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Racial and Ethnic Differences in Incident Hospitalized Heart Failure in Postmenopausal Women

The Women's Health Initiative

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Background—The differences in the incidence of heart failure by race/ethnicity and the potential mechanisms for these differences are largely unexplored in women.

Methods and Results—A total of 156 143 postmenopausal women free of self-reported heart failure enrolled from 1993 to 1998 at 40 clinical centers throughout the United States as part of the Women's Health Initiative and were followed up until 2005, for an average of 7.8 years, for incident hospitalized heart failure. Incident rates, hazard ratios (HRs), and 95% confidence intervals were determined by use of the Cox proportional hazard model comparing racial/ethnic groups, and population-attributable risk percentages were calculated for each racial/ethnic group. Blacks had the highest age-adjusted incidence of heart failure (380 in 100 000 person-years), followed by whites (274), Hispanics (193), and Asian/Pacific Islanders (103). The excess risk in blacks compared with whites (age-adjusted HR=1.45) was significantly attenuated by adjustment for household income (HR=0.97) and diabetes mellitus (HR=0.89), but the lower risk in Hispanics (age-adjusted HR=0.72) and Asian/Pacific Islanders (age-adjusted HR=0.44) remained despite adjustment for traditional risk factors, socioeconomic status, lifestyle, and access-to-care variables. The effect of adjustment for interim coronary heart disease on nonwhite versus white HRs for heart failure differed by race/ethnic group.

Conclusions—Asian/Pacific Islander and Hispanic women have a lower incidence of heart failure and black women have higher rates of heart failure compared with white women. The excess risk of incident heart failure in black women is explained largely by adjustment for lower household incomes and diabetes mellitus in black women, whereas the lower rates of heart failure in Asian/Pacific Islanders and Hispanics are largely unexplained by the risk factors measured in this study.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00000611.

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Key Words: continental population groups ■ heart failure ■ ethnic groups ■ incidence ■ population

Heart failure (HF) is recognized by a constellation of signs and symptoms and a neurohumoral response to cardiac dysfunction. HF develops as a consequence of many forms of cardiovascular disease and is not a single pathological entity. Rates of HF are reaching epidemic proportions, affecting >5 million people in the United States with >500 000 newly diagnosed cases each year.[1] Both the prevalence and morbidity associated with HF are increasing in the United States, with racial and ethnic disparities noted. Despite advances in therapy and an improvement in the 5-year survival rate, the prognosis is still relatively poor.[2,3] HF also imposes considerable economic impact on health services owing to the need for long-term, multipharmaceutical treatment, use of implantable defibrillators, and frequent hospitalizations.[4] Most

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previous work related to racial/ethnic differences in the prevalence of HF has suggested that differences may be attributable to the relative importance of different risk factors or access-to-care issues.[4–11] However, such prevalence studies are prone to bias and lack temporality. A few recent studies have examined racial/ethnic differences in incident HF but had limited numbers of incident cases of HF and limited numbers of racial/ethnic groups for comparison.[12,13] Also of interest are the sex differences in HF in both rates and risk factors because most studies of HF have included a limited number of women. Previous research suggests that women have more hypertension and valvular disease and less underlying coronary disease or dilated cardiomyopathy compared with men as potential risk factors for HF, but again, this research is limited to prevalence studies.[11,14]

Clinical Perspective on p 696

These limitations emphasize the need for larger prospective epidemiological studies clarifying the incidence and risk factors associated with HF in a multiracial cohort in postmenopausal women. We address the following research questions in a large, diverse nationwide cohort of postmenopausal women: Are there differences in the incidence of HF by race/ethnicity in postmenopausal women? If so, what sociodemographic, lifestyle, access-to-care, and traditional risk factors explain these differences? Which modifiable risk factors contribute to the burden of HF in different race/ethnic groups in postmenopausal women?

Methods

Study Population

The Women's Health Initiative (WHI) recruited women nationwide in 40 clinical centers between 1993 and 1998.[15–18] Study participants were women 50 to 79 years of age at baseline. Women were excluded if they did not plan to reside in the area for at least 3 years, had medical conditions predictive of <3 years of survival, or had complicating conditions such as alcoholism, mental illness, or dementia. Those eligible for either the clinical trials or observational arm completed baseline assessments, including several self-administered questionnaires of sociodemographic characteristics, medical history, reproductive and menstrual history, health behavior (including physical activity and diet), and family history of selected diseases. Trained staff obtained anthropometric measures, including height, weight, and waist circumference. After women sat quietly for 5 minutes, blood pressure was measured with a mercury manometer twice, 30 seconds apart, and the average was used in this analysis.

Medication use at baseline was ascertained by having the participants bring all the containers for medications taken for the 2 weeks before the baseline visit. Interviewers entered each medication into a central database, which assigned drug codes using Medi-Span software. Information was recorded on duration of use but not dose. White blood cell count and hemoglobin levels were measured via standardized automated technique on fresh samples at each local WHI site.

A standardized written protocol, centralized training of local clinical staff, local quality control, and periodic quality assurance visits by the Clinical Coordinating Center were used to maintain uniform data collection procedures at all study sites. Reproducibility of WHI questionnaire data was evaluated in a random subsample at 10 weeks with good to excellent reproducibility (weighted κ=0.77–0.99).[15]

Covariates

Race was self-reported as American Indian or Alaskan Native, Asian or Pacific Islander, black or African American, Hispanic/Latino, white (not of Hispanic origin), or other.

For analytic purposes, age was categorized by age groups as <50 to 59, 60 to 69, or 70 to ≥79 years; education was categorized as less than high school or more than high school; income was categorized as less than $20 000, $20 000 to $35 000, $35 000 to $50 000, $50 000 to $75 000, and more than $75 000 per year; cigarette smoking was categorized as current, past, or never; hormone status was categorized as current, past, or never. Hyperlipidemia was defined as taking cholesterol-lowering medication. Hypertension was defined by self-report and taking antihypertensive medications, systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg. Uncontrolled systolic blood pressure was defined as systolic blood pressure >150 mm Hg and taking antihypertensive medications. Diabetes mellitus defined by self-report of physician diagnosis and taking hypoglycemic medications. Atrial fibrillation was based on self-report and not medication use.

Prevalent coronary heart disease (CHD) was defined as self-reporting at baseline as having been hospitalized for a heart attack (myocardial infarction), coronary angioplasty or stent, coronary artery bypass graft surgery, or angina (chest pains from heart problems).

Physical activity was ascertained from a series of questions related to walking and exercise at strenuous levels and physical activity at moderate- and low-intensity levels. A composite variable was constructed imputing the midpoint of the range of frequency and duration of walking, strenuous exercise, and moderate- and low-intensity physical activity to determine the hours of activity per week for each type of physical activity. A metabolic equivalent (MET) value was assigned to each level of activity, and a total physical activity score (MET-h/wk) was computed for each participant.[17] Alcohol intake was ascertained by asking participants to estimate over the past 3 months the average frequency and quantity of drinking beer, wine, or liquor. Servings per week were estimated on the basis of 12 oz of beer equivalent to 6 oz of wine and 1.5 oz of liquor for each participant.

Outcomes

Incident hospitalized HF was ascertained yearly in WHI by medical record abstraction of self-report hospitalizations and classified by trained adjudicators using the standardized methodology as previously described.[18] Hospitalized HF requiring and/or occurring during hospitalization required physician diagnosis of new-onset or worsened congestive HF on the reported hospital admission and 1 or more of the following 4 criteria: HF diagnosed by physician and receiving medical treatment for HF; symptoms plus documentation in the current medical record of a history of an imaging procedure showing impaired left ventricular (LV) systolic or diastolic LV function; pulmonary edema/congestion on chest x-ray on the current admission; dilated ventricle(s), or "poor" LV or right ventricular function by echocardiography, radionuclide ventriculography, or other contrast ventriculography or evidence of LV diastolic dysfunction. This method was found to have an excellent 79% agreement rate (κ) comparing central adjudicated HF and local adjudication.[18]

Interim CHD was defined by adjudicated hospitalization for myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass graft, or angina after baseline and before the HF hospitalization.[18]

Statistical Methods

The frequency distribution of the variables of interest was inspected to rule out anomalies and outliers resulting from measurement artifacts. Correlations among covariates were examined to evaluate collinearity. Differences in covariates by race/ethnicity and by developing incident HF were assessed to look for potential confounding relationship through the use of ANOVA and χ^2 testing for continuous and categorical variables.

Women with self-reported HF at baseline (n=2048) were excluded from the cohort, as were those with missing, other, or Native American race (n=2926) and those with missing covariate data (n=691). Age-specific and age-adjusted rates using 2000 Census data for direct adjustment by race/ethnicity were calculated. Proportional hazards models were developed for incident hospitalized HF,

with adjustment for potential confounders based on the clinical literature and inclusion of other potential confounders found in the univariate analysis that differed by race and by incident HF at $P<0.10$. Because the entry criteria and time of observation were different between the observational study and clinical trial cohorts, we performed stratified analysis by cohort assignment and pooled the estimate of effect for each risk factor using the STRATA statement in proc PHREG in SAS.9.2. A C statistic or area under the receiver-operating characteristic curve, which compares the sensitivity and the 1−specificity, is presented to demonstrate how well the HF models discriminate cases of HF from noncases.

Population-attributable risk (PAR) percentages were calculated to evaluate the potential impact of risk factor reduction from the public health perspective using the following formula: $PAR=[p(r-1)]/[p(r-1)+1]\times 100\%$, where p is the proportion of the population with the risk factor and r is the relative risk estimate (hazard ratio) for the risk factor.

Results

The baseline cohort that included 156 143 postmenopausal women free of self-reported HF with complete data on confounders was analyzed; 84.3% were white, 9% were black, 4% were Hispanic, and 2.7% were Asian/Pacific Islanders. Table 1 shows the characteristics of the cohort by race/ethnicity. Significant differences between racial/ethnic groups were noted for sociodemographic factors such as age, education, and income; access-to-care and medication issues such as insurance status, hysterectomy, and hormone treatment; traditional risk factors for HF, including obesity, history of CHD, and diabetes mellitus; and lifestyle factors such as alcohol servings per week and vitamin D intake.

Incident hospitalized HF developed in an average of 7.8 years of follow-up in 3018 whites, 391 blacks, 82 Hispanics, and 37 Asian/Pacific Islanders. Age-specific and age-adjusted rates demonstrated differences by race, with blacks having the highest age-adjusted rate of incident hospitalized HF (Figure 1A and Table 2). This higher rate was greatest in the group of women <60 years of age. After multiple variable adjustments for other risk factors, whites and blacks had similar rates for HF, whereas Hispanics and Asian/Pacific Islanders had persistently lower rates of HF (Figure 1B and Table 3). The C statistic for the full multivariate model was C=0.84 (95% confidence interval, 0.83–0.85).

To better understand which risk factors might explain the racial/ethnic differences in the incidence of HF, we performed nested models (Tables 3 and 4) comparing each race/ethnicity group with white women regarding their risk of HF. As shown in Table 3, a model adjusting for age, income, and education had a modest effect on explaining differences between black and white women, had no effect on Asian/Pacific Islanders, and made more apparent the lower risk of HF in Hispanics. Adjusting for established risk factors for HF to the model removed the excess risk in black compared with white women and made more apparent the lower risk of HF in Asian/Pacific Islanders and Hispanics compared with whites. Adjusting for interim CHD in addition to age, socioeconomic status, and traditional risk factors had a modest effect on the inverse relationship between Hispanic and Asian/Pacific Islander race for incident HF compared with whites. This adjustment lead to a nonsignificant excess risk in black women compared with white women. Further adjustment for all potential confounders, including access to care, medications, and other medical conditions, to the model reversed the modest excess risk associated with adjusting for interim CHD in black women and had minimal effect on the point estimates of risk for the Hispanic or Asian/Pacific Islanders.

To further explore the risk attenuation of HF in black women compared with white women and the independent contribution of prevalent and interim CHD and other potential risk factors, we evaluated risk factor–specific models (Table 4). For black women, adjusting for age made more apparent the excess risk of HF compared with white women, whereas adjusting for diabetes mellitus, household income, education level, hysterectomy, and hormone replacement therapy use lowered the excess risk of HF compared with white women. Of note, adjusting for diabetes mellitus and household income removed the excess risk of HF completely in black women, whereas hypertension, obesity, and prevalent or interim CHD had no effect. For Hispanic women, adjusting for the confounding effects of age and interim CHD for HF led to point estimates of risk closer to the null compared with baseline risk levels, whereas adjusting for diabetes mellitus, household income, and education led to point estimates of a lower risk of HF for Hispanics compared with whites, suggesting potential mechanisms for differences in rates of incident HF for Hispanics. For Asian/Pacific Islander women, adjusting for household income and interim CHD had a modest effect on point estimates of the lower risk for HF compared with white women.

Population-attributable percentages for HF attributed to diabetes mellitus and interim CHD are shown in Figure 2. This measure of the public health impact of these risk factors, which accounts for both the prevalence of a risk factor and its relative risk, shows that diabetes mellitus has its greatest impact on Hispanic and black women and, to a lesser extent, Asian/Pacific Islander and white postmenopausal women. Interim CHD shows a greater overall impact on the modifiable risk of HF, with its greatest effect on Hispanics, followed by Asian/Pacific Islanders, whites, and then blacks.

Discussion

This analysis of a large prospective cohort of racially and ethnically diverse postmenopausal women revealed that black women, especially those ≤60 years of age, are at higher risk of incident hospitalized HF than their white counterparts, whereas Asian/Pacific Islanders and Hispanics had lower risks of incident hospitalized HF than white postmenopausal women. Adjusting for age, socioeconomic status, and known risk factors for HF removed the excess risk for black women but did not significantly attenuate the lower risk of HF found in the Asian/Pacific Islanders and Hispanics compared with whites. For black women, the higher risk of HF compared with white women was largely explained by adjustment for diabetes mellitus and lower income levels. Population-attributable risk percentages showed the greatest public health impact for interim CHD and diabetes mellitus, with differences by race/ethnicity on their relative attributable burden on incident HF.

Our age-adjusted incidence of hospitalized HF (271.1 per 100 000 person-years) is similar to that found in the Olmsted County study,[19] which had an age-adjusted incidence of 289

Table 1. Description of the Women's Health Initiative Cohort Free of Heart Failure at Baseline by Race/Ethnicity

	Asian/Pacific Islanders (n=4135)		Blacks (n=14 110)		Hispanics (n=6257)		Whites (n=131 641)		
Variable	n	%	n	%	n	%	n	%	*P**
Sociodemographic									
Age, y									
<50–59	1461	35.3	5912	41.9	3151	50.3	41 393	31.4	
60–69	1732	41.9	6015	42.6	2437	39.0	59 944	45.5	
70–≥79	942	22.8	2183	15.5	669	10.7	30 304	23.1	<0.01
Education									
Less than high school	210	5.1	1646	11.8	1670	27.2	4451	3.4	
High school or higher	1235	30.1	3659	26.3	1760	28.61	35 629	27.2	
Some college	838	20.4	3692	26.5	1427	23.2	36 952	28.3	
College or higher	1821	44.4	4934	35.4	1288	21.0	53 761	41.1	<0.01
Income, $									
<20 000	472	12.2	3894	29.9	2146	38.6	17 344	14.1	
20 000–<35 000	732	18.9	3179	24.4	1314	23.6	30 079	24.4	
35 000–<50 000	739	19.1	2367	18.2	907	16.3	25 996	21.1	
50 000–<75 000	940	24.2	2204	16.9	719	12.9	25 301	20.5	
≥75 000	994	25.6	1385	10.6	478	8.6	24 567	19.9	<0.01
Access to care and medications									
Insurance status									
No insurance	99	2.4	1158	8.4	1272	21.1	4492	3.4	<0.01
Medicare	1410	34.4	3887	28.2	1241	20.6	50 734	38.8	<0.01
Private insurance	3745	91.4	10 981	79.7	4098	67.9	116 206	88.9	<0.01
Medications									
Aspirin	491	12.0	1947	14.2	710	11.9	29 707	22.0	<0.01
Angiotensin receptor blockers	61	1.5	105	0.8	26	0.4	859	0.7	<0.01
β-Blocker	294	7.2	1176	8.6	321	5.4	11 047	8.5	<0.01
Multivitamin	1495	36.2	3634	25.1	1701	27.2	54 480	41.4	<0.01
Hormone therapy									
Never	1150	28.4	6569	47.4	2465	40.5	40 312	31.6	
Past	850	20.8	3452	24.9	1343	22.1	29 395	23.0	
Current	2087	51.1	3853	27.8	2284	37.5	57 879	45.4	<0.01
Medical condition									
Hysterectomy	1437	34.8	7806	55.3	2806	44.9	52 934	40.2	<0.01
Traditional risk factors									
Hyperlipidemia	828	20.5	2074	15.6	851	14.9	16 625	13.4	<0.01
Hypertension	1839	45.0	8219	60.2	2062	34.7	47 946	38.0	<0.01
Obesity	447	10.9	7139	51.1	2275	36.7	36 265	27.8	<0.01
Previous coronary heart disease	189	4.6	1333	9.5	349	5.6	7875	6.0	<0.01
Atrial fibrillation	134	3.3	667	4.9	165	2.7	5413	4.2	<0.01
Diabetes mellitus	237	5.7	1636	11.6	432	6.9	4192	3.2	<0.01
Cigarette smoking									
Never	2965	72.2	6863	49.6	3870	63.1	64 958	50.0	
Past	984	23.9	5383	39.0	1821	29.	56 619	43.5	
Current	161	3.9	1575	71.4	446	4.2	8507	6.5	<0.01
Lifestyle	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*†
Physical activity, MET-h/wk	13.1	14.2	9.7	12.8	10.5	13.7	12.9	13.8	<0.01
Alcohol, servings/wk	0.7	2.6	1.1	4.2	1.2	3.6	2.6	5.0	<0.01
Vitamin D intake, μg/d	4.57	5.82	2.94	5.14	3.41	5.54	5.22	6.29	<0.01
Physiology									
Systolic blood pressure, mm Hg	130	14.2	132	17.8	126	17.1	127	17.6	<0.01
Diastolic blood pressure, mm Hg	78	9.7	78	9.5	75	9.1	75	9.1	<0.01
Waist-to-hip ratio	0.82	0.07	0.82	0.08	0.82	0.08	0.81	0.08	<0.01
Waist circumference, cm	78.6	10.7	91.8	14.0	86.9	12.9	86.0	13.7	<0.01
Hemoglobin, g/dL	13.6	1.0	12.9	1.2	13.4	1.0	13.5	1.1	<0.01
White blood cell count, 10^3/mL	5.7	6.5	5.7	9.6	6.3	11.9	6.2	12.3	<0.01

MET indicates metabolic equivalent.

*P values obtained from the χ^2 test statistic using categorical variables.

†P values obtained with ANOVA for the continuous variable by race/ethnicity.

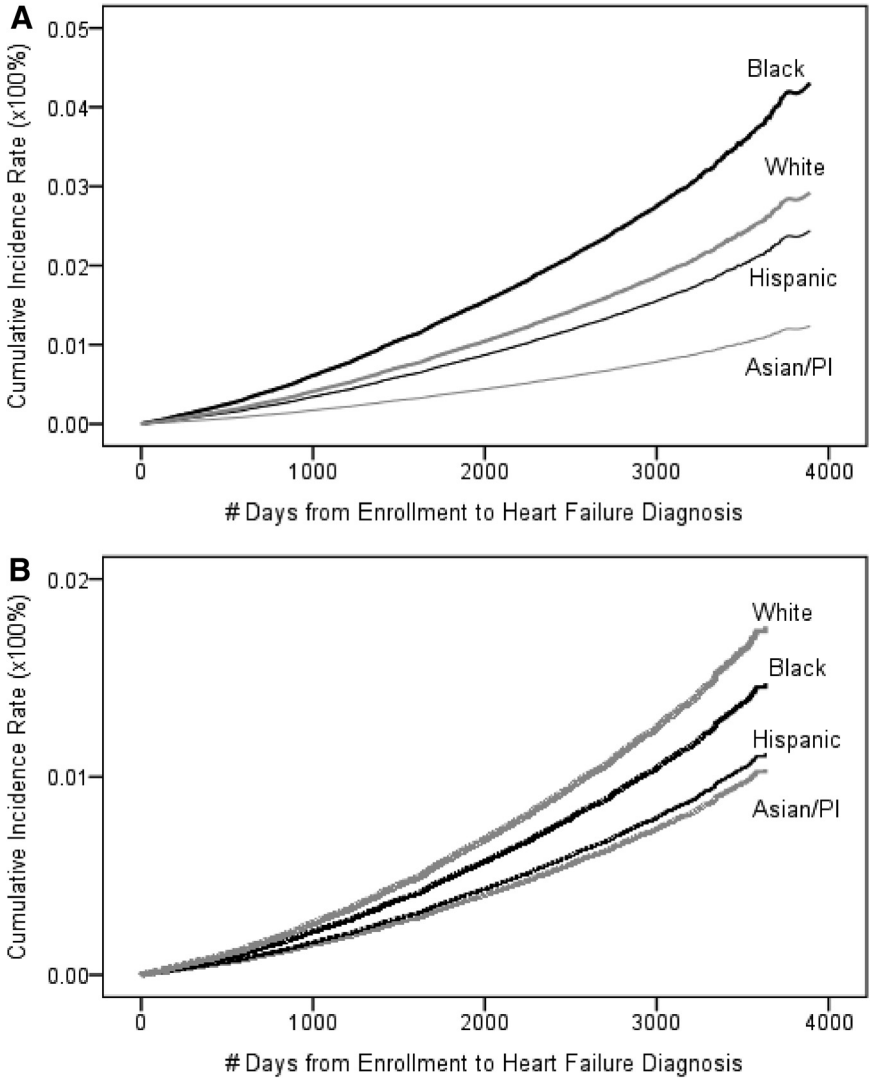

Figure 1. A, Age-adjusted cumulative incidence of heart failure in the Women's Health Initiative (WHI) cohort by race. **B**, Multivariate-adjusted cumulative incidence of heart failure in WHI cohort by race adjusted for age, income, education, insurance status, alcohol consumption, physical activity, current medical conditions (hypertension, diabetes, high cholesterol, coronary heart disease, atrial fibrillation, history of hysterectomy), and medication use (hormone replacement therapy, multivitamins, aspirin, angiotensin receptor blockers, β-blockers). PI indicates Pacific Islander.

per 100 000 person-years in women, and the crude incidence rate of 310 per 100 000 in the Multiethnic Study of Atherosclerosis (MESA),[12] but it differs from the Cardiovascular Health Study (CHS),[20] which had a crude incidence rate of 2460 per 100 000 person-years, and Health, Aging and Body Composition (ABC),[21] which had a crude incidence rate of 1170 per 100 000 person-years. The higher rates of incident HF in Health ABC and CHS are probably due to the older age of the CHS and Health ABC cohorts, the combination of men and women in the CHS estimates, differences in racial mix, geographic variation, and differences in the diagnostic criteria used.

A limited number of studies have evaluated the incidence of hospitalized HF in different race/ethnic groups of women. Alexander et al[22] calculated the population-based age-adjusted incidence of HF in California using administrative data in 1991 and found rates of 265 per 100 000 person-years for white women, 454 per 100 000 person-years for black women, 237 per 100 000 for Hispanic women, and 206 per 100 000 person-years for Asian/Pacific Islanders, very similar to our results. Using the MESA cohort, Bahrami et al[12] calculated rates of 240 per 100 000 person-years for whites, 460 per 100 000 person-years for blacks, 350 per 100 000 person-years for Hispanics, and 100 per 100 000 person-years

Table 2. Crude, Age-Adjusted, and Age-Specific Rates of Hospitalized Heart Failure by Race/Ethnicity (per 100 000 Person-Years)

	Whites	Blacks	Hispanics	Asian/Pacific Islanders	Total
Crude	293.0	364.9	176.6	118.3	290.4
Age-adjusted	274.0	380.0	193.1	103.2	271.1
Age <50–59 y	88.6	203.4	113.2	35.2	101.2
Age 60–69 y	258.8	408.8	178.9	107.4	265.0
Age 70–≥79 y	674.2	721.0	490.6	275.9	662.8

Table 3. Nested Models Predicting Incident Heart Failure in Postmenopausal Women

	Hazard Ratio (95% Confidence Interval)				
Racial/Ethnic Group	Model 1: Age	Model 2: Age+SES*	Model 3: Age, SES,* Established Risk Factors†	Model 4: Age, SES,* Established Risk Factors,† Interim CHD	Model 5: Age, SES,* Established Risk Factors,† Interim CHD, Additional Factors‡
White	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Asian/Pacific Islander	0.44 (0.31–0.62)§	0.45 (0.32–0.64)§	0.49 (0.35–0.69)§	0.55 (0.39–0.78)§	0.59 (0.47–0.83)§
Black	1.45 (1.29–1.64)§	1.19 (1.05-1.35)§	0.76 (0.67–0.87)§	0.88 (0.78–1.00)§	0.84 (0.73–0.95)§
Hispanic	0.72 (0.55–0.94)§	0.54 (0.41–0.72)§	0.54 (0.41–0.72)§	0.62 (0.47–0.82)§	0.63 (0.48–0.84)§

SES indicates socioeconomic status; CHD, coronary heart disease.

*Income and education level.

†Hypertension, diabetes mellitus, obesity, dyslipidemia, smoking status, and CHD at baseline.

‡Hysterectomy, atrial fibrillation, any health insurance, medication use (hormone replacement therapy, aspirin, angiotensin receptor blockers, β-blockers, multivitamin), physical activity level, and alcohol consumption.

§Statistically significant ($P<0.05$).

for Asian/Pacific Islanders; however, their estimates combined men and women and were based on only 79 incident cases of HF. These rates from MESA are comparable to the 60- to 69-year age-specific rates in our study for whites, blacks, and Asian/Pacific Islanders in WHI but are much higher than those found for Hispanic women (179 per 100 000 person-years) in the WHI cohort. Using the Coronary Artery Risk Development in Young Adults (CARDIA)

Table 4. Nested Models of Heart Failure, Adding Each Risk Factor Individually, Comparing Each Racial/Ethnic Group With White Postmenopausal Women

	Racial/Ethnic Group, Hazard Ratio (95% Confidence Interval)				*P* for Added Covariate
Model	Asian/Pacific Islander	Black	Hispanic	White	
Unadjusted model (model 1)	0.43 (0.30–0.60)	1.21 (1.07-1.36)	0.52 (0.40–0.68)	1.00 (Reference)	<0.001
Established risk factors					
Model 1+age	0.44 (0.31–0.62)	1.45 (1.29-1.64)	0.72 (0.55–0.94)	1.00 (Reference)	<0.001
Model 1+hypertension	0.38 (0.27–0.55)	1.23 (1.10-1.38)	0.56 (0.43–0.72)	1.00 (Reference)	0.35
Model 1+uncontrolled SBP	0.38 (0.27–0.55)	1.23 (1.10-1.38)	0.56 (0.43–0.72)	1.00 (Reference)	0.03
Model 1+diabetes mellitus	0.35 (0.24–0.50)	0.92 (0.81-1.03)	0.49 (0.38–0.63)	1.00 (Reference)	<0.001
Model 1+obesity (BMI ≥30 kg/m^2)	0.38 (0.27–0.55)	1.23 (1.10-1.39)	0.56 (0.43–0.72)	1.00 (Reference)	<0.05
Model 1+smoking status	0.37 (0.26–0.54)	1.23 (1.10-1.38)	0.56 (0.43–0.72)	1.00 (Reference)	0.77
Model 1+dyslipidemia	0.37 (0.26–0.54)	1.23 (1.10-1.38)	0.56 (0.43–0.72)	1.00 (Reference)	0.77
Model 1+previous CHD	0.38 (0.26–0.54)	1.22 (1.09-1.37)	0.56 (0.43–0.73)	1.00 (Reference)	<0.001
Socioeconomic factors					
Model 1+household income	0.41 (0.29–0.59)	0.99 (0.89-1.12)	0.41 (0.32–0.53)	1.00 (Reference)	<0.001
Model 1+education level	0.37 (0.26–0.53)	1.14 (1.01-1.28)	0.44 (0.34–0.57)	1.00 (Reference)	<0.001
Other medical issues					
Model 1+atrial fibrillation	0.37 (0.26–0.54)	1.23 (1.10-1.38)	0.56 (0.43–0.72)	1.00 (Reference)	0.84
Model 1+hysterectomy	0.38 (0.27–0.55)	1.17 (1.04-1.31)	0.55 (0.42–0.71)	1.00 (Reference)	<0.001
Access to health care and medication use					
Model 1+any health insurance	0.37 (0.25–0.53)	1.23 (1.09-1.38)	0.55 (0.43–0.72)	1.00 (Reference)	0.46
Model 1+ARB use	0.38 (0.26–0.55)	1.22 (1.09-1.37)	0.56 (0.43–0.73)	1.00 (Reference)	0.61
Model 1+aspirin use	0.38 (0.26–0.55)	1.22 (1.09-1.37)	0.56 (0.43–0.73)	1.00 (Reference)	0.75
Model 1+β-blocker use	0.38 (0.26–0.55)	1.22 (1.09-1.37)	0.56 (0.43–0.73)	1.00 (Reference)	0.98
Model 1+HRT use	0.38 (0.26–0.55)	1.12 (1.00-1.26)	0.53 (0.41–0.69)	1.00 (Reference)	<0.001
Model 1+multivitamin use	0.37 (0.25–0.53)	1.23 (1.09-1.38)	0.55 (0.43–0.72)	1.00 (Reference)	0.10
Lifestyle factors					
Model 1+alcohol consumption	0.38 (0.26–0.54)	1.24 (1.10-1.39)	0.56 (0.43–0.72)	1.00 (Reference)	0.80
Model 1+physical activity level	0.38 (0.26–0.55)	1.24 (1.10-1.39)	0.55 (0.42–0.72)	1.00 (Reference)	0.43
Proximal risk factors					
Model 1+interim CHD	0.44 (0.31–0.64)	1.24 (1.10-1.39)	0.62 (0.48–0.81)	1.00 (Reference)	<0.001

SBP indicates systolic blood pressure; BMI, body mass index; CHD, coronary heart disease; ARB, angiotensin receptor blocker; and HRT, hormone replacement therapy. *P* values reflect the effect of adding the risk factor on predicting heart failure in the Cox proportional hazard model, not differential effect across race/ethnicity gradient.

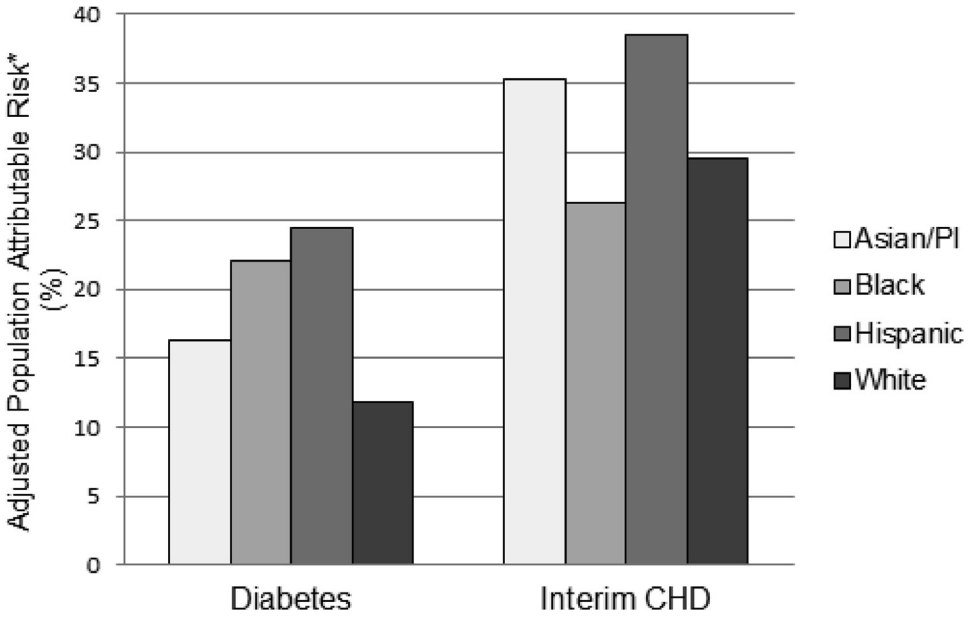

Figure 2. Population-attributable risk percentage of diabetes mellitus and interim coronary heart disease (CHD) for incident heart failure by race/ethnic group in postmenopausal women. PI indicates Pacific Islander. *Relative risk estimates adjusted for age, income, and education.

cohort, Bibbins-Domingo et al[13] estimated early HF rates in black women <50 years of age at 55 per 100 000 person-years, which is less than the 50- to 59-year age-specific rate of 203 per 100 000 person-years found in WHI. These differences may well be explained by the difference in rates of HF in premenopausal compared with postmenopausal women. In addition, in a comparison of the incidence rates of HF, how HF was defined, including both hospitalized and outpatient diagnosis versus only hospitalized HF, differed by study. For example, in MESA,[12] of the 79 cases of incident HF, ≈18% were based on outpatient diagnoses, whereas CHS,[20] Health ABC,[21] and CARDIA[13] relied on hospitalized HF or death, similar to the WHI study. The exclusion of outpatient diagnoses of HF may have underestimated mild or transient cases of HF (viral associated cardiomyopathies) but, given the large number of cases in whites and blacks, probably had little effect on overall incident rates, whereas in Hispanics and Asian Pacific Islanders with much fewer incident cases, the impact of misclassification might be greater and might tend to underestimate rates. However, the misclassification bias of not including outpatient HF diagnoses by risk factor is likely random and therefore would bias toward the null, leading to underestimation of risk factor associations by race/ethnicity.

A study in the United Kingdom[8] that evaluated southeast Asian women mainly from the Indian subcontinent compared with white women found minimally higher rates of hospitalized HF southeast Asians (430 per 100 000 person-years) compared with white women (410 per 100 000 person-years), contrary to the protective effects found in our study and in the California study, which is probably related to differences in Indo-Asian compared with Asians/Pacific Islanders found in the WHI and other US cohorts. The WHI had only a small number of women from the Indian subcontinent. Contrary to our findings and those of Alexander et al,[22] Thomas et al[9] recently published data from selected hospitals suggesting that Hispanics had greater risk for HF than whites. This cross-sectional analysis combined both men and women, and similar to many previous studies[4–8,10,11] on the ethnic differences in HF, it is limited in terms of determining true differences in rates because of its cross-sectional nature and concerns about prevalence-incidence bias, temporal bias, and incomplete adjustment for confounding bias. Also contrary to our findings, Bahrami et al[12] found higher rates of incident HF in Hispanics compared with whites in the MESA study, but this risk did not reach statistical significance, presumably related to sample size issues. Of interest is the fact that in MESA this increased risk in Hispanics was attenuated by household income and LV mass index and to a lesser extent by hypertension, suggesting potential mechanisms important to the Hispanic population. In WHI Hispanic women, adjustment for higher household incomes led to lower risk estimates of HF, whereas development of interim CHD led to higher estimates of HF compared with whites and hypertension had no confounding effect. The explanation for the differences in risk of HF in Hispanics between the different studies is unclear but may be related to different countries of origin for Hispanics (Caribbean, Central American, South American) and the degree of acculturation in the different studies.[9,12,22]

Why Hispanic and Asian women have lower rates of HF even after adjustment for age, socioeconomic status, and known cardiac risk factors than whites in our study remains unclear. A recent article on racial and ethnic differences in subclinical myocardial function in a population cohort free of cardiovascular disease using cardiac magnetic resonance imaging with tissue tagging found that Chinese Americans had the greatest magnitude of peak systolic strain and strain rates, consistent with the highest rate of systolic contraction,

whereas blacks had the lowest rates of peak systolic strain in the majority of wall regions and Hispanics had the lowest rate of contractility in all wall regions.[23] These regional differences in LV systolic function may provide a clue to the differential rates of HF by race and ethnicity.[23]

Risk factors for hospitalized HF found in this analysis are similar to those found in other prospective studies, including older age, lower educational attainment, lower income, diabetes mellitus, and CHD.[2,4,12,19] Hysterectomy was found to be a risk factor in this study, which had previously been reported as a risk factor for HF in the observational cohort of WHI.[24] Although we found hormone therapy and multivitamin use (borderline significance) to be protective, we believe these results may be confounded by past versus present use and markers for overall good health. We did not find hypertension to be a risk factor for HF in our analysis, whereas it has been found to be a risk factor in most other studies of HF.[2,4,12,19,25] We explored this anomaly using differing definitions of hypertension in the WHI data set and found that uncontrolled systolic blood pressure (systolic blood pressure >150 mm Hg and on antihypertensive medication) had a modest effect in predicting HF (Table 4) but no differential effect by race; therefore, we chose to use the more standard definition of hypertension for our nested model (Table 3) to be comparable to other studies.

The strengths of this study are that it is prospective, has an adequate sample size to evaluate racial and ethnic differences with reasonable power, and has >7.8 years of follow-up. Its limitations include the fact that although HF was a physician-adjudicated outcome using consistent clinical criteria, it was not a primary outcome of the WHI study, and thus its definition relied on clinical criteria that did not capture uniform quantitative assessment of systolic function or diastolic LV function, valvular pathology, or separate categorization for right HF. In addition, brain natriuretic peptide and other biomarkers of HF were not routinely assessed. Still, this measurement error would be nondifferential across race/ethnicity groups and thus would bias our results toward the null. Although dietary factors were measured in this cohort, they are not reported here because they are the focus of another report. Serum creatinine and cystatin C are currently not available to assess the role of chronic kidney disease in the origin of HF in WHI. Hemoglobin levels to evaluate anemia and white blood cell count as measures of inflammation were available for analysis but did not show an association with HF in the univariate analysis; therefore, they were not evaluated as confounding risk factors.

We did not evaluate Native Americans (0.44%) in the WHI primarily because of the small numbers and therefore unstable estimates of any potential findings. Missing data were limited to <1% of the sample and thus would have negligible effects on our findings.

Conclusions

Race and ethnicity appear to play an important role in the epidemiology of incident HF, with much lower rates found in Asian/Pacific Islanders and Hispanic postmenopausal women compared with white women. Confirming the results of previous studies, we found here that black women have the highest rates of HF, especially those <60 years of age. However, these differences are completely explained by the effects of income and diabetes mellitus and not by hypertension or CHD in this cohort. Different risk factors have different effects on the incidence of HF for each racial/ethnic group, providing some insight into potential different mechanisms explaining the differential rates of incident HF. Interim CHD and diabetes mellitus have the greatest modifiable public health impact on the incidence of HF and are variable in their attribution to the incidence of HF by race/ethnicity. The mechanism of the differential attribution of risk factors by race/ethnicity needs to be explored more deeply in future cohort studies with appropriate genomic and environmental exposure data.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Heart failure is increasing in prevalence, especially in older women, with differences noted by race/ethnicity. However, limited information is available on differences by race/ethnicity on the incidence of heart failure, which may differ from previous studies owing to the small number of cases of incident heart failure in racial/ethnic minorities and the incomplete assessment of potential biases. In addition, the potential mechanisms for these differences, including the role of traditional risk factors, lifestyle, socioeconomic status, and access-to-care issues in women, are not well explored. This study confirmed previous findings that black women had the highest rates of heart failure, especially at younger ages, but also demonstrated that this increased risk was completely abated when household income or diabetes mellitus was taken into account. Hispanic and Asian/Pacific Islander women not from the Indian subcontinent had lower rates of heart failure compared with whites, and this protective effect persisted after adjustment for all the above risk factors. Future research on the genetic and environmental interactions that lead to the differential rate of heart failure by race/ethnicity and the risk factors involved may lead to improved targeted preventive therapies.

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