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EDITORIAL COMMENT

Recognizing Breast Arterial Calcification as Atherosclerotic CVD Risk Equivalent

From Evidence to Action*

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Mammography is an established and widely accepted imaging modality for early detection of breast cancer. The American Cancer Society endorses annual mammography for breast cancer screening among all women older than 40 years of age (1). The U.S. Preventive Service Task Force recommends mammography every 2 years for all women aged 50 to 75 years and for selected high-risk women aged 40 to 50 years (2). In general, it is estimated 37 million mammograms are performed annually in the United States alone (3).

Largely because of age, the group of women routinely undergoing mammography are also candidates for atherosclerotic cardiovascular disease (ASCVD) risk assessment. Although cardiovascular disease remains the leading cause of mortality, morbidity, and cost in women, there is no consensus on national screening for early signs of actual disease, such as coronary artery calcium (CAC) testing. Instead, current guidelines continue to emphasize use of surrogate risk factor-based algorithm to estimate ASCVD risk and subsequent intensity of established interventions (4). However, especially among women, it is well established these approaches tend to underestimate presence and increasing burden of actual atherosclerotic disease, which may lead to underuse of preventive therapies in appropriately higher risk cases (4).

One possible way to overcome this bias is to use additional clinical data, already routinely available, that can stimulate formal ASCVD risk assessment and discussions for further testing in unclear situations. In the past many have advocated that we leverage detection of breast arterial calcifications (BAC), which are readily visible on mammography, to further inform ASCVD risk among women undergoing breast cancer screening (5). BAC reflects medial calcification of arteries (Mönckeberg arteriosclerosis), and has been associated with markers of subclinical atherosclerotic disease and risk of incident cardiovascular disease (5). However, to date the question of whether identification of BAC on routine mammogram potentially represents a valuable approach to appropriately identifying higher risk women without additional imaging, cost, or radiation to optimize ASCVD prevention strategies remains unresolved.

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In this issue of *iJACC*, Margolies et al. (6) present a single-center study from 292 women that details the interplay between traditional risk factor-based ASCVD risk estimates, BAC detected by digital mammography, and CAC determined from nongated chest computed tomography (CT) imaging for noncardiac clinical indications (6). Chest CT was used to derive a semiquantitative ordinal CAC score that has been validated to robustly relate to information obtained by traditional prospective gated cardiac CT. Presence of BAC was seen in 42% of women undergoing mammography as compared with more conservative estimate of 10% to 12% in the literature. This can likely be attributed to the fact that the authors used digital mammography and, more importantly, this was a highly selected and risk-enriched cohort with pulmonary disorders and at

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higher risk for lung cancer requiring chest CT testing and not representative of the general population of women undergoing routine mammography. Overall 47% of women had CAC on chest CT performed within 1 year of mammography. A significant new finding is that, in fully adjusted risk factor model, BAC seems to demonstrate the strongest independent association with elevated CAC (more so even than age or presence of hypertension). Furthermore, added information of BAC compared with risk factor–based estimates was superior in discriminating those with and without elevated CAC burden (6).

In our viewpoint, the most implicating finding of the current study lies within the BAC's robust positive predictive value of nearly 70% for identifying women with presence of CAC. Even among younger women, 50% with BAC had demonstrable CAC. This association may be slightly underestimated considering nearly 5% to 10% with any coronary calcification can be missed with nongated chest CT. In fact, recently Mostafavi et al. (7) demonstrated a superior positive predictive value of 83% for presence of any coronary artery disease on coronary CT angiography among a more represented population undergoing mammography. As such, even by conservative estimate of 10%, approximately 4 million women nationwide undergoing screening mammography will exhibit BAC, with 2 to 3 million of them likely to have signs of premature coronary atherosclerotic disease.

Whether the best use of BAC is to trigger additional testing or to directly inform preventive treatment decisions, either by flagging high-risk women to their providers or by reclassifying traditional ASCVD risk estimates, is worth further discussion. The study authors advocate that it may be reasonable to recommend further CAC testing in those with BAC, because it will allow matching intensity of therapy based on CAC burden. Alternatively, in the future one can consider breast cancer screening via dedicated breast CT instead of mammography. Thus, protocols to image the breasts for cancer and the chest for CAC at the same visit could represent an exciting dual-screening approach. Indeed, in selected women, triple screening for breast cancer, lung cancer, and atherosclerosis with CT seems a viable and realistic option.

Can these women be classified as high risk even without proceeding with CAC testing? Extrapolating from the current study, most of those with BAC will have presence of CAC; only 2 to 3 per 10 women will have CAC of 0 to be categorized as low ASCVD risk. This potential minimal misclassification is significantly less than what we observe with current guidelines that overestimate risk in approximately one-half of those considered for therapy. To put things into perspective, risk of coronary atherosclerotic disease with presence BAC if not greater, is likely comparable with diabetes, a condition associated with an approximately 50% chance of having any CAC in women of similar age. As a result, considering the low incremental information and added cost, the yield from supplementary CAC testing among BAC-positive women is likely minimal. We believe rather than debating what we should recommend in these situations, we are better off empowering our patients to take charge of their own decisions. These informed choices can only be facilitated by disclosing probability of subclinical ASCVD and reclassified risk with BAC to allow discussions whether the estimated benefit is worth committing to lifelong therapy.

Although it is exciting to contemplate future implications, at the same time, we should also take this opportunity to introspect on what has not been done so far, and why it took so long to have this conversation. Despite the fact that a tremendous amount of literature in the past has pointed attention that BAC significantly increases vulnerability for ASCVD outcomes (myocardial infarction, stroke, peripheral arterial disease, and even heart failure), lack of sustainable and standardization action by guidelines and societies in recognizing its risk, and subsequent incorporation in healthcare delivery protocols by the medical community, is discerning. Our stakeholders are well within their rights to question what threshold of critical information will inspire pragmatic changes in how we practice medicine.

Are more studies needed? Absolutely. Further investigations are critical to decipher interactions between ASCVD risk, BAC, and burden of atherosclerotic disease in predicting outcomes in more detailed granularity. However, as we aspiringly continue our journey toward new discoveries, we must also be cognizant not to discount existing knowledge that could provide significant value in our routine operations. Before pressing for new studies, let us pause to garner consensus on constructing best practices on what is already known. There is little doubt based on the principles of clinical equipoise that BAC detection should be actively pursued in all mammograms performed, and its reporting and subsequent management tracked as part of the core quality performance measures. Rather than another outcome study, our stakeholders are more likely to cherish investigations designed to explore better health-delivery models using information such as presented in the current study. The conventional response "lack of clinical trial" should not be allowed to justify current inertia, which has already impeded constructive dialogue

among stakeholders in other past similar situations. Unified advocacy efforts are the only solution to overcome what ails the current medical research enterprise. We owe this to the thousands of patients who have generously partnered with us in the past to produce this knowledge. Remaining a silent bystander waiting for another study and preserving status quo should not be an option.

For now, the excellent report by Margolies et al. (6) provides strong motivation for the following: supporting the widespread documentation of BAC in mammography reports; improving the education of primary care and radiology providers regarding the link between BAC and ASCVD; establishing related standard of care and performance measures; and stimulating further research for establishing best practices that can facilitate successful translation of this widely available, but often ignored, science.

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REFERENCES

1. Smith RA, Saslow D, Sawyer KA, et al. American Cancer Society guidelines for breast cancer screening: update 2003. CA Cancer J Clin 2003;53:141–69.

2. Force USPST. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2009;151:716–26, W-236.

3. Kerlikowske K. Evidence-based breast cancer prevention: the importance of individual risk. Ann Intern Med 2009;151:750–2.

4. Amin NP, Martin SS, Blaha MJ, Nasir K, Blumenthal RS, Michos ED. Headed in the right direction but at risk for miscalculation: a critical appraisal of the 2013 ACC/AHA Risk Assessment Guidelines. J Am Coll Cardiol 2014;63:2789–94.

5. Iribarren C, Molloi S. Breast arterial calcification: a new marker of cardiovascular risk? Curr Cardiovasc Risk Rep 2013;7:126–35.

6. Margolies L, Salvatore M, Hecht HS, et al. Digital mammography and screening for coronary artery disease. J Am Coll Cardiol Img 2016;9:350–60.

7. Mostafavi L, Marfori W, Arellano C, et al. Prevalence of coronary artery disease evaluated by coronary CT angiography in women with mammographically detected breast arterial calcifications. PLoS One 2015;1:e0122289.

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