



Mammographic detection of breast arterial calcification as an independent predictor of coronary atherosclerotic disease in a single ethnic cohort of African American women



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ABSTRACT

Objective: Accumulating data on predominantly Caucasian women suggests an association between breast arterial calcification (BAC) and coronary artery disease (CAD). We sought to comprehensively examine the correlation between mammographic BAC and CAD endpoints detected by cardiac computed tomography (CCT) in African American (AA) women.

Methods: Consecutive AA women who underwent digital screening mammography and CCT were identified. In blinded fashion, mammographic and CCT studies were reviewed. Patient-related pertinent covariates were assessed.

Results: Two-hundred-four AA women (median age, 52.5 years) were included. BAC was present in 42 women (20.6%). BAC was significantly associated with coronary artery calcium score >100 (odds ratio [OR], 7.66; 95% confidence interval [CI], 2.75–21.29; $P < 0.001$), atherosclerotic luminal narrowing (OR, 9.99; CI, 3.65–27.32; $P < 0.001$), and stenosis $\geq 50\%$ (OR, 5.48; CI, 1.97–15.23; $P = 0.001$) by CCT.

Conclusion: In AA women, BAC is associated with increased probability of coronary calcification, atherosclerosis, and CAD on CCT.

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1. Introduction

Large population-based studies indicate racial disparities among women regarding the prevalence and disease-specific mortality of coronary artery disease (CAD), with a higher risk

among African American (AA) women compared to Caucasian women [1,2].

Reddy et al. [3] studied a diverse population of women and reported that breast arterial calcification (BAC) varies by race. Interestingly, the prevalence of BAC among AA women was found to be higher than among Caucasian women [3]. However, previous studies on coronary artery calcification indicated that AA individuals develop relatively more non-calcified disease whereas more calcified disease is present in Caucasian individuals [2,4].

De facto, BAC is not mentioned within the current societal guidelines for interpreting and reporting mammographic findings [5]. This study aimed at evaluating the ability of mammographic BAC to predict the presence of coronary artery calcification,

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atherosclerotic luminal narrowing, and obstructive CAD, as assessed by cardiac computed tomography (CCT) in AA women.

2. Methods

2.1. Study design

Consecutive AA women were identified who had undergone digital screening mammography and CCT. All examinations were performed between 01/2007 and 06/2013. We defined 24 months to be the maximum time interval between mammography and CCT. Among patients with multiple examinations, only the initial CCT examination and the mammogram with the shortest time interval were included. Mammography preceded CCT in 126 subjects. All CCT examinations were clinically indicated, none were ordered in response to BAC detection. To further control for selection bias, patients with known CAD were excluded, but patients with incomplete demographic data ($n = 4$) were included in the final analysis. Three patients were excluded because of non-diagnostic image quality of the CCT dataset. The responsible Institutional Review Board approved our study. Informed patient consent was waived for this retrospective analysis.

2.2. Cardiac computed tomography

All CCT examinations were performed using first and second generation dual-source CT technology (Somatom Definition and Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany). Patients initially underwent a non-contrast enhanced coronary artery calcium scan. Parameters of the coronary CT angiography protocol for the first and second generation dual-source CT were as follows: gantry rotation time, 330/280 ms; collimation, 32/64 $\times$ 2 $\times$ 0.6 mm (z-flying focal spot); tube voltage, 80–120 kV; tube current, 320–650 mA s.

The specific coronary CT angiography acquisition protocol was chosen to minimize radiation dose exposure for each individual patient based on body mass index, heart rate and rhythm. Bolus tracking technique was applied. Study subjects received 50–90 mL iodinated contrast material (Ultravist, 370 mgI/mL iopromide, Bayer, Wayne, NJ), followed by a saline flush. A dedicated vascular kernel was chosen for image reconstruction.

An experienced observer reviewed all CCT examinations in blinded fashion. After Budoff et al. [6], a coronary calcium score >100 was considered significant. Atherosclerosis was defined as any atherosclerotic luminal narrowing. CAD was defined as $\geq 50\%$ luminal stenosis.

2.3. Screening mammography

Screening mammograms were performed using a full-field digital mammography system (Selenia Dimensions 2D, Hologic, Bedford, MA) with acquisition of standard views. An experienced observer interpreted the mammograms on a dedicated, calibrated workstation in blinded fashion. BAC was defined as vascular calcium deposition in one or both breasts. Modified from Loberant et al. [7], BAC was classified based on a 4-level Likert-scale (0 = no BAC, 1 = few punctate BAC, 2 = coarse BAC with tram track or ring appearance in <3 vessels, 3 = coarse BAC in ≥ 3 vessels) as exemplified in [Supplementary Fig. 1](#).

2.4. Statistical analysis

Categorical variables are presented as frequencies and percentages. Continuous variables are presented as means $\pm$ standard deviations. For normally and non-normally distributed data the

two-tailed unpaired Student t-test and Mann–Whitney U-test were used, respectively. For categorical variables, the association with CCT endpoints was analyzed with Chi-square testing.

Median calcium score was determined for each BAC severity group and compared using the Kruskal–Wallis test. Receiver operating characteristic analysis was used to calculate sensitivity, specificity and area under the curve (AUC) of BAC presence to predict a calcium score >100 and CAD. Potential confounders yielding $P < 0.1$ in univariate analysis were included in the multivariate regression models. Mammographic BAC presence and severity were entered for multivariate regression analysis separately. For intra- and interobserver variability assessment, 68 randomly selected mammographic and CCT studies were read by second experienced observers in blinded fashion. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Population characteristics and imaging results

The median time between CCT and screening mammography was 9 months (interquartile ranges, 5–13 months). The median coronary calcium score was 0, ranging from 0 to 2988. BAC was detected on digital screening mammograms of 42 subjects (21%). Mild, moderate, and severe BAC was found in 23, 15, and 4 women, respectively. Intra- and interobserver agreement was substantial for BAC presence ($\kappa = 0.95$ and $\kappa = 0.89$, respectively), BAC severity ($\kappa = 0.95$ and $\kappa = 0.85$, respectively), atherosclerosis ($\kappa = 0.96$ and $\kappa = 0.89$, respectively), and CAD (both $\kappa = 1$). Relevant population characteristics and imaging results are provided in [Table 1](#).

3.2. Univariate analysis

Results of the univariate analyses for the evaluation of pertinent covariates to predict calcium score >100 , presence of atherosclerosis, and CAD are listed in [Supplementary Table 1](#). Median calcium score was 0 in women without BAC and 45, 30 and 51 in patients with mild, moderate and severe BAC, respectively ($P < 0.001$). BAC presence had 66.7% sensitivity, 85.4% specificity, 4.57 positive likelihood ratio (+LR), and 0.39 negative likelihood ratio (–LR) for

Table 1
Population characteristics and imaging results ($n = 204$ African American women).

Demographics	
Age (years) ^a	52.5 (46–59)
Body mass index (kg/m ²) ^{a,b}	32.9 (28.3–37.1)
Hypertension	151 (74.0)
Diabetes mellitus	68 (33.3)
Hyperlipidemia	127 (62.3)
Tobacco abuse	93 (45.6)
Severe renal insufficiency	11 (5.4)
Cardiac computed tomography	
Symptomatic/asymptomatic	188 (92.2)/16 (7.8)
Coronary artery calcium score ^{a,c}	0 (0–10)
Coronary artery calcium score $>100^c$	24 (12.3)
Atherosclerotic luminal narrowing $<50\%$	44 (21.6)
CAD (i.e. luminal stenosis $\geq 50\%$)	24 (11.8)
1-vessel CAD	17 (8.3)
2-vessel CAD	5 (2.5)
3-vessel CAD	2 (1.0)
Digital screening mammography	
Presence of BAC (dichotomous)	42 (20.6)
Severity of BAC (Likert grade 0–3) ^a	0 (0–0)

Unless specified otherwise, data are frequency (%).

BAC: breast arterial calcification; CAD: coronary artery disease.

^a Data are medians (interquartile ranges).

^b Body mass index was assessable in 200/204 patients.

^c Coronary artery calcium score was obtained in 195/204 patients.

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