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Heart Failure With Preserved Ejection Fraction in African Americans

The ARIC (Atherosclerosis Risk In Communities) Study

Deepak K. Gupta, MD,* Amil M. Shah, MD, MPH,* Davide Castagno, MD,† Madoka Takeuchi, MS,* Laura R. Loehr, MD, PhD,‡ Ervin R. Fox, MD, MPH,§ Kenneth R. Butler, PhD,‖ Thomas H. Mosley, PhD,‖ Dalane W. Kitzman, MD,¶ Scott D. Solomon, MD*

Boston, Massachusetts; Turin, Italy; Chapel Hill and Winston-Salem, North Carolina; and Jackson, Mississippi

Objectives In an entirely African-American cohort, we compared clinical characteristics, cardiac structure and function, and all-cause mortality in patients with heart failure (HF) with preserved ejection fraction (HFpEF) in relation to patients with heart failure with reduced ejection fraction (HFrEF) and those without HF.

Background African Americans are at increased risk for HF. Nevertheless, there are limited phenotypic and prognostic data in African Americans with HFpEF compared with those with HFrEF and those without HF.

Methods Middle-aged African Americans from the Jackson, Mississippi, cohort of the ARIC (Atherosclerosis Risk In Communities) study (n = 2,445) underwent echocardiography between 1993 and 1995. HF prevalence was available in 1,962 patients for whom left ventricular ejection fraction (LVEF) could be quantified. Participants with HF were categorized as having HFpEF (LVEF ≥50%), HFrEF (LVEF <50%), or no HF, with comparisons made between groups.

Results HF was identified in 116 (5.9%) participants (HFpEF n = 85 [73%]; HFrEF n = 31 [27%]). Compared with those without HF, those with HFpEF were older, were more likely to be female, and had more frequent comorbidities and concentric hypertrophy. In relation to HFrEF, those with HFpEF were more likely to be female but less likely to have coronary heart disease, diabetes mellitus, chronic kidney disease, left atrial enlargement, and eccentric hypertrophy. Over a median 13.7 years of follow-up, risk of death differed between groups, with age- and sex-adjusted hazard ratios of 1.51 (95% confidence interval: 1.01 to 2.25) for HFpEF versus those without HF and 2.50 (95% confidence interval: 1.37 to 4.58) for HFrEF versus HFpEF.

Conclusions In this cohort of middle-aged African Americans, HFpEF was the most common form of HF and was associated with a substantially better prognosis than HFrEF but worse than those without HF. (J Am Coll Cardiol HF 2013;1:156–63)

African Americans, as compared with other racial groups, are at increased risk for the development of heart failure (HF) (1–3). Additionally, HF in African Americans occurs at a younger age and is associated with a higher prevalence of cardiovascular risk factors, particularly hypertension and diabetes mellitus, but lower frequency of coronary heart disease (CHD) (4–6). It has been suggested that the prevalence of heart failure and preserved ejection fraction (HFpEF) may be higher in African Americans than current estimates of HFpEF in the general population (5,7,8). However, findings are mixed regarding survival in African Americans with HF (3,4,6,9), and information is limited concerning prognosis in African Americans with HFpEF (10,11). We therefore aimed to describe differences in clinical characteristics, cardiac structure and function, and prognosis in a community-based sample of African Americans with HFpEF as compared with those with heart failure and reduced ejection fraction (HFrEF) and those without HF.

From the *Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts; †Division of Cardiology, University of Turin, Turin, Italy; ‡Department of Epidemiology, University of North Carolina, Chapel Hill, North Carolina; §Division of Cardiovascular Disease, University of Mississippi Medical Center, Jackson, Mississippi; ‖Department of Medicine-Geriatrics, University of Mississippi Medical Center, Jackson, Mississippi; and the ¶Cardiology and Geriatrics Sections, Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina. The ARIC study is supported by National Heart, Lung, and Blood Institute contracts HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C. Support was also provided by the National Heart, Lung, and Blood Institute training grant (T32 HL094301-02). All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Methods

Study population. The ARIC (Atherosclerosis Risk In Communities) study is an ongoing, prospective observational study of the natural history of atherosclerotic diseases

and cardiovascular risk factors. Detailed study rationale, design, and procedures have been previously published (12). The original cohort was recruited between 1987 and 1989 using probability sampling of middle-age (45 to 64 years) men and women from 4 communities in the United States (Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland). The Jackson field center enrolled an entirely African-American cohort. Subsequent follow-up visits occurred at 3-year intervals up to 1998, with annual telephone interviews conducted between visits. Institutional review boards from each site approved the study, and informed consent was obtained from all participants.

Transthoracic echocardiography was only performed in the Jackson, Mississippi, cohort during visit 3 (1993 to 1995). Of 2,445 participants who underwent transthoracic echocardiography, 1,962 were included in this analysis after sequential exclusion of 318 in whom left ventricular ejection fraction (LVEF) could not be calculated, 32 with missing HF status, 3 in whom incident HF occurred after visit 3 but before the echocardiogram, and 130 with missing covariate data.

Echocardiography. Two-dimensional (2-D), M-mode, and Doppler images were acquired with an Acuson 128XP/10c cardiac ultrasound machine with 2.5-, 3.5-, and 5.0-MHz transducers (Malvern, Pennsylvania). Quality control measures have been previously described (13). LV end-diastolic diameter, LV end-systolic diameter, and septal and posterior wall thicknesses were measured from 2-D images according to American Society of Echocardiography criteria. LV mass was calculated using the simplified cubed equation and indexed (LVMI) to height ($m^{2.7}$) with left ventricular hypertrophy (LVH) defined as LVMI $\geq$51 $g/m^{2.7}$ (14). Relative wall thickness was calculated as 2 $\times$ posterior wall thickness/LV end-diastolic diameter, with $\leq$0.42 considered normal. LVEF was calculated using the 2-D Teichholz method, with LVEF $\geq$50% and <50% defining preserved and reduced LVEF, respectively. Diastolic dysfunction was determined based upon transmitral Doppler E to A ratio, with $\leq$0.75 or >1.5 considered abnormal (15).

Definition of HF. Prevalent HF at visit 3 was defined by: 1) stage 3 or manifest HF according to Gothenburg criteria or the use of medications for HF at visit 1 (n = 82); or 2) hospitalization with International Classification of Diseases-Ninth Revision (ICD-9) code for HF (428.x) listed at discharge between visit 1 and 3 (n = 34) (3). The Gothenburg criteria are a validated scoring system composed of 3 components—cardiac, pulmonary, and therapy—in which stage 3 or manifest HF requires 1 point from each component (16). Participants with quantifiable LVEF by echocardiography and prevalent HF were categorized as HFpEF (LVEF $\geq$50%) or HFrEF (LVEF <50%).

Covariates. Established definitions for hypertension, obesity, diabetes mellitus, CHD, stroke, smoking status, and medication use were used as previously described in the ARIC study (17). Electrocardiographic LVH was determined by Cornell criteria. Pulmonary disease was defined as self-reported history of physician-diagnosed lung disease or asthma. Retinopathy, estimated glomerular filtration rate, ankle brachial index, hematologic parameters, lipids, and glucose were measured according to standardized protocols, with chronic kidney disease (CKD) and peripheral arterial disease defined as previously described (12,18–20). Ankle brachial index was available in 1,239 participants. All covariates were ascertained at visit 3, except for hemoglobin, white blood cell count, and creatinine, for which the most recent previous measures were used.

Abbreviations and Acronyms

CHD = coronary heart disease
CKD = chronic kidney disease
HF = heart failure
HFpEF = heart failure with preserved ejection fraction
HFrEF = heart failure with reduced ejection fraction
LV = left ventricular
LVEF = left ventricular ejection fraction
LVH = left ventricular hypertrophy
LVMI = left ventricular mass index

Outcome. The primary outcome was death from any cause. The follow-up period was defined as the time elapsed from the date of echocardiography to the date of death, date of last contact for those lost to follow-up, or December 31, 2008. Deaths were ascertained through annual phone calls to participants and ongoing surveillance of health department certificate files.

Statistical methods. For each of the 3 groups (no HF, HFpEF, and HFrEF), summary statistics for covariates were calculated as counts and percentages and medians and interquartile ranges for categorical and continuous data, respectively. Comparisons were then made between: 1) HFpEF and no HF; and 2) HFpEF and HFrEF. Chi-square or Fisher exact test and Wilcoxon rank-sum test were used to compare baseline characteristics. All-cause mortality rates were calculated (number of deaths divided by person-time at risk). Survival analysis was performed according to the Kaplan-Meier method, with the log-rank test used to assess for differences. Univariable and multivariable hazard ratios for death were estimated using Cox proportional hazards regression. Covariates included in multivariable models included age, sex, LVEF, and clinical characteristics. Propensity scores for HFpEF versus no HF and HFrEF versus HFpEF were calculated using clinical characteristics that significantly differed in univariate analyses between groups. The propensity score was then included in Cox proportional hazards models. Two-sided p values <0.05 were considered significant. Analyses were performed using Stata version 11.2 (Stata Corp., College Station, Texas).

Results

Prevalent HF was identified in 116 participants (5.9%) and further classified as HFpEF (n = 85 [73%]) and HFrEF (n = 31 [27%]). Those with HFpEF were older than those without HF but similar in age to those with HFrEF. Female sex was significantly more common in HFpEF as compared with those without HF and those with HFrEF. There were

JACC: Heart Failure Vol. 1, No. 2, 2013
April 2013:156–63

Table 1 Characteristics of the Jackson, Mississippi, Participants of the ARIC Cohort Who Underwent Echocardiography, Stratified According to HF Status

	HFpEF (n = 85)	No HF (n = 1,846)	No HF vs. HFpEF p Value	HFrEF (n = 31)	HFrEF vs. HFpEF p Value
Age, yrs	61.1 (57.1–66.5)	58.5 (54.6–63.8)	0.001	62.0 (54.9–65.7)	0.89
Female	72 (85)	1156 (63)	<0.001	20 (65)	0.036
Orthopnea	27 (32)	175 (9)	<0.001	13 (42)	0.38
PND	18 (21)	116 (6)	<0.001	12 (39)	0.09
Self-reported LE edema	55 (65)	588 (32)	<0.001	16 (52)	0.28
Hypertension	72 (85)	1,088 (59)	<0.001	26 (84)	1.00
Obesity*	60 (71)	831 (45)	<0.001	19 (61)	0.37
Diabetes mellitus	36 (42)	409 (22)	<0.001	21 (68)	0.021
Pulmonary disease	23 (27)	129 (7)	<0.001	5 (16)	0.33
Peripheral arterial disease	8 (14)	62 (5)	0.013	2 (10)	1.00
Coronary heart disease	11 (13)	69 (4)	0.001	10 (32)	0.027
Chronic kidney disease	1 (1)	55 (3)	0.72	8 (27)	<0.001
Stroke	4 (5)	42 (2)	0.14	5 (16)	0.056
Current tobacco use	10 (12)	371 (20)	0.07	4 (13)	1.00
Current alcohol use	17 (20)	579 (31)	0.03	5 (16)	0.79
Aspirin	50 (59)	852 (46)	0.026	13 (42)	0.14
Lipid-lowering medication	4 (5)	74 (4)	0.77	4 (13)	0.21
Antihypertensive medication	74 (87)	910 (49)	<0.001	28 (90)	0.76
Beta-blocker	12 (14)	163 (9)	0.10	4 (13)	0.87
ACE inhibitor	17 (20)	165 (9)	0.002	14 (45)	0.009
Diuretic	49 (58)	412 (22)	<0.001	21 (68)	0.39
Digoxin	8 (9)	20 (1)	<0.001	11 (36)	0.002
Heart rate, beats/min	68 (64–74)	68 (64–72)	0.32	72 (66–78)	0.20
Systolic BP, mm Hg	130 (120–141)	128 (117–142)	0.42	135 (122–154)	0.14
Diastolic BP, mm Hg	74 (68–81)	76 (70–83)	0.13	72 (64–92)	0.76
Pulse pressure, mm Hg	52 (45–65)	52 (43–63)	0.15	60 (51–72)	0.06
Body mass index, kg/m^2	32 (29–37)	29 (26–33)	<0.001	34 (27–40)	0.97
Total cholesterol, mg/dl	206 (182–227)	204 (180–231)	0.88	210 (184–245)	0.24
LDL-cholesterol, mg/dl	124 (105–154)	126 (102–151)	0.85	124 (104–156)	0.88
HDL-cholesterol, mg/dl	53 (41–64)	54 (43–66)	0.41	54 (42–66)	0.55
Triglycerides, mg/dl	110 (85–150)	98 (74–134)	0.007	117 (84–157)	0.85
WBC	5.3 (4.5–6.3)	5.1 (4.2–6.3)	0.25	6.4 (5.2–7.2)	0.019
Hemoglobin, g/dl	12.6 (11.9–13.3)	13.1 (12.2–13.9)	0.003	12.5 (11.7–13.4)	0.69
Creatinine, mg/dl	0.86 (0.76–0.96)	0.86 (0.76–1.06)	0.003	0.96 (0.86–1.26)	<0.001
eGFR, ml/min/1.73 m^2	93 (79–114)	90 (79–103)	0.66	78 (59–100)	0.006
Glucose, mg/dl	109 (96–156)	102 (94–118)	0.004	124 (97–203)	0.30
LVH on ECG (Cornell), %	3 (4)	125 (7)	0.37	8 (26)	0.001
QRS duration, ms	94 (87–103)	93 (86–101)	0.39	102 (92–109)	0.042
Advanced retinopathy, %	17 (20)	222 (12)	0.037	12 (39)	0.07
Ankle brachial index	1.05 (0.97–1.13)	1.10 (1.03–1.17)	0.002	1.03 (0.99–1.14)	0.99

Values are median (interquartile range) or n (%). *Obesity defined as body mass index ≥30 kg/m^2.

ACE = angiotensin-converting enzyme; ARIC = Atherosclerosis Risk in Communities; BP = blood pressure; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LDL = low-density lipoprotein; LE = lower extremity; LVH = left ventricular hypertrophy; PND = paroxysmal nocturnal dyspnea; WBC = white blood cell count.

no differences with regard to heart rate or blood pressure. As expected, symptoms of HF, such as orthopnea, paroxysmal nocturnal dyspnea, and lower extremity edema, were more common among those with HF compared with those without HF (Table 1).

Comorbidities were common among those with HFpEF (Table 1). In particular, hypertension, obesity, diabetes mellitus, pulmonary disease, peripheral arterial disease, and CHD were more frequent among those with HFpEF compared with those without HF. Of note, hypertension was highly prevalent, approaching 60%, even in those without HF. Comorbidities were also common among those with HFrEF—with diabetes mellitus, CHD, and CKD present more frequently than in those with HFpEF.

Cardiac structure and function differed between groups (Table 2). Those with HFpEF had increased wall thickness and LVMI compared with those without HF, although prevalence of diastolic dysfunction and left atrial enlargement did not differ between these 2 groups. In contrast, those with HFrEF had the highest LV wall thickness and

Table 2 Cardiac Structure and Function According to HF Status and LVEF Among Jackson, Mississippi, Participants of the ARIC Study

	HFpEF (n = 85)	No HF (n = 1,846)	No HF vs. HFpEF p Value	HFrEF (n = 31)	HFrEF vs. HFpEF p Value
LVEF, %	67 (59–75)	64 (56–71)	0.002	39 (28–44)	<0.001
FS 2D, %	37 (31–44)	34 (29–40)	0.002	19 (13–22)	<0.001
Mitral E velocity, cm/s	76 (66–89)	76 (65–87)	0.50	79 (63–92)	0.52
Mitral A velocity, cm/s	80 (67–91)	75 (64–88)	0.13	96 (72–106)	0.001
Mitral E/A	0.94 (0.79–1.12)	1.00 (0.84–1.19)	0.14	0.75 (0.66–1.10)	0.054
Diastolic dysfunction, %	23 (27)	460 (25)	0.70	22 (71)	<0.001
SWT, cm	1.22 (1.09–1.32)	1.16 (1.04–1.29)	0.028	1.27 (1.12–1.34)	0.35
PWT, cm	1.21 (1.09–1.36)	1.17 (1.06–1.31)	0.057	1.27 (1.20–1.41)	0.07
LVEDD, cm	4.35 (4.07–4.67)	4.34 (3.98–4.72)	0.76	5.43 (4.73–6.08)	<0.001
LVESD, cm	2.60 (2.42–2.99)	2.82 (2.45–3.20)	0.014	4.32 (3.59–5.32)	<0.001
LV mass, g	239 (202–285)	230 (188–276)	0.10	366 (304–436)	<0.001
LVMI, $g/m^{2.7}$	63 (51–74)	56 (47–68)	0.002	92 (75–101)	<0.001
LVH (LVMI ≥51 $g/m^{2.7}$)	64 (75)	1,183 (64)	0.037	29 (94)	0.035
RWT	0.57 (0.51–0.62)	0.54 (0.47–0.62)	0.057	0.48 (0.42–0.56)	<0.001
RWT ≥0.42	79 (93)	1668 (90)	0.57	23 (74)	0.01
LA diameter, cm	3.4 (3.1–3.8)	3.4 (3.0–3.7)	0.12	3.8 (3.3–4.3)	0.008
LA enlargement (>4 cm)	16 (19)	240 (13)	0.14	12 (39)	0.048
Aortic root diameter, cm	3.1 (2.8–3.3)	3.0 (2.8–3.2)	0.08	3.0 (2.8–3.3)	0.85
≥ Moderate regurgitation					
Mitral	0 (0)	13 (1)	1.00	3 (10)	0.02
Aortic	1 (1)	9 (1)	0.35	0 (0)	1.00
Tricuspid	2 (2)	29 (2)	0.65	1 (3)	1.00
LV geometry					
Normal	4 (5)	80 (4)	0.79	1 (3)	1.00
Concentric remodeling	17 (20)	583 (32)	0.023	1 (3)	0.039
Concentric hypertrophy	62 (73)	1,085 (59)	0.009	22 (71)	0.82
Eccentric hypertrophy	2 (2)	98 (5)	0.32	7 (23)	0.001

Values are median (interquartile range) or n (%).

2D = 2-dimensional; FS = fractional shortening; LA = left atrium; LV = left ventricular; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; LVMI = left ventricular mass index; PWT = posterior wall thickness; RWT = relative wall thickness; SWT = septal wall thickness; other abbreviations as in Table 1.

LVMI. Additionally, left atrial enlargement and mitral regurgitation were more frequent among those with HFrEF compared with those with HFpEF. Concentric hypertrophy was the most common LV geometry; however, it was significantly more frequent in patients with HFpEF compared with those without HF. Hypertrophy was present in nearly all participants with HFrEF, with eccentric hypertrophy more frequent in patients with HFrEF compared with those with HFpEF.

Over a median follow-up of 13.7 years, deaths occurred in 21%, 31%, and 61% of those without HF, with HFpEF, and with HFrEF, respectively (Table 3). Death rates in patients with HFpEF were increased compared with those without HF but were lower than those with HFrEF, even when adjusted for age. In age- and sex-adjusted Cox proportional hazard models, risk of death differed among groups. HFpEF was associated with a 51% increased risk of death compared with no HF (hazard ratio [HR]: 1.51; 95% CI: 1.01 to 2.25). HFrEF was associated with the worst survival, with 2.5 times the risk of death compared with HFpEF (HR: 2.50; 95% CI: 1.37 to 4.58). When further adjusted for LVEF, HFpEF was associated with 61% increased risk of death as compared with no HF (HR: 1.61; 95% CI: 1.08 to 2.41). Adjustment for differences in clinical characteristics attenuated the mortality risk associated with HFpEF versus no HF; however, those with HFrEF remained at significantly increased risk of death compared with those with HFpEF (Table 3, Fig. 1).

Discussion

In a community-based sample of middle-age African Americans, we found that demographic and clinical characteristics as well as cardiac structure and function significantly differed among patients with HFpEF, HFrEF, and no HF. By comparing patients with HFpEF with those without HF, we found that older age, female sex, hypertension, obesity, diabetes mellitus, and concentric hypertrophy were more common in patients with HFpEF. Similarly, diabetes mellitus, CKD, CHD, and left atrial enlargement were more common in patients with HFrEF than those with HFpEF. Survival differed among groups, with HFpEF portending a worse prognosis than no HF but not as severe as HFrEF. Together, these findings suggest that in African Americans, HFpEF and HFrEF may be distinct syndromes.

Representation of African Americans in observational studies and clinical trials is typically low; thus, HF in this population is not well understood (21,22). Moreover, few HF

JACC: Heart Failure Vol. 1, No. 2, 2013
April 2013:156–63

Table 3 Mortality Rates and Risk of Death According to HF Status and LVEF in African Americans

	No HF (n = 1,846)	HFpEF (n = 85)	HFrEF (n = 31)
Deaths and mortality rates			
Deaths, n (%)	393 (21)	26 (31)	19 (61)
Person-time, yrs	23,707	1,032	291
Deaths/100 person-yrs* (95% CI)	1.66 (1.50–1.83)	2.52 (1.72–3.70)	6.52 (4.16–10.22)
		HFpEF vs. Non HF	HFrEF vs. HFpEF
Hazard ratios (95% CI)			
Unadjusted		1.55 (1.04–2.30)	2.62 (1.45–4.75)
Age, sex adjusted		1.51 (1.01–2.25)	2.50 (1.37–4.58)
Age, sex, LVEF† adjusted		1.61 (1.08–2.41)	N/A
Age, sex, LVEF,† propensity score‡ adjusted		1.35 (0.87–2.09)	2.29 (1.19–4.42)

*Death rates standardized to median age (58.7 years) of cohort. †LVEF not included in comparison of HFrEF versus HFpEF. ‡Propensity score calculated with baseline characteristics that significantly differed between groups.
Abbreviations as in Tables 1 and 2.

studies focus specifically on African Americans (23) because most literature involving race in HF addresses differences among racial groups. This is in spite of a higher prevalence of cardiovascular risk factors and greater burden of HF among African Americans. The existing literature suggests that the development and progression of HF in African Americans may be characterized by predominantly non-ischemic etiologies, more severe natural history, and possibly a different response to pharmacotherapy when compared with predominantly white studies (9,21). By evaluating an entirely African-American cohort, our findings may advance understanding of HF in this high-risk population.

Approximately three-quarters of African Americans with HF in our cohort had HFpEF. This is concordant with 2 population-based studies of patients with ambulatory HF in which 57% to 76% had preserved systolic function (7,24) but differs from an ambulatory Veterans Administration population in which HFpEF was present in 25% (25). However, only 6% of those in the Veterans Administration study were female; therefore, the Veterans Administration population may not be representative of the typical HFpEF population (25). In comparison, 65% of the Jackson, Mississippi, cohort was female, which may be one explanation for the higher prevalence of HFpEF. Our findings are also consistent with population studies of patients with ambulatory HF that included multiple ethnicities and demonstrated a higher prevalence of HFpEF than HFrEF (26–28). However, our results contrast with those of studies evaluating African Americans hospitalized with acute decompensated HF in which HFpEF was prevalent in 29% to 43% (5,6,29), suggesting that the relative frequency of HFpEF and HFrEF may differ between hospitalized and ambulatory settings (30). Additionally, the finding that HFpEF was more common than HFrEF may be explained, in part, by the high prevalence of hypertension and relatively low frequency of CHD.

Regardless of preserved or reduced LVEF, comorbidities were common in HF. However, the pattern of clinical characteristics differed between patients with HFpEF and those with HFrEF. In addition to diabetes mellitus and CKD, CHD was more frequent in patients with HFrEF compared with those with HFpEF, although it was only present in one-third of those with HFrEF despite the high prevalence of atherosclerotic risk factors. Overall, CHD was not as common in patients with HF as typically described in predominantly white populations, which may be partially explained by the relatively high proportion of female and middle-age patients in this study. Hypertension, however, was present in 85% of those with HF. Together, these findings suggest that hypertension, along with other comorbidities such as obesity, diabetes mellitus, and CKD, rather than CHD, may be relatively more important factors in HF in African Americans.

The most striking finding related to cardiac structure was the marked prevalence of LVH in those with HF and among those without HF. Although hypertension may be the most common contributor to hypertrophy, other factors including obesity

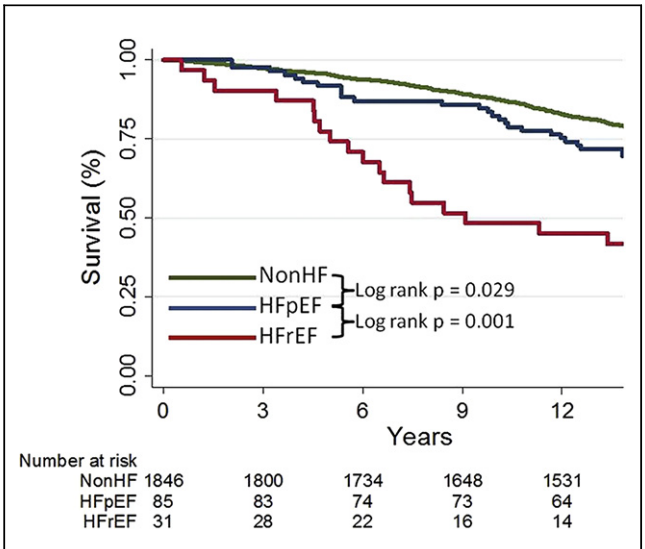

Figure 1 Survival in African Americans According to HF Status

Kaplan-Meier survival analysis in those without heart failure (nonHF), HF with preserved ejection fraction (HFpEF), and those with HF and reduced ejection fraction (HFrEF).

(31,32), diabetes mellitus (33,34), metabolic syndrome (35), and CKD (36) have previously been demonstrated to be associated with LVH. Several studies have shown that these comorbidities are common in HF, particularly among African Americans and Hispanics (4,37). In our analysis, these comorbidities were frequent in patients with HF, and a particularly worrisome finding was that concentric hypertrophy was present in 60% of those without HF. The high prevalence of hypertension and concentric LVH, a known marker of increased cardiovascular risk in African Americans (38), portends a potential increase in HF among this group (39).

There is also uncertainty regarding the risk of death in chronic HF among African Americans (5). Registries of hospitalized patients with HF suggest similar or better survival in African-American versus white patients (4–6,40). This is congruent with previous reports from the ARIC study demonstrating similar mortality rates between races at 30 days and 1 year; however, the longer follow-up time in the ARIC study revealed higher fatality rates in African Americans at 5 years post-HF hospitalization (3). Few studies have evaluated survival in HFpEF in African Americans. In a predominantly male Veterans Administration population, survival over 5 years of follow-up did not differ according to race among those with HFpEF; however, among African Americans, HFpEF appeared to be associated with a similar or slightly better prognosis than HFrEF (10). Results from the Duke Databank of Cardiovascular Disease suggest a better 5-year survival in patients with HFpEF (68%) (11), as compared with those with HFrEF (51%) (41), although a direct comparison of mortality between HFpEF and HFrEF in African Americans was not made.

We found that HFpEF was associated with a more benign prognosis than HFrEF. This is consistent with a meta-analysis of nearly 42,000 patients with HF that demonstrated a 32% lower risk of death in HFpEF compared with HFrEF, although stratification according to race was not reported (42). It is also consistent with the CHARM (Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity) trial (43) but differs from epidemiological data from Olmsted County, Enhanced Feedback for Effective Cardiac Treatment, and the Framingham Heart Study, in which mortality rates were similar between patients with HFpEF and those with HFrEF (44–46). This may, in part, be explained by differences in study populations because those studies that capture patients during or immediately following an acute hospitalization find that HFpEF and HFrEF have similar mortality, particularly among the elderly (30). In contrast, patients with ambulatory HF, such as those in the Cardiovascular Health and Strong Heart studies, which enrolled an older biracial population and Native Americans, respectively, demonstrated lower fatality rates in HFpEF versus HFrEF (26,27). However, representation of African Americans in these studies was generally low, limiting applicability to this race.

We also found the mortality rate in patients with HFpEF to be greater than that of those without HF. The risk of death in those with HFpEF was 61% higher than age-, sex-, and LVEF-matched participants without prevalent HF. However, adjustment for additional clinical characteristics attenuated this risk. It has been proposed that HFpEF is a collection of comorbidities and that the syndrome of HFpEF may not even exist (47). In contrast, pooled analyses of clinical trials of HFpEF and cardiovascular trials of patients without HF have demonstrated higher mortality rates in patients with HFpEF compared with those without HF (48). Our data in African Americans are consistent with these pooled analyses. Although adjustment for comorbidities attenuated this risk, the relatively small number of deaths in our HFpEF population limited our statistical power. Nevertheless, our findings highlight the importance of comorbidities in African Americans with HFpEF but do not mitigate the broader literature demonstrating that HFpEF is associated with a worse prognosis than no HF.

Recent literature also suggests that one-half of all deaths in HFpEF may not be related to cardiovascular causes (49–51), again emphasizing the impact of comorbidities (37,52). We extended these findings by showing that non-cardiovascular comorbidities were frequent among African Americans with HF. Furthermore, using ICD codes (recognizing their limitation in identifying cause of death), we observed a similar trend to previous reports, namely, that 58%, 44%, and 26% of deaths in those with no HF, HFpEF, and HFrEF, respectively, were due to noncardiovascular causes (Fig. 2). Together, these findings emphasize the importance of treating comorbidities, particularly among those with HFpEF, as a potential approach to improving outcomes (37,49,52,53).

Study limitations. Although we specifically evaluated an entirely African-American cohort over a long follow-up

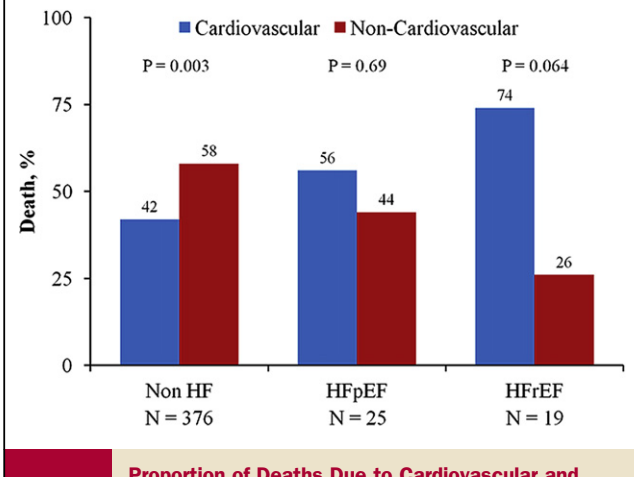

Figure 2 Proportion of Deaths Due to Cardiovascular and Noncardiovascular Causes According to HF Status in African Americans

Cause of death ascertained from International Classification of Diseases-Ninth Edition codes. Abbreviations as in Figure 1.

JACC: Heart Failure Vol. 1, No. 2, 2013
April 2013:156–63

period, limitations should be noted. The cross-sectional design precludes assessment of causality among clinical characteristics, cardiac structure and function, and HF. However, differences among patients with HFpEF, HFrEF, and no HF may provide insight into targets for future investigation. The definition for prevalent HF was based upon Gothenburg criteria and unadjudicated hospitalization ICD-9 codes, although these methods have been validated in the ARIC study (3,54). Importantly, this approach captured participants with previous or current symptoms of HF, as recommended by the American College of Cardiology/American Heart Association staging of HF (55). LVEF was not assessed at the time of incident HF, and it is possible that LVEF may have recovered between the incident HF event and our assessment. However, LVEF has previously been demonstrated to be similar between acute and chronic HF (56). Moreover, our findings suggest that LVEF measured after incident HF still imparts prognostic information. The Teichholz method was used to calculate LVEF because volumetric measurements were not available. Diastolic function was assessed with transmitral Doppler E/A ratio because estimation of left atrial volumes, tissue Doppler imaging, transmitral E-wave deceleration time, pulmonary venous flow, and isovolumic relaxation time were not obtained at echocardiography. Although diastolic dysfunction is frequently reported in HFpEF, we found it to be present in only 25% of participants with HFpEF, which did not differ between patients with HFpEF and those without HF, likely reflecting limitations in diastolic assessment. There may have been selection bias with regard to participants who presented for echocardiography or had interpretable images, such that the sickest individuals, including those with more severe HF, may be underrepresented. Inherent to the ARIC study's design, this study included a selected age range and consisted entirely of African Americans from Jackson, Mississippi. Therefore, our results may not be generalizable to younger, more elderly, or all African Americans. However, the mean age of African Americans in most HF registries is 63 to 64 years, falling within the range of our cohort (4–6,25). The observed mortality rates may not be directly applicable to a more contemporary time period due to temporal changes in HF management. Finally, the relatively low numbers of participants with prevalent HF may limit statistical power.

Conclusions

We found in a community-based sample of middle-age African Americans that demographic and clinical characteristics, as well as cardiac structure and function, significantly differed among patients with HFpEF, HFrEF, and no HF. HFpEF was more common than HFrEF and portended a worse prognosis than no HF but not as severe as HFrEF. Because this population bears a disproportionate burden of HF, focused investigation on African Americans is an important step to understanding HF and developing strategies for prevention, detection, and treatment.

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Reprint requests and correspondence: Dr. Scott D. Solomon, Brigham and Women's Hospital, Cardiovascular Division, 75 Francis Street, Boston, Massachusetts 02115. E-mail: ssolomon@rics.bwh.harvard.edu.

REFERENCES

1. Bibbins-Domingo K, Pletcher MJ, Lin F, et al. Racial differences in incident heart failure among young adults. N Engl J Med 2009;360:1179–90.
2. Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the Multi-Ethnic Study of Atherosclerosis. Arch Intern Med 2008;168:2138–45.
3. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). Am J Cardiol 2008;101:1016–22.
4. Thomas KL, Hernandez AF, Dai D, 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;161:746–54.
5. 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;168:1152–8.
6. Yancy CW, Abraham WT, Albert NM, et al. Quality of care of and outcomes for African Americans hospitalized with heart failure: findings from the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure) registry. J Am Coll Cardiol 2008;51:1675–84.
7. Martin TC. Comparison of Afro-Caribbean patients presenting in heart failure with normal versus poor left ventricular systolic function. Am J Cardiol 2007;100:1271–3.
8. Hogg K, Swedberg K, McMurray J. Heart failure with preserved left ventricular systolic function; epidemiology, clinical characteristics, and prognosis. J Am Coll Cardiol 2004;43:317–27.
9. Dries DL, Exner DV, Gersh BJ, Cooper HA, Carson PE, Domanski MJ. Racial differences in the outcome of left ventricular dysfunction. N Engl J Med 1999;340:609–16.
10. Agoston I, Cameron CS, Yao D, Dela Rosa A, Mann DL, Deswal A. Comparison of outcomes of white versus black patients hospitalized with heart failure and preserved ejection fraction. Am J Cardiol 2004;94:1003–7.
11. East MA, Peterson ED, Shaw LK, Gattis WA, O'Connor CM. Racial differences in the outcomes of patients with diastolic heart failure. Am Heart J 2004;148:151–6.
12. The ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol 1989;129:687–702.
13. Skelton TN, Andrew ME, Arnett DK, et al. Echocardiographic left ventricular mass in African-Americans: the Jackson cohort of the Atherosclerosis Risk in Communities study. Echocardiography 2003;20:111–20.
14. Nunez E, Arnett DK, Benjamin EJ, et al. Optimal threshold value for left ventricular hypertrophy in blacks: the Atherosclerosis Risk in Communities study. Hypertension 2005;45:58–63.
15. Redfield MM, Jacobsen SJ, Burnett JC Jr., Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. JAMA 2003;289:194–202.
16. Wilhelmsen L, Eriksson H, Svardsudd K, Caidahl K. Improving the detection and diagnosis of congestive heart failure. Eur Heart J 1989;10 Suppl C:13–8.

17. Folsom AR, Yamagishi K, Hozawa A, Chambless LE. Absolute and attributable risks of heart failure incidence in relation to optimal risk factors. Circ Heart Fail 2009;2:11–7.
18. Wong TY, Rosamond W, Chang PP, et al. Retinopathy and risk of congestive heart failure. JAMA 2005;293:63–9.
19. Kottgen A, Russell SD, Loehr LR, et al. Reduced kidney function as a risk factor for incident heart failure: the Atherosclerosis Risk in Communities (ARIC) study. J Am Soc Nephrol 2007;18:1307–15.
20. Folsom AR, Peacock JM, Boerwinkle E. Variation in PCSK9, low LDL cholesterol, and risk of peripheral arterial disease. Atherosclerosis 2009;202:211–5.
21. Yancy CW. Heart failure in African Americans. Am J Cardiol 2005;96: 3i–12i.
22. Franciosa JA, Ferdinand KC, Yancy CW. Treatment of heart failure in African Americans: a consensus statement. Congest Heart Fail 2010; 16:27–38.
23. Taylor AL, Ziesche S, Yancy C, et al. Combination of isosorbide dinitrate and hydralazine in blacks with heart failure. N Engl J Med 2004;351:2049–57.
24. Magana-Serrano JA, Almahmeed W, Gomez E, et al. Prevalence of heart failure with preserved ejection fraction in Latin American, Middle Eastern, and North African regions in the I PREFER study (Identification of Patients With Heart Failure and Preserved Systolic Function: an epidemiological regional study). Am J Cardiol 2011;108:1289–96.
25. Deswal A, Petersen NJ, Urbauer DL, Wright SM, Beyth R. Racial variations in quality of care and outcomes in an ambulatory heart failure cohort. Am Heart J 2006;152:348–54.
26. Gottdiener JS, McClelland RL, Marshall R, et al. Outcome of congestive heart failure in elderly persons: influence of left ventricular systolic function. The Cardiovascular Health Study. Ann Intern Med 2002;137:631–9.
27. Devereux RB, Roman MJ, Liu JE, et al. Congestive heart failure despite normal left ventricular systolic function in a population-based sample: the Strong Heart Study. Am J Cardiol 2000;86:1090–6.
28. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. J Am Coll Cardiol 1999;33:1948–55.
29. Ilksoy N, Hoffman M, Moore RH, Easley K, Jacobson TA. Comparison of African-American patients with systolic heart failure versus preserved ejection fraction. Am J Cardiol 2006;98:806–8.
30. Kitzman DW. Diastolic heart failure in the elderly. Heart Fail Rev 2002;7:17–27.
31. Fox E, Taylor H, Andrew M, et al. Body mass index and blood pressure influences on left ventricular mass and geometry in African Americans: the Atherosclerotic Risk in Communities (ARIC) study. Hypertension 2004;44:55–60.
32. Lorber R, Gidding SS, Daviglus ML, Colangelo LA, Liu K, Gardin JM. Influence of systolic blood pressure and body mass index on left ventricular structure in healthy African-American and white young adults: the CARDIA study. J Am Coll Cardiol 2003;41:955–60.
33. de Simone G, Palmieri V, Bella JN, et al. Association of left ventricular hypertrophy with metabolic risk factors: the HyperGEN study. J Hypertens 2002;20:323–31.
34. Lee M, Gardin JM, Lynch JC, et al. Diabetes mellitus and echocardiographic left ventricular function in free-living elderly men and women: the Cardiovascular Health Study. Am Heart J 1997;133:36–43.
35. Burchfiel CM, Skelton TN, Andrew ME, et al. Metabolic syndrome and echocardiographic left ventricular mass in blacks: the Atherosclerosis Risk in Communities (ARIC) study. Circulation 2005;112: 819–27.
36. Astor BC, Arnett DK, Brown A, Coresh J. Association of kidney function and hemoglobin with left ventricular morphology among African Americans: the Atherosclerosis Risk in Communities (ARIC) study. Am J Kidney Dis 2004;43:836–45.
37. Ather S, Chan W, Bozkurt B, et al. Impact of noncardiac comorbidities on morbidity and mortality in a predominantly male population with heart failure and preserved versus reduced ejection fraction. J Am Coll Cardiol 2012;59:998–1005.
38. Liao Y, Cooper RS, McGee DL, Mensah GA, Ghali JK. The relative effects of left ventricular hypertrophy, coronary artery disease, and ventricular dysfunction on survival among black adults. JAMA 1995; 273:1592–7.
39. Kamath S, Markham D, Drazner MH. Increased prevalence of concentric left ventricular hypertrophy in African-Americans: will an epidemic of heart failure follow? Heart Fail Rev 2006;11:271–7.
40. Gordon HS, Nowlin PR, Maynard D, Berbaum ML, Deswal A. Mortality after hospitalization for heart failure in blacks compared to whites. Am J Cardiol 2010;105:694–700.
41. Thomas KL, East MA, Velazquez EJ, et al. Outcomes by race and etiology of patients with left ventricular systolic dysfunction. Am J Cardiol 2005;96:956–63.
42. Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC). The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. Eur Heart J 2012;33:1750–7.
43. Solomon SD, Anavekar N, Skali H, et al. Influence of ejection fraction on cardiovascular outcomes in a broad spectrum of heart failure patients. Circulation 2005;112:3738–44.
44. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med 2006;355:251–9.
45. Bhatia RS, Tu JV, Lee DS, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006;355:260–9.
46. Lee DS, Gona P, Vasan RS, et al. Relation of disease pathogenesis and risk factors to heart failure with preserved or reduced ejection fraction: insights from the Framingham Heart Study of the National Heart, Lung, and Blood Institute. Circulation 2009;119:3070–7.
47. Packer M. Can brain natriuretic peptide be used to guide the management of patients with heart failure and a preserved ejection fraction? The wrong way to identify new treatments for a nonexistent disease. Circ Heart Fail 2011;4:538–40.
48. Campbell RT, Jhund PS, Castagno D, Hawkins NM, Petrie MC, McMurray JJ. What have we learned about patients with heart failure and preserved ejection fraction from DIG-PEF, CHARM-Preserved, and I-PRESERVE? J Am Coll Cardiol 2012;60:2349–56.
49. Lee DS, Gona P, Albano I, et al. A systematic assessment of causes of death after heart failure onset in the community: impact of age at death, time period, and left ventricular systolic dysfunction. Circ Heart Fail 2011;4:36–43.
50. Zile MR, Gaasch WH, Anand IS, et al. Mode of death in patients with heart failure and a preserved ejection fraction: results from the Irbesartan in Heart Failure With Preserved Ejection Fraction Study (I-PRESERVE) trial. Circulation 2010;121:1393–405.
51. Henkel DM, Redfield MM, Weston SA, Gerber Y, Roger VL. Death in heart failure: a community perspective. Circ Heart Fail 2008;1:91–7.
52. Kitzman DW. Outcomes in patients with heart failure with preserved ejection fraction: it is more than the heart. J Am Coll Cardiol 2012;59: 1006–7.
53. Shah SJ, Gheorghiade M. Heart failure with preserved ejection fraction: treat now by treating comorbidities. JAMA 2008;300:431–3.
54. Avery CL, Mills KT, Chambless LE, et al. Long-term association between self-reported signs and symptoms and heart failure hospitalizations: the Atherosclerosis Risk In Communities (ARIC) study. Eur J Heart Fail 2010;12:232–8.
55. Hunt SA, Abraham WT, Chin MH, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. J Am Coll Cardiol 2009;53:e1–90.
56. Gandhi SK, Powers JC, Nomeir AM, et al. The pathogenesis of acute pulmonary edema associated with hypertension. N Engl J Med 2001; 344:17–22.

Key Words: African-Americans ■ echocardiography ■ heart failure with preserved ejection fraction ■ heart failure with reduced ejection fraction ■ mortality.