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EDITORIAL COMMENT

Sharpening the Focus on Causes of Ethnic Differences in Aortic Stiffness*

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With cardiovascular disease responsible for the largest global burden of disease, there is a strong imperative to improve health systems for identifying and mitigating cardiovascular risk factors. The measurement of aortic stiffness can help in this regard, as it is a proven marker of organ damage that is associated with adverse cardiovascular outcomes independent of conventional Framingham risk factors (1). Normal and reference values have been derived for the gold standard measure of aortic stiffness (carotid-to-femoral pulse wave velocity) (2) and is recommended in some international guidelines as a credible biomarker in preventive cardiology to stratify individual risk (3). Increased aortic stiffness can be interpreted as a marker of early vascular aging (4), especially important in understanding exaggerated cardiovascular risk evident among specific patient, or ethnic, populations.

Black and Hispanic people present with a high prevalence of risk factors leading to early and severe cardiovascular disease (5). Multiple risk factors synergistically compound overall risk but this does not completely account for the notably higher prevalence of end-organ disease and cardiovascular mortality among Blacks. Yet, the risk situation for Hispanics is less clear because despite higher prevalence of certain risk factors (i.e., diabetes, obesity, hypercholesterolemia, inactivity) mortality outcomes are generally more favorable than would be expected, thus giving rise to the so-called "Hispanic Paradox" (6). In this issue of *iJACC*, Goel et al. (7) present data from the Dallas Heart Study in which aortic stiffness was compared between Whites, Blacks, and Hispanics on the expectation that aortic stiffness would be especially raised among Blacks, thereby offering a conceivable mechanistic pathway to explain disproportionate hypertension prevalence and end-organ disease above and beyond traditional risk factors. The main findings were that both Blacks and Hispanics had higher aortic stiffness compared with Whites after full adjustment for all available covariates known or suspected to be associated with large artery stiffness. Of the 3 ethnicities, aortic stiffness was highest among Blacks.

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The study has several positive features including being a large population-based, multiethnic probability sample that was specifically designed to understand ethnic differences in adult cardiovascular health, and thus should have good external validity. A strong methodological approach was also used to characterize stiffness phenotypes between ethnic groups by direct measurement with the advanced technique of cardiovascular magnetic resonance imaging. Although causal mechanisms cannot be resolved, the analysis provides hypothesis-generating information on ethnic-specific factors contributing to aortic stiffness and cardiovascular disease risk. Many questions arise in particular as to what may account for the excessively raised aortic stiffness observed among Blacks. Given that aortic stiffness is highly dependent on blood pressure (BP), and with higher BP associated with greater increases in aortic stiffness over time, the potential influence of this variable on the findings warrants closer inspection.

As a cross-sectional study (7) it is unable to be determined the extent to which long-standing

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hypertension may induce aortic remodeling such that stiffness remains higher for a given level of office cuff BP. In support of this proposal, data from the Bogalusa Heart Study indicate a stronger sensitivity of BP towards remodeling of the carotid artery in Blacks (8). Other investigations suggest a possible reduction in small artery elasticity independent of BP in Blacks (9). So for a given BP level, arterial structural abnormalities seem more likely with Black ethnicity. However, BP measurement itself could be influencing interpretation of these data. Differences of >20 mm Hg in central (aortic) systolic BP can occur between people with similar brachial cuff BP, thus measuring BP at the peripheral level may give an inaccurate estimation of the true aortic BP loading (10). Indeed, Heffernan et al. (11) have shown elevated central BP among young Black men despite similar cuff BP compared to Whites. If such central-to-brachial BP ethnic disparities came forth in future examination of the Dallas Heart Study cohort, this could go a long way to explaining their findings on aortic stiffness.

We have concentrated on the idea that an elevation in aortic stiffness is the consequence of raised BP, but as alluded by Goel et al. (7), aortic stiffness could be the cause of raised BP (12). The more complex reality is likely to be a combination of each view, where on the one hand hypertension can lead to structural arterial stiffening from increased circumferential wall stress and promotion of matrix synthesis (and wall thickening), whereas on the other, hypertension can result from a hemodynamic response to diffuse structural arterial stiffness. In either case, a positive feedback relationship resulting in exacerbation of both aortic stiffening and high BP is likely at play (13,14), and a phenomenon amplified in Black people. This emphasizes the obligation for better identification of the problem (raised stiffness and/or BP) and appropriate intervention to rectify, with the most likely effective means to achieve this by antihypertensive medications and lifestyle, in particular with regular exercise and dietary sodium reduction.

As with all stimulating research, many questions arise from the work by Goel et al. (7). Could the impairment of aortic remodeling and relatively smaller aortic area be due to defects in endothelial function? Is there any difference in salt and potassium intake between groups, and what could be their influence on arterial mechanics? How may ethnic differences in arterial wall structural components amplify stiffness (14)? What is the role of cardiac, and combined cardiac (left ventricular)-vascular interaction on stiffness? Is there a genetic component in the observed vascular abnormalities (15)? The Dallas Heart Study cohort gives an opportunity for exploring these latter 2 questions. Additionally, while acknowledging that it is impossible to account for all covariables, other socio-demographic factors not considered, but relevant to the question of ethnic differences in aortic stiffness, include such things as the level of physical fitness, depression (16), perceived racism (17), and menopause status (18), to name a few. Altogether the work of Goel et al. (7) sharpens the focus towards gaining better understanding of the underlying mechanisms involved in aortic stiffness and constitute an important step towards ultimately refining and maximizing intervention strategies to reduce risk among people of different ethnicity.

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