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Publication Date

2026-05-15

Breast arterial calcification and cardiovascular risk prediction in women with and without standard modifiable risk factors

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Background: Risk identification among women, particularly those without standard modifiable risk factors (SMuRFs) for cardiovascular disease (CVD), remains suboptimal. Breast arterial calcification (BAC), found incidentally on mammography, is a promising biomarker associated with CVD. We evaluated BAC's utility for predicting CVD and mortality between SMuRFless and SMuRF+ women. Among SMuRF+ women, we examined whether treatment of hypertension or hyperlipidemia modifies the relationship between BAC and CVD.

Methods: This single-center retrospective cohort study included 19,718 women aged 40–90 years who underwent screening digital mammography from 2006–2016. BAC was quantified using validated deep-learning software (cmAngio®, CureMetrix). SMuRFless women had no hypertension, hyperlipidemia, diabetes, smoking history, chronic kidney disease, prevalent CVD, or related preventive pharmacotherapy. The primary composite outcome included acute myocardial infarction, heart failure, stroke, and death; the secondary outcome was all-cause mortality.

Results: Mean age was 56.8±11.5 years. Prevalent risk factors (RFs) included hypertension (24%), hyperlipidemia (27%), and diabetes (7%). 8,813 women (42%) were SMuRFless; 18% of SMuRFless and 31% of SMuRF+ women were BAC-positive. Over a mean follow-up of 5.9±3.2 years, a composite event occurred in 4.8% of BAC-negative and 14% of BAC-positive women ($p<0.001$). Among SMuRF+ women, BAC was associated with a 50% higher adjusted risk of the composite outcome (aHR 1.50 [95% CI 1.30–1.73], $p<0.001$) and 51% higher mortality risk (aHR 1.51 [95% CI 1.25–1.82], $p<0.001$). Among SMuRFless women ≤60 years, there was a similar association between BAC and the composite outcome (aHR 1.51 [95% CI 0.96–2.36], $p=0.07$). Among women on lipid-lowering therapy (LLT), BAC was independently associated with a 44% increased risk of the composite outcome (aHR 1.44 [95% CI 1.18–1.76], $p<0.001$) and a 42% increased mortality risk (aHR 1.42 [95% CI 1.08–1.87], $p<0.001$). Among women on antihypertensive therapy, BAC was independently associated with a 45% increased risk of the composite outcome (aHR 1.45 [95% CI 1.19–1.76], $p<0.001$) and a 24% increased mortality risk (aHR 1.24 [95% CI 1.10–1.38], $p=0.006$). Women with RFs and BAC not receiving LLT or antihypertensive medication had highest risk across all subgroups.

Conclusion: Among women undergoing routine mammography, BAC identifies women at higher-risk for incident CVD and mortality. BAC provides incremental prognostic information in SMuRF+ women and may improve risk stratification in younger women without traditional RFs.

Keywords: coronary artery disease, risk stratification, breast arterial calcification, sex-specific biomarkers

Disclosure statement: The authors have no conflicts of interest to disclose relevant to the contents of this abstract.

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