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Incident Atrial Fibrillation Among Asians, Hispanics, Blacks, and Whites

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Background—Because the association between atrial fibrillation (AF) and race has only been rigorously compared in population-based studies that dichotomized participants as white or black, it is unclear whether white race confers elevated AF risk or black race affords AF protection.

Methods and Results—The Healthcare Cost and Utilization Project was used to identify patients receiving hospital-based care in California between January 1, 2005 and December 31, 2009. The association between race and incident AF was examined using Cox proportional hazards models. Interaction analyses were performed to elucidate the mechanism underlying the race-AF association. Among 13 967 949 patients, 375 318 incident AF episodes were observed over a median 3.2 (interquartile range 1.8–4.3) years. In multivariable Cox models adjusting for patient demographics and established AF risk factors, blacks (hazard ratio, 0.84; 95% confidence interval, 0.82–0.85; $P<0.001$), Hispanics (hazard ratio, 0.78; 95% confidence interval, 0.77–0.79; $P<0.001$), and Asians (hazard ratio, 0.78; 95% confidence interval, 0.77–0.79; $P<0.001$) each exhibited a lower AF risk compared with whites. AF risk among whites was disproportionately higher in the absence of acquired cardiovascular risk factors and diminished or reversed in the presence of comorbid diseases. Although Hispanics and Asians also had a lower adjusted risk of incident atrial flutter compared with whites, the risk of flutter was significantly higher among blacks.

Conclusions—In a large hospital-based cohort, whites have an increased risk of AF whether compared with blacks, Asians, or Hispanics. The heightened AF risk among whites is most pronounced in the absence of cardiovascular comorbidities. **(*Circulation*. 2013;128:2470-2477.)**

Key Words: arrhythmia ■ atrial fibrillation ■ atrial flutter ■ continental population groups ■ risk factors

More than 3 million Americans are presently living with atrial fibrillation (AF), and this number is expected to grow substantially in future years.[1] Although AF is the most common arrhythmia encountered in clinical practice, the underlying mechanisms responsible for its induction and perpetuation remain incompletely understood. Over the past decade, multiple studies have demonstrated that blacks, despite having a higher burden of traditional AF risk factors, experience a substantially lower rate of AF compared with whites.[2–6]

Clinical Perspective on p 2477

The relative strength of race compared with other established AF risk factors[2,6] suggests the mechanism responsible for the race–AF association plays an important role in disease pathogenesis. However, because AF rates have only been rigorously compared in studies that focused on white or black patients, it is unclear whether white race confers elevated AF risk or black race affords arrhythmia protection. Determining the direction of this relationship is critical to identifying the causal mechanism responsible for this association (eg, whether to search within African ancestry for a protective gene or European ancestry for a harmful gene), which could be broadly applicable to all patients with or at risk for AF.

Characterization of AF rates across multiple racial and ethnic groups is therefore necessary to fully appreciate how race enhances or mitigates risk. We sought to compare the incidence of AF among a large population of white, black, Hispanic, and Asian patients seeking care at California hospitals. To further explore underlying mechanisms, we also examined the interaction between established AF risk factors and the race–AF association.

Methods

All patients aged ≥18 years who received care in a California emergency department, inpatient hospital unit, or ambulatory surgery setting between January 1, 2005 and December 31, 2009 were identified using Healthcare Cost and Utilization Project (HCUP, Agency for Healthcare Research and Quality) California State Emergency Department Databases, State Inpatient Databases, and State Ambulatory Surgery Databases.[7] Individual databases specific

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to calendar year and healthcare setting were merged using an encrypted linkage variable to identify repeat visits for a given patient. Patients with missing admission date data, residence outside of the state of California, unknown race/ethnicity, or a race/ethnicity other than white, black, Hispanic, or Asian were excluded. Patients with prevalent AF (defined as AF at the first recorded hospital encounter) were also excluded from incident analyses. Individuals entered the study cohort at their first healthcare encounter and were censored upon the diagnosis of AF or at the time of inpatient death. Patients who did not experience either of these outcomes were administratively censored at the end of the study period (December 31, 2009).

Age, sex, race, income level, and insurance payer were recorded at each healthcare encounter by the discharging institution. Race and Hispanic ethnicity are reported separately in HCUP data, and race was coded as either white or other for the majority (94%) of individuals with Hispanic ethnicity. Because preliminary analyses revealed no substantial difference in incident AF risk between white Hispanics and other Hispanics when compared with white non-Hispanics, individuals with Hispanic ethnicity were treated as a single group and this designation superseded the coded race. Income level was categorized by quartiles using the median household income for the patient's ZIP code. Up to 25 International Classification of Diseases–9th Edition (ICD-9) codes and 21 Current Procedural Terminology (CPT) codes were provided for each encounter. AF was defined using the ICD-9 code 427.31. Because postoperative AF may have a different underlying mechanism than AF occurring outside of the acute surgical setting, AF was not recorded if a patient had undergone cardiothoracic surgery during the same hospitalization or within the previous 30 days.[3] Such patients remained under observation and could be diagnosed with AF outside of this blanking period. Other medical comorbidities postulated to confound or mediate the association between race and AF were also recorded using ICD-9 and CPT codes as previously described (Table I in the online-only Data Supplement).[3,8] Dichotomous medical comorbidity variables were accumulated at each healthcare encounter and carried forward over time.

Patients with the diagnosis of atrial flutter (AFL, ICD-9 code 427.32) were not considered to have met the AF end point. A secondary analysis examined the association between race and incident AFL. For this analysis, prevalent AFL was excluded and the diagnosis of AFL was blanked in the setting of recent cardiothoracic surgery. Patients were followed until the diagnosis of AFL irrespective of a preceding or concomitant AF diagnosis.

Statistical Analysis

Continuous variables with a normal distribution are presented as mean ± standard deviation (SD) and were compared using 1-way analysis of variance. Non-normally distributed continuous variables are presented as medians with interquartile ranges and were compared using Kruskal-Wallis tests. The association between categorical variables was determined using χ^2 tests. Logistic regression was used to determine the association between race and prevalent AF. Kaplan–Meier analysis was used to estimate the incidence of AF within the total population. The cumulative incidence of AF was also estimated, treating death as a competing risk. Because results from this analysis did not substantially differ from the standard Kaplan–Meier estimates, this methodology was not further implemented in multivariable models. Cox proportional hazards models were used to investigate the association between race and AF incidence both before and after controlling for known confounders. In these models, insurance payer, income level, and medical comorbidities were treated as time-dependent covariates. Nonlinearity of the relationship between age and AF was evaluated by modeling age with restricted cubic splines. Incorporating the cubic spline terms for age into the final model did not appreciably change the estimates for race/ethnicity, so the simpler model treating age as a continuous linear predictor was used. The proportional hazards assumption was assessed using Kaplan–Meier versus predicted survival plots and log-minus-log survival plots. The association between race and incident AFL was examined with the same adjusted Cox model as was used for the AF analysis.

Several sensitivity analyses were performed to more completely evaluate the association between race and AF. To determine whether differences in AF patterns could account for our results, patients with AF coded on all postdiagnosis healthcare encounters were considered to have continuous AF and individuals that had ≥1 subsequent hospital visit without an AF diagnosis were considered to have intermittent AF. The association between race and AF was then determined after stratifying the outcome by either intermittent or continuous AF. To more conservatively identify prevalent AF cases, a repeat analysis was performed after excluding individuals diagnosed with AF during the first year of observation. The influence of healthcare setting was investigated using 2 approaches: one analysis controlled for the initial location of presentation, whereas a second was stratified by location of AF diagnosis. Additional incident analyses were limited to AF identified as the primary inpatient admission diagnosis and AF diagnosed on ≥2 visits within 1 year. A final analysis only included patients aged ≥65 years. An AFL sensitivity analysis was also performed in which the outcome definition was narrowed to only those patients with AFL in the absence of a preceding or concomitant AF diagnosis. In this analysis, patients identified as having AF either before or at the same time as AFL were censored at the time of their AF diagnosis.

After determining the adjusted association between race and AF, we assessed for modification of racial differences in AF risk by traditional AF risk factors. Interaction terms for the comparison between whites and blacks, whites and Hispanics, and whites and Asians were all statistically significant and qualitatively similar. Non-white groups were therefore pooled to enhance interpretation of the interaction results.

To investigate the possibility that the observed associations between race and AF resulted from differences in AF ascertainment, we examined the relationship between race and 2 other medical diagnoses (ventricular tachycardia, ICD-9 427.1 and influenza, ICD-9 487.0, 487.1, or 487.8) using Cox proportional hazard models. If ascertainment bias explained the race/ethnicity and AF associations, we would expect to observe similar patterns for all three diagnoses. These analyses were adjusted for confounders identified a priori.

All analyses were performed using Stata 12 (StataCorp, College Station, TX). A 2-tailed $P<0.05$ was considered statistically significant. Certification to use deidentified HCUP data was obtained from the University of California, San Francisco Committee on Human Research.

Results

Between 2005 and 2009, HCUP data were available for 17 741 021 adult patients. From this population, individuals were excluded because of a missing date of initial hospitalization (n=152 602), a non-California primary residence (n=592 473), or race/ethnicity other than white, black, Hispanic, or Asian (n=2 734 055). A total of 293 942 patients had prevalent AF. After adjusting for the variables in Table 1, all races/ethnicities demonstrated a reduced odds of prevalent AF when compared with whites (blacks odds ratio, 0.53; 95% confidence interval [CI], 0.52–0.54; $P<0.001$; Hispanics odds ratio, 0.61; 95% CI, 0.60–0.62; $P<0.001$; Asians 0.68; 95% CI, 0.67–0.69; $P<0.001$).

Among the 13 967 949 patients included in the incident analysis, 7 918 726 (56.7%) were white, 1 074 150 (7.7%) black, 3 768 607 (27.0%) Hispanic, and 1 206 466 (8.6%) Asian. Nonwhite patients had a higher prevalence of Medicaid insurance, hypertension, and diabetes mellitus (Table 1).

A total of 375 318 incident AF episodes were observed over a median follow-up of 3.2 (interquartile range, 1.8–4.3) years (271 404 episodes among whites, 19 660 among blacks, 55 724 among Hispanics, and 28 530 among Asians). The overall incidence of AF was 9.03 (95% CI, 9.00–9.06) per 1000

Table 1. Baseline Patient Characteristics by Race

	White n=7 918 726	Black n=1 074 150	Hispanic n=3 768 607	Asian n=1 206 466	*P* Value*
Age, mean (SD), years	50.5 (19.2)	43.5 (17.8)	41.8 (17.8)	49.5 (18.8)	<0.001
Female, n (%)	4 378 438 (55.3)	622 038 (57.9)	2 205 843 (58.5)	773 994 (64.2)	<0.001
Insurance, n (%)					<0.001
Medicare	1 916 882 (24.2)	166 458 (15.5)	500 622 (13.3)	259 629 (21.5)	
Medicaid	460 330 (5.8)	188 494 (17.5)	695 596 (18.4)	131 346 (10.9)	
Private	4 219 166 (53.3)	397 339 (37.0)	1 559 487 (41.4)	639 607 (53.0)	
Self-Pay	772 731 (9.8)	218 582 (20.4)	658 877 (17.5)	89 650 (7.5)	
Other	547 202 (6.9)	102 938 (9.6)	352 678 (9.4)	85 968 (7.1)	
Income quartile, n (%)					<0.001
1 Lowest	1 355 149 (17.4)	496 275 (46.9)	1 288 682 (34.6)	193 561 (16.2)	
2	1 824 516 (23.5)	234 181 (22.1)	1 159 416 (31.1)	239 490 (20.0)	
3	2 128 149 (27.4)	211 276 (20.0)	817 445 (22.0)	336 607 (28.1)	
4 Highest	2 462 296 (31.7)	117 192 (11.0)	456 477 (12.3)	428 406 (35.7)	
HTN, n (%)	1 270 478 (16.0)	213 163 (19.8)	493 465 (13.1)	234 746 (19.5)	<0.001
Diabetes mellitus, n (%)	496 802 (6.3)	97 131 (9.0)	348 909 (9.3)	117 548 (9.7)	<0.001
CAD, n (%)	362 872 (4.6)	34 196 (3.2)	98 430 (2.6)	53 511 (4.4)	<0.001
HF, n (%)	136 429 (1.7)	26 009 (2.4)	43 865 (1.2)	19 303 (1.6)	<0.001
CTS,† n (%)	53 784 (0.7)	6337 (0.6)	20 033 (0.5)	7490 (0.6)	<0.001
Valvular disease, n (%)	91 767 (1.2)	6 884 (0.6)	17 922 (0.5)	10 338 (0.9)	<0.001
Pulmonary disease, n (%)	190 449 (2.4)	18 341 (1.7)	32 753 (0.9)	16 018 (1.3)	<0.001
CKD, n (%)	57 775 (0.7)	17 036 (1.6)	32 137 (0.9)	16 932 (1.4)	<0.001
First encounter location					<0.001
Ambulatory surgery	2 348 661 (29.7)	121 338 (11.3)	624 961 (16.6)	330 979 (27.4)	
Emergency department	3 832 666 (48.4)	726 341 (67.6)	2 236 495 (59.3)	523 901 (43.4)	
Inpatient hospitalization	1 737 399 (21.9)	226 471 (21.1)	907 151 (24.1)	351 586 (29.2)	

Baseline characteristics are for patients included in the incident AF analysis; individuals with prevalent AF have been excluded. AF indicates atrial fibrillation; CAD, coronary artery disease; CKD, chronic kidney disease; CTS, cardiothoracic surgery; HF, heart failure; HTN, hypertension; and SD, standard deviation.

**P* value for comparison of the reported characteristic across all races.

†Atrial fibrillation was blanked if diagnosed within 30 days after cardiothoracic surgery.

patient years. Age-, sex-, and race-specific rates of incident AF were higher than those previously reported in community dwelling adult cohorts (Table II in the online-only Data Supplement). The ratio of incident AF diagnoses between whites and non-whites was similar across the 3 studied healthcare settings (Figure 1). Both before and after multivariable

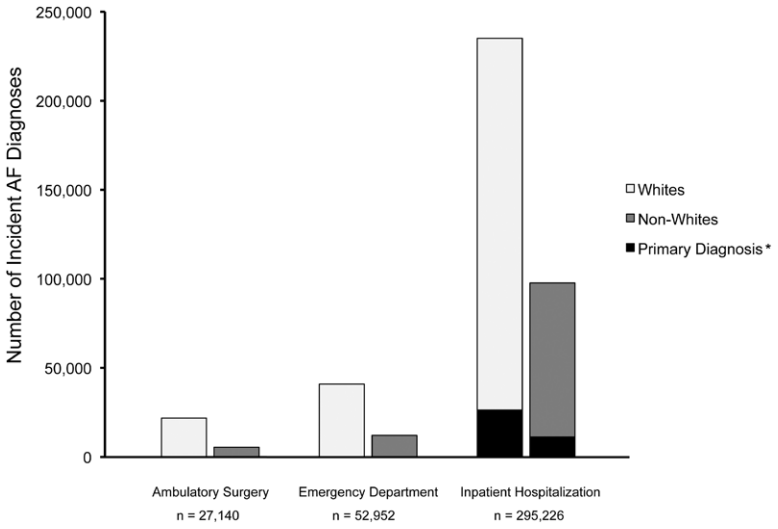

Figure 1. Atrial fibrillation diagnoses by healthcare setting. Distribution of the 375 318 incident atrial fibrillation diagnoses by location. *Primary diagnosis data were only available for inpatient hospitalizations.

adjustment, established AF risk factors were associated with an increased hazard of incident AF (Table III in the online-only Data Supplement). In age- and sex-adjusted analyses, and after adjusting for the covariates listed in Table 1, blacks, Hispanics, and Asians each exhibited a substantially reduced hazard of AF compared with whites (Table 2). There was evidence of heterogeneity in AF risk among the non-white races ($P<0.001$). Compared with non-Hispanic whites, a similarly reduced adjusted hazard of AF was observed among both white Hispanics (hazard ratio [HR], 0.76; 95% CI, 0.75–0.77; $P<0.001$) and other Hispanics (HR, 0.80; 95% CI, 0.79–0.81; $P<0.001$).

Using the same multivariable Cox proportional hazards model from the overall analysis, blacks, Hispanics, and Asians each had a reduced risk of incident intermittent (n=155 113) and continuous (n=36 790) AF compared with whites (Table IV in the online-only Data Supplement). Excluding AF cases diagnosed in the first year of observation did not substantively change the results, nor did controlling for location of initial healthcare utilization, stratifying by AF diagnosis location, or restricting the analysis to individuals age ≥65 years. Finally, sensitivity analyses limited to inpatient AF outcomes or AF coded twice within 1 year identified similar associations between race and AF.

Differences in AF risk between whites and non-whites were modified by several established AF risk factors. Specifically, the difference in AF risk between white and non-white races narrowed by ≈2 percentage points for each decade increase in age. For example, whites demonstrated an adjusted 32% increased risk of AF at age 50 (HR, 1.32; 95% CI, 1.30–1.34; $P<0.001$), although this heightened risk decreased to 25% at age 80 (HR, 1.25; 95% CI, 1.24–1.26; $P<0.001$, P value for interaction <0.001). In addition, the elevated risk of AF among whites was greater for men (HR, 1.29; 95% CI, 1.28–1.31; $P<0.001$) than women (HR, 1.24; 95% CI, 1.23–1.25; $P<0.001$, P value for interaction <0.001). Analysis of acquired AF risk factors revealed that the hazard of AF among whites was significantly higher in the absence of these comorbid conditions. In the presence of AF risk factors, however, the elevated hazard of AF among whites versus non-whites was significantly diminished or reversed (Figure 2).

Among the 375 318 patients with incident AF, 10 517 (2.8%) received a diagnosis of AFL before AF. An additional 22 876 (6.1%) individuals had AFL identified concurrent with incident AF. Of the 68 670 patients with incident AFL, 26 843 (39.1%) were diagnosed with AF before AFL. After adjusting for the same demographic and comorbidity variables used in the AF analysis, Hispanics and Asians each had a lower adjusted risk of AFL compared with whites (Table 2). Blacks, on the other hand, had a significantly higher risk of this arrhythmia. These relationships persisted in a sensitivity analysis limited to the 18 951 AFL patients without a preexisting or concomitant AF diagnosis.

To determine whether there were inherent biases in the HCUP data, we examined the relationship between race and a diagnosis of influenza or ventricular tachycardia. All non-white races each demonstrated an increased hazard of influenza compared with whites (Figure 3). The hazard of ventricular tachycardia among non-white races, however, was variable; blacks exhibited a significantly increased risk of this diagnosis, whereas the risk among Asians was reduced when compared with whites.

Discussion

In a large, diverse cohort of patients receiving care in California hospital-based healthcare facilities, blacks, Hispanics, and Asians each had a significantly lower hazard of AF when compared with whites. This reduced risk of arrhythmia persisted after controlling for multiple covariates associated with race and AF. These data indicate that an unidentified characteristic inherent to white race increases AF risk. In addition, the heightened risk associated with white race was most pronounced in the absence of established AF risk factors, compatible with the presence of alternative disease mechanisms.

The results of this investigation are consistent with prior research that has established a reduced risk of AF among

Table 2. Association Between Race, Incident Atrial Fibrillation, and Incident Atrial Flutter

	Black			Hispanic			Asian		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value	HR	95% CI	*P* Value
Incident atrial fibrillation									
Model 1	0.95	0.94–0.97	<0.001	0.83	0.82–0.84	<0.001	0.80	0.79–0.81	<0.001
Model 2	0.94	0.92–0.95	<0.001	0.81	0.80–0.82	<0.001	0.79	0.78–0.80	<0.001
Model 3	0.84	0.82–0.85	<0.001	0.78	0.77–0.79	<0.001	0.78	0.77–0.79	<0.001
Incident atrial flutter									
Model 1	1.25	1.21–1.29	<0.001	0.74	0.72–0.76	<0.001	0.83	0.81–0.85	<0.001
Model 2	1.27	1.23–1.31	<0.001	0.75	0.73–0.76	<0.001	0.82	0.80–0.84	<0.001
Model 3	1.09	1.06–1.12	<0.001	0.71	0.69–0.73	<0.001	0.81	0.79–0.83	<0.001

White race is the reference group for all comparisons. Model 1 is adjusted for age and sex. Model 2 is adjusted for age, sex, insurance payer, and income. Model 3 is adjusted for age, sex, insurance payer, income, history of cardiothoracic surgery, and presence of hypertension, heart failure, coronary artery disease, valvular heart disease, pulmonary disease, chronic kidney disease, and diabetes mellitus. CI indicates confidence interval; and HR, hazard ratio.

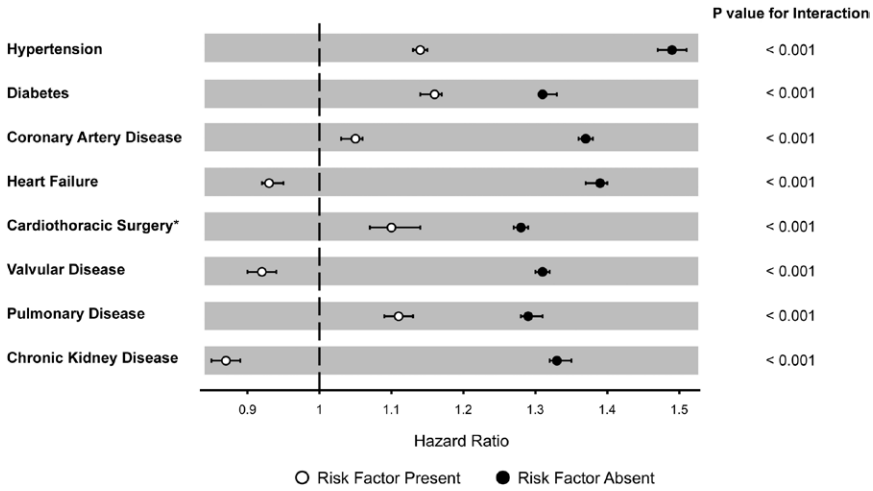

Figure 2. Race and atrial fibrillation interaction analysis by cardiovascular comorbidities. Hazard ratios for the adjusted risk of incident atrial fibrillation among whites compared with non-whites (blacks, Hispanics, and Asians combined) in the presence (white circles) and absence (black circles) of the described cardiovascular comorbidities. The higher risk of AF in whites is more pronounced in the absence of comorbidities and attenuated or reversed in the presence of comorbidities, resulting in statistically significant interactions for each comparison. *Atrial fibrillation was blanked if diagnosed within 30 days after cardiothoracic surgery. Error bars denote 95% confidence intervals.

blacks compared with whites.[2–6] Marcus et al[2] recently extended this observation to show that increased percent European ancestry within African Americans significantly predicts elevated AF risk. The dichotomous treatment of race in these prior studies, however, does not allow the relative protective or harmful influence of an individual race to be discerned.

The mechanism driving the lower observed risk of AF among blacks in this and previous studies remains unclear. Because blacks have both a greater burden of AF risk factors and higher rates of stroke, some authors have hypothesized that this race–AF paradox is explained by reduced AF ascertainment in blacks.[9,10] Higher rates of asymptomatic or paroxysmal AF, for example, could reduce the sensitivity of ECG screening, patient self report, or hospitalization records for the diagnosis of AF. Indeed, the association between P wave indices (a proposed marker of AF risk) and black race is consistent with this theory.[11] Continuous monitoring with implantable devices, however, does not support this phenomenon and instead corroborates the presently observed higher incidence of AF among whites.[12] To further evaluate for this proposed ascertainment bias, we used discharge coding patterns to classify AF as intermittent or continuous and stratified our analysis by AF type. Because the association between race and AF was consistent in these analyses, our results do not support the hypothesis that reduced AF ascertainment in blacks entirely accounts for the observed association between race and AF.

In addition to identifying a reduced hazard of AF among blacks compared with whites, we also observed a lower AF risk among both Hispanics and Asians. Studies reporting a reduced risk of AF among non-white races have been limited by the use of a single non-white comparator group,[4–6,13–16] absence of incident event data,[3–5,16–19] failure to adjust for comorbidities,[3,17,18] or enrollment of select populations (including patients with acute decompensated heart failure,[4] with acute myocardial infarction,[14] on hemodialysis,[20] and after coronary artery bypass graft surgery).[21] Our results provide a more comprehensive assessment of the risk of AF among a diverse population of patients seeking care at California hospitals without limitation to a specific disease condition. Factors that contribute to the elevated AF risk in whites are not well understood, but may include genetic effects or environmental exposures related to race. These results indicate that future research in this area should aim to identify factors that confer increased AF risk rather than focusing on protective characteristics unique to blacks. In addition, although recently published AF risk algorithms have incorporated white or black race to refine prediction,[22,23] the present findings and shifting United States demographics suggest future models should also include Asian race and Hispanic ethnicity.

The adjusted hazard of AF among blacks versus whites was smaller in the present study compared with previous reports.[2] This is potentially explained by patient characteristics and AF ascertainment. Although most previous investigations enrolled relatively healthy outpatients, the present study

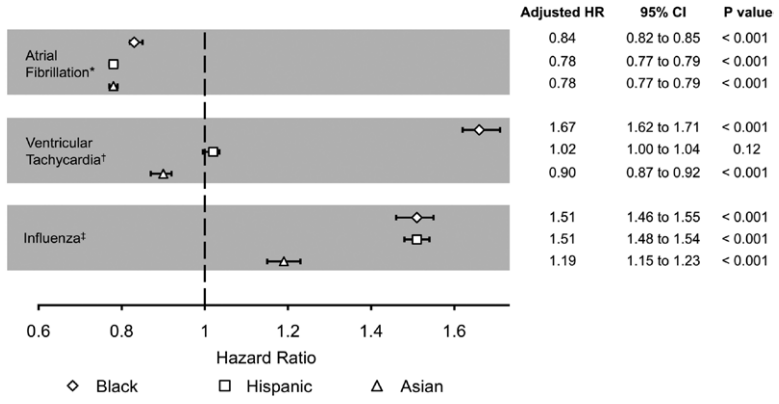

Figure 3. Adjusted association between race and medical diagnoses. Adjusted hazard ratios (HR) for atrial fibrillation, ventricular tachycardia, and influenza among blacks, Hispanics, and Asians using white race as reference group for all analyses. *Adjusted for age, sex, insurance payer, income, history of cardiothoracic surgery, and presence of hypertension, heart failure, coronary artery disease, valvular heart disease, pulmonary disease, chronic kidney disease, and diabetes mellitus. †Adjusted for age, sex, insurance payer, income, and history of coronary artery disease and heart failure. ‡Adjusted for age, sex, insurance payer, income, and history of pulmonary disease. Error bars denote 95% confidence intervals (CI).

included individuals only after an index hospitalization. This likely selected for a sicker population within which the association between race and AF risk may be less pronounced. Indeed, such an explanation is supported by our interaction findings. In addition, whereas we identified incident AF that necessitated or was present during a hospital encounter, previous investigations have used data from both outpatient and inpatient settings to identify cases. Access to outpatient primary care is reduced among many minority populations[24] and such patients are more likely to rely on hospital settings for their healthcare.[25,26] The reduced magnitude of the hazard ratio observed in the present study may therefore be expected if black patients are more likely to present to a hospital with incident AF (versus a physician's office). Despite this anticipated source of bias, blacks and other non-white races remained at a significantly decreased risk of AF. It should be further noted that the higher rates of incident AF observed in the HCUP population are likely attributable to differences in overall health between patients seeking care in a hospital-based setting and those enrolled in community-based cohorts, as mentioned above. Our incidence rate results, therefore, are not indicative of the absolute rate of AF in the overall California or United States populations.

Although AF risk was reduced among blacks, Hispanics, and Asians compared with whites, similar associations were not observed for the diagnoses of influenza or ventricular tachycardia. Although all non-white races demonstrated a significantly higher hazard of influenza when compared with whites, the association between race and ventricular tachycardia did not follow such a homogenous pattern. These analyses were performed with the express purpose of demonstrating that the observed relationship between race and AF was not a result of systematic bias related to database coding, nor was it solely a reflection of differences in the way various races use and receive healthcare. Further exploration and validation of racial/ethnic differences in influenza and ventricular tachycardia diagnoses was not undertaken.

To better understand the mechanism of differential AF risk by race, we leveraged the statistical power of our large database to study the interaction between known AF risk factors and the race-AF relationship. Although statistically significant, the differences in AF risk between non-white races did not appear to be clinically meaningful; all non-white races were therefore combined and compared with whites in our interaction analysis. We consistently observed that the hazard of AF among whites was higher in the absence of comorbidities. Approximately 30% of patients with AF lack other identifiable cardiopulmonary disease[27]; although we did not specifically study individuals with lone AF, our findings suggest that white race may be especially important in driving risk among this subgroup of AF patients. In the presence of acquired AF risk factors, the differential risk of AF between races was diminished. Patients with more comorbidities likely have greater contact with the medical system, which could result in enhanced detection of asymptomatic or paroxysmal AF. For example, a previous study among chronic kidney disease patients found no association between race and AF.[28] Although this finding could be explained by our interaction results (the race–AF association is attenuated in the presence of cardiovascular comorbidities), it also is consistent with the possibility that more healthcare access leads to a more equal detection of AF across different racial groups. However, our results indicate differential contact with the healthcare system cannot entirely account for the observed differences in AF by race; although the relative hazard of AF between white and non-white races was diminished in the setting of common medical conditions that require frequent medical follow up (including hypertension, diabetes mellitus, coronary disease, and pulmonary disease), this relative hazard generally remained significantly higher among whites. In addition, the significant interaction results indicate that the association between white race and AF is not an artifact of increased diagnostic suspicion among patients with AF risk factors.

Interestingly, the adjusted hazard of AFL by race did not mirror the AF results. Although the precise electrophysiologic mechanism of AF induction and perpetuation remains incompletely understood, it is thought that both an electrical trigger and anatomic substrate are necessary to initiate and sustain AF.[29] Typical AFL, on the other hand, is a macroreentrant circuit involving well-defined anatomic obstacles in the right atrium.[30] This rhythm also presumably requires an atrial trigger for initiation.[31] The link between AF and AFL is inadequately characterized; whereas some have argued that the 2 arrhythmias can exist independently, others believe the ability of the atrium to sustain AFL also implies the ability to clinically develop AF.[32–34] The differential risk of AF versus AFL by race could suggest that the racial differences in AF may in part be secondary to differences in left atrial anatomic substrate (versus electrical triggers), potentially identifying a mechanism underlying the race–AF association that warrants future investigation.

This study used an administrative database to longitudinally follow patients for the diagnosis of AF over 5 years. Strengths of this approach include the large sample size, which afforded the ability to examine a diverse sample of patients and provided the necessary statistical power to perform interaction analyses. However, limitations of this investigation should be recognized. Race was identified by the treating hospital, and additional efforts to verify patient race were not feasible. Similarly, outcome and confounder variables were determined using hospital ICD-9 coding. Notably, a previous study revealed administrative ICD-9 coding at a large health maintenance organization exhibited 95% sensitivity and 99% specificity for the diagnosis of AF when compared with record review by trained abstractors.[35] Nonetheless, we recognize that we were unable to capture patients diagnosed with AF in a nonsurgical outpatient setting, symptomatic patients who did not seek care, or asymptomatic AF patients. Because HCUP does not include data from all hospitals (for example, no Veterans Affairs data are provided), some California hospitalizations were not captured in our analysis. However, a very high proportion of California hospitals were represented. In 2009, for instance, 354 community hospitals (which include both private and academic centers) and 36 state/federal hospitals supplied data to the HCUP State Inpatient Database. HCUP only identified 3 nongovernment funded California hospitals (<1%) that did not contribute data. Because outpatient death is not captured by HCUP databases, it is possible

that substantially differential rates of death by race and AF status could bias our results. Some clinicians may confuse the diagnoses of AF and AFL,[36] reducing the validity of diagnostic coding for AFL.[37] This could potentially account for the differences in AF and AFL risk by race. Although our results are in agreement with previous investigations performed in well-characterized cohort studies (albeit limited to white and black patients) demonstrating a reduced risk of AF among blacks, it remains possible that blacks, Hispanics, and Asians more frequently seek hospital-based care for non-AF diagnoses compared with whites. Such bias could potentially account for the lower observed risk of AF in these patients. Finally, we are unable to exclude residual confounding resulting from unmeasured or incompletely characterized covariates, and the results of this observational analysis do not prove a direct, causal relationship between race and AF.

In conclusion, we observed a significantly lower hazard of AF among blacks, Hispanics, and Asians compared with whites after controlling for established risk factors. Furthermore, racial differences in AF risk are significantly reduced with the accumulation of cardiovascular comorbidities. These findings argue against a protective effect unique to black race and instead suggest unidentified mechanisms separate from traditional AF risk factors increase AF risk in whites.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Although atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice, the underlying mechanisms responsible for its induction and perpetuation remain incompletely understood. Blacks experience a substantially lower rate of AF compared with whites, and the relative strength of this association suggests the mechanism responsible for the race-AF association plays an important role in disease pathogenesis. Because AF rates have only been rigorously compared between black and white patients, it is unclear whether white race confers elevated AF risk or black race affords arrhythmia protection. The present investigation compared incident AF between whites, blacks, Hispanics, and Asians receiving hospital-based medical care in California. A significantly lower hazard of AF was observed among blacks, Hispanics, and Asians compared with whites both before and after controlling for established risk factors. These findings argue against a protective effect unique to black race and instead suggest an unidentified characteristic inherent to white race increases AF risk. In addition, the difference in AF risk between whites and non-whites was most pronounced in the absence of established AF risk factors. This further suggests that an unknown, alternative disease mechanism is driving these racial differences. As non-white racial and ethnic populations within the United States continue to grow, clinicians should be aware of the importance of race in AF prediction and incorporate this knowledge into their care of patients at risk for this frequently encountered disease.

SUPPLEMENTAL MATERIAL

Supplemental Table 1. International Classification of Diseases-9th Edition (ICD-9) and Current Procedural Terminology (CPT) Codes Used for Disease Identification

Diagnosis	ICD-9 / CPT Codes	
Atrial Fibrillation	ICD-9	427.31
Hypertension	ICD-9	401.X, 402.X, 403.X, 404.X, 405.X, 437.2
Diabetes	ICD-9	249.X, 250.X, 790.X, 791.5, 791.6, V458.5, V539.1, V654.6
Coronary Artery Disease	ICD-9	36.01, 36.02, 36.03, 36.05, 36.09, 36.1X, 411.0, 411.1, 411.8, 411.89, 412, 413.X, 414.X, 429.7, V458.2
Heart Failure	ICD-9	402.01, 402.11, 402.91, 404.91, 404.93, 425,X, 428.X
Cardiothoracic Surgery*	ICD-9	35.3X, 35.41, 35.42, 35.50, 35.51, 35.52, 35.53, 35.54, 35.60, 35.61, 35.62, 35.63, 35.70, 35.71, 35.72, 35.73 36.1X, 37.10, 37.11, 37.12, 37.24, 37.25, 37.31, 37.32, 37.33, 37.35, 37.40
Valvular Disease	ICD-9	394.X, 395.X, 396.X, 397.0, 397.1, 424.0, 424.1, 424.2, 424.3, V422, V433
Pulmonary Disease	ICD-9	494.2X, 491.8, 491.9, 492.0, 492.8, 494, 494.0, 494.1, 496
Chronic Kidney Disease	ICD-9	39.93, 54.98, 585.X, V420, V451, V451.1, V451.2, V560, V561, V562, V563.1, V563.2, V568, V56
	CPT	90921, 90925, 90935, 90937, 90945, 90947, 90989, 90993
Ventricular Tachycardia	ICD-9	427.1
Influenza	ICD-9	487.0, 487.1, 487.8

*Atrial fibrillation was blanked if diagnosed within 30 days after cardiothoracic surgery.

Supplemental Table 2. Incidence of Atrial Fibrillation per 1,000 Person Years by Age, Sex, and Race

Healthcare Cost and Utilization Project

	White		Black		Hispanic		Asian	
Age, y	Men	Women	Men	Women	Men	Women	Men	Women
65 - 69	20.9	13.5	18.7	14.4	16.2	11.0	15.3	9.7
70 - 74	31.9	22.7	26.5	21.0	24.4	18.1	22.6	15.9
75 - 79	46.1	34.3	34.7	29.3	34.4	26.8	32.3	24.2
≥ 80	65.7	50.5	42.4	38.2	45.6	38.7	48.8	39.4

	Atherosclerosis Risk in Communities Study[1]				Cardiovascular Health Study[2]*	
	White		Black			
Age, y	Men	Women	Men	Women	Men	Women
65 - 69	8.8	6.1	5.8	4.2	12.3	10.9
70 - 74	12.3	9.3	10.9	10.5	22.8	9.1
75 - 79	21.0	15.5	10.9	11.1	34.8	23.1
≥ 80	47.5	33.1	41.1	29.3	58.7	25.1

*Due to the low number of Black participants in the Cardiovascular Health Study (CHS), age, sex, and race-specific estimates of AF incidence are not provided. In the overall CHS cohort, the incidence of AF was 19.5 and 12.0 per 1,000 person years for Whites and Blacks, respectively; y, years.

Supplemental Table 3. Unadjusted and Adjusted Association Between Established Risk Factors and Incident Atrial Fibrillation

	Unadjusted HR	95% CI	P value	Adjusted HR*	95% CI	P value
Age (per year)	1.09	1.09 to 1.09	< 0.001	1.07	1.07 to 1.07	< 0.001
Male gender	1.38	1.37 to 1.38	< 0.001	1.42	1.41 to 1.43	< 0.001
HTN	4.73	4.70 to 4.76	< 0.001	1.11	1.10 to 1.12	< 0.001
Diabetes	3.07	3.05 to 3.10	< 0.001	1.12	1.11 to 1.13	< 0.001
CAD	6.21	6.17 to 6.26	< 0.001	1.21	1.20 to 1.22	< 0.001
HF	9.72	9.64 to 9.79	< 0.001	1.88	1.86 to 1.90	< 0.001
CTS†	4.33	4.27 to 4.39	< 0.001	1.27	1.25 to 1.29	< 0.001
Valvular Disease	7.51	7.43 to 7.59	< 0.001	1.54	1.52 to 1.56	< 0.001
Pulmonary Disease	5.66	5.61 to 5.71	< 0.001	1.34	1.33 to 1.35	< 0.001
CKD	6.53	6.46 to 6.60	< 0.001	1.30	1.29 to 1.32	< 0.001

CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; CTS, cardiothoracic surgery; HTN, hypertension; HF, heart failure; HR, hazard ratio. *Adjusted model included terms for insurance payer, income, and the atrial fibrillation risk factors listed in the above table. †Atrial fibrillation was blanked if diagnosed within 30 days after cardiothoracic surgery.

Supplemental Table 4. Association Between Race and Incident Atrial Fibrillation Stratified by AF Type

AF Type	Black			Hispanic			Asian		
	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value
Overall	0.84	0.82 to 0.85	< 0.001	0.78	0.77 to 0.79	< 0.001	0.78	0.77 to 0.79	< 0.001
Intermittent*	0.73	0.72 to 0.74	< 0.001	0.77	0.76 to 0.78	< 0.001	0.72	0.71 to 0.73	< 0.001
Continuous†	0.60	0.56 to 0.63	< 0.001	0.70	0.67 to 0.71	< 0.001	0.71	0.69 to 0.74	< 0.001

Hazard ratios describe the relative hazard of incident AF compared to Whites. *Patients with continuous AF were excluded. †Patients with intermittent AF were excluded. AF, atrial fibrillation; HR, hazard ratio; CI, confidence interval.

Supplemental References

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