American Heart Association.

Biomarkers in Cardiovascular Disease: The Dilemma of Racial Differences

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Racial differences in medicine are still a matter of debate, with the scientific community divided on the real meaning and relevance in medical research.[1,2] The view is that classic racial categories identify subgroups with different disease epidemiological features, pattern, and prognosis, posed for the so-called racial medicine. On the other hand, the concept that race is a social construct, without biological roots, led to the statement that the use of race as a biological factor is "problematic at best and harmful at worst." [3] Indeed, there is a tendency to assume that differences between subgroups are caused by genetics, rather than socioeconomic or cultural factors. This concept led to the use of the term ethnicity rather than race, with the aim of indicating a group of people who identify on the basis of a supposed shared genealogy or cultural similarities (eg, language, society, culture, or nation). Some scientists fear that the use of race as a variable in medicine can perpetuate historical discriminatory attitudes[2] (eg, limiting the use of particular drugs or procedures to a particular racial subgroup).

However, genetic studies show that there seems to be more genetic variation (95%) within a group than between so-called racial groups (5%).[4] To date, nearly all geneticists reject the concept that biological differences are caused by racial differences,[5] whereas epidemiological and clinical studies continue to find association between clinical findings and the social identities of research participants. In particular, in cardiovascular disease (CVD), the difference in drug response and its association with race have been well demonstrated[6]: the attenuated response to angiotensin-converting enzyme inhibitor therapy in black compared with white patients in heart failure and hypertension,[7–9] the prevalence of cardiovascular and metabolic diseases,[10,11] and prognosis,[12] when subjects are grouped on the basis of racial categories.

In European populations, statistics on ethnicity or race present challenges with acquiring data (ie, legal prohibitions, data protection provisions, and political reluctance). Mapping Europe on the basis of geographical location allows for collecting "race or ethnic statistics" that adjust for the aforementioned challenges.[13] In Europe, even when geographical location rather than race is considered, a recent report showed regional differences in levels of a gut microbiome-related biomarker, trimethylamine N-oxide, in a European population with >99% of patients being white regardless of confounders.[14] These discrepancies are a complex interaction between factors that include socioeconomic status, structural differences, and ethnic influences.

In this context, Hackler et al reported, in this issue of the *Journal of the American Heart Association* (*JAHA*), on the association between race and a panel of biomarkers, with known or possible informative cardiac and metabolic roles, in a multiethnic population cohort without known CVD[15] enrolled in the DHS (Dallas Heart Study).[16] In the final cohort of 2635 subjects (1638 black and 997 white), with a 10 years of follow-up, 32 biomarkers were investigated. The results showed the rate of CVD events in blacks was more than twice higher than in whites. In line with other studies,[17] diseases such as arterial hypertension and diabetes mellitus were more frequent in blacks, and a difference in echocardiographic parameters (left ventricular mass, left ventricular end-diastolic volume, and coronary calcium) was observed between blacks and whites.[18] For differences in biomarker levels after multivariate adjustment, when compared with whites, blacks showed significant differences in Lipoprotein(a) concentration, adipokine levels, inflammatory biomarkers, endothelial biomarkers, and myocyte injury/stress (lower NT-proBNP [N-terminal pro-B-type natriuretic peptide] and higher ST2 [cardiac biomarker]). Furthermore, black women had higher

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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J Am Heart Assoc. 2019;8:e014295. DOI: 10.1161/JAHA.119.014295.

rates of microalbuminuria, whereas black men had higher high-sensitivity troponin T levels. Notably, when these biomarkers were used in exploratory analyses for association with outcomes, differences in the rate of CVD were no longer significant, suggesting that these pathways can contribute or mediate the observed difference in CVD rate among the 2 groups.

The observed association of CVD events with blacks is mediated by the described different biological patterns expressed by the subjects (resulting in the difference in biomarkers). Even if the DHS has been deeply phenotyped, with data on traditional risk factors and possible confounders available (eg, socioeconomic status), the design of the study argues that these differences can be explained as genetic differences rather than as the presence of other factors (eg, social state, educational state, dietary habits, nutritional state, and physical activity); hence, these are ethnic differences more than racial differences. Accordingly, it has been demonstrated that the higher incidence rate of venous thromboembolism in blacks when compared with whites can be mostly explained by a difference in distribution of risk factors.[19] Similarly, in the present study, blacks had more insulin resistance and diabetes mellitus, black men were more often smokers, and black women had higher body mass index when compared with white women. Consistent with well-documented socioeconomic differences between blacks and whites that impact on CVD rate and prognosis,[20] black participants in the present study reported lower education and income compared with white participants.

Following a definition provided in the past by one of the authors of the present investigation,[21] there are 3 criteria that define the clinical usefulness of a biomarker: (1) it has to be accurate, reproducible, cost-effective, and time effective; (2) the biomarker must provide information that is not already available; and (3) the measurement of the biomarker should support the clinician in medical decision making. In line with these concepts, the present investigation focused on the strategy of investigating multiple biomarkers of several pathophysiological pathways that provided information that may be potentially useful in legitimate epidemiological observations.[21] To date, this appears the most promising strategy that can help to go beyond the limits of the current management of CVD.[22]

In conclusion, the present report describes differences of multiple biomarkers, possibly or known to be, related to cardiometabolic diseases in healthy subjects grouped on the basis of the definition of race as black and white. Even if limited by the fact that there is a consensus that "race" is a weak surrogate for various genetic and nongenetic factors in correlations with health status,[23] the finding of the present study can be considered as hypothesis generating, providing additional information about the dilemma of racial differences in medicine and allowing the pursuit of advancing tailored medicine.

Disclosures

None.

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Key Words: Editorials • biomarker • cardiovascular disease • racial differences