Editorial

Separate and Unequal: Cardiovascular Medicine in Black Americans

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Black patients in the United States fare worse with respect to key cardiovascular risk factors and outcomes, with substantially increased lifetime risk of hypertension, heart failure, and stroke than White patients.1 Race-based differences in outcomes are likely multifactorial and reflect imbalances in disease ascertainment as well as access to, and delivery of, care. Although most investigations of race-based disparities in cardiovascular medicine have focused on common diseases, 2 studies in the current issue of the Journal of the American Heart Association (JAHA) expand the focus on race to hypertrophic cardiomyopathy (HCM),2 a relatively rare cardiovascular disease managed best at specialty centers, and to the design of cardiovascular clinical trials3 with respect to enrollment of Black patients.

See Articles by Arabadjian et al. and Prasanna et al.

HCM is the most common genetic cardiomyopathy, with an estimated population prevalence of 1:500, and is an important cause of heart failure, sudden cardiac death, and stroke. Approximately 50% of HCM is caused by dominant mutations in sarcomere genes that are typically unique (or private) to individual families.4 The genetics of HCM are in contrast to genetic diseases, like sickle cell anemia or hemochromatosis, where endemic diseases (ie, malaria and bubonic plague) select for common variants that vary in population frequency among different races. As HCM is caused by spontaneous rare variants unrelated to selection pressures, the frequency is not expected to vary by race or ancestry.

Prior investigation of the presenting characteristics and outcomes of Black patients with hypertrophic HCM has revealed that Black patients are underrepresented in US HCM specialty centers, with 5% in a single-center study5 and 8% in a multicenter study.6 Moreover, Black patients are younger, are more likely to have hypertension and obesity, are more likely to present with apical hypertrophy,7 and have a higher burden of severe heart failure symptoms.8 In the largest study examining race-based differences in HCM to date, Black patients were less likely to undergo genetic testing, and less likely to have a sarcomere mutation when testing was performed.6 In that study, septal reduction therapies were less frequently used in Black patients, whereas the use of implantable cardioverters-defibrillators did not differ by race.

In their study, Arabadjian et al further investigate race-based differences in HCM expression and outcomes.2 Like several prior studies, this was a single-center investigation of a large HCM referral program nested within an academic medical center (New York University). They restricted their analysis to self-identified White and Black patients and excluded patients with prior septal reduction therapies in whom preprocedural cardiac imaging was unavailable. Relatively unique to this investigation was the categorization of patterns of left ventricular remodeling into basal, subbasal, or diffuse based on the distribution of hypertrophy and the choice

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of composite outcomes, particularly "major HCM interventions," which were composed of septal reduction therapy, transcatheter mitral edge-to-edge anastomosis, and implantable cardioverter-defibrillator placement for primary prevention.

The key findings were generally in keeping with prior investigation. Black patients were again underrepresented, accounting for 13% of the final cohort, in comparison with the demography of New York City, which is 24% Black individuals (US Census data). The authors leveraged the strengths of a single-center study by providing more detailed phenotypic characterization than is typically available in a multicenter study. For example, the relatively high frequency of cardiac magnetic resonance imaging in Black and White patients (79% versus 58%), use of medical therapy, and comorbidities were notable. Compared with White patients, Black patients were more likely to have apical remodeling (39% versus 15%) and diffuse left ventricular hypertrophy (11% versus 4%), whereas White patients were more likely to have basal left ventricular hypertrophy and associated left ventricular outflow tract obstruction. Genetic testing was performed in <50% of patients, but neither the provision of genetic testing nor the frequency of sarcomere mutations differed by race in this underpowered analysis. The key outcome difference reported was the higher rate of implantable cardioverter-defibrillator therapies in Black patients; however, this was based on a limited number of ventricular tachyarrhythmia events (n=5), which included antitachycardia pacing.

Although Arabadjian et al add to our understanding of race and HCM, much remains to be done. A key limitation of this study is shared with all prior scholarship in this field. Ascertainment of HCM in Black and White patients is different. Not only are Black patients underrepresented, the paths by which a Black patient is referred into an HCM center is different than in White patients. In this study, the patients excluded from analysis for prior septal reduction therapy were almost exclusively White patients (99%), indicating that White patients were more likely referred to New York University for management of obstruction. Thus, we have limited capacity to gain insight into race-based differences in biology by simply comparing baseline characteristics of all-comer Black and White patients in this cohort. Indeed, the null hypothesis that there are no race-based differences in HCM biology is strong. On what prior basis would we expect sarcomere mutation expression to differ according to the construct of race? One method for overcoming this limitation is to focus race-based comparative analysis in the subset of patients with sarcomeric HCM. This addresses the heterogeneity of the population with non-sarcomeric HCM, in whom underling risk factors likely contribute to subsequent outcomes. Even then, using race (especially self-reported) as a proxy for modifying genetic factors is inadequate. Indeed, the shared legacy of structural racism, including decreased access to care and burden of other relevant cardiovascular risk factors (namely, hypertension), is more likely to influence differences in HCM outcomes in Black patients than ancestry. Future studies should include socioeconomic and ancestral data to understand how these factors impact the journey of Black patients with HCM. Most important, the HCM community should identify the key barriers that have prevented Black patients from receiving care at a referral center, an established priority in consensus guidelines. This will include educating referring providers to suspect HCM when left ventricular hypertrophy is identified in Black patients, and to ensure that access to specialty care is not limited by transportation, insurance, or other socioeconomic factors that differ by race.

The challenge of improving access to cardiovascular outcomes for Black patients extends to participation in clinical trials, where Black patients are underrepresented well below the burden of cardiovascular disease they bear. Different factors that influence the low representation of Black patients in clinical trials are difficult for trialists to address, including socioeconomic status, access to transportation, and distrust of the biomedical research establishment. However, using the design of clinical trials to recruit Black patients is directly under the control of investigators and is the subject of a study from Prasanna et al. They focused on cardiology treatment trials conducted in the United States in the past 20 years, which were supported by the National Institutes of Health. On the basis of the burden of cardiovascular disease in the Black community, the investigators considered adequate diversity when ≥25% of a study cohort was Black race.

They searched for qualifying clinical trials using clinicaltrials.gov, and reviewed protocols where available to characterize the plan for recruitment of Black study subjects as passive, active, or community based. The latter involved the use of community spaces or community members outside of medical institutions to recruit participants. They identified 100 trials that met their inclusion criteria, of which 62 had available study protocols. Among this group, the racial breakdown of study participation was reported for 53 trials, with 19 achieving enrollment of ≥25% Black participants. However, they did not identify that different recruitment strategies (eg, passive versus active versus community based) were associated with an increase in Black subject participation. Moreover, the representation of Black patients in trials did not increase over time.

Certain design elements limit the insight that can be gained from this study and could have underestimated the magnitude of the problem. Focusing on studies where the recruitment plan was available may have biased toward studies that prioritized diverse recruitment. Moreover, the generic 25% target does not reflect the catchment of the patient population available
to investigators. For example, studies conducted in diseases overrepresented in Black patients (eg, pulmonary hypertension secondary to sickle cell anemia) or in regions with a large Black population should have much higher Black representation. Important study elements are absent from their analysis, including the number of patients included in each trial and the diseases studied. Moreover, the investigators are underpowered to examine the effect of different recruitment strategies. Despite these limitations, the authors are to be congratulated for prioritizing study design in addressing this key disparity. Future work could include prospectively studying different recruitment strategies as an experiment nested within traditional clinical trials. Funding agencies and regulators should monitor diversity prospectively and actively incentivize investigators to enroll Black patients. The power of randomization should be used to achieve these goals.

Both studies highlight work that is required to improve the cardiovascular care of Black patients, yet demonstrate the limitations of contemporary disparities research in cardiovascular medicine. One strength of both studies is the role played by nurse investigators in this critical scholarship. Nurses may provide a less anachronistic approach to the problem of disparities than the traditional academic community. The power of unconventional study design and personnel was perhaps best exemplified in the Black barbershop study, which should serve as inspiration for future investigators.

ARTICLE INFORMATION

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REFERENCES

1. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al.; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2021 update. Circulation. 2021;143:E254–E743. DOI: 10.1161/CIR.0000000000000950.

2. Arabadjian M, Yu G, Sherrid MV, Dickson VW. Disease expression and outcomes in Blacks and Whites with hypertrophic cardiomyopathy. J Am Heart Assoc. 2021;10:e019978. DOI: 10.1161/JAHA.120.019978.

3. Prasanna A, Miller HW, Wu Y, Peeler A, Ogungbe O, Plante TB, Juraschek SP. Recruitment of Black adults into cardiovascular disease trials. J Am Heart Assoc. 2021;10:e021108. DOI: 10.1161/JAHA.121.021108.

4. Cirino AL, Harris S, Lakdawala NK, Michels M, Olivotto I, Day SM, Abrams DJ, Charron P, Caleshu C, Semsarian C, et al. Role of genetic testing in inherited cardiovascular disease: a review. JAMA Cardiol. 2017;2:1153–1160. DOI: 10.1001/jamacardio.2017.2352.

5. Wells S, Rowin EJ, Bhatt V, Maron MS, Maron BJ. Association between race and clinical profile of patients referred for hypertrophic cardiomyopathy. Circulation. 2018;137:1973–1975. DOI: 10.1161/CIRCULATIONAHA.117.032838.

6. Eberly LA, Day SM, Ashley EA, Jacoby DL, Jeferies JL, Colan SD, Rossano JW, Semsarian C, Pereira AG, Olivotto I, et al. Association of race with disease expression and clinical outcomes among patients with hypertrophic cardiomyopathy. JAMA Cardiol. 2020;5:83–91. DOI: 10.1001/jamacardio.2019.4638.

7. Sorensen LL, Pinheiro A, Dimanov VL, Pozios I, Nowbar A, Liu H, Luo H-C, Lin X, Olsen NT, Hansen TF, et al. Comparison of clinical features in blacks versus whites with hypertrophic cardiomyopathy. Am J Cardiol. 2016;117:1815–1820. DOI: 10.1016/j.amjcard.2016.03.017.

8. Watkins H. Time to think differently about sarcomere-negative hypertrophic cardiomyopathy. Circulation. 2021;143:2415–2417. DOI: 10.1161/CIRCULATIONAHA.121.053527.

9. Bailey ZD, Feldman JM, Bassett MT. How structural racism works—racist policies as a root cause of U.S. racial health inequities. N Engl J Med. 2020;384:768–773. DOI: 10.1056/NEJMp2025396.

10. Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, Evanovich LL, Hung J, Joglar JA, Kantor P, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy. Circulation. 2020;142:E254–E743. DOI: 10.1161/CIR.0000000000000937.

11. Tahhan AS, Vaduganathan M, Greene SJ, Alrohaibani A, Raad M, Gafeer M, Mehran R, Fonarow GC, Douglas PS, Bhatt DL, et al. Enrollment of older patients, women, and racial/ethnic minority groups in contemporary acute coronary syndrome clinical trials: a systematic review. JAMA Cardiol. 2020;5:714–722. DOI: 10.1001/jamacardio.2020.0359.

12. Victor RG, Lynch K, Li N, Blyler C, Muhammad E, Handler J, Brettler J, Rashid M, Hsu B, Faxon-Drew D, et al. A cluster-randomized trial of blood-pressure reduction in black barbershops. N Engl J Med. 2018;378:1291–1301. DOI: 10.1056/NEJMoa1712520.