with different levels of severity of summed breast arterial calcification score, the current smoking status was found 5.6% in none group where no such cases was found in mild, moderate and severe were not found and followed by ex-smoker was in 13.9%, 16.7%, 8.3% and 10%, non-smoker 19.4%, 16.7%, 25% and 30%, hypertension was in 13.9%, 8.3%, 8.3% and 10%, diabetes was in 2.8%, 8.3%, 8.3% and 10%, total cholesterol was in 5±1.0, 5.6±2.1, 5.1±2.0 and 5±2.1, ASSIGN score was in 15±10, 14±8, 19±12 and 21±12, coronary artery calcium score was in 0 (0,42), 3 (0, 127), 2 (0, 96) and 10 (0, 55), any coronary artery disease on CCTA was in 19.4%, 8.3%, 8.3% and 10%, obstructive coronary artery disease on CCTA was in 5.6%, 16.7%, 8.3% and 10%, Family history was in 19.4%, 16.7%, and 10% cases (Table III). In assessing the risk factors associated with different levels of severity of summed breast arterial calcification score, S. McLenachan *et al.*, in their study reported the current smoking status was found 20% in none group and 1% in moderate group and followed by ex-smoker was in 31%, 40%, 28% and 10%, non-smoker 49%, 60%, 69% and 90%, hypertension was in 34%, 17%, 38% and 53%, diabetes was in 8%, 7%, 9% and 16%, total cholesterol was in 5±2.0, 5.7±2.1, 5.2±2.0 and 5.1±2.1, ASSIGN score was in 16±10, 15±8, 20±12 and 22±12, coronary artery calcium score was in 0 (0,43), 24(0, 128), 19(0, 97) and 10(0, 56), any coronary artery disease on CCTA was in 49%, 63%, 63% and 61%, obstructive coronary artery disease on CCTA was in 12%, 30%, 12% and 19%, Family history was in 49%, 29%, 50% and 52% cases [23]. The diagnostic accuracy of breast arterial calcification on mammography was evaluated to predict the presence of coronary artery disease on coronary computed tomography angiography (CCTA) where any coronary artery calcification 5 was found in TP, 14 was in TN, 3 was in FP, 14 was in FN, 2 was in sensitivity, 7 was in specificity, 6 was in PPV, 5 was in NPV and .545 was in AUC and followed by coronary artery calcification (>400 AU) was in 1, 27, 8, 1, 3, 6, 1, 9 and 0.554, any coronary artery disease on CCTA was in 5, 14, 3, 14, 2, 7, 6, 5 and 0.546, obstructive coronary artery disease on CCTA was in 2,

25, 7, 4, 3, 7, 2, 8 and 0.556 (Table IV). S. McLenachan *et al*., in their study evaluated the diagnostic accuracy of breast arterial calcification on mammography to predict the presence of coronary artery disease on coronary computed tomography angiography (CCTA) where any coronary artery calcification 58 was found in TP, 157 was in TN, 35 was in FP, 154 was in FN, 27 was in sensitivity, 82 was in specificity, 62 was in PPV, 51 was in NPV and 0.546 was in AUC and followed by coronary artery calcification (>400 AU) was in 8, 295, 85, 16, 33, 78, 9, 95 and 0.555, any coronary artery disease on CCTA was in 58, 157, 35, 152, 28, 92, 62, 51 and 0.547, obstructive coronary artery disease on CCTA was in 19, 273, 74, 39, 33, 79, 20, 88 and 0.557 [23].

CONCLUSION

BAC on mammography is a potential woman-specific risk predictor for CAD and is also related to the growth of coronary atherosclerosis proven by CCTA having important clinical implications. BAC is also strongly associated with the development of CAC and CAP. A woman having BAC along with 1 or more of cardiovascular risk factors are found to be present like diabetes, hypertension, lipid profile, inflammatory status also has risk of CAD and should be treated timely and properly as similarly anticipated for CAC. Besides, discovery of BAC on mammography has no additional cost or radiation exposure and can also benefit the patients with increased risk of CAD by helping to find the necessary preventive measures. Based on the results of this study, it is recommended that patients with BAC should be timely informed of their cardiovascular risk factors and should be given timely treatment and encouraged to adapt appropriate lifestyle.

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