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Effect of Race on Outcomes (Stroke and Death) in Patients >65 Years With Atrial Fibrillation

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Abstract

Atrial fibrillation (AF) is associated with stroke and death. We sought to determine whether there are any racial differences in the outcomes of death and stroke in patients with AF. We used Medicare administrative data from January 1, 2010, to December 31, 2011, to identify 517,941 patients with newly diagnosed AF. Of these, 452,986 patients (87%) were non-Hispanic white, 36,425 (7%) were black, and 28,530 (6%) were Hispanic. The association between race and outcomes of death and stroke were measured using Cox proportional hazard models. Over a median follow-up period of 20.3 months, blacks had a significantly higher hazard of death (hazard ratio [HR] = 1.46; 95% confidence interval [CI] 1.43 to 1.48; $p < 0.001$) and stroke (HR = 1.66; 95% CI 1.57 to 1.75; $p < 0.001$), compared with white patients. After controlling for pre-existing co-morbidities, the higher hazard of death in blacks was eliminated (HR 0.95; 95% CI 0.93 to 0.96; $p < 0.001$) and the relative hazard of stroke was reduced (HR = 1.46; 95% CI 1.38 to 1.55; $p < 0.001$). Similarly, Hispanics had a higher risk of death (HR = 1.11; 95% CI 1.09 to 1.14; $p < 0.001$) and stroke (HR = 1.21; 95% CI 1.13 to 1.29; $p < 0.001$) compared with whites. The relative hazard of death was lower in Hispanics (HR 0.82; 95% CI 0.80 to 0.84; $p < 0.001$) compared with whites, after controlling for pre-existing co-morbidities, and the relative hazard of stroke was also attenuated (HR = 1.11; 95% CI 1.03 to 1.18; $p < 0.001$). In conclusion, in patients >65 years with newly diagnosed AF, the risks of death and stroke are higher in blacks and Hispanics compared with whites. The increased risk was eliminated or significantly reduced after adjusting for preexisting co-morbidities. AF may be a marker for underlying co-morbidities in black and Hispanic patients who may be at a higher mortality risk.

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Disclosures

The other authors have no conflicts to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.amjcard.2015.04.012>.

Several studies have shown that despite having higher risk factors for developing atrial fibrillation (AF), the risk of AF is lower in black Americans compared with white Americans.^{1–5} A recent study found similar results in Hispanics.⁶ However, less is known about differences in AF-related outcomes by race and ethnicity. Race-based differences in outcomes have been reported in other cardiovascular conditions, such as acute myocardial infarction (AMI) and cardiac arrest, where blacks had worse outcomes than the whites.^{7,8} Although both AMI and cardiac arrest are acute conditions, AF is a chronic condition and racial differences in outcomes with AF have not been adequately studied. To address this gap in knowledge, we used Medicare data to examine whether the risk of death and stroke in patients with newly diagnosed AF differed by a patient's race.

Methods

We used data obtained from the Centers for Medicare and Medicaid (CMS) for years 2009 through 2012, including (1) Beneficiary Summary File Base and Chronic Condition segments, (2) Inpatient (part A) and Carrier (part B) Standard Analytic Files, and (3) Pharmacy Drug Event (part D). Patients were included in the study if they had a new AF diagnosis during the period January 2010 to December 31, 2011. New AF was defined based on previously published algorithms (i.e., 1 inpatient claim or 2 outpatient claims within a year with *International Classification of Diseases, Ninth Revision, Clinically Modification (ICD-9-CM)* code 427.31 as primary or first secondary diagnosis, with no previous AF diagnoses during the previous 12 months). Patients were excluded if they were <66 years at the time of diagnosis (to ensure at least 12 months of Medicare eligibility before diagnosis), were enrolled in a Medicare managed care during the observation period, or were not enrolled in a Part D drug prescription plan at the time of AF diagnosis.

Patient race or ethnicity was determined using the race code developed by the Research Triangle Institute (RTI) that is available on the CMS Beneficiary Summary File.⁹ The RTI race code is an enhanced race/ethnicity designation based on first and last name algorithms. The RTI race code agrees excellently with self-reported race, with kappa coefficients 0.80 for Hispanic beneficiaries and 0.90 for black beneficiaries.

Additional patient characteristics were identified in the CMS enrollment and encounter data. Dual enrollment in Medicaid at the time of AF diagnosis was identified from the CMS Beneficiary Enrollment Summary. Co-morbid conditions were identified in inpatient and outpatient claims during the 12 months before the first AF diagnosis date and were defined using algorithms originally developed by Elixhauser et al.¹⁰ Previous cerebrovascular events were identified using previously published algorithms, as were previous bleeding episodes.^{11,12}

Risk scoring systems were used to assess the risk of stroke and bleeding. To assess the risk of stroke, the CHA₂DS₂-VASc risk scores were calculated based on a point system reflecting the presence of congestive heart failure (1 point), hypertension (1 point), age more than or equal to 75 years (2 points), diabetes (1 point), previous stroke (2 points), vascular disease (1 point), age 65 to 74 (1 point), and female gender (1 point).^{11,13} A modified HAS-BLED risk score was also calculated to assess bleeding risk based on the presence of

hypertension, previous stroke, advanced age, renal disease, liver disease, and alcohol abuse.¹⁴ Finally, we identified the date of first oral anticoagulant prescription fill after initial AF diagnosis in part D event data to control for potential confounding because of differences in the use of oral anticoagulants by race.

Our primary outcome was death through December 31, 2012. The secondary outcome was stroke, as identified on inpatient Standard Analytic Files claims for years 2010 to 2012 and included acute hospitalizations admitted as emergent or urgent with a primary diagnosis of cerebral infarction (*ICD-9-CM* codes 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, and 434.91). Dates of death were identified on the Beneficiary Summary File. For each patient, the date of the first occurrence of each outcome after AF diagnosis was identified. Patients who did not experience the outcome of interest were censored on December 31, 2012.

Data analysis encompassed bivariable and multivariable methods. First, characteristics of patients as of the date of first AF diagnosis were compared by race and ethnicity. Categorical variables (e.g., presence of hypertension) were compared using the chi-square statistic, whereas continuous or interval variables (e.g., age), were compared using analysis of variance. Subsequently, we created for each patient a longitudinal record that included the date of first AF diagnosis, pre-existing patient characteristics and co-morbidities, oral anticoagulant use, and number of days to first stroke and death. Cox regression models were used to evaluate the relative hazard of stroke and death by race. The exponentiated value of the regression coefficients associated with black race or Hispanic ethnicity provides the relative hazard of each outcome in black patients (or Hispanic), relative to non-Hispanic white patients. Initial models included race/ethnicity indicators only, whereas subsequent models controlled for the patient demographic and co-morbid conditions displayed in Table 1, using a statistical criterion of $p < 0.05$ to identify variables eligible for inclusion in multivariable models. A second set of risk adjustment models were estimated that further controlled for the use of oral anticoagulants after initial AF diagnosis, treating oral anticoagulant use as a time-dependent indicator variable set to 1 after the first prescription fill. We also examined the interaction between race or ethnicity and gender to determine whether racial differences are consistent for men and women. The final risk adjustment models for stroke and death are shown in the Supplementary Table 1. Finally, we conducted sensitivity analyses to examine the consistency of our findings across patient strata defined by age category (age 66 to 74, 75 to 84, and 85 years), stroke risk (i.e., CHA₂DS₂-VASc score 0 to 4, 5 to 6, and 7), and setting of initial AF diagnosis (inpatient vs outpatient).

Results

A total of 517,941 non-Hispanic white, non-Hispanic black, or Hispanic patients met criteria for newly diagnosed AF and were included in the study. Of these, 452,986 (87%) were whites, 36,425 (7%) were blacks, and 28,530 (6%) were Hispanics. Patient baseline demographics by race are presented in Table 1. Although the mean age was similar across groups, the prevalence of several co-morbid conditions was significantly higher for blacks and Hispanics compared with whites. The mean CHA₂DS₂-VASc score was higher in blacks and Hispanics, compared with whites, indicating higher risk of stroke. Black and

Hispanic patients were also significantly more likely to be dually enrolled in Medicaid compared with white patients. White patients were more likely to receive oral anticoagulants within 90 days of the initial AF diagnosis, compared with black or Hispanic patients (40% vs 35% and 34%, respectively).

Over a median follow-up period of 20.3 months per patient (interquartile range 13.1 to 27.4 months), 136,271 whites (30%), 14,850 blacks (41%), and 9,343 Hispanics (33%) died. Overall, 12,337 whites (2.7%), 1,504 blacks (4.1%), and 910 Hispanics (3.2%) experienced stroke. Table 2 lists unadjusted rates of death and stroke per 100 person-years of follow-up for white, black, and Hispanic patients.

In unadjusted analyses, black patients had a significantly higher hazard of death (hazard ratio [HR] = 1.46; 95% confidence interval [CI] 1.43 to 1.48; $p < 0.001$) and stroke (HR = 1.66; 95% CI 1.57 to 1.75; $p < 0.001$), compared with white patients (Table 3). Hispanic patients also had a higher risk of death (HR = 1.11; 95% CI 1.09 to 1.14; $p < 0.001$) and stroke (HR = 1.21; 95% CI 1.13 to 1.29; $p < 0.001$) compared with white patients.

After adjusting for patient demographics and co-morbidities, the higher hazard of death was eliminated in blacks compared with whites, with mortality slightly lower for blacks after risk adjustment (HR 0.95; 95% CI 0.93–0.96; $p < 0.001$). In addition, the relative hazard of stroke was reduced (HR = 1.46; 95% CI 1.39 to 1.55; $p < 0.001$). In Hispanics, the relative hazard of death was even lower, compared with whites, after controlling for preexisting co-morbidities (HR 0.82; 95% CI 0.80 to 0.84; $p < 0.001$). The relative hazard of stroke remained higher for Hispanics but was somewhat attenuated compared with analyses that did not control for co-morbidities (HR = 1.11; 95% CI 1.03 to 1.18; $p = 0.003$). These differences persisted in analyses that further controlled for the use of oral anticoagulants after AF diagnosis.

There were no significant interactions between race and gender in models estimating the likelihood of stroke (data not shown in Supplementary Table 1). That is, the higher likelihood of stroke for black and Hispanic patients, relative to white patients, was roughly the same for men and women. Similarly, we found that the significantly lower mortality for Hispanic patients, compared with white patients, was present in men (HR = 0.81; 95% CI 0.77 to 0.85; $p < 0.001$) and women (HR = 0.83; 95% CI 0.81 to 0.85; $p < 0.001$). However, although black women had significantly lower hazard of death compared with white women (HR = 0.94; 95% CI 0.92 to 0.96; $p < 0.001$), there was no difference in the hazard of death for black and white men.

In analysis stratified by age, the hazard of death for black and Hispanics relative to white patients was generally consistent for patients aged 66 to 74, 75 to 84, and 85 years. However, the relative hazard of stroke decreased with increasing age. For example, the hazard of stroke for black relative to white patients decreased from 1.48 to 1.32 for patients aged 66 to 74 and those aged 85 years (Table 4). A similar pattern was found when the study patients were stratified by CHA₂DS₂-VASc category (0 to 4, 5 to 6, and 7). The relative hazard of stroke for black patients decreased from 1.71 for patients with low

CHA₂DS₂-VASc scores to 1.37 for patients with high CHA₂DS₂-VASc scores. Results were similar, although less pronounced, for Hispanic patients.

Discussion

This large-scale analysis of differences in outcomes of AF by race found significantly higher hazard of death and stroke for black and Hispanic Medicare beneficiaries, >65 years, with newly diagnosed AF compared with white beneficiaries. The higher likelihood of death for blacks and Hispanics was eliminated, and the higher risk of stroke was significantly reduced after controlling for differences in preexisting co-morbidities.

Although smaller studies have investigated outcomes of AF by race, the association of all-cause mortality and AF by race has not been reported before in a large-scale study. A substudy of the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study trial compared the survival with rate and rhythm control in Caucasians, African-Americans, and Hispanics.¹⁵ Although the overall survival rates were similar in all the 3 races, the event-free survival was higher in Caucasians followed by Hispanics and lowest in African-Americans over a follow-up period of 5 years. However, this study was not powered to examine racial differences in outcomes because of the small number of African-Americans (n = 265) and Hispanics (n = 132). A substudy of the Atherosclerosis Risk in Communities trial demonstrated that AF increased the risk of sudden cardiac death significantly more for blacks than nonblack participants, with more than a twofold difference in the relative risks associated with AF.¹⁶ Another recent study compared the effect of race on in-hospital outcomes of AF in patients hospitalized with CHF. Although there was no racial difference in in-hospital mortality, black patients had a longer length of stay compared with whites and were less likely to be discharged on warfarin.¹⁷

Racial differences have also been reported in the incidence and severity of stroke in general populations.¹⁸ In the national Reasons for Geographic and Racial Differences in Stroke (REGARDS) study cohort of 27,744 participants, blacks were 1.5 times more likely to experience stroke compared with white participants, after controlling for age and gender.¹⁹ There is also evidence that blacks have more severe and disabling strokes compared with whites.²⁰ Mexican-Americans have also been reported to have a higher risk of recurrent stroke than non-Hispanic whites.²¹ It is possible that subclinical AF may account for this higher incidence of stroke in minority populations. However, a recent study of patients with implanted pacemaker or defibrillator found lower incidence of newly diagnosed symptomatic and asymptomatic AF in blacks compared with white Europeans, although the blacks had higher risk factors for developing AF.²²

An important finding of this study is that the higher risk of death in black and Hispanic patients, compared with the white patients was eliminated after controlling for differences in co-morbidities. This suggests that the diagnosis of AF in blacks and Hispanics may be a marker for other co-morbidities that increase the risk of death.

Blacks and Hispanics with AF had significantly more congestive heart failure, hypertension, diabetes mellitus, cardiomyopathy, and previous stroke at the time of AF diagnosis. A

possible explanation is racial differences in access to care and socioeconomic conditions resulting in late diagnosis and treatment of AF. This has been well described in other health conditions but was not specifically addressed in our study.²³ Another possible hypothesis that may need to be tested in further studies is whether AF in whites is more likely to be a primary event because of genetic predisposition and is more likely to be secondary to risk factors and co-morbidities in blacks and Hispanics. A recent study demonstrated novel genetic markers for AF on chromosome 4 in patients of the European ancestry.²⁴ It is not known if similar genetic markers also exist in blacks.

The increased risk of stroke in blacks and Hispanics compared with the whites persisted even after accounting for measured confounders and differences in the use of oral anticoagulants. The hazard of stroke is higher in blacks versus whites among the subset of patients with low CHA₂DS₂-VASc scores, suggesting that there is greater unmeasured risk for blacks in that group. It is possible that the low CHA₂DS₂-VASc scores may be because of underdiagnosis of the risk factors for stroke. The other possibilities include unmeasured confounding factors, differences in treatment intensity, access to health care, and compliance.

The major strength of our study is the large patient population including blacks and Hispanics. Moreover, the study benefits from the recent inclusion of modified race information in CMS data files, resulting in substantial improvements in the accuracy of indicators for race and ethnicity compared with older data—particularly for subjects of Hispanic ethnicity.⁹ A second strength is the longitudinal nature of Medicare data, allowing us to track outcomes over multiple years. Of note, the overall mortality rate in this study is consistent with previously published survival rates for a community-based cohort of adults with new-onset AF.²⁵

The limitations of our study include its retrospective nature. Although our study included an elderly population, where AF is more prevalent, the data may not be extrapolated to the younger patient population. In addition, our identification of patients with new AF is dependent on the accuracy of *ICD-9-CM* diagnosis codes. Nevertheless, previous studies suggest reasonable accuracy of claims data for identifying AF. Jensen et al²⁶ identified 16 studies that validated algorithms to identify AF from electronic health data, including data from Medicare. Positive predictive values ranged from 70% to 96% and sensitivity from 57% to 95%. Because patients must have >1 AF-related encounter to meet the CMS definition of chronic AF, we expect that our approach has good sensitivity and excellent specificity, based on similar previous studies.^{27,28} Our assessment of stroke also depends on the accuracy of the *ICD-9-CM* diagnosis codes, which has also shown to have good positive predictive value in administrative data.²⁹ In addition, administrative data generally do not contain important prognostic indicators, such as laboratory test results. Nevertheless, our analysis incorporates multiple widely used risk scores (e.g., CHA₂DS₂-VASc) that have been shown to predict outcomes and important indicators of co-morbidities. Finally, we did not consider the use of surgical and nonsurgical interventions that may affect outcomes (e.g., catheter ablation).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Patient demographics and clinical comorbidities*

	Whites (N=452,986)	Blacks (N=36,425)	Hispanics (N=28,530)
Variables			
Age (years), mean (SD)	79.2 (8.07)	78.8 (8.3)	79.1 (7.83)
Age Category (years):			
66 to 74	149,339 (43.5%)	13,134 (46.8%)	9,202 (41.4%)
75 to 84	177,038 (51.6%)	13,694 (48.8%)	11,953 (53.7%)
85 years	16,654 (4.9%)	1,229 (4.4%)	1,087 (4.9%)
Males	185,935 (41.1%)	12,476 (34.3%)	11,415 (40%)
Dual enrollment in Medicaid	114,966 (25.4%)	25,543 (70%)	21,779 (76%)
Hypertension	37,097 (82%)	33,546 (92%)	25,128 (88%)
Heart failure	164,571 (36.3%)	19,349 (53.1%)	13,436 (47.1%)
Pulmonary circulatory disease	53342 (11.8%)	6638 (18.2%)	3531 (12.4%)
Prior stroke	74,025 (16.3%)	10,360 (28.4%)	6490 (22.7%)
Prior myocardial infarction	60,192 (13%)	5,825 (16%)	6,490 (22.7%)
Prior bleeding	120,371 (27%)	12,229 (34%)	9,130 (32%)
Malignancy	81,376 (18%)	6,473 (17.8%)	4,121 (14.4%)
Renal failure	85,902 (19%)	13,448 (37%)	7,962 (28%)
Diabetes Mellitus	149,114 (33%)	18,858 (52%)	15,600 (55%)
Dementia	40,378 (9%)	6,379 (18%)	3,745 (13%)
Obesity	35,592 (7.9%)	4,439 (12.2%)	3,202 (11.2%)
HAS-BLED score, mean (SD)	2.55 (1.02)	3.03 (1.12)	2.89 (1.13)
CHA ₂ DS ₂ -VASc score, mean (SD)	4.75 (1.58)	5.49 (1.58)	5.34 (1.58)
CHA ₂ DS ₂ -VASc score			
0–2	35,665 (7.9%)	1,085 (3.0%)	1,168 (4.1%)
3	60,245 (13.3%)	2,650 (7.3%)	2,277 (8.0%)
4	98,820 (21.8%)	5,667 (15.6%)	4,620 (16.2%)
5	116,117 (25.6%)	8,910 (24.5%)	7,110 (24.9%)
6	84,570 (18.7%)	8,904 (14.4%)	7,044 (24.7%)
7 or more	57,569 (12.7%)	9,209 (25.3%)	6,311 (22.1%)

* p< 0.001 for all comparisons based on Chi-square test for categorical variables and analysis for variance for mean CHA₂DS₂-VASc, HAS-BLED, and patient age.

Table 2

Number of initial outcome events and initial events per 100 person-years (95% confidence interval) of follow-up after initial AF diagnosis for white, black, and Hispanic patients

	Events (Total and per 100 person-years)*		
	Whites	Blacks	Hispanics
Death - Number Events	136,271	14,850	9,343
- Per 100 Person-years	18.48 (95% CI, 18.39–18.58)	27.72 (95% CI, 27.27–28.16)	20.76 (95% CI, 20.34–21.18)
Stroke - Number Events	12,337	1,504	910
- Per 100 Person-Years	1.70 (95% CI, 1.68–1.74)	2.89 (95% CI, 2.75–3.05)	2.06 (95% CI, 1.94–2.21)

* Rate calculated as $100 \times (\text{Number of Events} / \text{Total person-years of follow-up})$. Lower Limit of Confidence Interval calculated as Rate divided by D, and Upper Limit calculated as Rate multiplied by D, where $D = \exp[1.96 \times \text{square root of } (1/\text{number of events})]$.

Table 3

Unadjusted and risk adjusted relative outcomes for black and Hispanic patients, relative to White patients

Admission for Stroke			
	Unadjusted	Risk Adjusted	Risk adjusted plus anticoagulant indicator
Black vs. White	1.66 (1.57–1.75; p<.001)	1.46 (1.39–1.55; p<.001)	1.44 (1.36–1.52; p<.001)
Hispanic vs white	1.21 (1.13–1.29; p<.001)	1.11 (1.03–1.18; p=.003)	1.08 (0.01–1.16; p=.02)
Death			
	Unadjusted	Risk Adjusted	Risk adjusted plus anticoagulant indicator
Black vs. White	1.46 (1.43–1.48; p<.001)	0.95 (0.93–0.96; p<.001)	0.94 (0.92–0.96; p<.001)
Hispanic vs white	1.11 (1.09–1.14; p<.001)	0.82 (0.80–0.84; p<.001)	0.81 (0.79–0.83; p<.001)

Table 4

Risk adjusted hazard of stroke or death for black and Hispanic patients, relative to White patients, stratified by age category and CHADS₂-Vasc score

By Age Category	Age 66 to 74 (n=171,729)	Age 75 to 84 (n=202,685)	Age 85 plus (n=143,527)
Stroke			
Black vs White	1.48 (1.33–1.65; p<.001)	1.54 (1.41–1.68; p<.001)	1.32 (1.20–1.46; p<.001)
Hispanic vs White	1.22 (1.06–1.40; p=.005)	1.13 (1.02–1.25; p=.024)	1.02 (0.90–1.15; p=0.75)
Death			
Black vs White	0.91 (0.88–0.94; p<.001)	0.98 (0.95–1.01; p=0.11)	0.93 (0.90–0.96; p<.001)
Hispanic vs White	0.79 (0.75–0.83; p<.001)	0.81 (0.78–0.84; p<.001)	0.88 (0.85–0.91; p<.001)
By CHA ₂ DS ₂ -VAsc	0–4 (n=212,197)	5–6 (n=232,655)	7 or more (n=73,089)
Stroke			
Black vs White	1.71 (1.51–1.94; p<.001)	1.43 (1.32–1.54; p<.001)	1.37 (1.24–1.50; p<.001)
Hispanic vs White	1.25 (1.07–1.45; p=.004)	1.05 (0.95–1.16; p=.34)	1.10 (0.98–1.24; p=.11)
Death			
Black vs White	1.00 (0.96–1.04; p=0.95)	0.94 (0.92–0.96; p<.001)	0.96 (0.93–1.00; p=0.03)
Hispanic vs White	0.79 (0.75–0.83; p<.001)	0.82 (0.79–0.84; p<.001)	0.88 (0.85–0.92; p<.001)