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Epidemiology of Incident Heart Failure in a Contemporary Elderly Population: The Health, Aging, and Body Composition Study

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Abstract

Background—Race- and gender- specific epidemiology of incident heart failure (HF) in a contemporary elderly cohort is not well described.

Methods—We studied 2934 participants without HF enrolled in the Health ABC Study (age 73.6 ±2.9 years, 47.9% men, 58.6% white, 41.4% black) and assessed incidence of HF, population attributable risk (PAR) of independent risk factors for HF, and outcomes of incident HF.

Results—During a median follow-up of 7.1 years, 258 (8.8%) participants developed HF (13.6/1000 person-years). Men and blacks were more likely to develop HF. No significant sex-based differences were observed in risk factors. Coronary heart disease (whites: PAR 23.9%, blacks: PAR 29.5%) and uncontrolled blood pressure (whites: PAR 21.3%, blacks: PAR 30.1%) carried the highest PAR in both races. In blacks, 6 out of 8 risk factors assessed (coronary heart disease, uncontrolled blood pressure, left ventricular hypertrophy, reduced glomerular filtration rate, smoking, and increased heart rate) had >5% higher PAR compared to whites, leading to a higher overall proportion of HF attributable to modifiable risk factors in blacks vs. whites (67.8% vs. 48.9%). Participants who developed HF had a higher annual mortality (18.0% vs. 2.7%). No racial difference in survival after HF was noted; however, rehospitalization rates were higher in blacks (62.1 vs. 30.3/100 person-years, P<.001).

Conclusions—Incident HF is common in the elderly; a large proportion of HF risk was attributed to modifiable risk factors. Racial differences in risk factors for HF and in hospitalization rates after HF need to be accounted for prevention and treatment efforts.

Keywords

Heart failure; epidemiology; risk factors; race; sex

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Heart failure (HF) is primarily a disease of the elderly, with an annual incidence of 10/1000 after age 65 years, which doubles every decade thereafter.[1] Subjects older than 65 years represent >75% of prevalent HF cases in the United States.[2] In a recent European study, participants older than 70 years accounted for 88% of new HF cases.[3] Although some data suggest a relative improvement in survival after development of HF recently,[4, 5] other studies, especially in the elderly, challenge this notion.[6] Nevertheless, the absolute survival rate for these patients remains poor and the actual number of HF deaths has increased by 20.5% over the last decade, reflecting the increasing prevalence of HF and the aging of the population. In patients older than 67 years, median survival is generally less than 3 years after hospitalization for HF.[7, 8] The annual hospitalization rate for these patients now exceeds over a million in the United States, 80% of patients hospitalized with HF are older than 65 years, and readmission rates as high as 50% within 6 months of discharge have been reported.[9]

Risk factors and outcomes for HF in the general population have been well described.[4, 8, 10, 11] However, many of these data are old, derived from primarily white subjects, and mostly in relatively young or middle-aged populations. The risk factor profile for cardiovascular diseases is changing with increasing prevalence of obesity, metabolic syndrome, and diabetes.[12] Similarly, the therapeutic profile for risk factors like hypertension or coronary heart disease (CHD) has evolved over time, with increased use of ACE inhibitors and statins. This may affect both the development of HF and outcomes thereafter. Also, recent literature suggests substantial differences in disease development and progression among sex- and race-based sub-groups.[13, 14] Understanding and quantifying these differences is imperative for planning appropriate preventive and therapeutic interventions. The sex- and race-related risk factor profile and population attributable risk (PAR) for HF risk factors in the contemporary elderly population are not known. In this study, we sought to assess the epidemiology of incident HF in the elderly participants enrolled in the Health, Aging and Body Composition (Health ABC) Study.

METHODS

Study Population and Outcomes

The Health ABC Study is a population-based study of 3075 community-dwelling men and women aged 70 to 79 years at enrollment. To be eligible, participants had to report no difficulty in walking one-quarter mile or climbing 10 stairs without resting. Participants were identified from a random sample of white Medicare beneficiaries and all age-eligible black community residents in designated zip codes areas surrounding Pittsburgh and Memphis. Exclusion criteria included difficulties with activities of daily living, obvious cognitive impairment, inability to communicate with the interviewer, intention of moving within 3 years, or participation in a trial involving a life-style intervention. All participants provided written informed consent and the Institutional Review Boards at both study sites approved the study protocol.

Baseline data were collected in 1997–1998. Cardiovascular disease status at baseline, including prevalent HF, was based on ICD 9-CM codes as reported by Medicare and Medicaid Services for the years 1995–1998; self-reported history; and use of selected drugs. All participants were asked to report any hospitalizations and every 6 months they were asked direct questions to elicit information about interim cardiovascular events. All admissions with an overnight stay were evaluated for cardiovascular events by reviewing the medical records at each site. All hospitalizations and deaths were reviewed by the Health ABC Diagnosis and Disease Ascertainment committee and underlying causes of death were determined by central adjudication.

Of the 3075 subjects enrolled at in the Health ABC Study, 95 had definite or possible HF at baseline, and 46 were excluded due to missing data on HF status. The final cohort analyzed for this study included 2934 participants.

Study Definitions

Incident HF—All first admissions with an overnight stay confirmed to be related to HF were classified as incident HF. Local adjudicators classified events as HF, based on symptoms, signs, chest radiograph results, and echocardiographic findings, using criteria similar to those used in the Cardiovascular Health Study.[15] Briefly, physician diagnoses of HF were confirmed by documentation in the participants' medical records of a constellation of symptoms (i.e., shortness of breath, fatigue, orthopnea, paroxysmal nocturnal dyspnea) and physical signs (i.e., edema, pulmonary rales, gallop rhythm, displaced left ventricular apical impulse) or by clinical findings such as evidence of pulmonary edema on chest radiograph. Although ejection fraction was not available for all incident HF hospitalizations, when it was available it was considered part of the clinical picture. The diagnosis of CHF was also confirmed if, in addition to having a physician diagnosis of HF, the participant was receiving medical therapy for HF, including diuretics, digitalis, angiotensin-converting enzyme inhibitors, and beta-blockers.

The HF criteria required at least HF diagnosis from a physician *and* treatment for HF (i.e. a current prescription for a diuretic agent and either digitalis or a vasodilator); these criteria have been used in previous studies.[16] Since HF was not allowed as a cause of death, there were no deaths considered as due to incident HF.

Risk Factors Definitions—History of coronary revascularization, electrocardiographic evidence of myocardial infarction, or self-reported history of myocardial infarction or angina accompanied by anti-anginal medications was considered definite evidence of CHD; self-reported history of CHD without medications was considered as probable CHD. Hypertension was classified as definite if there was both a history of hypertension or physician diagnosis and use of antihypertensive medications; history or medications alone were classified as probable hypertension. Diabetes was considered present if the participant reported history of diabetes or use of anti-diabetic medications. Smoking was classified as current, past (if $\geq$ 100 lifetime cigarettes), or never. Cerebrovascular disease was based on history of stroke, transient ischemic attack, or carotid intervention. Depression was defined as self-reported depression accompanied by medication use. Left ventricular hypertrophy (LVH) was determined from the baseline electrocardiogram by the following criteria[17]: R >26mm in either lead V5 or V6, or R >20mm in any of leads I, II, III, aVF, or R >12mm in lead aVL, or R in lead V5 or V6 plus S in lead V1 >35mm.

Risk Factors for Incident HF—We have previously reported independent predictors of incident HF in the Health ABC Study.[18] Nine variables were independently associated with HF development: age, history of smoking and CHD, LVH, systolic blood pressure and heart rate, and serum glucose, albumin, and creatinine levels; sex and race were both considered but neither was independently associated with incident HF. For PAR calculation purposes, continuous predictors were dichotomized using clinically relevant cut-off points. Systolic blood pressure was dichotomized as controlled vs. uncontrolled at 140 mmHg, fasting glucose at 125 mg/dl, resting heart rate at 75 bpm,[19] and albumin at 3.8 mg/dl [20]; creatinine was converted to glomerular filtration rate (GFR) by MDRD formula [21] and a cut-off of 60ml/min/1.73m^2 was used to define impaired GFR. Smoking (current yes/no) and CHD status (definite yes/no) were collapsed into binary predictors. We classified independent risk factors into two groups: modifiable (CHD, systolic blood pressure, glucose, LVH and smoking) and potentially modifiable (renal function, albumin, and heart rate). Age was included in regression models

for multivariable PAR calculation, but PAR of age was omitted from the tables since age cannot be modified.

Statistical Analysis

We compared continuous variables with the rank-sum test and categorical variables with the Fisher's exact test. Cumulative event rates were obtained with the Kaplan-Meier method and compared with the log-rank statistic. Raw and adjusted hazard ratios (HR) and the corresponding confidence intervals (CI) were obtained by Cox models. Interaction terms were fitted where appropriate.

Because of the sampling approach of the Health ABC Study, the study sample is not representative of the race distribution of the elderly population in the United States. Therefore, we opted to calculate only race-specific PAR estimates, and did not calculate pooled PARs. Sex-specific and sex-stratified (Mantel-Haenszel combined) rate ratio (RR) estimates for the risk factors of interest were calculated. Unadjusted (univariable) PARs were calculated with the standard formula [22]:

$$PAR_{unadjusted} = [\text{Prevalence} * (RR - 1)] / [\text{Prevalence} * (RR - 1)] + 1$$

This formula, however, is only valid when no confounding exists.[23] Therefore, we also calculated adjusted (multivariable) PARs using a Poisson regression model with incident HF as the outcome and the factors described above as predictors.[24] Briefly, the predicted number of cases is calculated for the full model (N_{full}) - which equals the actual number of cases. Next, the effect of the risk factor of interest is "removed" by setting the value of the covariate to zero and the predicted number of events is calculated ($N_{removed}$). The adjusted PAR for the risk factor becomes then:

$$PAR_{adjusted} = 1 - (N_{removed} / N_{full})$$

Similarly, it is possible to calculate the total preventable fraction, i.e. the proportion of cases that could be prevented if these risk factors were eliminated, by setting all the covariates to zero; notably, the sum of the individual PARs does not add up to the total preventable fraction. Also, although maximum likelihood estimators have been shown to produce reliable point estimates and CIs of PAR in simulation studies,[24] no formal method to compare PAR for a risk factor between groups has been developed to date.

Hospitalizations were analyzed as count data over time at risk; RRs and CIs were obtained by Poisson regression. All analyses were performed with Stata 10.0. Adjusted PARs were calculated with a Stata module written by Tony Brady, PHLS Statistics Unit, U.K., (http://www.stata.com/stb/stb42).

RESULTS

Incident HF

The mean age of participants was 73.6±2.9 years; 47.9% were men and 58.6% white. After 7.1 years median follow-up (25%–75%, 6.6–7.5 years), 258 participants (8.8%) developed HF (annual rate: 1.36%, 95% CI, 1.21%–1.54%). The baseline characteristics of participants are presented in Table 1. Figure 1 presents the Kaplan-Meier estimates of incident HF in race- and sex-based subgroups; men and blacks were more likely to develop HF than women and whites. Annual rate was 1.63% in black vs. 1.19% in white participants (age-adjusted HR: 1.41, 95%

CI, 1.11–1.80, P=.006); and 1.58% in men vs. 1.17% in women (age-adjusted HR 1.34, 95% CI, 1.05–1.71, P=.021). Sex-race interaction term was not statistically significant (P=.470).

Population Attributable Risks

Tables 2 and 3 present the prevalence and the unadjusted (univariable) and adjusted (multivariable) PARs for the independent risk factors. Increased systolic blood pressure, heart rate, and fasting glucose levels, LVH, smoking, and decreased albumin levels, all were more prevalent in blacks than whites (P<.001 except for heart rate P=0.005 and albumin P=.01). In contrast, decreased GFR was more prevalent among white participants (P=.001). Prevalence of CHD was comparable across race (P=.48). The preventable fraction due to modifiable risk factors was 48.9% in whites (95% CI, 35.1%–59.8%) vs. 67.8% in blacks (95% CI, 55.1%–76.8%). Uncontrolled systolic blood pressure and CHD had the higher PARs (>20%) in both race groups both in unadjusted and adjusted analyses. Adjusted PARs for all independent risk factors except serum glucose were higher in blacks than whites with LVH, smoking, and GFR <60 ml/min/1.73m^2 being approximately 10% higher.

Outcomes After Incident HF

During a median of 2.1 years (25%–75%, 0.7–4.4 years) after initial hospitalization for HF, 121 of 258 participants with HF died (46.9%), representing an 18.0% (95% CI, 15.0%–21.5%) annual mortality. In addition, 312 all-cause readmissions were recorded (46.3 per 100 person-years); of these, 252 (80.8%, 37.4 per 100 person-years) were related to HF. In comparison, participants who remained HF-free throughout the study had an annual mortality of 2.72% (95% CI, 2.49%–2.97%) and a hospitalization rate of 21.9 per 100 person-years (RR 2.11, 95% CI, 1.88–2.37, P<.001).

Table 4 summarizes the outcomes after incident HF in the race- and sex- based subgroups. Overall survival did not differ between whites and blacks (log-rank χ^2=0.00, P=.984), however there was a significant race-sex interaction (white male vs. female HR: 0.70, 95% CI, 0.41–1.21, P=.202, black male vs. female HR: 2.10, 95% CI, 1.23–3.60, P=.007, P=.015 for interaction), Figure 2. Rates of all-cause rehospitalization were two-fold higher in blacks compared to whites (62.1 vs. 30.3 per 100 person-years, RR: 2.05, 95% CI, 1.62–2.60, P<.001). This effect was mainly due to HF-related readmissions: blacks had 53.2 HF-related hospitalizations per 100 person-years compared to 21.3 for whites (RR: 2.50, 95% CI, 1.90–3.30, P<.001). The differences in rehospitalization rates between race-based subgroups persisted after controlling for age and number of concomitant conditions (data not shown). No race-sex interaction was observed for all-cause and HF rehospitalization rates (P=.36 and P=.71, respectively, for the interaction terms).

Data on ventricular function during hospitalization for HF were not prospectively collected in the Health ABC Study; therefore, the available data are based on chart reviews. Data on left ventricular ejection fraction (LVEF), obtained by either echocardiography or left ventriculography reports during the index HF hospitalization, were available in 197/258 (76.4%) of participants. Median LVEF was 40% (interquartile range, 26–55) without difference between the white and the black participants (median LVEF 40% for both groups). However, LVEF was higher in female participants (median LVEF 46% vs. 35% in males, P=.011); no race-sex interaction was observed. Participants with LVEF >40% (n=97, 49.2%) had subsequent age-adjusted mortality 14.9, all-cause hospitalization rate 51.3, and HF rehospitalization rate 38.6 per 100 person-years. In comparison, participants with LVEF ≤ 40% (n=100, 50.8%) had age-adjusted mortality 23.2 (HR: 1.46, 95% CI, 0.98–2.18, P=.063), all-cause hospitalization rate 53.5 (RR: 1.04, 95% CI 0.82–1.32, P=.74) and HF rehospitalization rate 46.3 per 100 person-years (RR: 1.20, 95% CI 0.92–1.57, P=.18).

DISCUSSION

In the current study, we found a high rate of incident HF in the elderly, poor prognosis for these participants once they developed HF, and race related differences in risk factor profile for incident HF. Considering the worsening risk factor profile for HF in the population (e.g. diabetes, hypertension), aging of the population, and the increasing HF prevalence, our study underscores the need for focused HF prevention efforts.

Heart Failure Incidence

The rate of incident HF in our study was similar to a recent study comprising of elderly population [25]; however these rates are lower as compared to data from administrative databases. [6, 26] Varying rates for incident HF have also been reported by the Framingham Heart Study, the Cardiovascular Health Study, and from the Olmsted County, Minnesota.[4, 5, 10] These differences are likely related to different age groups, racial mix, geographic variation etc. from which these cases were ascertained. Our study most likely underestimated HF rate as the definition of incident HF required hospitalization and some patients with new onset HF may not require hospitalization. Also, diagnosing HF is challenging and studies have used primarily sign and symptoms; medication profile review; and cardiac imaging based assessment; some studies have utilized chart reviews whereas others have used administrative databases. This becomes more complicated when assessing HF with preserved ejection fraction as its signs and symptoms are non-specific, there is no standard medication profile, and imaging characteristics are complicated.

Irrespective of the precise quantitative assessment, several themes are similar across all these studies, including a high incidence rate, worsening profile with aging, and either stagnant or increasing incidence rates over the last several decades. These trends have tremendous implications as the population demographics are changing. With the aging of the 78 million baby boomers, 1 in 5 Americans are expected to be over 65 years by 2050.[27] This trend is projected to significantly impact healthcare and healthcare economics since the use of formal and informal services strongly correlate with age. Without effective prevention efforts, the current HF epidemic can be expected to significantly worsen in the near future.

Risk Factors for HF

Although risk factors for HF have been described, [10] those data have limitations as many are older studies on primarily white younger participants. Many studies have assessed risk factors in isolation rather than assessing their multivariable independent association. Risk factor profile for cardiovascular diseases is changing with increasing obesity prevalence, and race and sex related differences in risk factors and outcomes for incident HF in the elderly were not assessed in these studies.[12–14] In the current study, for example, most of the modifiable risk factors were significantly more prevalent among blacks (compared to their white counterparts) and constituted a major driving force for the higher incidence of heart failure in blacks. Lastly, although literature on HF risk factors is rich, data on PAR are limited,[28, 29] and only the Cardiovascular Health Study has specifically addressed this issue.[10]

In the Cardiovascular Health Study, the investigators assessed PAR for all significant associations with HF. Several of these maybe be collinear and hence may “dilute” the true effect of modifiable risk factors. For example, CHD, ankle-arm index, carotid intima medial thickness, stroke, and electrocardiographic evidence of ST-T wave changes were all included in the analysis due to their statistical significance. They may however be related to a common domain of vascular atherosclerosis as a risk factor. Indeed, the CHD attributable risk was only 13%. Assessment of PAR requires binary categorization of continuous variables; such categorization was not based on clinically used cut-offs, e.g. C-reactive protein >7 mg/dl.

Lastly, sex- or race- based analysis was not performed and we found significant differences in this regard.

We observed that CHD and uncontrolled blood pressure were the leading causes of HF in both race and sex based subgroups. We also observed that a substantial proportion of HF is attributed to metabolic and cardio-renal factors, including glucose and renal abnormalities as described previously [30, 31], and low albumin levels. It is not clear whether low albumin signifies cachexia, inflammation, or comorbidity burden; or hypoalbuminemia precipitates symptomatic HF due to fluid extravasation.[32] Increased heart rate has been reported as a HF risk factor, and may represent a surrogate of vasovagal imbalance or a physiologic response to worsening cardiac function.[33] Although much work is needed to assess which of these risk factors can be modified and how much, if any, HF risk reduction may be achieved, it is still notable that most risk factors were either modifiable or amenable to potential intervention.

Two observations regarding racial differences merit special comment. First, LVH appears to affect mainly blacks, which is consistent with the high prevalence of uncontrolled blood pressure in blacks. However, the risk associated with LVH was additive and independent from that associated with uncontrolled blood pressure; in fact, LVH was encountered in 8.6% of participants with systolic blood pressure <140mmHg. Second, the higher incidence of HF observed in blacks is accompanied by a higher prevalence of modifiable risk factors and, thus, a higher preventable fraction of incident HF. With the exception of increased fasting glucose, PAR for all risk factors was higher in blacks, with 6 out of 8 assessed risk factors (CHD, uncontrolled blood pressure, LVH, reduced GFR, smoking, and increased heart rate) having >5% higher PAR.

Outcomes after HF Development

Despite the selection bias resulting in a relatively lower comorbidity burden compared to general population, mortality after hospitalization for HF in the Health ABC Study was high (annual rate 18.0%), similar to that reported by recent community-based studies.[5, 8] In fact, studies assessing temporal trends in mortality post-HF development demonstrate either none or only modest improvements over the last few decades.[8] These results suggest that either the benefit from recent advances in HF therapy observed in “real-life” patient population are significantly less than in the clinical trial setting; or that they may not have yet been translated into routine clinical practice; or that HF characteristics at the community level are different than those in clinical trials.

In concordance with a retrospective cohort study,[34] we observed significantly higher all-cause and HF readmission rates in blacks, whereas mortality did not differ overall across race; there was however a race-sex interaction with black men presenting the highest mortality among race-sex subgroups. Nevertheless, the latter finding should be interpreted with caution because of the relatively small number of events.

Value of Population Attributable Risk

The PAR for a risk factor represents the proportional reduction in disease risk that would be achieved by eliminating the risk factor from the population, assuming however a causal relation. The relative importance of risk factors in the population as defined by PAR can help guide policy makers in planning public health interventions. It has to be noted however, that the absolute PAR estimates are highly dependent on the definition of risk factors and in the multivariate setting also on the presence or absence of other risk factors.

Limitations

Diagnosis of incident HF in our study was based on HF hospitalization and therefore we likely underestimated the true incidence. Echocardiography was not performed at baseline. Thus, participants with subclinical prevalent structural heart disease may have been included in the analysis. The Health ABC Study did not collect detailed data on valvular heart disease; however it is unlikely that a very large proportion of participants had significant subclinical valvular heart disease that would impact these results overall.[29] Also, because ventricular function during hospitalization for HF was not prospectively assessed, we could not reliably assess the differential impact of risk factors on development of HF with preserved vs. reduced LVEF. The available data on LVEF are based on chart reviews and do not refer to a single modality. Therefore, we cannot be confident that the distribution of LVEF is representative of the elderly population hospitalized with new-onset HF. Finally, the causes of the observed differences in outcomes between groups cannot be ascertained in this study. These differences may represent race, gender, severity of illness, or therapy related differences and need further study.

Conclusion

In this study we observed a high incidence for HF in the elderly. Race-based differences in risk factors were noted. Outcomes after development of HF remain poor. However, most risk factors for HF are either modifiable or potentially amenable to interventions. Therefore HF prevention efforts may succeed in reducing the community-based burden of HF. Considering the worsening risk factor profile and aging of the population, such efforts should be considered a public health priority.

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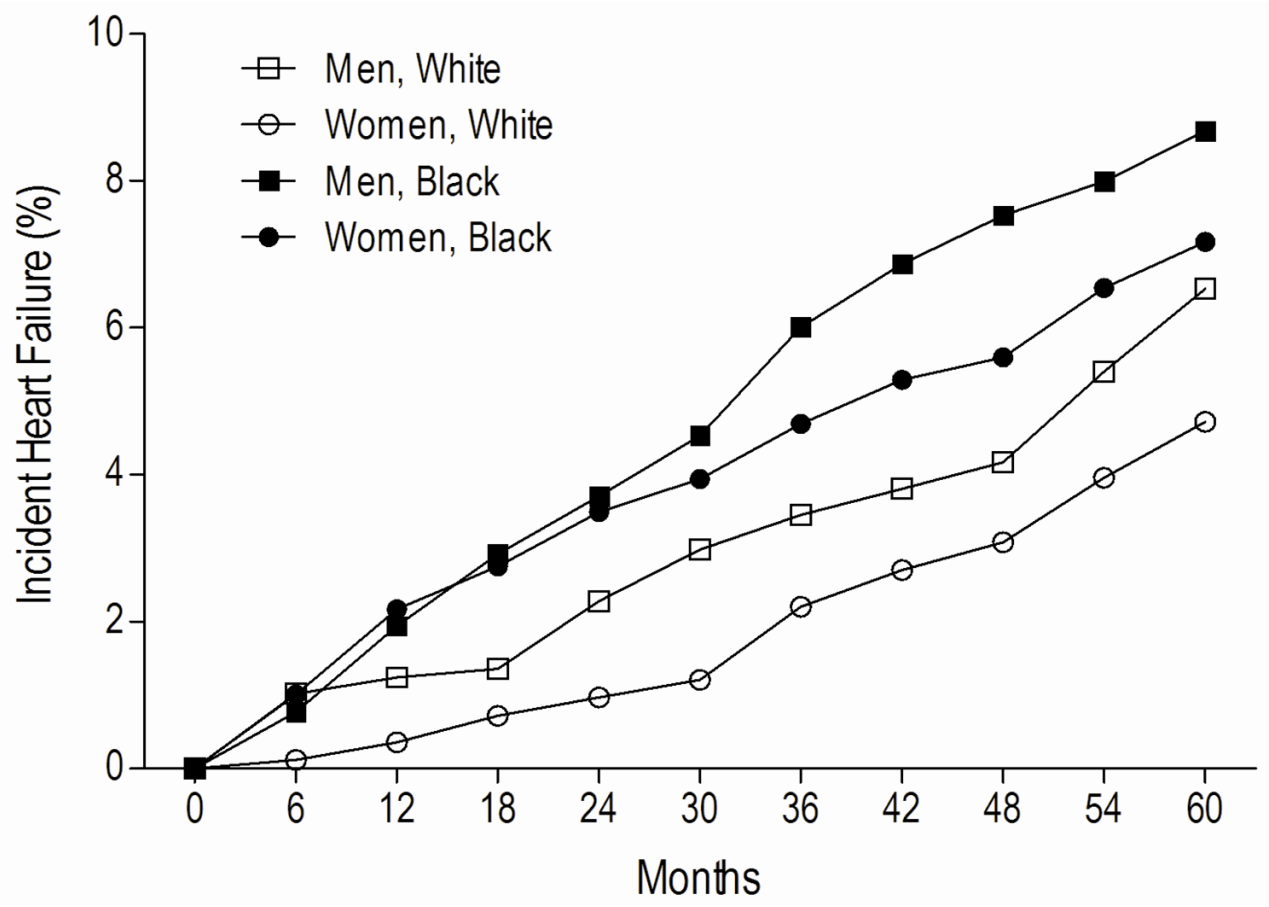

Figure 1. Incident heart failure by sex and race

In the Health ABC cohort, men and blacks were more likely to develop HF than women and whites (stratified log-rank χ^2 for sex 7.30, P=.007; for race 7.85, P=.005).

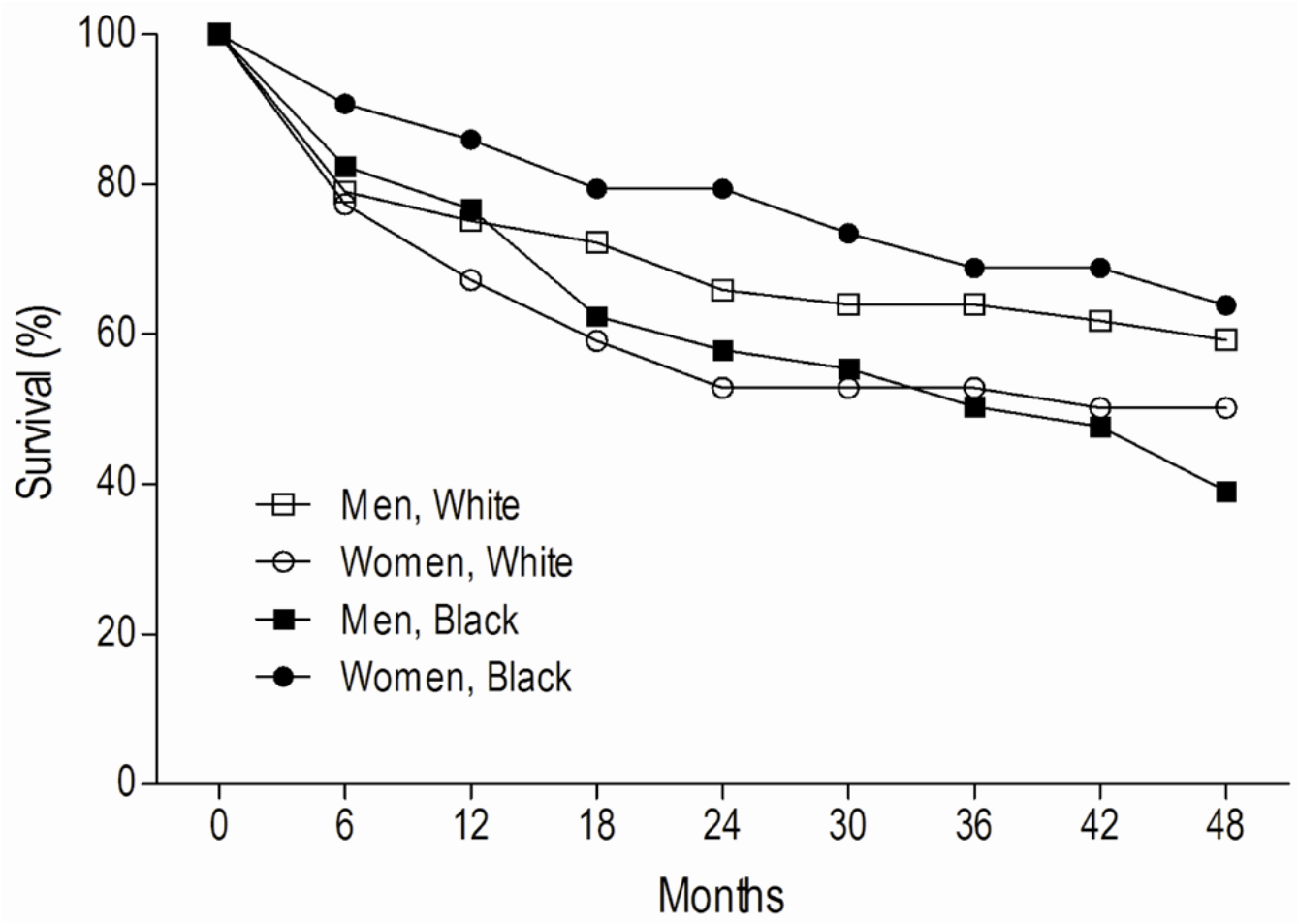

Figure 2. Mortality after incident heart failure by sex and race

Overall survival did not differ between whites and blacks; however, there was a statistically significant race-sex interaction, with black men showing a higher mortality than white men compared to their female counterparts.

Table 1

Baseline Participant Characteristics

Characteristic	Overall (n=2934)	Heart Failure on Follow-up (n=258)	No Heart Failure on Follow-up (n=2676)	*P*
Age, years	73.6 (2.9)	74.2 (2.9)	73.6 (2.9)	.001
Males, %	47.9	54.3	47.3	.037
Whites, %	58.6	52.3	59.2	.034
Smoking status				
Current, %	10.5	17.1	9.9	0.02
Past, %	45.0	44.7	45.0	
Marital Status				
Never Married, %	5.1	5.8	5.1	
Married, %	54.5	49.2	55.1	.149
Widowed, %	31.0	37.1	30.4	
Divorced/Separated, %	9.3	7.9	9.5	
Education				
< than high school, %	10.6	10.2	10.7	
High school, %	40.8	41.8	40.7	.945
Post high school, %	48.6	48.0	48.6	
Body mass index, kg/m^2	27.3 (4.8)	28.1 (4.9)	27.3 (4.8)	.013
<25	32.7	30.6	32.9	
25–30	41.9	36.4	42.5	.014
>30	25.4	33.0	24.6	
Systolic blood pressure, mmHg	136 (21)	144 (24)	135 (20)	<.001
Systolic blood pressure >140mmHg,%	36.6	51.9	35.1	<.001
Diastolic blood pressure, mmHg	71 (12)	73 (13)	71 (12)	.070
Heart rate, beats/minute	65 (11)	68 (12)	65 (11)	.003
Heart rate >75 beats/minute, %	16.4	24.1	15.7	.001
Left ventricular hypertrophy, %	11.9	17.8	11.3	.003
Hypertension				
Definite,%	43.4	58.0	41.9	<.001
Possible, %	10.1	10.9	10.0	
Diabetes, %	14.8	23.4	13.9	<.001
Depression				
Definite, %	2.1	2.0	2.1	.608
Possible, %	7.9	6.2	8.0	
Cerebrovascular disease, %	6.8	9.9	6.5	.001
Coronary heart disease				
Definite, %	16.5	36.0	14.7	.001
Possible, %	3.1	3.6	3.1	
Glucose fasting, mg/dl	104 (34)	114 (46)	103 (33)	<.001
Glucose fasting >125mg/dl, %	13.1	22.1	12.3	<.001
Creatinine, mg/dl	1.05 (0.41)	1.16 (0.58)	1.04 (0.39)	.001

Characteristic	Overall (n=2934)	Heart Failure on Follow-up (n=258)	No Heart Failure on Follow-up (n=2676)	*P*
eGFR, ml/min/1.73m^2	73 (16)	70 (19)	73 (16)	.035
eGFR <60 ml/min/1.73m^2, %	20.5	28.1	19.7	.002
Albumin, g/dl	3.98 (0.31)	3.94 (0.32)	3.98 (0.31)	.039
Albumin <3.8 g/dl, %	22.7	28.1	22.2	.041
Total cholesterol, mg/dl	203 (38)	198 (40)	204 (38)	.030
High density lipoprotein, mg/dl	54 (17)	52 (17)	55 (17)	.012
Low density lipoprotein, mg/dl	122 (35)	119 (35)	122 (35)	.255
Triglycerides, mg/dl	137 (77)	134 (70)	137 (78)	.527

Continuous variables are expressed as mean (SD).

eGFR=estimated glomerular filtration rate

Table 2

Prevalence and unadjusted rate ratios and population attributable risk for the modifiable risk factors of incident heart failure

White (n=1720)	Men (n=886)		Women (n=834)			Combined		
Risk Factors	**Prevalence, %**	**RR (95% CI)**	**Prevalence, %**	**RR (95% CI)**	**P (M-H)**	**Prevalence, %**	**RR (95% CI)**	**PAR, %**
			Modifiable					
Systolic BP >140 mmHg	32.5	1.91 (1.21–3.02)	32.7	1.78 (0.99–3.17)	.84	32.6	1.86 (1.33–2.61)	21.6
Coronary Heart Disease	23.3	2.66 (1.66–4.22)	10.1	2.67 (1.24–5.29)	.99	16.9	2.66 (1.84–3.84)	22.4
Glucose >125 mg/dl	14.6	2.30 (1.34–3.82)	5.5	1.43 (0.38–3.90)	.41	10.2	2.09 (1.34–3.25)	10.8
Left Ventricular Hypertrophy	7.0	0.74 (0.20–1.96)	6.5	1.22 (0.32–3.31)	.49	6.7	0.92 (0.45–1.87)	-
Current Smoking	5.1	1.32 (0.42–3.21)	7.7	2.72 (1.17–5.64)	.22	6.3	1.96 (1.12–3.42)	4.8
			Potentially Modifiable					
eGFR <60 ml/min/1.73m^2	20.5	1.18 (0.65–2.01)	28.6	1.69 (0.93–3.03)	.35	24.4	1.39 (0.96–2.04)	7.2
Albumin <3.8 g/dl	19.5	1.32 (0.74–2.33)	22.6	1.40 (0.71–2.60)	.88	21.0	1.35 (0.91–1.99)	6.3
Heart Rate >75 bpm	14.5	1.32 (0.68–2.37)	15.1	1.98 (0.97–3.77)	.35	14.8	1.57 (1.03–2.39)	7.2
Black (n=1214)	**Men (n=520)**		**Women (n=694)**			**Combined**		
			Modifiable					
Systolic BP >140 mmHg	42.3	1.90 (1.10–3.34)	42.1	2.02 (1.20–3.44)	.87	42.2	1.96 (1.37–2.81)	28.3
Coronary Heart Disease	17.6	4.77 (2.72–8.30)	14.6	2.82 (1.56–4.93)	.17	15.9	3.68 (2.54–5.34)	27.4
Glucose >125 mg/dl	18.9	1.67 (0.86–3.08)	16.2	1.73 (0.90–3.14)	.94	17.3	1.70 (1.13–2.57)	10.5
Left Ventricular Hypertrophy	18.3	2.31 (1.25–4.13)	19.6	1.90 (1.06–3.28)	.61	19.0	2.08 (1.42–3.04)	15.9
Current Smoking	21.0	1.88 (1.01–3.35)	13.0	1.75 (0.85–3.32)	.87	16.4	1.82 (1.20–2.76)	11.5
			Potentially Modifiable					
eGFR <60 ml/min/1.73m^2	14.8	2.57 (1.35–4.68)	14.8	2.25 (1.19–4.03)	.73	14.8	2.40 (1.60–3.59)	15.5
Albumin <3.8g/dl	26.4	1.35 (0.73–2.42)	24.2	1.41 (0.76–2.46)	.92	25.1	1.38 (0.94–2.03)	8.6
Heart Rate >75 bpm	18.9	1.93 (1.03–3.47)	18.7	1.74 (0.95–3.04)	.79	18.8	1.82 (1.23–2.70)	12.8

* Mantel-Haenszel test for homogeneity (low significance indicates comparable effects).

BP=blood pressure, eGFR=estimated glomerular filtration rate, PAR=Population Attributable Risk, RR=Rate Ratio for Incident Heart Failure

Table 3

Adjusted rate ratios and population attributable risk for modifiable risk factors of incident heart failure

	White (n=1686)		Black (n=1167)	
Risk Factors	**RR (95% CI)**	**PAR, %**	**RR (95% CI)**	**PAR, %**
Modifiable				
Systolic Blood Pressure >140 mmHg	1.80 (1.27–2.55)	21.3	1.95 (1.33–2.84)	30.1
Coronary Heart Disease	2.72 (1.89–3.90)	23.9	3.31 (2.26–4.85)	29.5
Glucose >125 mg/dl	2.08 (1.35–3.22)	11.3	1.37 (0.88–2.14)	7.3
Left Ventricular Hypertrophy	0.90 (0.44–1.84)	-	2.20 (1.47–3.30)	19.5
Current Smoking	2.04 (1.15–3.64)	5.5	2.08 (1.37–3.16)	15.0
Modifiable Fraction		48.9		67.8
Potentially Modifiable				
eGFR <60 ml/min/1.73m^2	1.29 (0.88–1.87)	6.8	2.14 (1.42–3.24)	16.2
Albumin <3.8 g/dl	1.46 (0.98–2.16)	8.5	1.63 (1.09–2.44)	12.7
Heart Rate >75 bpm	1.45 (0.94–2.23)	6.7	1.97 (1.30–2.99)	15.7
Potentially Modifiable Fraction		20.5		38.6

eGFR=estimated glomerular filtration rate, PAR=Population Attributable Risk

Note: population attributable risks are *not* additive and *do not* add up to 100%

Table 4

Mortality and rehospitalization rates after incident HF

	Mortality			All-cause Re-hospitalization			Heart failure Re-hospitalization		
	Rate	**Hazard Ratio (95% CI)**	**p**	**Rate**	**Rate Ratio (95% CI)**	**p**	**Rate**	**Rate Ratio (95% CI)**	**p**
White (n=135+	18.0			30.3			21.3		
Male (n=82)	16.7	0.70 (0.41–1.21)	.20	30.4	1.02 (0.68–1.52)	.94	19.6	0.82 (0.52–1.32)	.42
Female (n=53)	20.0	Referent	-	30.0	Referent	-	23.8	Referent	-
Black (n =123)	18.0			62.1*			53.2†		
Male (n=58)	26.3	2.10 (1.23–3.60)	.007	63.9	1.05 (0.80–1.38)	.73	57.2	1.26 (0.84–1.51)	.43
Female (n=65)	12.3	Referent	-	60.9	Referent	-	50.8	Referent	-

Rates refer to events per 100 person-years

*RR 2.05 (95% CI, 1.62–2.60), P<.001 compared to white participants

†RR 2.50 (95% CI, 1.90–3.30), P<.001 compared to white participants