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Do breast arterial calcifications on mammography predict elevated risk of coronary artery disease?

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ABSTRACT

Purpose: To determine whether breast arterial calcifications (BAC) seen on mammography correlates with coronary artery calcium score on coronary CT as it may serve as a potential marker for increased risk of developing symptomatic coronary artery disease (CAD).
Materials and methods: Retrospective review of the imaging database at our institution identified 145 female patients who underwent coronary CT within a year of screening or diagnostic mammography. The coronary calcium score on CT was calculated by multiplying area of calcification by weighted value assigned to its highest Hounsfield unit and summed for all lesions and expressed as Agaston score. Calculated scores were risk stratified for developing CAD as follows: 0—no risk; 1–10—minimal; 11–100—mild; 101–400—moderate; >400—high risk. Percentile distribution of calcium score adjusted by age, gender and race was calculated based on results of the Multi-Ethnic Study of Atherosclerosis (MESA), which excluded patient with diabetes and chronic renal disease. The mammograms were reviewed by MQSA-certified breast radiologists who were blinded to patients' coronary calcium scores. Mammograms were interpreted for presence or absence of BAC. The calcium scores and corresponding percentiles were correlated with BAC on mammography. Cardiac risk factors such as, diabetes, hypertension, hyperlipidemia, family history of CAD and smoking, were recorded for each patient.
Results: BAC correlated with coronary calcium score of >11 ($p = 0.0001$), corresponding to mild or greater risk of developing CAD. Specifically, coronary calcium score of >11 was seen in 68% (25/37) of patients with BAC and 31% (34/108) of patients without BAC. Accounting for race, gender and age, presence of BAC showed statistically significant correlation with percentile scores of >25. Namely, 70.4% (19/27) of patients with BAC vs. 44.6% (41/92) of patient without BAC showed percentile score of >25 for developing CAD. Statistically significant association was observed of BAC with diabetes ($p = 0.01$) and chronic renal disease ($p = 0.005$). BAC showed no significant associated with hyperlipidemia, hypertension, smoking and family history of CAD.
Conclusion: BAC does predict coronary artery calcium score of >11, which indicates mild or greater risk of developing CAD. In addition, statistically significant correlation exists between BAC and cardiac risk factors, namely diabetes and chronic renal disease. Our study suggests that BAC on mammography can be utilized as a potential marker for increased risk of developing CAD.
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1. Introduction

Coronary artery disease (CAD) remains the leading cause of death among women in the United States [1,2]. While significant advances have been made in the field of CAD prevention, a large majority of patients still present with myocardial infarction or even death as the initial manifestation of underlying disease [3]. In addition, CAD related mortality has declined in men, but has remained unchanged in the women, which may relate to unique pathophysiologic features of CAD in the female population [4,5]. Risk stratification algorithms are of great importance in CAD prevention and treatment. The Framingham Risk Score was developed to stratify patients as low risk (10-year CAD risk <10%), intermediate risk (10-year CAD risk 10–20%) and high risk (10-year CVD risk >20%) based on risk factors including age, sex, diabetes, smoking, blood pressure, lipid profile and weight. However, many coronary

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Fig. 1. Mediolateral oblique (MLO) view of the right breast demonstrates characteristic morphology of breast arterial calcifications (arrow) as parallel, "tram-track" calcifications.

events were documented in patients with no such risk factors and over half of the events occurred in patients in the low to intermediate risk category [6,7]. This fact has led to development of new methods for risk assessment such as carotid intima-media thickness, ankle-brachial index, inflammatory markers (namely C-reactive protein) and coronary artery calcium score on CT (CAC-CT). Of these, CAC-CT score is the most robust risk indicator based on multiple longitudinal cohort studies and is currently endorsed by American Heart association and American College of Radiology for screening asymptomatic patients with low to intermediate risk [8–10]. While clinically valuable, additional radiation, cost, need for dedicated personnel and equipment limit usage of CAC-CT as large scale intervention.

Breast arterial calcifications (BAC) is a potential new risk stratification tool, which involves no additional cost or radiation, as a majority of women older than 40 undergo screening mammography every year. BAC demonstrates characteristic appearance on mammography as parallel, linear, "tram-track" calcifications (Fig. 1). BAC prevalence is reported as approximately 12.7% in multiple screening programs, which increases with age and is found in approximately 50% of women by the age of 80 [11]. However, BAC prevalence varies based on race/ethnicity. One study of over 1900 women, found that Hispanic women have the highest prevalence of BAC at 34%, whereas Asian women have the lowest prevalence of only 7%. Prevalence was found to be 25% in the white population and 24% in African-American women [12].

In this study, we examined the role of BAC as a potential female-specific risk factor for cardiovascular disease. We studied the relationship between BAC and CAC-CT scores in women who underwent digital screening or diagnostic mammography within a year of undergoing CAC-CT. Since BAC prevalence is dependent on age and race/ethnicity, we converted CAC-CT scores to percentile scores based on the Multi-Ethnic Study of Atherosclerosis (MESA) data to account for these variables. MESA is a prospective cohort study designed to investigate subclinical cardiovascular disease in a multiethnic cohort free of clinical cardiovascular disease. This allows comparison of patient's CAC-CT score relative to others with the same age, gender and race/ethnicity who do not have clinical cardiovascular disease or treated diabetes. We then compared BAC to percentile scores corrected for age and race of each patient, which has not been previously reported. In addition, we investigated relationship between BAC and CAD risk factors including diabetes, hypertension, smoking, renal disease, dyslipidemia and family history of CAD.

2. Materials and methods

This retrospective study was approved by the institutional review board at our institution. Review of the imaging database at our institution identified 145 female patients who underwent coronary CT within a year of screening or diagnostic mammography. The mammograms were reviewed by MQSA certified breast radiologists who were blinded to patients' coronary calcium scores. The mammograms were interpreted for the presence or absence of BAC. The coronary calcium score on CT was calculated by multiplying area of calcification by weighted value assigned to its highest Hounsfield unit and summed for all lesions. Calculated scores were risk stratified for developing CAD as follows: 0—no risk; 1–10—minimal; 11–100—mild; 101–400—moderate; >400—high risk.

Percentile distribution of calcium score adjusted by age, gender and race was calculated based on results of the Multi-Ethnic Study of Atherosclerosis (MESA), which excluded patient with diabetes and chronic renal disease. The calcium scores and corresponding percentiles were correlated with BAC on mammography.

Cardiac risk factors including diabetes, hypertension, hyperlipidemia, family history of CAD and smoking, were obtained from online medical records and recorded for each patient.

2.1. Statistical analysis

Student *t*-test analysis was performed to compare age between BAC positive and negative groups. Data was analyzed using $\chi 2$ tests for categorical groups. P values for categorical variables were calculated using two-tailed Fisher exact tests. P value of <0.05 was considered to indicate statistical significance.

3. Results

Of the 145 patients, 37 had BAC on mammography and 108 had no BAC on mammography. Average age of BAC positive and negative groups was, 56 and 61, respectively, with no statistically significant difference.

In the BAC negative subgroup, the number of patients in each coronary artery calcium score category decreased with increasing score (Fig. 2). The opposite trend was observed in BAC positive population (Fig. 3), where the number of patients in each coronary artery calcium score category increased with increasing score. This trend was most notable between coronary artery score categories greater or less than 11–100. Coronary calcium score of >11 was seen in 68% (25/37) of patients with BAC and 31% (34/108) of patients without BAC ($p = 0.001$) (Table 1, Fig. 4). Therefore, BAC correlates with coronary calcium score of >11 corresponding to mild or increased risk of developing CAD.

Accounting for race, gender and age, the presence of BAC showed statistically significant correlation with percentile scores of >25 ($p = 0.03$). In patients with BAC on mammography, 70.4% (19/27)

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