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# Digital Mammography and Screening for Coronary Artery Disease

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## ABSTRACT

**OBJECTIVES** This study sought to determine if breast arterial calcification (BAC) on digital mammography predicts coronary artery calcification (CAC).

**BACKGROUND** BAC is frequently noted but the quantitative relationships to CAC and risk factors are unknown.

**METHODS** A total of 292 women with digital mammography and nongated computed tomography was evaluated. BAC was quantitatively evaluated (0 to 12) and CAC was measured on computed tomography using a 0 to 12 score; they were correlated with each other and the Framingham Risk Score (FRS) and the 2013 Cholesterol Guidelines Pooled Cohort Equations (PCE).

**RESULTS** BAC was noted in 42.5% and was associated with increasing age ($p < 0.0001$), hypertension ($p = 0.0007$), and chronic kidney disease ($p < 0.0001$). The sensitivity, specificity, positive and negative predictive values, and accuracy of BAC >0 for CAC >0 were 63%, 76%, 70%, 69%, and 70%, respectively. All BAC variables were predictive of the CAC score ($p < 0.0001$). The multivariable odds ratio for CAC >0 was 3.2 for BAC 4 to 12, 2.0 for age, and 2.2 for hypertension. The agreements of FRS risk categories with CAC and BAC risk categories were 57% for CAC and 55% for BAC; the agreement was 47% for PCE risk categories for CAC and 54% by BAC. BAC >0 had area under the curve of 0.73 for identification of women with CAC >0, equivalent to both FRS (0.72) and PCE (0.71). BAC >0 increased the area under the curve curves for FRS (0.72 to 0.77; $p = 0.15$) and PCE (0.71 to 0.76; $p = 0.11$) for the identification of high-risk (4 to 12) CAC. With the inclusion of 33 women with established CAD, BAC >0 was significantly additive to both FRS ($p = 0.02$) and PCE ($p = 0.04$) for high-risk CAC.

**CONCLUSIONS** There is a strong quantitative association of BAC with CAC. BAC is superior to standard cardiovascular risk factors. BAC is equivalent to both the FRS and PCE for the identification of high-risk women and is additive when women with established CAD are included. (J Am Coll Cardiol Img 2016;9:350–60) © 2016 by the American College of Cardiology Foundation.

Breast cancer and cardiovascular disease affect millions of women; cardiovascular disease is the leading cause of mortality (1) and breast cancer is the most feared disease (2). Women are commonly screened for breast cancer with mammography; 47.5% of women between 40 and 49 and 57.2% of women between 50 and 74 had mammograms in 2011 (3). However, there is no routine screening for coronary artery disease (CAD). Nonetheless, the presence or absence of breast arterial calcification (BAC) has been correlated with CAD (3-14) and with the presence or absence of coronary artery calcium (CAC) in a limited number of studies (7-9,14). This study was designed to quantitatively evaluate the relationship between BAC on digital mammography and CAC on noncontrast computed tomography (CT) scans, and their correlation with the Framingham Risk Score (FRS) (15) and the 2013 Cholesterol Guidelines Pooled Cohort Equations (PCE) (16). A significant relationship would provide the opportunity

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for large-scale cardiac risk assessment of peri- and post-menopausal women undergoing mammography without additional cost and radiation exposure.

## METHODS

Institutional review board approval was obtained for this HIPAA-compliant study and informed consent was waived. A search of the radiology department database was made for all women who had mammograms and noncontrast CT scans of the chest for routine clinical indications, and complete risk factor information, within 1 year of each other during the years of 2011 to 2013. A total of 325 asymptomatic women were identified; 33 had established CAD by chart review and were excluded from further analysis, leaving 292 subjects for primary analysis. Selected analyses of the entire cohort of 325 patients are provided in Online Figure 1 and Online Table 1.

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**CT SCAN.** Chest CT scans were acquired on the following scanners: GE VCT 64 slice (General Electric Medical Systems, Milwaukee, Wisconsin); and Siemens Somatom Definition AS-40 slice, Siemens DEFINITION AS128, and Siemens SENSATION 64 Cardiac (Siemens Medical Solutions, Forchheim, Germany) with 5-mm slice thickness, 120 kVp, and mA varying according to the patient size.

A chest radiologist with more than 20 years of experience measured the ordinal CAC score as previously described (17). Each of the 4 main coronary arteries was identified (left main, left anterior descending, circumflex, and right) and the extent of CAC in each artery was categorized as being absent, mild, moderate, or severe and scored as 0, 1, 2, or 3, respectively. The extent of CAC was classified as mild when less than one-third of the length of the entire artery showed calcification, moderate when one-third to two-thirds of the artery showed calcification, and severe when more than two-thirds of the artery showed calcification. With 4 arteries thus scored, each participant received a score from 0 to 12. The CAC scores were divided into 3 categories of increasing severity: 0, 1 to 3, and 4 to 12, which have been shown to be strongly predictive of cardiac outcomes in a long-term follow-up of 8,782 patients (17).

**DIGITAL MAMMOGRAPHY.** Standard full-field digital mammograms were acquired in the craniocaudal and mediolateral oblique positions on either a GE Essentials Unit General Electric (Buc, France) or Hologic Dimensions Unit (Bedford, Massachusetts). A second radiologist with more than 20 years of experience in mammography, blinded to the CAC results, reviewed the mammograms of the 325 women. All mammograms were reviewed on standard 5 megapixel mammography monitors. All standard tools including magnification and inversion were available for use at the radiologist's discretion. For those women with BAC, the number of vessels involved in each breast was recorded and numerically coded as 1 to 6; if there were more than 6 BAC, then 6 was coded. The longest length of vessel involvement was recorded as none (scored as 0), less than one-third (scored as 1), between one-third and two-thirds (scored as 2), and greater than two-thirds (scored as 3). The density of calcium in the most severely affected segment was recorded as none (scored as 0), mild with clear visualization of the lumen and/or only 1 vessel wall involved (scored as 1), moderate with clouding of the lumen and calcification of both tangential walls (scored as 2), and severe with no visible lumen (scored as 3) (**Figure 1**). Thus each woman received an ordinal BAC score between 0 and 12 after summing up these 3 numbers for each breast. As with the CAC score, the BAC results were divided into 3 categories of increasing severity: 0, 1 to 3, and 4 to 12.

**RISK FACTORS.** Risk factor history was obtained for all patients based on chart review and the 10-year FRS and PCE scores were calculated. The FRS were divided into the conventional low (<10%), intermediate (10% to 20%), and high (>20%) risk categories. The PCE were classified as <5% (statins not needed), 5% to 7.4% (reasonable to offer moderate intensity statins), and ≥7.5% (should be treated with moderate/high intensity statins).

**STATISTICS.** All statistical analyses were performed using SAS version 9.2 (Statistical Analysis System, Cary, North Carolina). Frequencies and descriptive statistics were obtained for all the variables. Quantitative data were compared using chi-square tests, Fisher exact tests, and Student *t* tests. Logistic regression analysis was used to address the relationship of the prevalence and extent of CAC to BAC findings while adjusting for the other available risk factor of age. The age categories in years were <60, 60 to 69, and ≥70. The extent of CAC was analyzed for the 3 CAC categories and their relationship to the 3 BAC categories using polytomous logistic regression analysis. The dose-response relationship of CAC on the BAC score (using both linear and quadratic terms) was analyzed using regression analysis and the F statistic was used to test the significance of the linear and quadratic terms. Logistic regression analysis was

**ABBREVIATIONS AND ACRONYMS**

**BAC** = breast arterial calcification

**CAC** = coronary artery calcium

**CAD** = coronary artery disease

**CI** = confidence interval

**CT** = computed tomography

**FRS** = Framingham Risk Score

**IQR** = interquartile range

**OR** = odds ratio

**PCE** = 2013 Cholesterol Guidelines Pooled Cohort Equations

**ROC** = receiver-operating characteristic