

# Racial and Ethnic Differences in Heart Failure Etiology, Prognosis, and Management

Sheila Sahni · Tamara B. Horwich · Gregg C. Fonarow

Published online: 23 November 2014  
© Springer Science+Business Media New York 2014

**Abstract** Heart failure (HF) remains a major health care burden for the USA. Racial/ethnic groups in the USA are at increased risk for developing HF and incur higher rates of morbidity. Understanding the variations in the clinical syndrome of HF among different racial/ethnic groups is fundamental to addressing how to effectively treat these sub-groups. Despite evidence-based guideline-recommended medical and device therapy for HF, eligible patients from various racial/ethnic groups suffer disparities in receiving guideline-based HF therapy. The initiation of performance improvement programs has improved adherence to guideline-based therapy. The racial/ethnic differences that exist regarding the etiology and responses to medical therapy are fundamental to addressing ways to improve access to care, adherence, and overall survival in these at-risk groups. The review outlines racial/ethnic variations in the etiology, prognosis, and management with medical and device therapy for HF.

**Keywords** Heart failure · Race/ethnicity · Prognosis · Quality of care

## Introduction

Approximately 5.1 million adult Americans have the clinical syndrome of heart failure (HF), and this disease state results in substantial morbidity, mortality, and health care expenditures [1]. The prevalence is only increasing with a projected rise of

46 % over the next 20 years resulting in an estimate of over 8.1 million Americans affected. African-Americans, Hispanics, and potentially other racial/ethnic populations are at increased risk for developing HF, do so at an earlier age, experience higher morbidity, and possibly greater risk of death in younger age groups [2]. Epidemiological data suggests that by the year 2050, minorities will represent 50 % of the US population with Hispanics contributing the largest proportion of increase. Understanding racial/ethnic differences in the etiology, prognosis, and management of HF may be crucial in helping to guide initiatives aimed at promoting health equity, reducing the financial burden of HF, and improving outcomes.

The majority of data on racial/ethnic differences in patients with HF have been drawn from cross-sectional studies. Studies have demonstrated that African-American patients have a disproportionate greater burden of HF, higher rates of hypertensive heart disease as the etiology of HF, lower left ventricular ejection fractions (EF), and more symptomatic HF than white patients. Racial/ethnic differences in survival of patients with HF have been inconsistent with some studies reporting either similar or lower survival for African-American patients while others higher survival compared with white patients. There are even more limited data on the clinical characteristics, treatments, and outcomes for other race/ethnic groups. This leaves a large proportion of racial/ethnic groups that are not represented including those of Hispanic origin, Asians, Native Americans, and mixed race individuals. The United States Census Bureau 2000 definition of racial and ethnic categories is shown in Table 1 [3]. It is also important to acknowledge that published guidelines on HF management are based on studies that were performed on a predominantly white, non-Hispanic population. Of the literature available on treatment efficacy in non-white populations, the overwhelming majority is limited to data available on African-American patients. Given this degree of diversity, there remains a continued need for further understanding of racial/ethnic

This article is part of the Topical Collection on *Race + Ethnicity Disparities*

S. Sahni · T. B. Horwich · G. C. Fonarow (✉)  
Ahmanson-UCLA Cardiomyopathy Center, Ronald Reagan-UCLA  
Medical Center, 10833 LeConte Ave, Room 47-123 CHS, Los  
Angeles, CA 90095-1679, USA  
e-mail: GFonarow@mednet.ucla.edu

**Table 1** Census 2000 Race and Ethnic Categories in the United States

Categories	US citizens with origins from:	Percent of US population <sup>a</sup>	
Race <sup>b</sup>	White	Europe, the Middle East, or North Africa	75.1
	Black or African-American	Africa or Haiti	12.3
	American Indian or Alaska Native	North, South, or Central America with ongoing tribal affiliation or community attachment marked by an enrollment in a tribe such as Rosebud Sioux, Chippewa, or Navajo	0.9
	Asian	Far East, Southeast Asia, or Indian Subcontinent	3.6
	Native Hawaiian or other Pacific Islander	Hawaii, Guam, Samoa, or other Pacific Islands such as Tahitian, Mariana Islander, or Chuukese	0.1
	Some other race	For those who do not identify with any of the above five categories. Of note, the majority of who note this category identify with Hispanic origin	5.5
Ethnic	Hispanic or Latino	Heterogeneous group with ancestral linkage to Spain and Spanish-speaking nations of the Caribbean and Central and South America	12.5

Adapted from reference 3

<sup>a</sup> Abstracted data from Census 2000 of 97.6 % of 281,421,906 responders who reported one race

<sup>b</sup> As defined by the Office of Management and Bureau in October 1997

differences in all aspects of HF including epidemiology, etiology, prognosis, management, and outcomes. The following review highlights racial/ethnic variations in the etiology, prognosis, and management with medical and device therapy for HF.

### Racial Variations in HF Epidemiology and Etiology

Despite the homogenous presentation of the clinical syndrome of HF, the etiologies remain heterogeneous among patients of different racial/ethnic backgrounds. This heterogeneity is due to several factors including risk factor profile, genetics, socioeconomic status, and toxic exposures. Better understanding of the racial/ethnic variations in HF etiology may allow for improved prevention, risk stratification, early detection, and management for patients at risk for or with early signs of HF.

#### African-Americans

For individuals less than the age of 75, African-Americans have the highest incidence of HF [1]. The prospective Multi-Ethnic Study of Atherosclerosis (MESA) cohort study evaluated the incidence of HF in 6814 individuals by four race/ethnic groups: whites, African-Americans, Hispanic, and Chinese. During a 4-year follow-up period, the following incidences were observed (in 1000 person-years): African-Americans (4.6 %), Hispanics (3.5 %), whites (2.4 %), and Chinese Americans (1.0 %). The prevalence of elevated systolic blood pressure, obesity, diabetes mellitus, and total serum cholesterol were all significantly higher ( $p < 0.01$ ) in African-Americans compared with other races. The main determinants for the higher incidence of HF observed in African-Americans

compared with other racial/ethnic groups as noted in this large cohort study are attributed to their higher prevalence of hypertension and diabetes mellitus [2]. Previously published analyses from the Get With The Guidelines (GWTG)-HF program have also confirmed this finding [4•]. The underlying basis for the increased prevalence of diabetes mellitus and hypertension in African-Americans continues to be an area of ongoing research and debate [5].

Additionally, African-Americans with HF are more likely to have a non-ischemic etiology compared with whites. The MESA study revealed that African-American individuals had the highest incidence of HF due to non-ischemic etiology. Among the four racial/ethnic groups who did not suffer an interim myocardial infarction (MI), African-Americans had the highest incidence (3.5 per 1000 person-years) of HF followed by Hispanic (2.1), white (1.5), and Chinese Americans (0) [2]. Previously published analyses from the GWTG-HF program have also revealed that African-Americans and Hispanics have a higher rate of non-ischemic etiologies compared with whites [4•].

Another prospective cohort from the Coronary Artery Risk Development in Young Adults (CARDIA) study included over 5000 participants nearing equal proportions of African-Americans and whites who were followed prospectively for 20 years to evaluate for the incidence of heart failure among young adults age 18 to 30. During a 20-year follow-up, 27 total participants developed incident heart failure of whom 26 were African-American ( $p = 0.001$ ). The cumulative incidence of heart failure by race and gender was 1.1 % (95 % confidence interval [CI], 0.6 to 1.7) in African-American women, 0.9 % (95 % CI, 0.5 to 1.4) in African-American men, 0.08 % (95 % CI, 0 to 0.5) in white women, and 0 % in white men (95 % CI, 0 to 0.4). Independent predictors of HF in African-

American males between the ages of 18 to 30 were higher diastolic blood pressure (hazard ratio [HR] per 10.0 mm Hg, 2.1; 95 % CI, 1.4 to 3.1), higher body mass index (HR per 5.7 units, 1.4; 95 % CI, 1.0 to 1.9), lower high-density lipoprotein cholesterol (HR per 13.3 mg per deciliter [0.34 mmol per liter], 0.6; 95 % CI, 0.4 to 1.0), and kidney disease (HR, 19.8; 95 % CI, 4.5 to 87.2) [6•]. The strikingly younger age and high prevalence of obesity, hypertension, and diabetes mellitus among African-American patients with HF indicate that health improvement efforts should focus on early prevention of these risk factors in an attempt to reduce the incidence of HF and its long-term morbidity and mortality in these populations.

### Hispanics

Based on the aforementioned MESA data, Hispanics have the second highest incidence of HF following African-Americans [2]. Similar to the African-American race, individuals of Hispanic origin are plagued with a high burden of risk factors including obesity, hypertension, and diabetes mellitus [7••]. As previously stated, a non-ischemic etiology of HF is more common in individuals of Hispanic origin [2, 4•, 7••]. Additionally, Hispanics tend to have a higher prevalence of rheumatic heart disease [8] and Chagas' disease [9] etiologies for HF compared with non-Hispanic whites [7••], likely related to geographical factors.

### Chinese and South Asians

There is minimal published data to help clarify the epidemiology and etiology of HF in Asians and Southeast Asians. Most recently, Choi et al performed a cross-sectional study from two HF clinics with a large volume of South Asian and Chinese patients in Ontario, Canada, to define the clinical characteristics of these two racial sub-groups compared with non-Chinese/non-South Asians. Over an 11-year period, the racial breakdown of the 1671 patients managed by the HF clinics was 11 % Chinese, 13 % South Asian, and 76 % non-Chinese/non-South Asians. Compared with non-Chinese/non-South Asians, more South Asian patients reported a history of angina (25 vs. 17 %,  $p=0.01$ ) and had previous MI (70 vs. 52 %,  $p=0.0025$ ). Conversely, Chinese patients reported less history of MI (30 vs. 52 %,  $p=0.0014$ ) and coronary artery disease (CAD) (50 vs. 69 %,  $p=0.004$ ) when compared with non-Chinese/non-South Asians, respectively. For the Chinese population, there was a trend towards left ventricular EF greater than 45 % [10•]. The authors hypothesize that the most common etiology of HF in the Chinese population is likely related to hypertension as a risk factor [10•, 11]. Based on these findings, the extrapolated etiologies are more likely ischemia and CAD for the South Asian population and risk factor related for Chinese patients [10•].

Another cohort study from the UK observed approximately 5800 patients admitted with HF over a 13-year period. There were 5057 white patients (87.4 %) and 336 (5.8 %) South Asian patients admitted with HF with a follow-up period ranging from 3 to 42 months. Patterns of in-hospital comorbidities concurrent with and up to 5 years prior to the incident admission for HF revealed that compared with white patients, South Asian patients had statistically significant more acute MI (15.2 vs. 27.1 %), hypertension (29.3 vs. 43.8 %), and diabetes (16.2 vs. 45.8 %), respectively. Additionally, South Asian patients admitted with HF were about 8 years younger than white patients admitted. This large cohort study further supports the high prevalence of risk factors in the South Asian sub-group and their presentation of disease at younger ages as compared with whites [12].

Based on the above-mentioned etiologies among these racial/ethnic sub-groups, targeting modifiable risk factors as identified by "Stage A" of the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for HF is an important strategy for prevention and risk stratification for racial/ethnic groups with HF [13••].

### Racial Variation in HF Prognosis and Outcomes

Understanding patterns in hospital readmission rates for HF remains an important quality of care measure and essential metric for Medicare reimbursement. Racial/ethnic differences in HF admissions, readmissions, and in-hospital mortality remain key targets for improving outcomes and affecting long-term prognosis. In a retrospective analysis of Medicare data of individuals hospitalized with their first-listed diagnosis of HF (International Classification of Diseases, Ninth Revision, Clinical Modification code 428), Brown et al. examined the prevalence of HF hospitalizations over a 10-year period for whites, African-Americans, Hispanic, and Asian enrollees. Discharge outcomes were also analyzed for HF patients hospitalized in the final year of analysis. Compared with whites, the likelihood of HF hospitalization was 1.5 times higher in African-Americans, 1.2 times higher in Hispanics, and 0.5 times less likely in Asians ( $p<0.05$  for all). Compared with whites, all ethnic groups were more likely to be discharged home. African-Americans and Hispanics, but not Asians, had lower in-hospital mortality compared with whites. One potential explanation for higher readmissions in African-American and Hispanic patients is poorer access to outpatient HF management programs [14]. This sheds light on the importance of improving outpatient healthcare delivery and HF management among racial/ethnic minorities.

It is important to acknowledge that there are discrepancies in the data regarding the impact of race on readmission rates and overall mortality especially with respect to the African-

American race. Another retrospective analysis looking at administrative data from Medicare showed that 30-day readmission rates for HF did not differ between African-American and white patients. However, this study was limited to 30-day readmissions rates only and does not reflect long-term outcomes or patterns among other racial/ethnic groups. Additionally, racial differences among non-Medicare individuals are not accounted for in these conclusions [15]. Medicare data regarding readmission rates for enrollees of Hispanic origin appear more consistent with another such study revealing higher risk-adjusted readmission rates for Hispanic patients compared with whites (27.9 vs. 25.9 %, odds ratio [OR] 1.11, 95 % CI 1.07–1.14,  $p < 0.001$ ). These findings are consistent with previously mentioned studies and allude to Hispanics likely having poor access to outpatient resources limiting their ability to optimize their HF regimen [16•].

Furthermore, a retrospective analysis from the Acute Decompensated Heart Failure National Registry Database (ADHERE) evaluated race-related differences in in-hospital mortality between African-American and white patients [17]. ADHERE is a national registry with greater than 200,000 patients with acute decompensated HF episodes from a total of 274 community, tertiary, and academic centers well distributed in the USA [18]. There were 105,872 white patients and 29,862 African-American patients with ADHF episodes entered into the database from September 2001 to December 31, 2004. An aggregate of unadjusted in-hospital outcomes between these two racial groups was calculated, in addition to a multivariate analysis for three pre-specified sub-groups of ADHF: ischemic origin, non-ischemic origin, and new-onset heart failure. In all sub-sets, African-Americans had a lower in-hospital mortality compared with whites. African-American patients were found to have higher rates of admission to an intensive care unit (ICU) setting but with overall shorter ICU duration and length of stay in hospital. This study was novel in its incorporation of broader patient characteristics including nearly equal gender, age range spanning 45 to 75 years, and utilization of different hospital settings [17].

This study illustrates two essential points for understanding racial variations in HF prognosis. First, in-hospital outcomes can be quite favorable for African-American patients. Second, racial disparities in HF management are not revealed within the inpatient setting. This analysis allows for hypothesis generation that perhaps the disparities are occurring at the outpatient level with African-Americans. One potential explanation for the lower in-hospital mortality observed is that African-American patients may have limited access for continual healthcare management for various reasons not limited to resource poor settings and low socioeconomic status (SES). This may suggest that African-American patients may be presenting to tertiary care inpatient facilities more frequently because of poor outpatient resources and therefore may actually have a lower level of disease progression when admitted

compared with white patients who may have more advanced symptoms at the time of admission given that they likely have greater outpatient HF management support [17].

A recent retrospective analysis using the GWTG-HF registry linked to Medicare data evaluated for race-related differences in short- and long-term HF outcomes. Data from 213 hospitals including a total of 47,149 patients, 83.2 % white, 10.5 % African-American, 5.0 % Hispanic, and 1.4 % Asian/Pacific Islander patients, were analyzed for 30-day and 1-year rehospitalization and mortality rates for HF among these four race/ethnic groups. Compared with whites, African-Americans and Hispanics had lower short-term mortality 30 days post discharge: African-Americans 4.3 %, Hispanics 4.4 %, and whites 6.3 % ( $p < 0.001$ ). Compared with whites, African-Americans and Hispanics had higher 30-day and 1-year cardiovascular (CV) readmissions while Asians had readmission rates similar to whites. All racial/ethnic groups had lower 30-day and 1-year mortality that was statistically significant in comparison with whites. After adjusting for patient and hospital characteristics for both short- and long-term follow-up, higher readmission rates persisted for African-Americans and Hispanics; however, the observed differences in mortality rates compared with whites became slightly lower for African-Americans and similar for Hispanics. Asian patients when compared with whites had similar outcomes except for slightly higher risk of short-term readmission. After adjusting for SES, the observed difference between Hispanics and whites for 30-day readmission and 1-year all-cause readmission rates became statistically non-significant. However, mortality endpoints did not change. This reduction in risk, after adjusting for SES factors, is illustrative of how SES factors influence rehospitalization in this ethnic minority [19••].

Similarly, the previously mentioned UK cohort study of South Asian patients with HF also observed race-related differences in HF outcomes. Unadjusted in-hospital mortality rates were lower in South Asian patients compared with white patients (13 vs. 19 %), respectively. Multivariate analyses revealed 18 % lower risk of death for South Asian patients with similar rates of readmission compared with white patients [12]. Interestingly, another recent retrospective analysis from the GWTG-HF registry evaluated for associations between B-type natriuretic peptide levels (BNP), length of stay, in-hospital mortality, and quality of care for in-hospital HF admissions among the four different racial groups: white, African-American, Asian, and Hispanics. While multivariate analysis revealed that elevated BNP levels correlated with greater length of stay and higher in-hospital mortality, there were no ethnic differences in the prognostic implications of BNP values among whites, African-American, Asians, and Hispanics [20•]. The lack of race-related differences in BNP elevation prognostication is important since BNP is a powerful HF prognostic tool.

## Racial Variations in HF Management and Outcomes

Given the racial differences that continue to be determined in the etiology of HF, the next natural question becomes, should our standard therapies vary based on race? For HF with reduced EF (HFrEF), several pharmacotherapies including angiotensin-converting enzyme inhibitors (ACEI), beta-blockers (BB), and aldosterone receptor antagonists (ARA) have become guideline-recommended standard of care. The most fundamental question regarding racial variations is whether or not the standard group of HF medications recommended by the ACC/AHA guidelines is of equal efficacy among these racial/ethnic groups (Table 2).

### Angiotensin-Converting Enzyme Inhibitors

Race-based differences have been shown among a few of the class I recommended guideline medications for HF. The evidence for the class I recommendation of ACEIs in HF management arises from several pivotal randomized controlled trials in HF. One such study, the Studies of Left Ventricular Dysfunction (SOLVD), randomized 2500 HF patients on a background of conventional HF therapy to either placebo or enalapril and observed a 16 % risk reduction in mortality with enalapril use [21]. Given that 80 % of patients enrolled in SOLVD were male and Caucasian, the Vasodilator-Heart Failure Trial II (V-HeFT-II) study evaluated for race-based differences in enalapril therapy among the same treatment population. The addition of enalapril to the combination of hydralazine/isosorbide dinitrate for HF treatment showed a statistically significant reduction in death for white patients but not African-Americans [22]. Following this, Exner et al. performed a match-cohort design study pooling data from the prevention and treatment SOLVD trials to test this hypothesis in a larger population of African-American patients. The

matched cohort-design matched four white patients to each African-American patient with respect to age, sex, left ventricular EF, trial, and treatment. Compared with placebo, enalapril was associated with a 40 % risk reduction in HF hospitalizations (95 % confidence interval [CI], 0.27–0.57) in white patients. This significant association was not demonstrated in African-American patients [23–25]. A decrease response to ACE inhibitors in African-American patients with hypertension has been demonstrated in previous clinical trials and is hypothesized to be associated with lower plasma renin levels [26–28]. Additionally, the benefits of ACEI-related kinin activity on the myocardium have been attributed to endogenous nitric oxide (NO) release. African-Americans are known to have a lower rate of bioactivity of NO which may be another explanation for their decreased response to ACEI therapy [29].

Shekelle et al. performed a meta-analysis for ACEIs from the two SOLVD studies, which were the only two that included an adequate number of African-American patients and data to allow for HR calculations. A pooled relative risk (RR) analysis revealed an estimate of 0.89 (95 % CI, 0.74–1.06) in African-American patients and 0.89 (95 % CI, 0.82 to 0.97) in white patients. Although the RR reduction for African-American patients was not statistically significant, the authors concluded that because the estimates of effect were the same for both groups, there is no evidence to suggest that African-Americans benefit less from ACEI therapy when compared with whites [30].

### Beta Blockers

Within the class of BB therapy, the US Carvedilol Heart Failure Trials Program evaluated for race-related differences in carvedilol therapy compared with placebo for death or hospitalizations from any cause. Twenty percent of the

**Table 2** Outcomes in guideline-directed medical therapy for heart failure in African-American patients

Study	Therapy <sup>a</sup>	Outcome	Race	Adjusted RR (95 % CI)	<i>p</i> value for interaction
Exner et al. [23]	Enalapril	Hospitalization for HF	African-American	0.86 (0.64–1.16)	0.005
			Non-African-American	0.51 (0.37–0.70)	
Yancy et al. [31]	Carvedilol	Death from any cause or hospitalization for any reason	African-American	0.52 (0.31–0.88)	0.33
			Non-African-American	0.70 (0.53–0.92)	
Verganey et al. [35•]	Spironolactone	All-cause mortality	African-American	0.87 (0.46–1.59)	0.030
			Non-African-American	0.70 (0.59–0.82)	
Zaiean et al. [37•]	ICD/CRT	24-month mortality	African-American	0.68 (0.42–1.08)	0.355
			Non-African-American	0.59 (0.46–0.76)	

<sup>a</sup> Therapy vs. placebo

ICD implantable cardioverter defibrillator, CRT cardiac resynchronization therapy, HF heart failure. RR denotes relative risk and is the risk of therapy group relative to that in the placebo groups. CI denotes confidence interval. *p* values for interaction are for the comparison between the effect of the guideline-directed therapy in African-American patients and the effect in non-African-American participants

population studied was African-American which is one of the highest percentages among HF trials. Carvedilol lowered the risk of death from any cause by 56 % in African-Americans and 68 % in non-African-Americans [31]. However, this benefit is not equivalent across all BBs. In a sub-group analysis from the Beta-Blocker Evaluation of Survival Trial (BEST), bucindolol therapy revealed a survival benefit only in whites and adverse effect on mortality in African-Americans. Genetic sub-studies of the BEST trial suggest genetic polymorphisms to be the cause for this apparent race-related difference in BB therapy [32]. Furthermore, the Cardiac Insufficiency Bisoprolol Study II (CIBIS-II) revealed a mortality benefit for stable HF patients, but only approximately 0.3 % of patients enrolled were African-American given that it was conducted in Scandinavian and European countries [33].

Shekelle et al. performed a meta-analysis pooling data from four large randomized controlled trials of beta-blockers (BEST, COPERNICUS, MERIT-HF, and the US Carvedilol) in HF. Collectively, a total of 1172 African-Americans and greater than 8000 white patients were used to perform a race-stratified analysis. The pooled random effects estimates of the RR of the effect on mortality for African-American patients was 0.97 (95 % CI, 0.68 to 1.37), and for white patients, it was 0.69 (95 % CI, 0.55–0.85). However, after excluding data from BEST, the pooled random effects estimate of the RR was 0.67 (95 % CI, 0.68 to 0.85) for African-Americans. The authors concluded that point estimates of effect were similar enough to those observed in white patients and that the lack of statistically significant results for African-American patients compared with placebo was likely the result of a small sample size in the trials [30].

Moreover, a recent retrospective analysis evaluated the effect of BBs on echocardiographic parameters of LV dysfunction in a multiethnic population of 418 patients of 185 African-Americans, 159 Hispanics, and 74 Caucasians. Baseline measurements of LV ejection fraction (LVEF), LV end-diastolic dimension (LVEDd), and degree of mitral regurgitation were recorded and followed by repeat measurements after 1 year of BB therapy. Compared with the other races ( $p < 0.01$ ), Hispanics had the least improvement in LVEF (2 %) and more LVEF decline (24.5 %) and LVEDd decline. While the study was not designed to determine the cause of race-related differences, it highlights that there is room to understand how factors such as socioeconomic, lifestyle, genetic, and ethnic differences play a role in differences among multiethnic groups [34].

#### Aldosterone Receptor Antagonists

A sub-analysis of the Randomized Aldactone Evaluation Study (RALES) between African-American and non-African-American (whites, Asian, other) suggested a

decreased clinical benefit of the use of spironolactone in the combined endpoints of reduction of HF hospitalization and death. Rates of hyperkalemia were higher in non-African-Americans compared with African-Americans while African-Americans had higher rates of hypokalemia suggesting decreased effectiveness of spironolactone in this group. Additionally, more non-African-Americans attained the maximal dose compared with African-Americans. This analysis, however, was limited by small absolute numbers as only 7 % of the study participants were African-American. Outcomes observed may be affected by the fact that compared with non-African-Americans, more African-Americans were on digoxin and fewer were on beta-blockers and achieved lower doses of spironolactone therapy [35•].

#### Hydralazine and Isosorbide Dinitrate

While the prior studies are based on post-hoc analyses or observational, retrospective data, a seminal paper published in 2004 was the first large-scale randomized controlled trial to test a treatment strategy based on race alone. The African-American Heart Failure Trial (A-HeFT) randomized 1050 self-identified African-American patients with New York Heart Association (NHYA) classes III to IV symptoms for 3 months and evidence of LV systolic dysfunction who were on standard neurohormonal therapy for HF to fixed-dose hydralazine plus isosorbide dinitrate versus placebo. The study was stopped early due to increased mortality in the placebo group versus the therapy group (10.2 vs. 6.2 %,  $p = 0.02$ ). The treatment group had a significant improvement in 43 % in survival (HR 0.57,  $p = 0.01$ ). The subsequent race-specific indication for this combination therapy sparked controversy regarding stratifying treatments based on race [36]. This ushered in an era in which race-based differences in treatment strategies were now a potential option. These results also highlight the benefit of nitric oxide enhancing therapies in African-American patients with HF previously mentioned [29].

#### Implantable Cardioverter Defibrillator and Cardiac Resynchronization Therapy

A recent pre-specified analysis of the IMPROVE-HF (Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting) registry evaluated for race-related differences in the clinical effectiveness of implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) on mortality. Among outpatients with HF who received CRT pacemaker (P), CRT defibrillator (D), and ICD therapy, there was a significant survival benefit among all patients with no difference in clinical effectiveness based on race alone suggesting equal benefit across racial/ethnic groups [37•]. These findings are consistent with

previous sub-analyses from randomized control trials evaluating the mortality benefit of device therapy in this patient population [38, 39].

Ultimately, there remain unanswered questions regarding racial-related differences in HF management given that racial/ethnic groups are a minority which are largely underrepresented in clinical trials. There continues to be a need for further research to understand race-related differences in guideline-recommended medical therapy to ultimately improve HF outcomes for this group who remain at increased risk.

### Addressing Racial Disparities with the Use of Performance Improvement Programs to Improve HF Outcomes

The elimination of disparate health care was one of the principle goals of Healthy People 2010 and remains an important mission of health care reform [40]. A number of studies reveal that within various clinical settings, racial/ethnic minorities, particularly African-Americans, African-American patients are less likely to receive guideline-recommended medical and device therapy leaving them at increased risk for HF morbidity/mortality. It is essential to understand that racial/ethnic disparities exist in HF management and affect HF outcomes for this high-risk group. Narrowing or eliminating racial/ethnic disparities is paramount to improving HF outcomes for minority groups.

A number of performance improvement (PI) initiatives have become implemented to improve adherence to guideline-recommended medical and device therapy for HF. An analysis of GWTG-HF was performed to evaluate for temporal trends in rates of ICD use stratified by race. GWTG-HF is a hospital-based quality improvement program enabling health care providers to treat patients who are hospitalized with HF, CAD, or stroke according to guidelines consistently. A total of 11,880 unique patients enrolled in the GWTG-HF program from 2005 to 2009 underwent ICD placement either during the index hospitalization for HF, prescribed prior to discharge, or had it placed prior to the index hospitalization for HF. There was a statistically significant improvement in adherence to guideline-based therapy particularly among the African-American race [41••]. Similarly, another retrospective analysis from another PI initiative, IMPROVE-HF examined a total of 7605 patients from 155 outpatient practices with HF, prior MI, and LVEF less than 35 %. The racial breakdown was 9.0 % African-American, 42.6 % whites, and 46.5 % undocumented. After implementation of PI programs, there was a significant improvement observed for all three race groups on four of the seven individual quality measures: ARA, CRT with or without CRT, and HF education. This illustrates how PI initiatives can improve adherence to guideline-directed therapy and narrow the apparent racial/ethnic disparities previously observed

which is important for racial/ethnic minorities who have poor access to healthcare resources for optimal HF management [42].

### Conclusions

There are important racial and ethnic differences in the etiology, prognosis, treatment patterns, and quality of care of HF. African-American, Hispanic, and potentially other racial/ethnic populations are at increased risk for developing HF at a younger age, experience higher rates of morbidity and possibly mortality, and may receive disparate quality of care compared with white patients. Current ACC/AHA guideline recommendations for HF, with the exception of the hydralazine/isosorbide dinitrate combination, make no further race/ethnic-related distinctions given the lack of race-specific randomized data. Despite the available recommendations, many eligible racial/ethnic minorities are not receiving guideline-directed medical and device therapy. Evidence from PI initiative programs reveal that disparities among racial/ethnic groups can be overcome and adherence can improve making them an essential part of narrowing racial disparities in HF. There still remain significant opportunities to understand racial/ethnic-related differences in HF management to eliminate disparities and improve HF outcomes.

### Compliance with Ethics Guidelines

**Conflict of Interest** Gregg Fonarow worked as a consultant for Medtronic, Novartis, Johnson and Johnson, Amgen, Bayer, Boston Scientific, The Medicines Company, and Gambro. Fonarow is employed as the Elliott Corday Professor of Cardiovascular Medicine and Science; Fonarow has received grants from the NIH and AHRQ. Sheila Sahni and Tamara Horwich have no conflicts of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

**Conflict of Interest** SS and TBH, none; GCF consulting for Amgen, Bayer, Gambro, Janssen, Medtronic, Novartis.

### References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulatory*. 2014;129:e28–292.

2. Bahrami H, Kronmal R, Bluemke DA, Olson J, Shea S, Liu K, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. *Arch Intern Med.* 2008;168(19):2138–45.
3. Grieco EM and Cassidy RC. Overview of race and Hispanic origin. US Census Bureau. Issued March 2001. Available at <http://www.census.gov/prod/2001pubs/c2kbr01-1.pdf>. Accessed August 4, 2014.
4. Thomas KL, Hernandez AF, Dai D, Heidenreich P, Fonarow GC, Peterson ED, et al. Association of race/ethnicity with clinical risk factors, quality of care, and acute outcomes in patients hospitalized with heart failure. *Am Heart J.* 2011;161(4):746–54. *Retrospective analysis illustrating HF risk factors and in-hospital mortality rates for African American and Hispanic patients admitted with HF.*
5. Yancy CW. Heart failure in African Americans: pathophysiology and treatment. *J Card Fail.* 2003;9(5 Suppl Nitric Oxide):S210–5.
6. Bibbins-Domingo K, Pletcher MJ, Lin F, Vittinghoff E, Gardin JM, Arynchyn A, et al. Racial differences in incident heart failure among young adults. *N Engl J Med.* 2009;360(12):1179–90. *Evaluates the incidence of HF over a 20-year period among whites and African Americans revealing important predispositions to HF in African American race.*
7. Vivo RP, Krim SR, Cevik C, Witteles RM. Heart failure in Hispanics. *J Am Coll Cardiol.* 2009;53(14):1167–75. *State of the art review of HF in Hispanics.*
8. Becker TM, Wiggins CL, Key CR, Samet JM. Ethnic differences in mortality from acute rheumatic fever and chronic rheumatic heart disease in New Mexico, 1958–1982. *West J Med.* 1989;150:46–50.
9. Leiby DA, Rentas FJ, Nelson KE, Stambolis VA, Ness PM, Parnis C, et al. Evidence of *Trypanosoma cruzi* infection (Chagas' disease) among patients undergoing cardiac surgery. *Circulation.* 2000;102:2978–82.
10. Choi D, Nemi E, Fernando C, Gupta M, Moe GW. Differences in the clinical characteristics of ethnic minority groups with heart failure managed in specialized heart failure clinics. *JACC Heart Fail.* 2014;2(4):392–9. *Recent retrospective analysis from two specialty HF clinics highlighting clinical characteristics of Chinese and South Asians patients with HF.*
11. Sanderson JE, Ts TF. Heart failure: a global disease requiring a global response. *Heart.* 2003;89:585–6.
12. Blackledge HM, Newton J, Squire IB. Prognosis for South Asian and white patients newly admitted to hospital with heart failure in the United Kingdom: historical cohort study. *BMJ.* 2003;327(7414):526–31.
13. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey Jr DE, Drazner MH, et al. ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;62:e147–239. *ACCF/AHA HF guidelines outline an algorithm for identifying patients at different stages of HF, diagnostic strategies, and oral and device therapy for management.*
14. Brown DW, Haldeman GA, Croft JB, Giles WH, Mensah GA. Racial or ethnic differences in hospitalization for heart failure among elderly adults: Medicare, 1990 to 2000. *Am Heart J.* 2005;150(3):448–54.
15. Dharmarajan K, Hsieh AF, Lin Z, Bueno H, Ross JS, Horwitz LI, et al. Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. *JAMA.* 2013;309(4):355–63.
16. Rodriguez F, Joynt KE, López L, Saldaña F, Jha AK. Readmission rates for Hispanic Medicare beneficiaries with heart failure and acute myocardial infarction. *Am Heart J.* 2011;162(2):254–261.e3. *Demonstrates higher rates of readmissions amongst elderly Hispanics with HF.*
17. Kamath SA, Drazner MH, Wynne J, Fonarow GC, Yancy CW. Characteristics and outcomes in African American patients with decompensated heart failure. *Arch Intern Med.* 2008;168(11):1152–8.
18. Adams KF, Fonarow GC, Emerman CL, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100 000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J.* 2005;149(2):209–16.
19. Vivo RP, Krim SR, Liang L, Neely M, Hernandez AF, Eapen ZJ, Peterson ED, Bhatt DL, Heidenreich PA, Yancy CW, Fonarow GC. Short- and long-term hospitalization and mortality for heart failure in four racial/ethnic populations. *J Am Heart Assoc.* 2014;In press. *Highlights variations in mortality and short- and long-term readmissions amongst 4 different racial/ethnic groups admitted with HF.*
20. Krim SR, Vivo RP, Krim NR, Qian F, Cox M, Ventura H, et al. Racial/Ethnic differences in B-type natriuretic peptide levels and their association with care and outcomes among patients hospitalized with heart failure: findings from Get With The Guidelines-Heart Failure. *JACC Heart Fail.* 2013;1(4):345–52. *Retrospective analysis revealing race-related differences in the prognostic value of BNP levels for HF admissions.*
21. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med.* 1991;325(5):293–302.
22. Carson P, Ziesche S, Johnson G, Cohn JN. Racial differences in response to therapy for heart failure: analysis of the vasodilator-heart failure trials: Vasodilator-Heart Failure Trial Study Group. *J Card Fail.* 1999;5:178–87.
23. Exner DV, Dries DL, Domanski MJ, Cohn JN. Lesser response to angiotensin-converting-enzyme inhibitor therapy in black as compared with white patients with left ventricular dysfunction. *N Engl J Med.* 2001;344(18):1351–7.
24. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. *N Engl J Med.* 1992;327:685–91.
25. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med.* 1991;325:293–302.
26. Preston RA, Materson RA, Reda DJ, et al. Age-race subgroup compared with renin profile as predictors of blood pressure response to antihypertensive therapy. *JAMA.* 1998;280:1168–72.
27. Case DB, Wallace JM, Kein HJ, Weber MA, Sealey JE, Laragh JH. Possible role of renin in hypertension as suggested by renin-sodium profiling and inhibition of converting enzymes. *N Engl J Med.* 1977;296:641–6.
28. Cody RJ, Laragh JH, Case DB, Atlas SA. Renin system activity as a determinant of response treatment in hypertension and heart failure. *Hypertension.* 1983;5(Suppl III):III-36–42.
29. Campia U, Choucair WK, Bryant MB, Waclawiw MA, Cardillo C, Panza JA. Reduced endothelium-dependent and -independent dilation of conductance arteries in African Americans. *J Am Coll Cardiol.* 2002;40(4):754–60.
30. Shekelle PG, Rich MW, Morton SC, Atkinson CS, Tu W, Maglione M, et al. Efficacy of angiotensin-converting enzyme inhibitors and beta-blockers in the management of left ventricular systolic dysfunction according to race, gender, and diabetic status: a meta-analysis of major clinical trials. *J Am Coll Cardiol.* 2003;41(9):1529–38.
31. Yancy CW, Fowler MB, Colucci WS, et al. Race and the response to adrenergic blockade with carvedilol in patient with chronic heart failure. *N Engl J Med.* 2001;344:1358–65.
32. Beta-Blocker Evaluation of Survival Trial Investigators. A trial of the beta-blocker bucindolol in patients with advanced chronic heart failure. *N Engl J Med.* 2001;344(22):1659–67.
33. CIBIS-II Investigators and Committees. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. *Lancet.* 1999;353(9146):9–13.



34. Kelesidis I, Varughese CJ, Hourani P, Zolty R. Effects of  $\beta$ -adrenergic blockade on left ventricular remodeling among Hispanics and African Americans with chronic heart failure. *Clin Cardiol*. 2013;36(10):595–602.
35. Vardeny O, Cavallari LH, Claggett B, Desai AS, Anand I, Rossignol P, et al. Race influences the safety and efficacy of spironolactone in severe heart failure. *Circ Heart Fail*. 2013;6(5):970–6. *Highlights race-related differences between African Americans and non-African Americans with spironolactone therapy.*
36. Taylor AL, Ziesche S, Yancy C, Carson P, D'Agostino Jr R, Ferdinand K, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. *N Engl J Med*. 2004;351:2049–57.
37. Ziaieian B, Zhang Y, Albert NM, Curtis AB, Gheorghiane M, Heywood JT, et al. Clinical effectiveness of CRT and ICD therapy in heart failure patients by racial/ethnic classification: insights from the IMPROVE HF registry. *J Am Coll Cardiol*. 2014;64(8):797–807. *Retrospective analysis from IMPROVE HF illustrating equal clinical effectiveness of ICD/CRT-D therapy amongst different race/ethnic groups.*
38. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med*. 1999;341(25):1882–90.
39. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346(12):877–83.
40. U.S. Department of Health and Human Services. Office of Disease Prevention and Health Promotion. Healthy People 2010. Washington, DC. Available at [http://www.cdc.gov/nchs/healthy\\_people/hp2010.htm](http://www.cdc.gov/nchs/healthy_people/hp2010.htm). Accessed September 12, 2014.
41. Al-Khatib SM, Hellkamp AS, Hernandez AF, Fonarow GC, Thomas KL, Al-Khalidi HR, et al. Trends in use of implantable cardioverter-defibrillator therapy among patients hospitalized for heart failure: have the previously observed sex and racial disparities changed over time? *Circulation*. 2012;125(9):1094–101. *Demonstrates how enrollment in a quality improvement program improves adherence to guideline-recommended therapy in eligible patients.*
42. Reynolds D, Albert NM, Curtis AB, Gheorghiane M, Heywood JT, McBride ML, et al. Race and improvements in the use of guideline-recommended therapies for patients with heart failure: findings from IMPROVE HF. *J Natl Med Assoc*. 2012;104(5–6):287–98. *Demonstrates how enrollment in an outpatient quality improvement program narrows race-based differences in health care delivery in outpatient cardiology settings.*