Breast Arterial Calcification
Expanding the Reach of Cardiovascular Prevention

A large proportion of cardiovascular events occur among women whose 10-year estimated atherosclerotic cardiovascular disease risk is <7.5%, and thus guidelines would not routinely recommend statins for such patients before their events. Additional strategies beyond the measurement of traditional risk factors are therefore needed to identify women who might benefit from medical therapy, based on unexpected higher risk. Coronary artery calcium (CAC) seen on a noncontrast chest computed tomogram is the most potent marker of subclinical cardiovascular disease (CVD), and has been shown to enhance risk prediction in women. However, CAC testing is usually not covered by insurance companies, limiting its widespread use as a screening tool for subclinical CVD.

Given that millions of women undergo mammograms each year, there has been growing interest in whether the presence of breast arterial calcification (BAC), which is easily detected on a standard mammogram, could help inform cardiovascular risk assessment. Unlike CAC, which represents calcification in the intima, BAC is found along the circumference of the media giving it a tram-track appearance when the burden is severe (Figure). Some studies of BAC described it simply as present versus absent, whereas others attempted to use a semiquantitative assessment based on the density and extent of calcium in each artery, and the number of arteries involved. BAC prevalence varies widely depending on the population’s age and comorbidities, ranging from 10% to 12% in healthier population-based cohort studies, to 60% to 70% among women >70 years of age or with chronic kidney disease. BAC is thought to develop primarily through pathways related to mineral metabolism and bone formation, but there may be a role for inflammation as well. Although traditional cardiovascular risk factors such as age, hypertension, and diabetes mellitus are associated with BAC presence, BAC has an inverse association with smoking, which is consistent with other studies of medial calcification. Reproductive factors such as parity and breastfeeding are also associated with BAC.

Several observational studies have demonstrated that the presence of BAC provides important prognostic information related to cardiovascular risk. In a systematic review of the data related to BAC and CVD, Hendricks et al cited studies that used either hospital admission data or municipal death records to examine the association of BAC and CVD events. The authors reported a hazard ratio of 1.32 (95% confidence interval [CI], 1.08–1.60) for incident coronary heart disease, 1.44 (95% CI, 1.02–2.05) for coronary heart disease mortality, 1.29 (95% CI, 1.01–1.66) for CVD mortality, and 1.52 (95% CI, 1.18–1.98) for heart failure.

Exactly why BAC signifies an increased cardiovascular risk is not well understood. It may simply represent long-term exposure to known cardiovascular risk factors. BAC has also been shown to be indicative of medial calcification in other vascular beds. Medial calcification is known to increase vascular stiffness and likely explains the association of BAC with heart failure, in addition to coronary heart disease and stroke. Studies of women with chronic kidney disease are particularly helpful, given...
that chronic kidney disease is associated with diffuse vascular calcification. In a comparison of women with and without end-stage kidney disease (n=71 in each group, matched for age, race, and diabetes status), Duhn et al\(^3\) found that 63\% of the women with end-stage kidney disease had BAC versus 17\% of the women without end-stage kidney disease. Radiographs of the extremities to assess associations of BAC with peripheral arterial calcification were also available in 62 women. Of 21 women with peripheral arterial calcification, 19 (90\%) also had BAC. Conversely, 19 of 31 (61\%) of the women with BAC also had peripheral arterial calcification; however, mammography is more sensitive for arterial calcification than radiography.

More recently, a study by Margolies et al\(^4\) provided the most detailed assessment of the association between BAC and CAC. The authors studied a convenience sample of 292 women referred for a mammogram who also underwent a clinically indicated nongated chest computed tomogram within a year of the mammogram. Incidental CAC was determined using an established semiquantitative scoring system based on the extent of CAC in each coronary artery. BAC was quantified based on the number of vessels involved, density of calcium, and the longest length of calcium in an artery. Among women 39 to 59 years of age with BAC>0, 52\% had CAC, with 13\% being moderate to severe; among women 60 to 69 years of age with BAC>0, 67\% had CAC, with 31\% being moderate to severe. The authors also stratified women based on their 10-year estimated atherosclerotic CVD risk and found that, among lower-risk women with a 10-year estimated risk of <5\% or 5\% to 7.4\%, the prevalence of BAC>0 was 23\% and 34\%, respectively. Among women with a 10-year estimated risk \(\geq 7.5\%\), 60\% had BAC. After adjusting for age and traditional risk factors, only the presence of moderate to severe BAC (odds ratio, 3.2; 95\% CI, 1.8–5.9), age (odds ratio, 2.0; 95\% CI, 1.5–2.6), and hypertension (odds ratio, 2.2; 95\% CI, 1.3–3.8) remained significant predictors of a CAC>0.

Although BAC is considered a benign finding from an oncological perspective, its presence suggests that a woman’s cardiovascular risk could be higher than predicted by risk factors alone. Simultaneous screening for breast cancer and CVD has tremendous appeal, particularly given that measurement of traditional risk factors does not adequately represent cardiovascular risk for many women. However, there are currently no guidelines regarding the reporting of BAC and so it is often omitted. BAC should instead be treated as any other clinically relevant incidental finding, and be mentioned in the conclusion of the mammogram report. To make such a change acceptable to radiologists, a method of quantification and reporting that does not compromise workflow is needed. A semiquantitative assessment of mild, moderate, or severe BAC would suffice. In addition, it would be important to educate the providers who are most likely to order mammograms, such as those in primary care and gynecology, about the clinical significance of BAC. Further research is also warranted about how BAC changes over time, particularly in relation to the progression or treatment of cardiovascular risk factors.

How should clinicians and patients respond to a positive BAC result? Its presence should prompt clinicians to perform a comprehensive assessment of women’s traditional risk factors and lifestyle, and to initiate medication when appropriate based on existing treatment guidelines. If the patient does not already have a clear indication for a statin, then one could proceed to formal CAC testing. Margolies et al\(^5\) reported a specificity and positive predictive value of BAC for CAC of 83 and 53,
respectively, among women aged 39 to 59 years; of 66 and 67, respectively, among women aged 60 to 69 years; and of 53 and 86, respectively, among women aged ≥70 years. However, it is important to consider that the women in the study by Margolies et al were referred for chest computed tomogram and, therefore, not representative of the general population. The American College of Cardiology/American Heart Association Guideline on the Assessment of Cardiovascular Risk supports the use of statin therapy if the CAC score is >300 or >75th percentile based on age and sex. Although most insurance companies do not cover CAC testing, it can often be obtained for $75 to $250. Further cardiac workup with a stress test or coronary angiogram in the absence of symptoms is not indicated.

As with CAC screening, there is the theoretical concern that a diagnosis of BAC might have negative psychological consequences. Studies of adults who have undergone CAC testing have not substantiated such concerns. Although a small percentage of individuals with CAC>0 reported feeling worried about their cardiovascular risk, they were also more likely than adults without CAC to change their diet and initiate lipid-lowering therapy. Providers can convey the information about BAC so that women are both aware of its clinical significance and understand that controlling their cardiovascular risk factors can substantially decrease their risk of future events. If providers help women feel empowered to engage in their health care, then the detection of BAC can be a source of motivation rather than fear. It also represents an opportunity to reinforce that women are more likely to die of CVD than breast cancer.

But perhaps the greatest power in a joint screening for breast cancer and CVD lies in the potential to prevent BAC or CAC from developing in the first place. Breast cancer and CVD share several modifiable risk factors: diabetes mellitus, smoking, physical inactivity, poor diet, and obesity. If women were counseled each time they had a mammogram that controlling their risk factors could help them avoid 2 of the deadliest conditions for women, then the message of prevention could gain considerable strength.

**DISCLOSURES**

None.

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**FOOTNOTES**

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**REFERENCES**


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