Circulation: Arrhythmia and Electrophysiology

EDITORIAL

Race and Socioeconomic Status Regulate Lifetime Risk of Atrial Fibrillation

See Article by Mou et al

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Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, affects over 33 million people worldwide and significantly increases risk for stroke, heart failure, and death.[1] Genetic and acquired AF risk factors contribute to the initiation and maintenance of AF in susceptible individuals; however, this interaction is complex and incompletely characterized across race-ethnicities.[2,3] Data from large-scale genome-wide association studies suggest that genetic susceptibility to AF varies across race-ethnic groups, and there is also a differential response to antiarrhythmic therapy based on these differences.[4,5] Thus, it has become increasingly accepted that race-ethnicity is a strong modifier of both genetic and acquired risk factors in AF.[6,7]

Most clinical studies to date are limited by the enrollment of a predominantly white population of European descent.[8] This potential enrollment bias may lead to under- or overestimation of AF incidence and other sequelae in nonwhite groups.[9] More recent data suggest that both African Americans (AAs) and Hispanic/Latinos may disproportionately experience hospitalizations, stroke, and heart failure resulting from AF. However, the mechanisms for these observations remain poorly understood especially in light of the AF paradox that AAs and Hispanic/Latinos have been reported to have a lower incidence of AF, despite higher prevalence of AF risk factors in some populations.[7,9,10] More broadly, the INTERSTROKE study (International Stroke), which included 32 countries on 6 continents, demonstrated that AF incidence and stroke risk vary by race-ethnic origin and geography and that risk of AF sequelae remains highest among Southeast Asians.[11] Conversely, clinical studies such as the MESA (Multi-Ethnic Study of Atherosclerosis) and the CHS (Cardiovascular Health Study) have shown a more limited role for race-ethnicity associated genetic background in the promotion of certain AF mechanisms, such as the contribution of FGF (fibroblast growth factor)-23 to atrial dysfunction.[12] Thus, although clinical studies have determined that AF may be modified by race-ethnic background, the contributing mechanisms remain largely unknown. This creates a critical need for clinical and translational studies that help define AF and related stroke risk factors among different race-ethnicities.

The National Institutes of Health–sponsored ARIC (Atherosclerosis Risk in Communities) Study is a prospective epidemiological study of atherosclerosis in 4 communities, which examines cardiovascular disease risk and incidence by race, sex, location, and date.[13] This has been a powerful study for the determination of how race-ethnicity influences the incidence of cardiovascular disease in primarily white and AA populations. In this issue of *Circulation: Arrhythmia and Electrophysiology*, Mou et al[14] use this valuable resource to provide more granular data on AF incidence in AAs versus whites in the ARIC Study and determine the lifetime risk of AF controlled for

Key Words: Editorials ■ atrial fibrillation ■ ethnic groups ■ incidence ■ prevalence ■ risk factors

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socioeconomic status. The group studied 15 343 ARIC patients for whom detailed socioeconomic status data and AF data were available. AF was determined from ECGs, hospital discharge records, and death certificates. Individual predicted 5-year risk was calculated based on the CHARGE-AF score (Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation), a validated AF risk scoring system in diverse populations in the United States and Europe.[15] The investigators determined that white men had a higher CHARGE-AF score at baseline than white women and AA men and AA women and that across categories of income and education, white patients had a lower prevalence of cardiovascular risk factors than AA patients. Overall, white men had a significantly higher incidence of AF than AA women, AA men, and white women. Lifetime risk of AF in whites was 33% and in AAs was 21%. Income and educational attainment were inversely associated with lower rates of AF, but not lifetime risk of AF, especially in white women. The authors postulated that this effect may have been mediated by longer survival in patients in higher socioeconomic groups, especially because age is a strong determinant of AF incidence.

From the data, it is clear that age is a major driving force for the development of AF in both AAs and whites and across demographic characteristics such as income, educational attainment, and sex. Even after incorporating death as a competing risk in the ARIC population, white men had a significantly higher risk of developing AF versus the other groups; although interestingly, AF incidence was similar among both AA men and AA women, corresponding to a similar baseline CHARGE-AF score. There are as yet little genetic data to support this finding. One possibility includes a report by Schnabel et al,[16] who described that whereas the chromosome 4q25 AF risk single-nucleotide polymorphism rs4611994 is associated with AF risk in both AA and whites, the *IL6R* gene single-nucleotide polymorphism rs4845625 is associated with AF risk in whites, but did not reach significance in AA patients. Whether this genetic association may explain these findings in the current ARIC study remains to be determined. Another interesting observation in this study is the cumulative incidence of AF among the 4 groups, showing that white women had a similar cumulative incidence of AF to AA women and AA men until about 77 years of age, when there was a marked increase in rate of AF incidence. Further studies may provide more insight into the potential mechanism(s) of this departure in AF risk among white women patients susceptible to AF.

The lifetime risk for AF in European white has been determined by the Framingham Heart Study,[17] but the study by Mou et al[14] is the first to estimate the lifetime risk in AAs and determine whether socioeconomic status plays a role in AF incidence. Additional strengths of this study include a well-characterized and large cohort of white and AAs followed over 2 decades, a validated approach for the ascertainment of AF and the novel finding AA women have increased lifetime risk for AF when compared with AA men. Though the study has many strengths there are a few limitations that should be addressed in future investigations. First, as the authors note, AF burden is commonly a driver of AF outcomes, such as heart failure and stroke.[18,19] In this study, we do not have the benefit of knowing whether patients developed paroxysmal, persistent, or permanent AF. Similarly, ARIC has historically provided rich data on heart failure outcomes, cognitive decline, and stroke, and these data would be helpful to further define the functional significance of AF incidence. Second, although ARIC primarily defined AA and white populations, data on other ethnicities enrolled would be helpful to determine how complexity across races affects AF outcomes. Third, detection of AF was periodic, which could have theoretically missed paroxysms of AF; although outside the scope of the original ARIC Study, implantable loop recorders would be a useful adjunct to more completely quantify incidence in this population. Fourth, a major focus of this analysis was the relationship between lifetime risk of AF and socioeconomic status. However, family income and individual education was self-reported and has not been validated.

The authors are to be commended for a thoughtful, thorough evaluation, and comparison of AF incidence in AA and white patients enrolled in the ARIC Study. Given that the mechanisms of AF are complex and include a significant acquired and genetic component, a fundamental understanding of the roles of race-ethnicity in AF risk is incomplete without granular data describing incidence in nonwhite populations. Further studies into this complex interaction will be needed to achieve the goals of precision medicine and treatments for individuals susceptible to AF.

ARTICLE INFORMATION

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Sources of Funding

This work was in part supported by National Institutes of Health K08 HL130587 (M. McCauley) and R01 HL092217 and R01 HL138737 (D. Darbar) grants.

Disclosures

None.

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Circ Arrhythm Electrophysiol. 2018;11:
doi: 10.1161/CIRCEP.118.006584
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 1941-3149. Online ISSN: 1941-3084