Coronary Calcium, Race, and Genes

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Measurement of coronary calcium has become a useful tool in the investigation of coronary disease and risk, as evidenced by the companion articles in this issue examining the relationship of race and genetic factors to coronary calcium.1,2 Newman et al3 report racial differences in coronary calcium measures in older adults participating in the Cardiovascular Health Study. Among 471 white and 143 black participants with an average age of 80 years, median coronary calcium scores were lower in blacks than in whites, particularly in men, even after adjustment for other black-white differences. Black men were only 20% as likely, and black women 71% as likely, as whites to have increased calcium scores. In the small subgroup of participants with myocardial infarction, who might be expected to be more similar, calcium scores still were lower among blacks than whites.

These findings may cause us to question the premise that coronary calcium and clinically overt coronary disease have common antecedents, but other explanations should first be considered. More limited access to medical care and less aggressive risk factor management in blacks might be expected to produce more, rather than less, coronary disease in blacks, and in fact, blacks recruited into the Cardiovascular Health Study generally had worse health indicators at entry than their white counterparts.6 Of the many biases that may be considered. More limited access to medical care and less aggressive risk factor management in blacks might be expected to produce more, rather than less, coronary disease in blacks, and in fact, blacks recruited into the Cardiovascular Health Study generally had worse health indicators at entry than their white counterparts.6 Of the many biases that may be considered. 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The real issue may then not be to explain black-white differences in calcium but to explain interindividual differences in calcium-overt disease relationships so that calcium measures may be more effectively used to guide therapy. While one could argue strenuously against the concept of...
tailored therapeutic approaches based on race, which in itself has little biologic meaning, one could strongly support the concept of tailored approaches based on differences in risk factors and subclinical disease indicators. Much needed research to develop these approaches, unfortunately, remains to be done.

The article by Lange et al\textsuperscript{2} reports a genome-wide linkage scan in 105 Caucasian sibships drawn from the Genetic Epidemiology Network of Arteriopathy (GENOA) study. Coronary calcium was assessed by using similar methods as the previous study but was dichotomized above and below the 70th percentile value rather than analyzed as a continuous, or quantitative, trait. Regions on chromosomes 6 and 10 were shared more often among siblings similar for calcium presence than among siblings dissimilar for this trait. Linkage was stronger for the chromosome 10 region, which contains genes related to collagen and bone formation. No excess sharing was seen in regions linked to a number of previously reported candidate genes.

Lange et al\textsuperscript{2} note that their sample had a high prevalence (77%) of hypertension and that this may have influenced their ability to detect linkages in regions not previously identified by other investigators and vice versa. That genetic variants may have different associations with outcome in the presence of different risk factors has been demonstrated repeatedly, for example, for the apolipoprotein E4 allele and coronary risk factors such as smoking and elevated cholesterol.\textsuperscript{9,10} Common apolipoprotein E genotypes have even been shown to modify the relationship of common risk factors and coronary calcium prevalence.\textsuperscript{11} It is conceivable, and perhaps rather likely, that the impact of genetic polymorphisms on disease risk differs in the presence of other risk factors such as hypertension. If this is true, it could be quite relevant to the understanding of racial/ethnic differences in clinical coronary disease and coronary calcification, particularly for those who would interpret racial differences as evidence of genetic or biologic differences by race. Although there clearly are racial differences in allele frequencies at many loci, there is much more genetic variation within racial/ethnic subgroups than between them.\textsuperscript{12} The combination of (1) differing frequencies of genetic variants related to calcification and (2) different prevalences and severities of risk factors for calcification among racial/ethnic groups may indeed be expected to manifest as racial differences in the presence and prognostic significance of coronary calcium. The search is on for genes related to coronary calcification and, perhaps more importantly, the genetic variants that affect the relationship of calcium to development of overt disease. These variants must not be studied in isolation, without consideration of the other risk factors with which they undoubtedly interact, just as black-white differences must not be interpreted without consideration of the many social, medical, and physiological concomitants of race.

What are the clinical implications of these findings? They would appear limited at present, as the clinical implications of coronary calcium itself have yet to be fully elucidated. It is probably reasonable to conclude that low calcium scores in blacks should not deter the practicing physician from optimal risk factor management, just as they should not in whites. The significance of absent calcium, which is taken by many researchers to indicate a very low likelihood of subsequent coronary events, may be less clear in blacks, but this remains to be determined in long-term studies including adequate and population-based samples of blacks. In the interim, calcium imaging can potentially be utilized as a motivational tool for encouraging coronary risk reduction, regardless of race, when calcium is present. The implications of its absence in designing preventive strategies for coronary disease, particularly among blacks, remain to be determined.

References


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