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Atrial Fibrillation and the Risk of Myocardial Infarction

Elsayed Z. Soliman, MD, MSc, MS, **Monika M. Safford, MD**, **Paul Muntner, PhD**, **Yulia Khodneva, MD, PhD**, **Farah Z. Dawood, MD**, **Neil A. Zakai, MD**, **Evan L. Thacker, PhD**, **Suzanne Judd, PhD**, **Virginia J. Howard, PhD**, **George Howard, DrPH**, **David M. Herrington, MD, MHS**, and **Mary Cushman, MD, MSc**

Epidemiological Cardiology Research Center, Department of Epidemiology and Prevention, Wake Forest School of Medicine, Winston Salem, North Carolina (Soliman); Section on Cardiology, Department of Internal Medicine, Wake Forest School of Medicine, Winston Salem, North Carolina (Soliman, Dawood, Herrington); Division of Preventive Medicine, University of Alabama at Birmingham (Safford, Khodneva); Department of Epidemiology, University of Alabama at Birmingham (Muntner, Thacker, V.J. Howard); Department of Medicine, University of Vermont, Burlington (Zakai, Cushman); Department of Biostatistics, University of Alabama at Birmingham (Judd, G. Howard).

Abstract

IMPORTANCE—Myocardial infarction (MI) is an established risk factor for atrial fibrillation (AF). However, the extent to which AF is a risk factor for MI has not been investigated.

OBJECTIVE—To examine the risk of incident MI associated with AF.

DESIGN, SETTING, AND PARTICIPANTS—A prospective cohort of 23 928 participants residing in the continental United States and without coronary heart disease at baseline were enrolled from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort between 2003 and 2007, with follow-up through December 2009.

Corresponding Author: Elsayed Z. Soliman, MD, MSc, MS, Epidemiological Cardiology Research Center (EPICARE), Department of Epidemiology and Prevention, Wake Forest School of Medicine, Medical Center Boulevard, Winston Salem, NC 27157 (esoliman@wakehealth.edu).

Author Contributions: Drs Khodneva and Safford had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Soliman, Safford, Dawood, Zakai, Cushman.
Acquisition of data: Soliman, Safford, Judd, V. J. Howard, G. Howard, Cushman.
Analysis and interpretation of data: Soliman, Safford, Muntner, Khodneva, Zakai, Thacker, Judd, Herrington.
Drafting of the manuscript: Soliman, Khodneva, Dawood, G. Howard.
Critical revision of the manuscript for important intellectual content: Safford, Muntner, Khodneva, Zakai, Thacker, Judd, V. J. Howard, G. Howard, Herrington, Cushman.
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MAIN OUTCOMES AND MEASURES—Expert-adjudicated total MI events (fatal and nonfatal).

RESULTS—Over 6.9 years of follow-up (median 4.5 years), 648 incident MI events occurred. In a sociodemographic-adjusted model, AF was associated with about 2-fold increased risk of MI (hazard ratio [HR], 1.96 [95% CI, 1.52–2.52]). This association remained significant (HR, 1.70 [95% CI, 1.26–2.30]) after further adjustment for total cholesterol, high-density lipoprotein cholesterol, smoking status, systolic blood pressure, blood pressure–lowering drugs, body mass index, diabetes, warfarin use, aspirin use, statin use, history of stroke and vascular disease, estimated glomerular filtration rate, albumin to creatinine ratio, and C-reactive protein level. In subgroup analysis, the risk of MI associated with AF was significantly higher in women (HR, 2.16 [95% CI, 1.41–3.31]) than in men (HR, 1.39 [95% CI, 0.91–2.10]) and in blacks (HR, 2.53 [95% CI, 1.67–3.86]) than in whites (HR, 1.26 [95% CI, 0.83–1.93]); for interactions, $P = .03$ and $P = .02$, respectively. On the other hand, there were no significant differences in the risk of MI associated with AF in older (≥75 years) vs younger (<75 years) participants (HR, 2.00 [95% CI, 1.16–3.35] and HR, 1.60 [95% CI, 1.11–2.30], respectively); for interaction, $P = .44$.

CONCLUSIONS AND RELEVANCE—AF is independently associated with an increased risk of incident MI, especially in women and blacks. These findings add to the growing concerns of the seriousness of AF as a public health burden: in addition to being a well-known risk factor for stroke, AF is also associated with increased risk of MI.

Atrial fibrillation (AF) is a major public health problem owing to its increasing prevalence and strong association with morbidity and mortality.[1,2] Patients with AF have 4 to 5 times the risk of stroke and about double the risk of mortality compared with those without AF.[3–6]

Myocardial infarction (MI) is an established risk factor for AF,[7] with AF occurring in 6% to 21% of patients with MI.[8] Conversely, sporadic cases of thromboembolic acute MI also have been reported in patients with AF,[9–16] and presence of AF during acute MI has been associated with increased risk of developing in-hospital reinfarction.[8] These findings suggest that AF could also be a risk factor for MI. However, evidence from population studies to support this assertion is lacking. Therefore, we examined the association between AF and risk of incident MI in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study,[17] a large biracial population-based cohort study.

Methods

The study protocol was reviewed and approved by the participating institutions' institutional review boards. Informed consent was obtained initially on the telephone and subsequently in writing during an in-person evaluation.

The goals and design of the REGARDS study have been published elsewhere.[17] Briefly, the study was designed to investigate causes of regional and racial disparities in stroke mortality, oversampling blacks and residents of the southeastern stroke belt region (North Carolina, South Carolina, Georgia, Alabama, Mississippi, Tennessee, Arkansas, and Louisiana). During the period from January 2003 to October 2007, participants (n = 30 239) were recruited from a commercially available list of residents using a combination of postal

mailings and telephone. Using a computer-assisted telephone interview, trained interviewers obtained demographic information and medical history focused on cardiovascular disease. An in-home brief physical examination was conducted 3 to 4 weeks after the telephone interview.

For this report, individuals with prevalent coronary heart disease (CHD) (self-reported history of MI or coronary revascularization procedure at baseline or evidence of prior MI on the baseline electrocardiogram [ECG]) were excluded. We also excluded participants with missing information on AF or no follow-up. Events through December 31, 2009, were included in this analysis.

Ascertainment of MI Events

All CHD events were adjudicated by a team of experts following published guidelines. Details of the CHD adjudication have been described elsewhere.[18] For MI, medical records were examined for the presence of signs or symptoms of myocardial ischemia; a rising and/or falling pattern in cardiac troponin or creatine phosphokinase-MB level over 6 hours or longer with a peak value twice the upper limit of normal or higher (diagnostic cardiac enzymes); and ECG changes consistent with myocardial ischemia or MI, guided by the Minnesota code and classified as evolving diagnostic, positive, nonspecific, or not consistent with ischemia.[19] Definite MIs were those with diagnostic enzyme levels or ECG. Probable MIs (about 3% of MI cases) were those cases with elevated but not diagnostic (ie, equivocal) enzyme levels with a positive but not diagnostic ECG or cases where enzyme data were missing with a positive ECG in the presence of ischemic signs or symptoms. Fatal and nonfatal definite and probable MIs were included as events in this study.

Ascertainment of AF

Details of ascertainment of AF have been published elsewhere.[20] Briefly, AF was identified at baseline from 2 sources: (1) a study-scheduled ECG recorded during the in-home visit that was centrally read by electrocardiographers blinded to clinical data; and (2) a history of physician diagnosis of AF reported by the participants during the computer-assisted telephone surveys assessing medical history and health status. These 2 AF ascertainment methods have been equally predictive of stroke in the REGARDS study.[20]

Covariates

Age, sex, race, income, education, and smoking status were self-reported. Annual income was dichotomized at $20 000, and education was dichotomized at high school diploma. Smokers were defined as having smoked at least 100 cigarettes in their lifetime and smoking now, even occasionally. Data on blood pressure–lowering drugs and regular aspirin use were based on self-report, while use of digoxin, warfarin, and statin were based on pill-bottle review. Body mass index (BMI) was calculated from height and weight measured during in-home visit using a standardized protocol. Blood pressure was measured using an aneroid sphygmomanometer after a seated rest of 5 minutes with both feet on the floor. Two measures were obtained following a standardized protocol and averaged. Blood and urine markers included levels of total cholesterol, high-density lipoprotein (HDL) cholesterol, fasting glucose, high-sensitivity C-reactive protein (CRP), serum creatinine, and urinary

albumin and creatinine from a spot urine specimen. Diabetes was classified as present if the fasting glucose level was 126 mg/dL or higher (non-fasting glucose, ≥200 mg/dL [n = 229]) or if participant was taking diabetes medications. (To convert glucose to millimoles per liter, multiply by 0.0555.) We used current use of digoxin at baseline as a proxy for heart failure diagnosis similar to previous reports from REGARDS.[21] CHADS2 score (congestive heart failure; hypertension; age, ≥75 years; diabetes mellitus; and prior stroke) was calculated using 1 point for each category except for prior stroke, which was given 2 points.[22] Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI equation (Chronic Kidney Disease Epidemiology Collaboration).[23] Urinary albumin and creatinine were used to define the albumin to creatinine ratio (ACR).

Statistical Analysis

Characteristics of the analysis population were tabulated by AF status at baseline. Age-adjusted incidence rates of MI per 1000 person-years in participants with and those without baseline AF were calculated in the entire study population and in prespecified age, sex, and race subgroups. Cox proportional hazards analysis was used to examine the association between baseline AF with incident MI in a series of models with incremental adjustments as follows: model 1 adjusted for age, sex, race, region of residence, education level, and income; model 2 adjusted for model 1 covariates plus total cholesterol, HDL cholesterol, smoking status, systolic blood pressure, BMI, diabetes, use of antihypertensive medications, warfarin, aspirin, or statin, and history of noncardiac vascular disease (stroke, peripheral vascular disease, and aortic aneurysm); model 3 adjusted for model 2 covariates plus eGFR lower than 60 mL/min/1.73m^2, log-transformed CRP, and log-transformed ACR.

In a sensitivity analysis, we used AF ascertained by more restricted methods such as“ECG only” and by “ECG and/or history of a physician diagnosis plus warfarin use.” Other analyses included further adjustment for baseline heart failure as well as stroke events and chest pain hospitalizations that occurred during follow-up (included in the model as time-updated variables), separately. We also examined whether using death as a competing risk affected the results.

Models with identical incremental adjustment for the main analysis were examined in subgroups of participants stratified by age (using 75 years as a cut point in the main analysis and 65 years in additional analysis), sex, and race. Interaction between AF and each of these variables was examined in the full model. Because we observed significant interaction by sex and race, we also examined the age-adjusted risk of MI associated with AF in black men, black women, white men and white women, separately.

To investigate whether warfarin and aspirin modified the risk of MI associated with AF, we conducted subgroup analysis stratified by warfarin and aspirin use. We also examined the risk of MI in participants with AF and a CHADS2 score of 1 or lower; AF and a CHADS2 score higher than 1; and no AF (reference group).

The assumptions of proportionality were met. Individuals were censored at the time of their event, death, or the end of follow-up. Statistical significance for all analyses was considered as $P < .05$. Analyses were conducted using SAS 9.3 (SAS Institute) except for competing

risk Cox proportional hazards regression models, which were fitted using STATA version 12 (STATA Inc).

Results

After excluding participants with no follow-up data (n = 569), prevalent CHD at baseline (n = 5227), or missing data on AF status (n = 515),we found that 23 928 participants remained, and all of these were included in the analysis. At baseline, AF was present in 1631 participants; 268 AF cases were detected from the study baseline ECG, and the rest from medical history; 168 AF cases were detected by both methods. Table 1 lists the baseline characteristics of the study population stratified by AF status. Compared with those without AF, participants with AF were older, were less likely to be black and men, had more CHD risk factors such as diabetes and hypertension, and had worse kidney function.

Over 6.9 years of follow-up (median 4.5 years), 648 MI events occurred. The age-adjusted incidence rate of MI in participants with AF (12.0 [95% CI, 9.6–14.9] per 1000 person-years) was double the rate in those without AF (6.0 [95% CI, 5.6–6.6] per 1000 person-years) ($P < .001$). Figure 1 shows the unadjusted cumulative incidence of MI events by baseline AF status.

In a sociodemographically adjusted Cox proportional hazards model, AF was associated with a 96% increase in MI risk compared with no AF (HR, 1.96 [95% CI, 1.52–2.52]) (Table 2). This compares with a HRs of 1.77 (95% CI, 1.14–2.76) and 1.62 (95% CI, 0.93–2.82) when AF was ascertained by more restricted methods such as AF by ECG and/or history of a physician diagnosis plus warfarin use and AF by ECG only, respectively.

The association between AF and MI remained significant after further adjustment for traditional CHD risk factors and potential confounders (HR, 1.70 [95% CI, 1.26–2.30]) in the fully adjusted model; ie, model 3 (Table 2). Further adjustment for baseline heart failure (HR, 1.68 [95% CI, 1.24, 2.28]) or stroke events (HR, 1.71 [95% CI, 1.27–2.30]) and chest pain hospitalization (HR, 1.67 [95% CI, 1.24–2.25]) as time-updated variables, or using death as a competing risk (sub-HR, 1.65 [95% CI, 1.21–2.27]), did not appreciably alter the results.

In subgroup analysis, no statistically significant interaction by participant age (≥75 years vs <75 years) was detected ($P = .44$ for interaction) (Table 2). Similar results were obtained when we used 65 years as a cut point, comparing age 65 years or older (HR, 2.06 [95% CI, 1.44–2.94]) with younger than 65 years (HR, 1.28 [95% CI, 0.74–2.21]) ($P = .45$ for interaction). On the other hand, significant differences were observed in the sex and race subgroups. As summarized in Table 2, in a multivariable-adjusted model, the association was stronger in women than in men ($P = .03$ for interaction) and stronger in blacks than in whites ($P = .02$ for interaction). A similar direction of associations among these subgroups was observed when we used a more restricted method for ascertainment of AF such as AF by ECG and/or history of a physician diagnosis plus warfarin use (See eTable 1 in the Supplement) or by ECG only (See eTable 2 in the Supplement).

In sex-race stratified analyses, the MI association with AF was strongest in black men, followed by white women, then black women, but nonsignificant in white men (multivariable-adjusted HRs and 95% CIs, 2.91 [95% CI, [1.62–5.23]) for black men; 2.33 [1.27–4.28] for white women; 2.17 [1.19–3.98] for black women; and 0.86 [0.58–1.56] for white men) (Figure 2).

In a multivariable model similar to model 3 summarized in Table 2, the risk of MI associated with AF in warfarin users was significantly less than that in nonusers (HR, 0.76 [95% CI, 0.29–1.94]) vs (HR, 1.92 [95% CI, 1.42–2.60]) (P = .02 for interaction). On the other hand, no statistically significant difference in the risk of MI associated with AF was observed between aspirin users and nonusers (HR, 2.13 [95% CI, 1.44–3.15] in aspirin users vs HR, 1.36 [95% CI 0.86–2.15] in nonusers) (P = .15 for interaction).

Atrial fibrillation with higher CHADS2 score was associated with higher risk of MI. As summarized in Table 3, compared with no AF, AF in the setting of a CHADS2 score higher than 1 was associated with a 95% increased risk of MI (HR, 1.95 [95% CI, 1.33–2.86]). This compares with only a 40% increased risk if the CHADS2 score was 1 or lower (HR, 1.40 [95% CI, 0.91–2.17]).

Discussion

Key Findings

In this analysis from the REGARDS study, one of the largest US cohort studies, we showed that AF was significantly associated with increased risk of incident MI independent of common CHD risk factors and potential confounders. These findings add to the growing concerns of the seriousness of AF as a public health burden: in addition to being a well-known risk factor for stroke, it is also associated with increased risk of MI.

The risk of MI associated with AF differed by sex and race, with women and blacks having significantly stronger association between AF and MI than men and whites. These findings add to the accumulating evidence of the sex and race differences in cardiovascular disease outcomes and the potential differences in the impact of risk factors among sexes and races. Since we adjusted for several potential confounders, it is less likely that our observed sex and race differences were confounded by differences in AF-associated morbidities. Investigating whether genetic background, emerging risk factors, access to health care, awareness, and adherence to medication regimens contribute to these sex and race differences needs further investigation. In the REGARDS study, our research group has previously shown that blacks and women are less likely to be aware of having AF or to be treated with warfarin.[24] The excess risk of MI coupled with the tendency to under-treat AF may magnify the risk of poor outcomes in these 2 groups.

In a stratified analysis by warfarin use, the risk of MI associated with AF was lower in warfarin users than in nonusers, suggesting an effect modification by warfarin use. This accords with previous reports showing that warfarin might provide a protective effect against MI after acute coronary syndromes[25] and in patients with AF who are prescribed anticoagulation for stroke prevention.[26] A risk-benefit analysis is needed for routine use of

anticoagulation in prevention of MI in patients with AF at high risk, such as those with higher CHADS2 scores. As we showed, AF plus higher CHADS2 score was associated with higher risk of MI.

Possible Explanations

Our results of increased risk of MI in AF and the known increased risk of AF in MI[7] suggest a bidirectional relationship between these 2 conditions, with each leading to the other. Similar bidirectional relationships between AF and chronic kidney disease[27,28] and between AF and heart failure[29] have been reported.

A bidirectional relationship between AF and MI could be partially explained by the fact that AF and MI share similar risk factors, and therefore, common pathophysiologic processes might drive both outcomes. That is, in susceptible individuals, both AF and MI may eventually occur, and it is just a matter of which comes first. Similarly, it is also possible that sub-clinical CHD is associated with higher prevalence of AF and also associated with higher risk for the development of incident MI. That is, AF may not be a risk factor for incident MI but rather a marker of prevalent CHD that in turn places individuals at higher risk for MI events. These explanations, however, ignore the potential impact of AF on the risk profile that could lead to MI. For example, higher levels of inflammatory markers are associated with increased risk of both AF and MI, suggesting a role of inflammation in developing both conditions.[30–34] When AF occurs, however, it creates and sustains an inflammatory and prothrombotic environment (ie, AF-induced inflammation),[35] which subsequently can increase the risk of MI. An AF-induced increase in peripheral prothrombotic risk through systemic platelet activation, thrombin generation, and endothelial dysfunction as well as inflammation have been shown in several studies.[36–48]

Coronary thromboembolism with subsequent MI could be another potential explanation for the increased risk of MI in patients with AF. Although the actual incidence of coronary embolism is unknown, it is generally considered rare. The rarity of coronary embolization has been attributed to differences between the caliber of the aorta and the coronary arteries, location of the coronary vessels at the root of the aorta, emergence of the coronary arteries at a right angle, the bulk and swiftness of the blood current in this portion of the aorta, and the fact that the major part of coronary filling occurs in diastole.[49] Nevertheless, several sporadic cases of MI due to coronary embolism have been reported,[9–16] suggesting that occurrence of coronary embolism could be higher than it is thought to be. Furthermore, in a postmortem study of 419 patients with MI, coronary embolization accounted for as many as 55 (13%) of these cases. A coronary lesion was considered to be embolic in that study if at autopsy a source was apparent and the occluded artery demonstrated no evidence of mural disease including arteritis or significant atherosclerosis with an essentially normal intima at the site of occlusion. Atrial fibrillation was the underlying disease predisposing to coronary embolization in 24% of these cases.[49] These findings suggest that coronary embolization, which may not be as rare as we think, could be one of the mechanisms explaining our findings.

Another potential explanation for the increased risk of MI in patients with AF could be derived from the notion that some patients with AF present with episodes of poorly

controlled ventricular response resulting in demand infarction, referred to as type 2 MI.[50] In a cohort of unselected hospital patients, one-fourth of all MIs were type 2 MIs, and about half of those patients had no significant coronary artery disease, with tachyarrhythmias being one of the most frequent mechanisms.[51]

Limitations

Our results should be read in the context of a number of limitations. Although we used 2 methods for AF ascertainment (study-scheduled ECG and history of a physician diagnosis), it remains possible that some paroxysmal and/or intermittent AF cases were not detected. This would misclassify some participants and put them in the “no AF” group. Nevertheless, this misclassification would likely attenuate the association between AF and MI, and therefore, our results should be considered as conservative.

Heart failure was not systematically assessed in the REGARDS study. Hence, we used current digoxin use as a proxy for heart failure similar to previous REGARDS articles.[21] It has been reported that digoxin use has a specificity of about 99% and a sensitivity of about 28% for the diagnosis of heart failure.[52]

Data on the actual onset of AF were not available, and therefore we could not adjust for the time between AF onset and baseline visit. Also, we could not conduct analysis of AF as a time-updated predictor because only prevalent AF is available in the REGARDS cohort at this stage.

Finally, REGARDS by design included only whites and blacks; hence, our results may not be applicable to other racial or ethnic groups. Similar to other studies using a similar observational design, residual confounding is always a possibility. However, we adjusted for several risk factors and potential confounders, thus lessening this concern.

Despite these limitations, this is the first report to our knowledge from a large biracial population-based study showing an increased risk of MI associated with AF in the general population. Other strengths include the substantial accumulating number of events, rigorous physician adjudication of study end points, and long follow-up time.

In conclusion, we showed that AF was independently associated with an increased risk of incident MI in the REGARDS study. This risk was stronger in women and blacks than in men and whites.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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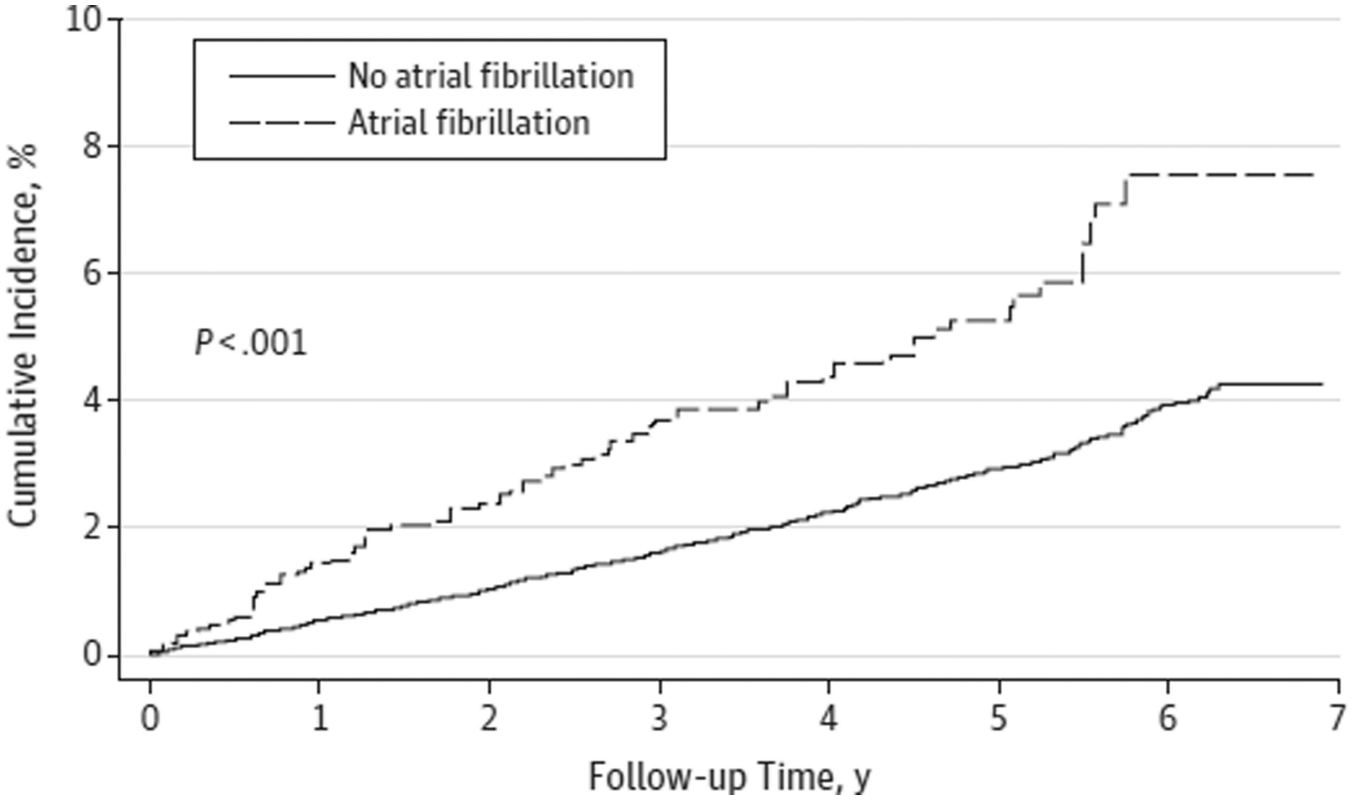

Figure 1.
Unadjusted Cumulative Incidence of Myocardial Infarction by Baseline Atrial Fibrillation Status

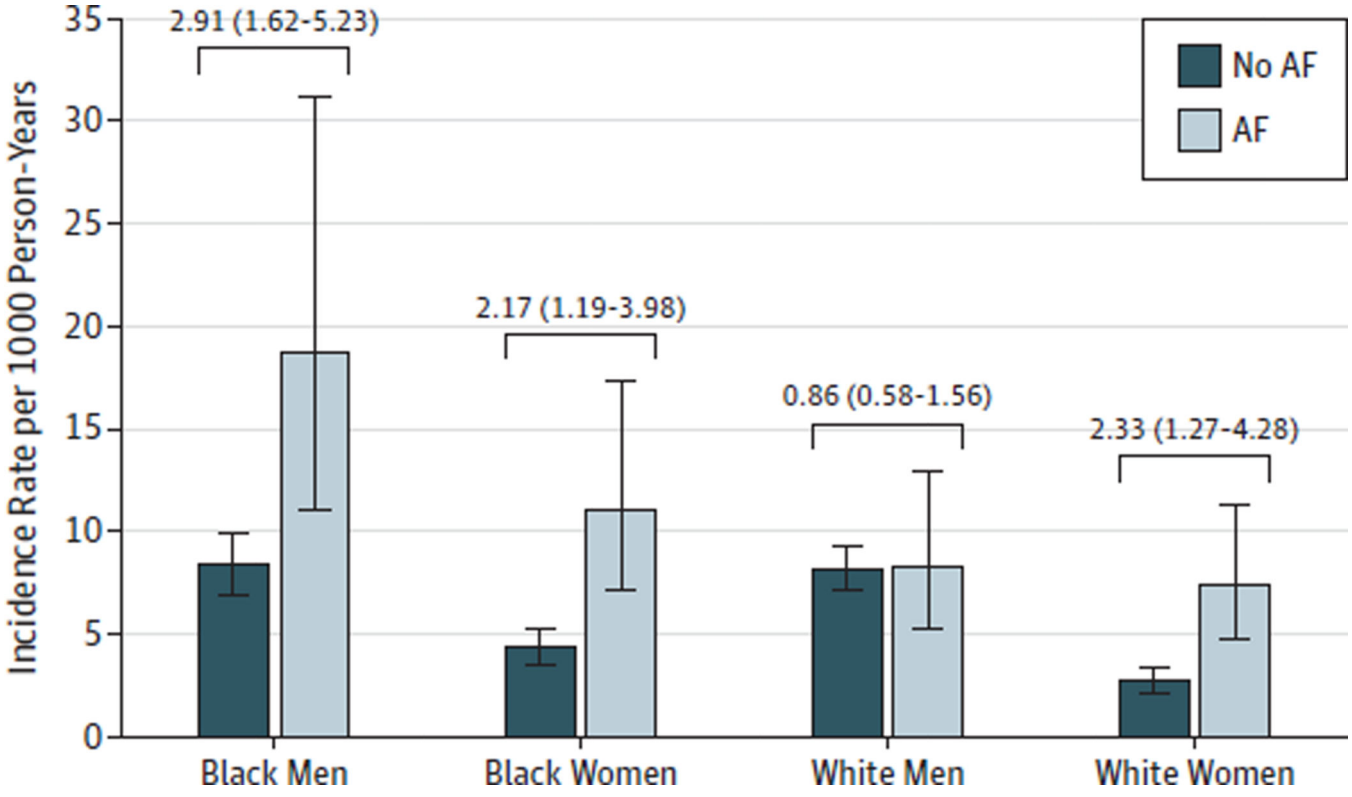

Figure 2.

Sex-Race Stratified Age-Adjusted Incidence Rates and Multivariable-Adjusted Hazard Ratios of Myocardial Infarction by Atrial Fibrillation (AF) Status

Data specified across horizontal braces are reported as hazard ratio (95% CI). All models were adjusted for age, sex, race, region of residence, education level, income, total cholesterol, high-density lipoprotein cholesterol, smoking status, systolic blood pressure, body mass index, diabetes, blood pressure–lowering drug use, warfarin use, aspirin use, statin use, history of noncardiac vascular disease (stroke, peripheral artery disease, and aortic aneurysm), estimated glomerular filtration rate lower than 60 mL/min/1.73 m^2, log-transformed C-reactive protein, and log-transformed albumin to creatinine ratio.

Table 1

Baseline Characteristics of REGARDS Study[17] Participants Stratified by Atrial Fibrillation Status

Characteristic	Atrial Fibrillation (n = 1631)	No Atrial Fibrillation (n = 22 297)	*P* Value
Age, mean (SD), y	66.5 (9.7)	63.9 (9.3)	<.001
Men, %	38.4	42.0	.01
African American, %	37.9	42.4	<.001
Education ≤high school, %	39.4	36.6	.001
Annual income <$20 000, %	24.5	19.0	<.001
BMI, mean (SD)	29.6 (6.8)	29.3 (6.2)	.04
Current smoking, %	12.8	14.3	.08
Diabetes, %	22.8	19.1	.003
Hypertension, %	65.2	55.6	<.001
History of noncardiac vascular disease, %[a]	11.1	6.2	<.001
Antihypertensive medication use, %	59.3	47.9	<.001
Systolic blood pressure, mean (SD), mm Hg	127 (17)	127(16)	.37
Total cholesterol, mean (SD), mg/dL	191 (40)	196 (39)	<.001
HDL-Cholesterol, mean (SD), mg/dL	52 (17)	53 (16)	.06
LDL-Cholesterol, mean (SD), mg/dL	112 (34)	117(40)	<.001
Triglycerides, median (25th-75th percentile), mg/dL	112 (83–161)	109 (80–155)	.004
Statin use, %	33.1	27.9	<.001
Warfarin use, %	19.9	1.4	<.001
Aspirin use, %	41.2	37.5	.003
C-reactive protein, median (25th-75th percentile), mg/L	2.6 (1.1–6.1)	2.2 (0.9–4.9)	<.001
Estimated glomerular filtration rate <60 mL/min/1.73 m^2, %	13.7	9.1	<.001
Albumin to creatinine ratio, median (25th-75th percentile), mg/g	8.9 (5.2–21.7)	7.0 (4.5–14.0)	<.001

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

SI Conversions: To convert cholesterol to millimoles per liter, multiply by 0.0259; triglycerides to millimoles per liter, multiply by 0.0113.

[a]Noncardiac vascular disease included stroke, peripheral artery disease, or aortic aneurism.

Table 2

Risk of incident MI associated with baseline AF in all participants and subgroups of age, sex and race

Subgroups	Participants with AF		Participants with no AF		Model 1†	Model 2*	Model 3‡	Interaction p-value#
	Participants (n)	Events (n)	Participants (n)	Events (n)	HR (95% CI)	HR (95% CI)	HR (95% CI)	
All participants	1,631	78	22,297	570	1.96(1.52–2.52)	1.80(1.35–2.40)	1.70(1.26–2.30)	N/A
Age<75 years	1245	48	19094	428	1.85(1.34–2.54)	1.69(1.19–2.40)	1.60(1.11–2.30)	0.44
Age ≥ 75 years	386	30	3203	142	2.32(1.52–3.54)	2.08(1.25–3.46)	2.00(1.16–3.35)	
Men	627	35	9353	367	1.49(1.04–2.14)	1.56(1.04–2.33)	1.39(0.91–2.10)	0.034
Women	1004	43	12944	203	2.65(1.85–3.81)	2.16(1.43–3.26)	2.16(1.41–3.31)	
Black	618	35	9458	247	2.71(1.87–3.94)	2.56(1.71–3.83)	2.53(1.67–3.86)	0.018
White	1013	43	12839	323	1.54(1.09–2.18)	1.34(0.89–2.03)	1.26(0.83–1.93)	

Abbreviations: MI, myocardial infarction; AF, Atrial fibrillation; HR (95% CI), hazard ratio and 95% confidence interval

*Model 1, adjusted for age, sex, race, region of residence, education level and income

†Model 2, Model 1 covariates plus, total cholesterol, HDL cholesterol, smoking status, systolic blood pressure, body mass index, diabetes, blood pressure lowering drugs, warfarin use, aspirin use, statin use, history of non-cardiac vascular disease (stoke, peripheral artery disease and aortic aneurysm).

‡Model 3, Model 2 plus estimated glomerular filtration rate < 60 ml/min/1.73 m^2, log-transformed C-reactive protein, and log-transformed albumin-to-creatinine ratio

#Interaction tested in the fully adjusted models

Table 3

Risk of Incident MI Associated With Baseline AF Stratified by the Level of CHADS2 Score

			Model[a]	
CHADS2 Level	**Participants, No.**	**MI Events, No.**	**HR (95% CI)**	***P* Value**
No AF	22 297	570	1 [Reference]	NA
AF and CHADS2 score ≤1	983	30	1.40 (0.91–2.17)	.13
AF and CHADS2 score >1	648	48	1.95 (1.33–2.86)	<.001

Abbreviations: AF, atrial fibrillation; CHADS2, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke (calculated using 1 point for each category except 2 points for prior stroke)22; HR, hazard ratio; MI, myocardial infarction; NA, not applicable.

[a]Model adjusted for age, sex, race, region of residence, education level, income, total cholesterol, high-density lipoprotein cholesterol, smoking status, systolic blood pressure, body mass index, warfarin use, aspirin use, and statin use.