The Scientific Journal of Medical Scholar

Volume 1, issue 3 , May 2022

Original Article

The Role of Breast Arterial Calcification on Mammogram as a Predictor for Risk of Coronary Artery Disease in Women

Abdallah Mohamed Sobhy*; Ahmed Mohamed Fekry Eldeek; Elsayed Mohamed Abd El-Hamid

Department of Radiology, Damietta Faculty of Medicine, Damietta, Egypt.

ABSTRACT

Introduction and Aim: Cardiovascular disease is a leading cause of death worldwide. Thus, the detection of mammographic arterial calcifications can be an early, noninvasive instrument for predicting the possible development of coronary heart disease in women. The current work aimed to assess the significance of Breast arterial calcification (BAC) detected by digital mammogram and its relation to coronary artery calcium score and degree of coronary artery stenosis if present.

Patients and methods: The study included 100 female patients submitted to digital mammography for breast cancer screening programs and showed BAC then coronary artery calcification (CAC) score and multidetector coronary computed tomography angiography (MDCCTA) had done to determine the severity of coronary artery stenosis.

Results: The age was ranged between 40 and 80 years; the mean was 56.7+9.42 years. The prevalence of positive BAC and CAD were 50% and 10%, respectively. Hypertension, diabetes mellitus (DM), hyperlipidemia, and Family history of cardiovascular disease was higher in the BAC (+) than in BAC (-) group. The presence of BAC appears to strongly and proportionately correlate with CAC Score and Coronary artery stenosis as determined by coronary CTA (r =0.809, and r = 0.811, respectively).

Conclusion: BAC can indicate a risk of CAD development. Besides, there was a significant correlation between BAC and some cardiac risk factors (e.g., age, family history of CAD, and DM).

Keywords: Mammography; Computed Tomography; Breast; Arterial calcifications; Coronary artery disease.

* Corresponding author
Email: abdallahsobhy70@gmail.com

INTRODUCTION

Breast cancer and coronary artery disease (CAD) remain the leading cause of morbidity and mortality among women. Preventive measures and screening tools are required to reduce associated morbidity or mortality [1]. A major percentage of CAD populations still present by myocardial infarction (MI) or even death, irrespective of crucial advances in the field of CAD prevention [2]. In asymptomatic females, the use of routine CAD screening is a matter of intense controversy. However, in clinical practice, breast cancer is commonly screened by mammography [3].

Breast arterial calcification (BAC) is medial calcific sclerosis, with characteristic linear, parallel opacity, presented as a "tram track" on a mammogram. BAC is a relatively common finding on mammogram with a prevalence rate of 29.4%. However, BAC is not considered a warning sign for breast cancer. Thus, sporadically reported [4].

However, several trials reported that the BACs are linked to atherosclerosis and associated with an increased risk of CAD or CV events [5]. Besides, there is an increase in interest if BAC existence could improve the risk assessment of CV events. To reduce radiation exposure and cost, the potential link between BAC and cardiovascular disease could be identified from mammography, which could be considered an opportunity to improve risk stratification [6].

Multiple trials have demonstrated a significant link between BAC and coronary arterial calcification (CAC). Coronary artery calcium score was introduced as a promising tool to stratify the risk of CVD, reflected in the 2018 updated 2018 guidelines of the American Heart Association (AHA) on blood cholesterol management [2].

AIM OF THE WORK

This study aimed to evaluate the significance of BAC detected by digital mammogram and its relation to coronary artery calcium score and degree of coronary artery stenosis if present.

PATIENTS AND METHODS

This study included 100 female patients, more than or equal to forty years of age, who underwent digital mammography for breast cancer screening programs and showed BAC then CAC score and MDCTCA had done to determine the severity of the coronary artery stenosis. All Patients were subjected to full clinical assessment (history and clinical examination). The clinical evaluation included an inquiry about potential risk factors, positive family history of any heart disease, and any cardiac incidents reported by the patient herself.

Screening mammograms were completed using a full-field digital system (Fuji film Amulet Innovality Digital Mammography, Japan) to acquire standard views. Mammograms were assessed for BAC by a radiologist. BAC was recognized as vascular calcification (VC) in one or both breasts. The BAC grade was determined using a classification scale defined by Loberant *et al*. [7].

Calcium scoring was performed using 80 dual MDCT systems (TOSHIBA Aquilion Prime 80 dual CT Scanner). A coronary CT calcium scan image was transmitted to a 3-dimensional (3D) workstation (Vitrea) and analyzed by an independent radiologist. CAC score was measured using the Agatston scoring system; the score is calculated using a weighted value allocated to the highest calcification density in a specific coronary artery.

According to the calcium score, CAD grading is zero grade for no evidence for CVD, minimal for scores one to 10, Mild for 11 to 100, Moderate for scores 100 to 400, and severe for scores higher than 400. CMDCTA was used to assess the coronary arteries to diagnose CAD. According to the severity of the artery stenosis, patients were classified into three groups. The first is normal, with no stenosis, the second is non-significant stenosis for luminal narrowing of < 50%, and significant stenosis for luminal narrowing of ≥ 50%.

Statistical analysis: data were analyzed, organized, presented in tables and suitable graphs and analyzed according to standard statistical methods using the computer program SPSS (Statistical package for social science) version 22.0 (IBM®SPSS®, Chicago, USA). Frequencies and descriptive statistics were calculated for studied variables. Categorical variables were compared by chi-square tests and quantitative by Student "t" tests. Pearson's correlation was used to address the correlation of the prevalence and extent of CAC to BAC. P-values < 0.05 was statistically significant.

RESULTS

One hundred females completed the study. Their age ranged between 40 to 80 years, and the mean age was 56.7±9.42 years. They were allocated for digital mammography for the screening of breast cancer. Fifty percent showed breast arterial calcifications (BAC). Then those patients performed CAC score and MDCTCA to determine the severity of coronary artery stenosis.

Coronary problems were discovered in 10% of the total population and 20% of BAC positive group. BAC positive patients were significantly older than BAC negative patients. In addition, the percentage of positive family history of (CVD) is 64% in the total population, with a significant increase in positive when compared to the negative group. Also, 40% of studied females had diabetes, with a significant increase in diabetes in the positive group. Hypertension was reported in 51.0% and hyperlipidemia in 42.0%, with no significant difference between positive and negative BAC groups (Table 1). According to Loberant et al. [7], grade 0 was reported in 50% of studied populations, grade- I was found in 32%, grade II discovered in 11%, and grade III in 7% (Figure 1). In addition, CAC Scoring revealed that no evidence of CVD was found in 50.0% of the total population, minimal disease in 40%, mild in 5.0%, moderate in 3%, and severe in 2% (Figure 2). CMDCTA revealed that 80.0% of positive BAC patients were normal (had no stenosis), 14% had non-significant stenosis, and significant stenosis was reported in 6.0%.

In the current work, there was a strong (r>0.07), proportional (positive) correlation between BAC severity and each of coronary artery stenosis and CAC (Table 2).

Table (1): Patient characteristics and risk factors

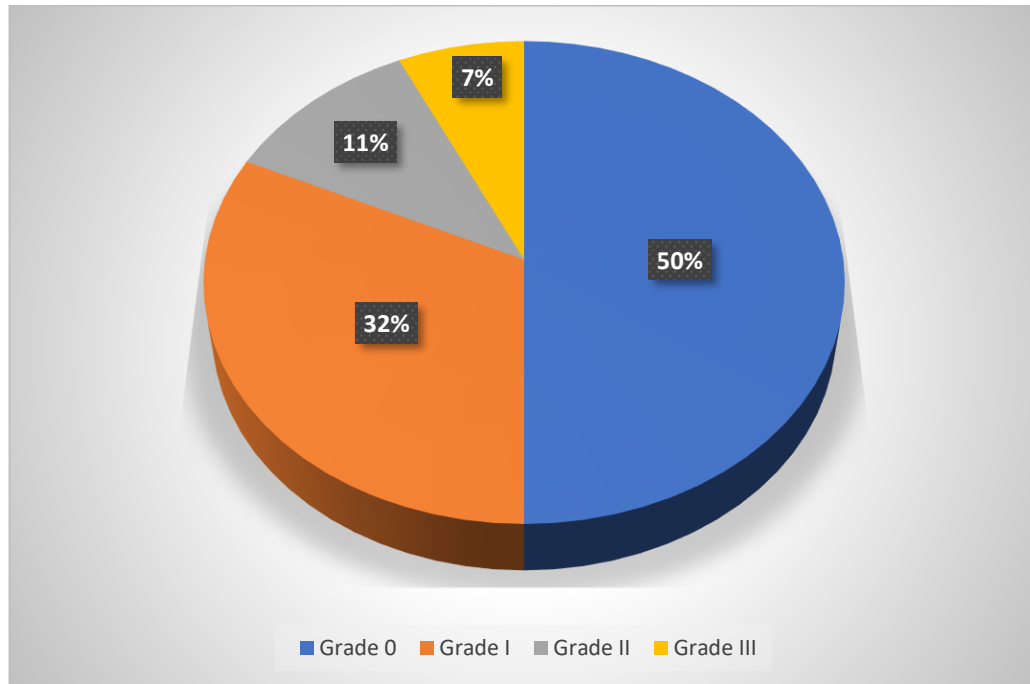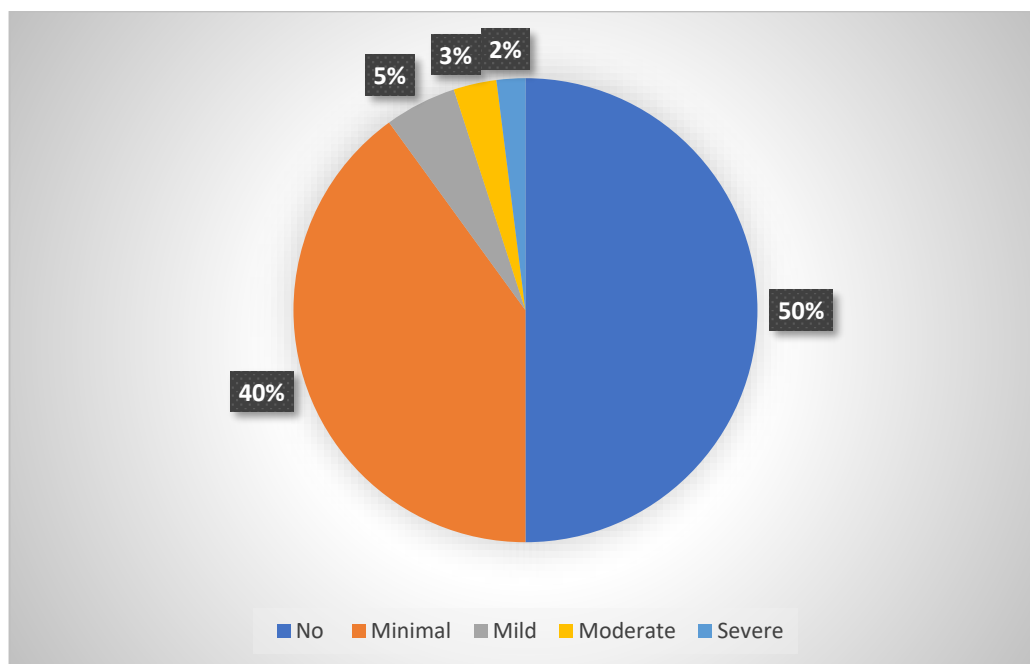|	Negative BAC (n=50)	Positive BAC (n=50)	P - Value
Age	54.5 + 7.79	58.8 + 8.60	0.02*
Family history of CVD	24 (48%)	41 (82%)	<0.001*
DM	14 (28)	26 (52%)	<0.014*
Hypertension	27 (54%)	34 (77%)	0.15
Hyper-Lipidemia	17 (34%)	25 (50%)	0.11

Figure (1): Percentage of BAC severity in total population.

Figure (2): Percentage of CAC severity in total population

Table (2): The relation between BCA and CAC Score.

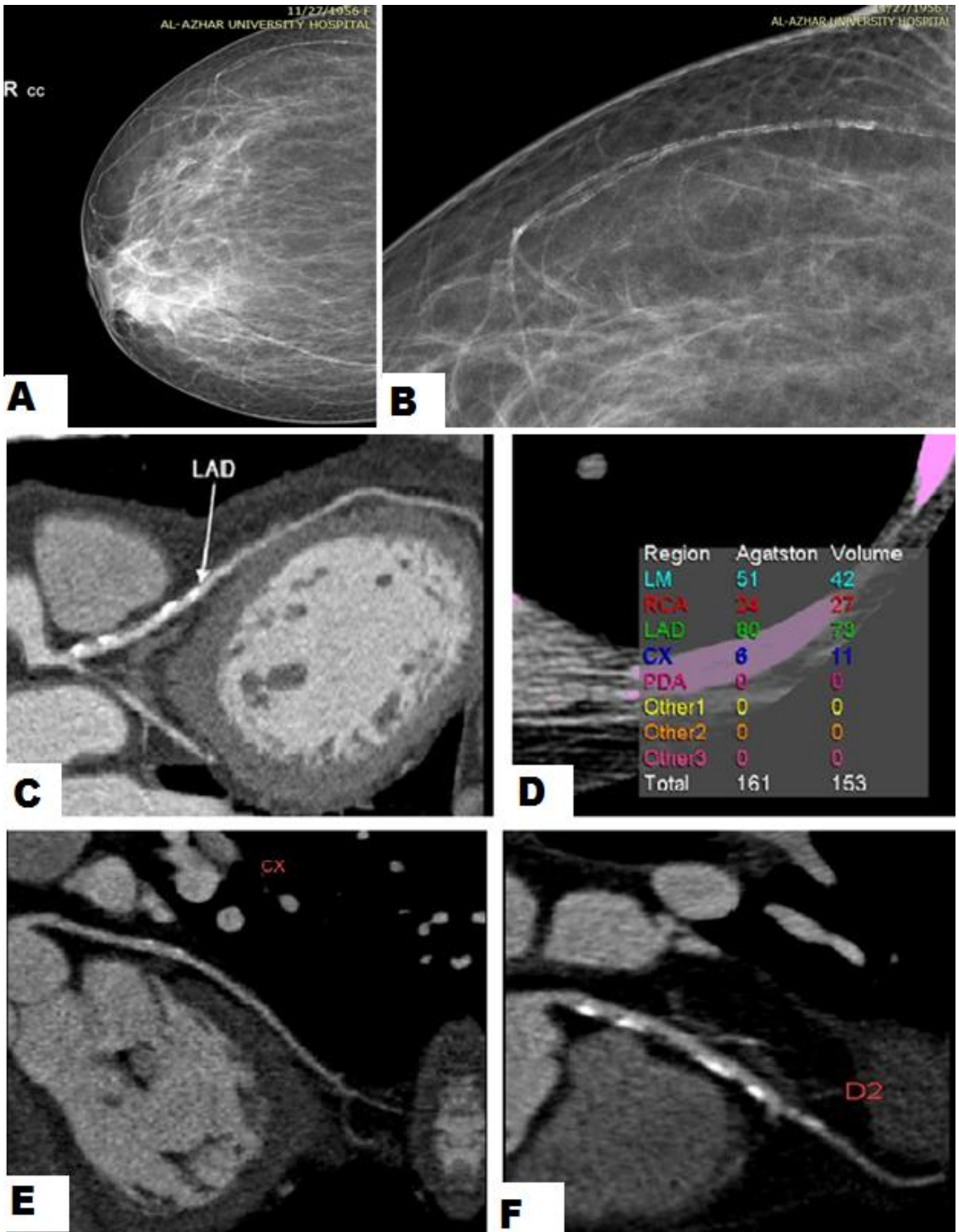|	BAC Severity	
	r	p
Coronary Artery Stenosis	.811**	<0.001
CAC	.809**	<0.001
**. Correlation is significant at the 0.01 level		

Figure (3): (A&B) images show CC view of right breast showing BAC Grade I (minor punctate vascular calcification). (C, D, E&F)) images show Curved MPR images and Calcium scoring showing: Calcium scoring 161, LM bifurcate to LAD & LCX, the proximal and middle part of LAD show multiple calcified plaques with mild stenosis <50%. LCX show two small marginal calcified plaque seen at the middle part with no significant stenosis.

DISCUSSION

CVD still a significant etiology of death, causing 1/4th of deaths in the United States [8].

Mammography is a vital substitute screening tool to recognize the risk of CAD in females. The past decades witnessed an increasing interest in BAC. BAC could be defined as a medial arterial calcification, usually discovered accidentally on mammography. It may represent a reflection of coronary calcification [4].

BAC is found in about 1/5 of patients who come to evaluate suspected CAD, and BAC existence and grade are associated with the CV risk score. Patients without BAC are unlikely to have CAD [9].

It has been proposing that this accidental finding might be a marker of generalized vascular disease [6].

For this reason, a large number of research studies have been conducted to investigate the link between BAC and CVD, its markers, and potential risk factors. However, evidence that the presence of BAC is associated with an increased risk of CVD morbidity and mortality is currently growing up.

Few studies are present to compare between BAC and CAC. In one semi-quantitative study of 74 post-menopausal females, there was a strong correlation (0.55 to 0.89) between BAC and CAC [10].

Margolies *et al*. followed up 499 females for up to 9 years and reported a significant link between BAC and subsequent development of CAC. However, they did not quantify CAC or BAC [11]. Thus, in the current work, we aimed to investigate if there was an association or correlation between mammographic BAC and CVD and related risk factors. Hence, BAC recognition during routine mammography represented an important determinant factor in the identification of asymptomatic females at increased risk of future CVD that may be candidates for more specific treatment [12]

We found that BAC's prevalence is 50% (50 BAC-positive women out of 100). Then there was a significantly high association of BAC inpatients and more severe coronary artery stenosis, besides a high association of BAC and CAC scoring.

Our results were in line with some studies. For example, Fathala *et al*. [13] demonstrated that BAC detected by the routine mammographic investigation was considered as an independent risk factor for multiple CV events among females.

Moradi *et al*. [14] had reported a significantly higher prevalence of BAC in women with more severe stenosis of the coronary artery. They studied 74 post-menopausal females aged < 65 who had routine mammography and determined their CAC score. They graded their mammograms according to two main factors (severity and extension). They reported a strong correlation between the existence & severity of BAC with CAC.

In addition to Margolies *et al*. [11] found that calcifications in the breast arteries are related to CAC occurrence. However, they suggested that mammograms may not be a useful tool in females' CAD risk assessment.

Another study has demonstrated a positive relationship between BAC and diagnosed CAD. Penugonda *et al*. [15] A study of 94 women who had a mammographic examination and invasive coronary angiography (ICA) reported that BAC was not linked to CV risk factors, suggesting that BAC, is not a useful predictor for CAD in intermediate high-risk patients.

In another case-control study, Ali *et al*. reported that, BAC was a risk factor for CAD development. Other risk factors included hypertension and a positive family history of CAD [16].

Zgheib *et al*. [17] researched with the participation of 172 females who underwent coronary artery catheterization and correlated findings with their mammographic study. They did not found any correlation between BAC and coronary angiography–confirmed CAD, even when CAD severity was considered.

A difference in the pathophysiological basis of BAC and coronary atherosclerosis could interpret these conflicting data. BAC mainly affects the arterial media, while coronary atherosclerosis affects the arterial intima. The abnormalities on the functional and microvascular CV circulation, rather than vascular stenosis, tend to be a more predominant CAD feature in females. Therefore, it is possible that BAC has a role in the development of microvascular abnormalities, even in the absence of angiographic CAD, and it could have a role in CVD risk in females [18].

But our finding could be attributed to the effects of CVD risk factors as a covariate. It means that both BAC and the presence of more significant coronary artery stenosis could be independently correlated with these risk factors. In our study, we examined the prevalence of BAC with conventional CAD risk factors. In our analysis, age, a family history of CAD, smoking, DM, hypertension, and hyperlipidemia were compared between positive and negative BAC patients. There was a strong link between BAC and many CAD risk factors, including age, a family history of CAD, and DM. Simultaneously, there were statistically differences in hypertension and hyperlipidemia.

The association between BAC and CAC risk factors has been investigated in previous trials. For example, Margolies *et al*. [11] found an association between BAC and potential risk factors, such as patient age, hypertension, hyperlipidemia, diabetes, smoking, and chronic kidney disease (CKD).

Fathala *et al*. [13] reported that BAC positive females were markedly older than BAC negative women and found a strong correlation between BAC and CAC, DM, hypertension.

However, Penugonda *et al*. [15] found that BAC was not associated with any of CV risk factors.

The evidence on the association between CAD and BAC is currently debated, with some negative and some negative associations, including the current one. However, the relation between BAC and CAC appears to be more consistent, with the vast majority of previous trials with a positive correlation between the scores of BAC and CAC.

Our study had many limitations. It is a retrospective single-center study, with inability to exclude selection bias. The application of study results to general populations must be done with caution. The study sample was relatively small with no long-term follow-up, limiting our results on the long-term occurrence of CV events. Finally, the study was conducted on the local population with inability to apply the study on the population with a certain social background.

In conclusion: BAC can predict and indicates mild or higher risk for CAD development. We suggested that BAC on mammography can be used to marker an increased risk of developing CAD, even in asymptomatic females. However, further large-scale prospective research with long-term outcomes is necessary.

Declaration of Financial and Non-Financial Relationships and Activities of Interest: None to be declared

REFERENCES

1. Jiang X, Clark M, Singh RK, Juhn A, Schnatz PF. Association of breast arterial calcification with stroke and angiographically proven coronary artery disease: a meta-analysis. Menopause. 2015; 22 (2): 136-43. doi: 10.1097/GME. 0000000000000300.

2. Chadashvili T, Litmanovich D, Hall F, Slanetz PJ. Do breast arterial calcifications on mammography predict elevated risk of coronary artery disease? Eur J Radiol. 2016 Jun; 85(6):1121-4. doi: 10.1016/j.ejrad.2016.03.006.

3. Yoon YE, Kim KM, Han JS, Kang SH, Chun EJ, Ahn S, Kim SM, Choi SI, Yun B, Suh JW. Prediction of Subclinical Coronary Artery Disease with Breast Arterial Calcification and Low Bone Mass in Asymptomatic Women: Registry for the Women Health Cohort for the BBC Study. JACC Cardiovasc Imaging. 2019 Jul;12(7 Pt 1): 1202-1211. doi: 10.1016/j.jcmg.2018.07.004.

4. Ryan AJ, Choi AD, Choi BG, Lewis JF. Breast arterial calcification association with coronary artery calcium scoring and implications for cardiovascular risk assessment in women. Clin Cardiol. 2017 Sep;40(9):648-653. doi: 10.1002/clc.22702.

5. Nasir K, McEvoy JW. Recognizing breast arterial calcification as atherosclerotic CVD risk equivalent: from evidence to action. JACC Cardiovasc Imaging. 2016 Apr; 9 (4): 361-3. doi: 10.1016/j.jcmg.2015.09.017.

6. Suh JW, Yun B. Breast arterial calcification: A potential surrogate marker for cardiovascular disease. J Cardiovasc Imaging. 2018 Sep;26(3):125-134. doi: 10. 4250/jcvi.2018.26.e20.

7. Loberant N, Salamon V, Carmi N, Chernihovsky A. Prevalence and Degree of Breast Arterial Calcifications on Mammography: A Cross-sectional Analysis. J Clin Imaging Sci. 2013 Sep 27; 3:36. doi: 10.4103/2156-7514.119013.

8. Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, *et al*. Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. J Am Coll Cardiol. 2017 Jul 4;70(1):1-25. doi: 10.1016/j.jacc.2017.04.052.

9. McLenachan S, Camilleri F, Smith M, Newby DE, Williams MC. Breast arterial calcification on mammography and risk of coronary artery disease: a SCOT-HEART sub-study. Clin Radiol. 2019 Jun;74(6):421-428. doi: 10.1016/j.crad.2019.01.014.

10. Trimboli RM, Codari M, Guazzi M, Sardanelli F. Screening mammography beyond breast cancer: breast arterial calcifications as a sex-specific biomarker of cardiovascular risk. Eur J Radiol. 2019; 119:108636. doi: 10.1016/j.ejrad.2019. 08.005.

11. Margolies L, Salvatore M, Hecht HS, Kotkin S, Yip R, Baber U, Bishay V, Narula J, Yankelevitz D, Henschke C. Digital Mammography and Screening for Coronary Artery Disease. JACC Cardiovasc Imaging. 2016 Apr;9(4):350-60. doi: 10.1016/ j.jcmg.2015.10.022.

12. Iribarren C, Molloi S. Breast Arterial Calcification: a New Marker of Cardiovascular Risk? Curr Cardiovasc Risk Rep. 2013 Apr;7(2):126-135. doi: 10.1007/s12170-013-0290-4.

13. Fathala AL, Alabdulkarim FM, Shoukri M, Alanazi M. Association between breast arterial calcifications found on mammography and coronary artery calcifications in asymptomatic Saudi women. Ann Saudi Med. 2018 Nov-Dec;38(6):433-438. doi: 10.5144/0256-4947.2018.433.

14. Moradi M, Adibi A, Abedi M. Relationship between breast arterial calcification on mammography with CT Calcium scoring and coronary CT angiography results. Adv Biomed Res. 2014 Feb 28;3:79. doi: 10.4103/2277-9175.127992.

15. Penugonda N, Billecke SS, Yerkey MW, Rebner M, Marcovitz PA. Usefulness of breast arterial calcium detected on mammography for predicting coronary artery disease or cardiovascular events in women with angina pectoris and/or positive stress tests. Am J Cardiol. 2010;105(3):359-61. doi: 10.1016/j.amjcard. 2009. 09.039.

16. Ali EA, Fouad H, Razek NA, Saeed OM, Helmy SM. Evaluation of mammography detected breast arterial calcifications as a predictor of coronary cardiac risk. Egypt J Radiol Nucl Med 2019; 50: 81 (8 pages). doi:10.1186/s43055-019-0095-7.

17. Zgheib MH, Buchbinder SS, Abi Rafeh N, Elya M, Raia C, Ahern K, Smith MC, *et al*. Breast arterial calcifications on mammograms do not predict coronary heart disease at coronary angiography. Radiology. 2010; 254 (2): 367-73. doi: 10.1148/ radiol.09090102.

18. Fathala AL, Alfaer F, Aldurabi A, Shoukri M, Alsergani H. Breast arterial calcification on mammography does not predict coronary artery disease by invasive coronary angiography. Ann Saudi Med. 2020;40(2):81-86. doi: 10.5144/0256-4947.2020.81.

The Scientific Journal of Medical Scholar