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A Global Perspective of Racial Differences and Outcomes in Patients Presenting with Acute Heart Failure

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Conflicts of interest

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65 **Abstract**

66 Important racial differences in characteristics, treatment, and outcomes of patient with acute heart
67 failure (AHF) have been described. The objective of this analysis of the International REgistry to
68 assess medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure (REPORT-
69 HF) registry was to estimate racial differences in patients with AHF according to country income
70 level.

Research Letter

Important racial differences in characteristics, treatment, and outcomes of patients hospitalized for acute heart failure (AHF) exist.(1) Compared to White patients, Black patients in the United States (US) are younger with a high prevalence of comorbidities.(1) Similar findings in low- compared to high-income countries,(2) suggest a role for systemic socioeconomic factors in determining the characteristics and outcomes of patients with AHF.(1) We hypothesized that Black patients from the US would have a clinical profile and outcomes more similar to non-black patients from lower- and middle- income world-regions rather than to White patients in the US. Therefore, we investigated racial differences in patients with AHF according to country income level in the International REgistry to assess medical Practice with lOngitudinal obseRvation for Treatment of Heart Failure (REPORT-HF) registry.

REPORT-HF was a prospective, observational cohort study enrolling patients with a primary diagnosis of AHF from 44 countries and 358 sites between July 23, 2014, and March 24, 2017. Information on demographics, medical history, precipitant to hospitalization, treatment, and outcomes were collected (2). Precipitants were reported by the local investigator. Race was self-reported and classified as Black, White, Asian, Native American, Pacific Islander or other. We focused on Black, White, and Asian patients, with the primary comparison between Black and White patients in the US, given that the majority of Black patients were from the US, and other patients stratified by race and country income level based on 2017 World Bank criteria (3). Out of the original 18,553 patients, 16,212 patients self-identified as Black, White, or Asian. Other ethnicities were excluded due to low numbers. We investigated differences between ethnicities across regions using the Chi-squared-test, multivariable logistic regression, and Cox regression analyses. We allowed clustering of estimates around the center variable, adjusted for the MAGGIC

risk score(4), and tested for interactions between race for different outcomes. We calculated the MAGGIC risk score based on age, sex, ejection fraction, systolic blood pressure, body mass index (BMI), New York Heart Association class (NYHA), smoking status, history of smoking, diabetes, previous diagnosis of HF and being on ACEi/ARB or β -blockers. The MAGGIC score was imputed using Multivariate Imputation by Chained Equations with averaging over 5 imputation sets using default settings in R.

Of 16,212 patients, 9,656 identified as White, 833 as Black, and 5,723 as Asian; Black patients were mainly from the US (84%); White patients from middle- and high-income countries (MHICs, 96%); and Asian patients from low- and middle-income countries (81%). Black patients and patients from low-income regions were commonly <55 years (*Figure A*). In the US, Black compared to White patients were younger (odds ratio [OR] 1.93, 95% confidence interval [CI] 1.43-2.60), had more hypertension (OR 2.20, 95%CI 1.62-2.98), anemia (OR 1.27, 95%CI 1.07-1.50), and chronic kidney disease (CKD, OR 1.55, 95%CI 1.22-1.98); and less atrial fibrillation (AF, OR 0.48, 95%CI 0.38-0.60), or coronary artery disease (CAD, OR 0.67, 95%CI 0.52-0.87, *Figure B, supplementary table 1*) in multivariable analyses. In the rest of the world, patients from low-income countries were younger (OR 2.86, 95%CI 2.26-3.61), and had more anemia (OR 1.38, 95%CI 1.14-1.68) compared to those from high-income countries. Uncontrolled hypertension and non-adherence to medication/diet were more common precipitants for Black (39%) than White (24%) patients in the US ($P<0.05$, *Figure C*), and globally (35% versus 14% respectively, $P<0.001$). Black patients in the US (OR 0.57, 95%CI 0.42-0.77 versus White) were less likely to undergo coronary angiography when adjusting for CAD. There were no racial differences in HF medication at discharge (ACEi/ARB, β -blockers, and MRAs) in patients with left ventricular ejection fraction <40% in the US and globally.

In-hospital and 1-year post-discharge mortality was similar among races in the total cohort, or in the US; the lower in-hospital mortality for Black patients in the USA may reflect their younger age (*Figure D/E*). However, country income level modified this association, with higher mortality in Black patients compared to non-Black patients in middle-income countries but not in high-income countries (*Figure D/E*, $P_{\text{interaction}} < 0.05$). The one-year rehospitalization rate for AHF was much higher in the USA than in other world-regions and highest among Black patients in the US, compared to White patients in the US and other races globally ($P < 0.001$, *Figure E*).

This analysis shows that, (1) Black patients from the US and patients (predominantly Asian) from low-income countries were younger and had a high-risk factor burden. (2) One in three hospitalized Black patients in the USA was admitted with uncontrolled hypertension or non-adherence to diet/medication; and (3) despite similar discharge medications, 1-year rehospitalization rates were higher for Black compared to White patients. Our data confirm racial differences in AHF in the US,^(1,5,6) and extend prior studies by highlighting these racial differences in the context of regions of lower socioeconomic status in the world. Racial differences in mortality appeared worse in middle- compared to high-income regions, suggesting that racial disparities in outcomes might be amplified in regions at lower economic development. The high rates of readmission for HF precipitated by non-adherence to diet/medication, or uncontrolled hypertension in Black patients might be reduced by a targeted post-discharge strategy to prevent early readmission. (1) Limitations of the present analysis include potential selection bias of centers able to produce high quality data with limited loss to follow-up, non-adjudication of outcomes, precipitants to hospitalization were reported by the treating physician. Structural racism and physician bias might have led to more misclassification of Black patients as being non-adherent to

medication or diet. The number of black patients included outside of North America was low in REPORT-HF limiting our ability to disentangle race and country in our analysis.

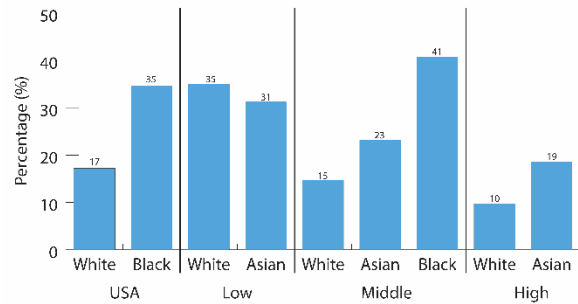
In conclusion, our results from a large global AHF cohort demonstrate significant racial differences and call for efforts to address the poor outcomes especially among Black patients.

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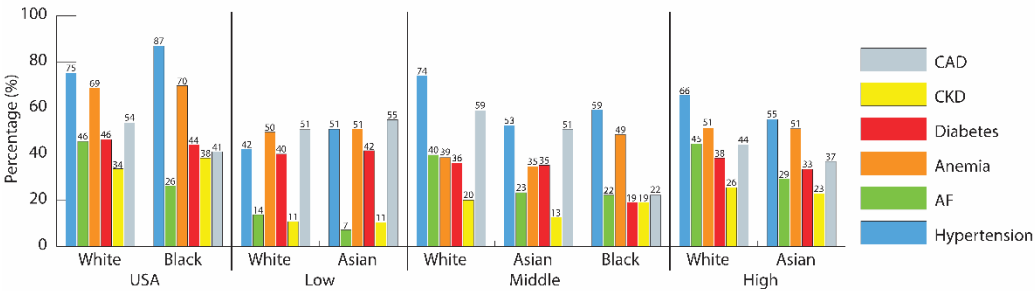
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Figure: Proportion of patients <55 years (A), prevalence of comorbidities (B), precipitating factors (C), in-hospital mortality (D), and post-discharge outcomes (E) according to race, USA and country income level. Abbreviations: ACS, acute coronary syndrome; AF, atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; HHF, hospitalization for heart failure; MI, myocardial infarction; USA, United States of America; WHF, worsening heart failure

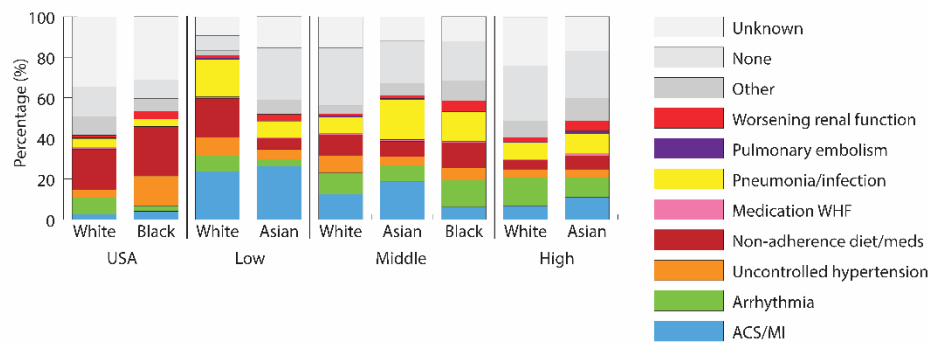
A: Proportion of patients <55 years



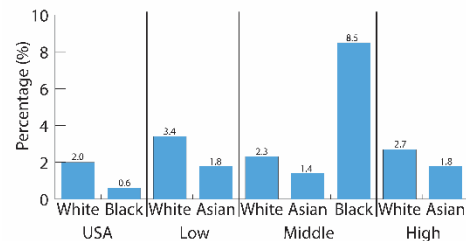
B: Prevalence of comorbidities



C: Prevalence of precipitants



D: In-hospital mortality



E: 1-year post-discharge outcomes

