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Linzi Li Date

Association of atrial fibrillation with severity of coronary artery disease: the Emory Cardiovascular Biobank (EmCAB)

By

Linzi Li
Master of Science in Public Health

Department of Epidemiology

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Alvaro Alonso
Committee Chair

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By

Linzi Li

B.S., Fudan University, 2016
MPH, Emory University, 2018

Thesis Committee Chair: Alvaro Alonso, MD, PhD

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Abstract

Association of atrial fibrillation with severity of coronary artery disease: the Emory Cardiovascular Biobank (EmCAB)

By Linzi Li

Background

Existing literatures suggest that atrial fibrillation (AF) can lead to coronary artery disease (CAD). However, little information is known regarding the association between AF and CAD severity.

Methods

We conducted cross-sectional and prospective cohort analysis of 7737 participants in the Emory Cardiovascular Biobank (EmCAB). At enrollment, data on AF history and four CAD severity measurements were collected: presence of 70% coronary stenosis, presence of 50% coronary stenosis, number of vessels with 50% coronary stenosis and the Gensini score. Different models were used to examine the association between each measurement and AF history. During follow-up, occurrence of incident MI, fatal MI and all-cause death were obtained as primary endpoints. We used Cox regression model to examine AF and each endpoint. Sex-specific and race-specific estimates were also calculated in both analyses.

Results

At baseline, no association was found between AF and presence of 50% and 70% stenosis, and numbers of vessels with 50% stenosis. AF was associated with 4.92 (95% CI -8.91, -0.93) points lower Gensini score in the crude model, but not in the adjusted model (beta coefficient: -4.66, 95% CI -9.71, 0.39). In the Longitudinal analysis, there was no evidence supporting association between AF and nonfatal MI, fatal MI and any MI. The risk of all-cause mortality among AF patients was 1.66 times (95% CI 0.91, 1.49) that among non-AF patients in the crude model. However, the association no longer existed after adjusting for covariates. In the dataset with imputed covariates, AF was associated with all-cause mortality in both crude and adjusted models (adjusted HR 1.26, 95% CI 1.03, 1.53). Similar results were found in strata of sex and race.

Conclusion

In the EmCAB, AF was associated with all-cause mortality but not with CAD severity.

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Table of contents

Introduction

Coronary artery disease (CAD) is one of the most common cardiovascular diseases (CVDs), with a prevalence of 6.7% among US adults and a leading cause of death [1-3]. Typical manifestations of CAD include angina, myocardial infarction (MI) and sudden cardiac death [1, 4]. Coronary atherosclerosis is the major pathophysiologic process leading to CAD and, therefore, CAD prevention requires identification of risk factors for the development of coronary atherosclerosis.

Atrial fibrillation (AF) is a highly prevalent cardiac arrythmia. Approximately, 1 in 3 to 5 individuals will develop AF in their lifetime [5]. In the United States, AF affected 2.7 to 6.1 million people in 2010 [5]. In 2030, the AF prevalence is estimated to increase to 12.1 million as the population ages [3]. AF can lead to severe complications, including CAD and MI. AF and CAD often co-occur and share risk factors, such as older age, hypertension, obesity, diabetes, and smoking [3]. Compared to a CAD prevalence in the US general population of 7%, that among AF patients is higher, ranging from 17% to 47% [6-9]. A meta-analysis of 16 cohort studies reported that AF is associated with increased risk of MI in follow-up [10]. In addition, AF and CAD may share pathophysiologic pathways. Coronary atherosclerosis plays a key role in the development of CAD, and AF has been found associated with arterial stiffness, which is a correlate of atherosclerosis [11, 12].

Based on this previous evidence, AF could contribute to the development and progression of CAD. However, evidence on the association between AF and CAD severity is lacking. Clarifying the impact of AF on CAD severity could improve our understanding of mechanisms linking AF and CAD. Therefore, we examined the association between AF and the severity of

CAD in the Emory Cardiovascular Biobank (EmCAB). We hypothesized that existing AF is associated with more severe CAD.

Methods

Study population

Study participants were selected from the EmCAB, an ongoing prospective registry of patients who are undergoing cardiac catheterization at 3 Emory Healthcare sites in Atlanta [13]. A detailed cohort profile has been published elsewhere [13]. At enrollment, patients are interviewed to collect demographic characteristics, detailed family and medical history, medication usage, health behaviors, and neuropsychological functioning prior to catheterization. Study personnel review medical records to confirm self-reported history of MI and other chronic conditions, and to document previous angiographic findings and coronary revascularization history. During follow-up, telephone interviews are conducted at year 1 and year 5 by study personnel.

In this study, we excluded patients who underwent cardiac transplant surgery and had missing AF data at enrollment, with 7737 patients being included in this analysis. The EmCAB has been approved by the institutional review board (IRB) at Emory University (Atlanta, Georgia, USA), and participants have provided written informed consent.

Study design

We examined the relationship between existing AF at enrollment and baseline severity of CAD cross-sectionally first, and then we examined prospectively the association between AF status at enrollment and incident MI, fatal MI and all-cause mortality during the follow-up. For the longitudinal study design, we excluded those who already had MI at baseline.

Determination of AF and characterization of CAD severity

At enrollment, patients' medical records were reviewed by trained personnel to confirm self-reported history of AF. For the cross-sectional analysis, severity of CAD was determined using four measurements: presence of 70% coronary stenosis, presence of 50% coronary stenosis, number of vessels with 50% coronary stenosis, and the Gensini score. These measurements were obtained from the baseline coronary angiography evaluation. A previous study has demonstrated good inter-observer agreement for these measurements [14]. 70%/50% stenosis was defined as presence of >70%/50% stenosis in any of major epicardial vessels. Number of vessels with 50% stenosis was the number of major epicardial vessels with >50% stenosis (range 0-12). Gensini score is a non-linear scale that quantifies CAD severity based on the degree of luminal narrowing. The scale weights lesions by prognostic significance [15]. For the longitudinal analysis, the primary endpoints were the occurrence of incident MI, fatal MI and all-cause death, which were ascertained during follow-up phone interview and verified by medical records [13].

Covariates

Covariates in this study include age, sex, race (black, non-black), body mass index (BMI), smoking status (current, past, never), education (high school graduate or less, some college, college graduate), high density lipoprotein cholesterol (HDL) concentration, low density lipoprotein cholesterol (LDL) concentration, triglycerides concentration, diabetes history, hypertension history, hypercholesterolemia history, estimated glomerular filtration rate (eGFR), medications use (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker). Demographic characteristics and medication use were self-reported. Chronic conditions were verified from chart review and laboratory readings were from blood samples collected at enrollment [13].

Statistical analysis

Baseline demographic and clinical characteristics of participants were described as mean (SD) or median (IQR) for continuous variables and frequency counts (percentage) for categorical variables. Participants' characteristics were summarized separately among total, those with and without AF history. For the cross-sectional analysis, different statistic models were used to examine the association between AF history and CAD severity measurements: logistic regression models were constructed to examine the association between AF and presence of 70% and 50% stenosis calculating odds ratios (ORs) with 95% confidence intervals (95% CIs); a Poisson regression model was used to examine the association between AF and the number of vessels with >50% stenosis and calculate incidence rate ratio (IRRs) and predicted counts with 95% CIs; linear regression was performed to examine the association between AF and Gensini score and calculate adjusted mean differences with 95% CI. All the models were run with and without adjustment for covariates, and then stratified by sex and race. For the longitudinal analysis, Cox proportional hazard models were used to calculate the hazard ratios (HRs) with 95% CIs of developing nonfatal MI, fatal MI, any MI and all-cause mortality by AF status at baseline. The time of follow-up was days from initial enrollment to any endpoints above, death, lost to follow up, or February 29, 2020, whichever occurred first. Similarly, crude and fully-adjusted models were run in total population and by sex and race. The interactions between AF and sex and race were also tested.

To minimize the effect of missing covariates in the fully-adjusted models, we used multiple imputation by chained equation (MICE) to impute all missing covariates in the multivariable models by including completely collected variables [16]. All the models stated above were re-conducted after creating 25 imputed datasets.

Results

Table 1 shows the baseline characteristics of 7737 participants, 651 of whom had AF history. In comparison with those who did not have AF history, participants with AF history were older, more likely to be male and non-black, less likely to have diabetes, and had lower BMI, HDL, LDL, triglycerides and eGFR levels. Among participants with and without AF, 71.5% and 69.9% had presence of 50% stenosis, and 56.1% and 58.1% had presence of 70% stenosis, respectively. The means (standard deviation) number of vessels with 50% stenosis were 1.7 (1.9) and 1.7 (1.8) and the medians (25^{th} percentile, 75^{th} percentile) of Gensini scores were 4 (0, 16) and 6 (0, 24) among those with and without AF history.

AF and CAD severity at baseline

At baseline, there was no evidence supporting an association between AF and presence of 70% and 50% stenosis, and numbers of vessels with 50% stenosis, in both crude and fully-adjusted models (Table 2). Comparing those with AF to those without AF, the adjusted ORs were 0.83 (95% CI 0.63, 1.09) and 0.92 (95% CI 0.69, 1.24) for presence of 70% and 50% stenosis. The adjusted rate of having vessels with 50% stenosis among participants with AF was 1.01 (95% CI 0.92, 1.11) times that among participants without AF. The predicted numbers of vessels with 50% stenosis in the fully-adjusted model were 1.08 (95% CI 0.96, 1.22) and 1.07 (95% CI 0.99, 1.16) for those with and without AF. In the crude model, AF was associated with Gensini score as AF patients had 4.92 (95% CI -8.91, -0.93) points lower than non-AF patients. However, the association was not significant after adjusting for covariates (beta coefficient: -4.66, 95% CI -9.71, 0.39).

In the stratified analysis (Table 3), similar results were found except that AF was associated with lower odds of presence of 70% stenosis among females (interaction p-value in

fully-adjusted model: 0.02). The crude OR was 0.70 (95% CI 0.50, 0.97) and the adjusted OR was 0.53 (95% CI 0.32, 0.87).

Relationship between AF and MI and all-cause mortality

After excluding those who had MI history and had admission due to MI at baseline, 4652 participants remained in the longitudinal analysis (Table 4). During a mean follow-up time of 4.6 years, 98 (2%) participants developed nonfatal MI, 51 (1%) participants had fatal MI and 1079 (23%) participants died. The incident rates of all-cause mortality among those without AF was lower than that among those with AF (49.3 per 1000 person-year vs. 68.7 per 1000 person-year). No significant association was found between AF and nonfatal MI, fatal MI and any MI. In the fully-adjusted model, the HRs were 0.82 (95% 0.29, 2.28) for nonfatal MI, 0.51 (95 % CI 0.12, 2.23) for fatal MI and 0.74 (95% CI 0.32, 1.72) for any MI. In the crude model, the risk of all-cause mortality among AF patients was 1.66 (95% CI 1.37, 2.01) times that among non-AF patients. In the fully-adjusted model, however, the risk of all-cause death was not significantly higher for AF patients (HR: 1.16, 95% CI 0.91, 1.49). In the strata of different sex and race, results were similar to that in the total population (Table 5), with no significant interactions found between AF and sex and race.

Sensitivity analysis

The results using the dataset with imputed covariates were slightly different from the main analysis. In the cross-sectional analysis (Supplemental Table 1), AF showed protective effect on presence of 70% stenosis (OR: 0.89, 95% CI 0.80, 0.99). Additionally, the Gensini scores among AF patients were not significantly lower than that among non-AF patients in both crude and adjusted models. Other results were consistent with those of the main analyses. In the longitudinal analysis (Supplemental Table 2), the results were similar to the main analyses

except that for all-cause death: AF was associated with all-cause death in both crude and adjusted models. Adjusted for covariates, the risk of all-cause death was 26% (95% CI 3%, 53%) higher among AF patients than non-AF patients.

Discussion

In this prospective cohort study, we found no association between existing AF and more severe CAD at baseline. Over follow-up of more than 4 years, existing AF was not related to fatal or nonfatal MI incidence but related to all-cause mortality.

Our study findings are somewhat inconsistent with previous research findings. In the REduction of Atherothrombosis for Continued Health (REACH) prospective registry of stable outpatients with either established atherothrombotic disease or ≥3 risk factors for atherothrombosis, the prevalence of having CAD history among AF patients was significantly higher than that among non-AF patients (69% vs. 58%, $p<0.001$) [17]. During 1-year of follow up of 63,589 patients, among those with and without AF history, the adjusted rates of developing nonfatal MI were 1.36% and 1.11%, which were not significantly different ($p=0.13$); the all-cause mortality rates were 4.3% and 2.3%, which were significantly different between groups ($p<0.001$) [17]. The study population in the REACH study is similar to patients in EmCAB, and the results regarding incident nonfatal MI and all-cause mortality are compatible. However, several prospective cohort studies in community-based samples, including REGARDS, ARIC and the Women's Health Study (WHS), have reported strong association between AF and future incident MI events, independent of other CAD risk factors [18-20]. In the ARIC study, the association between AF and increased risk of MI (particularly non-ST elevation MI) presented in women, but not in men [18]. Their inconsistency with our results could be due to several reasons.

First, the study populations in the three community-based cohorts are relatively healthier populations. The REGARDS and the ARIC studies sampled from general residents in specific areas in the United States, and the WHS study recruited female health care professionals who were initially healthy at enrollment. Among CVD patients, the relationship between AF and CAD would be more complicated, and the impact of competing events might not be avoidable over time. Second, the follow-up times in these studies were longer than that in EmCAB. Participants in WHS and ARIC were followed up over 15 years, and those in the REGARDS were followed up 6.9 years on average, while the mean follow-up time in EmCAB was 4.6 years [18]. Within longer period of follow-up time, there is a higher chance of observing incident MI cases and death. Third, the number of events in the longitudinal analysis of EmCAB was relatively small, limiting statistical power and precision of estimates of association, especially after stratification by sex and race.

To our knowledge, there is little information regarding how Gensini score could help in identifying high risk of severe CAD among patients with AF. Two scores to predict stroke risk among AF patients, CHA_2DS_2 and CHA_2DS_2-VASc, have been showed effective in assessing risk of thromboembolism in non-valvular AF patients [21, 22]. These two scores have been reported to be highly correlated with Gensini score and were predictive of the risk of severe CAD, [23] which implies the potential predictive ability of Gensini score for severe CAD among AF patients. Future investigations of Gensini score and AF are needed.

Consistent with other studies reporting increased mortality in persons with AF [24], our study also found that AF is associated with approximately 26% higher risk of all-cause mortality. Given the increasing prevalence of AF due to population aging within the next decades, the AF-associated mortality is also likely to increase, which would induce huge substantial burden on the

healthcare system. Thus, early detection of AF and identification of individuals at higher risk of developing AF, followed by evidence-based preventive and therapeutic interventions will be key to stymie this epidemic.

Our study has strengths. First, we used both cross-sectional and longitudinal study designs which provides different perspectives in answering the study question. Second, the EmCAB study has extensive data collection of epidemiologic and clinical information from a single healthcare system. This study design is good for minimizing the heterogeneity in treatment. Third, all enrolled participants in EmCAB had coronary angiographic information which allowed for investigation of AF and different measurements of CAD severity. However, there are several limitations in our study. First, the temporality between AF and measurements of CAD severity was not established. Coronary angiographic information was not collected again during follow-up. Second, for the longitudinal analysis, the relatively small number of events and missing covariates limited the statistical power, though this was partially addressed using multiple imputation approaches. The statistically significant results in the sensitivity analysis between AF and all-cause death suggested meaningful impact of missing covariates. Third, the results may not be generalizable to other populations, especially healthier populations.

In conclusion, AF was associated with all-cause mortality but not with CAD severity in the EmCAB study. Whether this lack of association is specific to this particular patient population or whether the association between AF and CAD is restricted to specific subgroups deserves further investigation.

DISCLOSURES

None.

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Table 1. Baseline characteristics of participants by AF history status in EmCAB

	Total (N=7737)	with AF history (n=651)	without AF history (n=7086)
Age, y	62.7(12.7)	68.7(12.3)	62.1(12.6)
Male, %	4863(63.1)	441(68.2)	4422(62.6)
Black, %	1801(23.3)	94(14.4)	1707(24.1)
BMI	29.9(6.6)	29.2(6.4)	29.9(6.6)
Smoking status, %			
Current	2295(32.9)	203(34.6)	2092(32.8)
Past	601(8.6)	30(5.1)	571(9)
Never	4071(58.4)	354(60.3)	3717(58.3)
Education, %			
High school graduate or less	2745(40.8)	194(34.3)	2551(41.4)
Some college	1572(23.4)	135(23.9)	1437(23.3)
College graduate	2414(35.9)	236(41.8)	2178(35.3)
HDL, mg/dL	42.9(13.9)	42.4(14.1)	43(13.9)
LDL, mg/dL	93.8(37.8)	86.6(33.6)	94.4(38)
Triglycerides, mg/dL	147(121.2)	128.8(108.6)	148.7(122.2)
Diabetes, %	2618(34.9)	204(31.7)	2414(35.2)
Hypertension, %	5880(77.9)	513(78.9)	5367(77.8)
Hypercholesterolemia, %	5266(69.8)	447(69)	4819(69.9)
eGFR, mL/min per 1.73 m2	74.1(25.1)	65.8(23.1)	74.9(25.1)
Medications, %			
ACE/ARB	4129(53.3)	395(60.7)	3734(52.7)
Aspirin	5819(75.2)	480(73.7)	5339(75.3)
Clopidogrel	3326(43)	216(33.2)	3110(43.9)
Statin	5356(69.2)	456(70.1)	4900(69.1)
Beta-blocker	5130(66.3)	522(80.2)	4608(65)
CAD, % (50% stenosis)	4246(70)	374(71.5)	3872(69.9)
CAD, % (70% stenosis)	3504(58)	293(56.1)	3211(58.1)
Number of vessels with 50% stenosis, n	1.7(1.8)	1.7(1.9)	1.7(1.8)
Gensini angiographic score, median(IQR)	6(22)	4(16)	6(24)

Notes: Some frequencies may not add up to total sample size due to missing values; Data are shown as frequency (percentage) or mean (SD) for continuous variables of the sample.

Table 2. Associations between CAD severity measurements and AF history at baseline (N=7737), EmCAB

CAD severity measurements	crude	95% CI	fully-adjusted	95% CI
Presence of stenosis (70%)				
OR	0.92	0.77, 1.10	0.83	0.63, 1.09
Presence of stenosis (50%)				
OR	1.09	0.89, 1.32	0.92	0.69, 1.24
Numbers of vessels with 50% stenosis				
IRR	1.04	0.96, 1.12	1.01	0.92, 1.11
predicted count				
with AF history	1.72	1.59, 1.85	1.08	0.96, 1.22
without AF history	1.65	1.61, 1.70	1.07	0.99, 1.16
Gensini angiographic score				
coefficient	-4.92	-8.91, -0.93	-4.66	-9.71, 0.39

Notes: Fully-adjusted models adjusted for age, sex, race, BMI, smoking status, education, HDL, LDL, triglycerides, diabetes, hypertension, hypercholesterolemia, eGFR, medications (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker); Observations in the fully-adjusted model may not be 7737 due to missing covariates.

Table 3. Associations between CAD severity measurements and AF history at baseline by sex and race(N=7737), EmCAB

CAD severity measurements	Sex				Race			
	Male(N=4863)		Female(N=2874)		Black(N=1801)		Non-black(N=5936)	
	crude	fully-adjusted	crude	fully-adjusted	crude	fully-adjusted	crude	fully-adjusted
Presence of stenosis (70%)								
OR	0.98(0.78, 1.24)	1.02(0.73, 1.42)	0.70(0.50, 0.97)	0.53(0.32, 0.87)	0.95(0.59, 1.55)	1.01(0.46, 2.18)	0.85(0.70, 1.04)	0.82(0.61, 1.10)
Interaction p-value			0.09	0.02			0.68	0.92
Presence of stenosis (50%)								
OR	1.12(0.86, 1.46)	1.16(0.79, 1.69)	0.94(0.68, 1.30)	0.65(0.41, 1.05)	1.03(0.63, 1.69)	0.79(0.36, 1.74)	1.02(0.82, 1.26)	0.98(0.71, 1.34)
Interaction p-value			0.41	0.07			0.96	0.26
Numbers of vessels with 50% stenosis								
IRR	1.02(0.93, 1.11)	1.00(0.89, 1.11)	1.01(0.85, 1.19)	1.03(0.84, 1.28)	0.88(0.70, 1.12)	0.93(0.70, 1.23)	1.04(0.96, 1.13)	1.02(0.92, 1.13)
predicted count								
with AF history	1.99(1.83, 2.17)	1.39(1.21, 1.59)	1.15(0.98, 1.34)	0.76(0.59, 0.98)	1.24(0.98, 1.56)	0.63(0.44, 0.89)	1.80(1.66, 1.94)	1.18(1.04, 1.34)
without AF history	1.96(1.90, 2.01)	1.39(1.26, 1.53)	1.13(1.08, 1.19)	0.74(0.63, 0.87)	1.40(1.32, 1.48)	0.67(0.54, 0.84)	1.73(1.68, 1.78)	1.16(1.06, 1.27)
Interaction p-value			0.92	0.86			0.20	0.63
Gensini angiographic score								
coefficient	-5.15(-10.65, 0.35)	-2.65(-9.60, 4.31)	-5.85(-10.95, -0.75)	-8.46(-15.21, -1.71)	-6.57(-14.92, 1.79)	-9.82(-19.89, 0.25)	-4.84(-9.40, -0.29)	-9.44(-30.57, 11.69)
Interaction p-value			0.87	0.35			0.74	0.40

Notes: Fully-adjusted models adjusted for age, sex, race, BMI, smoking status, education, HDL, LDL, triglycerides, diabetes, hypertension, hypercholesterolemia, eGFR, medications (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker); Observations in the fully-adjusted model may not be 7737 due to missing covariates.

Table 4. Association between AF history and incident MI in EmCAB (N=4652)

	nonfatal MI		fatal MI		incident MI		all-cause mortality	
	without AF history	with AF history	without AF history	with AF history	without AF history	with AF history	without AF history	with AF history
case, n	93	5	47	4	140	9	964	115
Incidence rate (per 1000 Pys)	4.75	2.99	2.4	2.39	7.16	5.38	49.28	68.69
HR								
crude	ref	0.62(0.25, 1.52)	ref	0.99(0.36, 2.75)	ref	0.74(0.38, 1.46)	ref	1.66(1.37, 2.01)
fully-adjusted	ref	0.82(0.29, 2.28)	ref	0.51(0.12, 2.23)	ref	0.74(0.32, 1.72)	ref	1.16(0.91, 1.49)

Notes: Fully-adjusted models adjusted for age, sex, race, BMI, smoking status, education, HDL, LDL, triglycerides, diabetes, hypertension, hypercholesterolemia, eGFR, medications (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker); Observations in the fully-adjusted model may not be 4652 due to missing covariates.

Table 5. Association between AF history and incident MI in EmCAB by sex and race (N=4652)

		nonfatal MI		fatal MI		incident MI		all-cause mortality	
		without AF history	with AF history	without AF history	with AF history	without AF history	with AF history	without AF history	with AF history
Male									
	case, n	59	4	29	3	88	7	360	52
	Incidence rate (per 1000 Pys)	4.98	3.57	2.45	2.68	7.43	6.25	32.73	55.19
	HR								
	crude	Ref	0.72(0.26, 1.99)	Ref	1.09(0.33, 3.57)	Ref	0.84(0.39, 1.82)	Ref	1.68(1.25, 2.24)
	fully-adjusted	Ref	0.80(0.24, 2.64)	Ref	0.39(0.05, 3.03)	Ref	0.65(0.23, 1.81)	Ref	1.12(0.76, 1.66)
Female									
	case, n	34	1	18	1	52	2	245	29
	Incidence rate (per 1000 Pys)	4.41	1.80	2.34	1.80	6.75	3.61	34.29	57.64
	HR								
	crude	Ref	0.39(0.05, 2.83)	Ref	0.76(0.10, 5.69)	Ref	0.51(0.13, 2.11)	Ref	1.67(1.14, 2.46)
	fully-adjusted	Ref	0.75(0.10, 5.85)	Ref	0.91(0.08, 10.4)	Ref	1.00(0.23, 4.38)	Ref	1.34(0.82, 2.19)
interaction p-value	crude		0.45		0.70		0.41		0.84
	fully-adjusted		0.78		0.57		0.76		0.85
Black									
	case, n	32	1	13	0	45	1	219	19
	Incidence rate (per 1000 Pys)	7.31	5.25	2.97	0.00	10.28	5.25	50.39	106.41
	HR								
	crude	Ref	0.66(0.09, 4.82)	Ref	NA	Ref	0.48(0.07, 3.45)	Ref	1.80(0.97, 3.32)
	fully-adjusted	Ref	0.83(0.10, 6.64)	Ref	NA	Ref	0.62(0.08, 4.78)	Ref	1.52(0.63, 3.65)
Non-black									
	case, n	61	4	34	4	95	8	745	96
	Incidence rate (per 1000 Pys)	4.02	2.70	2.24	2.70	6.26	5.39	53.95	75.78
	HR								
	crude	Ref	0.67(0.24, 1.83)	Ref	1.20(0.43, 3.39)	Ref	0.86(0.42, 1.77)	Ref	1.65(1.29, 2.13)
	fully-adjusted	Ref	0.78(0.24, 2.54)	Ref	0.60(0.13, 2.72)	Ref	0.75(0.30, 1.90)	Ref	1.18(0.85, 1.63)
interaction p-value	crude		0.86		0.98		0.53		0.90
	fully-adjusted		0.92		0.99		0.72		0.60

Notes: Fully-adjusted models adjusted for age, sex, race, BMI, smoking status, education, HDL, LDL, triglycerides, diabetes, hypertension, hypercholesterolemia, eGFR, medications (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker); Observations in the fully-adjusted model may not be 4652 due to missing covariates.

Supplemental Table 1. Associations between CAD severity measurements and AF history at baseline in EmCAB, model using multiple imputation by chained equation (MICE)

CAD severity measurements	crude	95% CI	fully-adjusted	95% CI
Presence of stenosis (70%)				
OR	0.94	0.86, 1.02	0.89	0.80, 0.99
Presence of stenosis (50%)				
OR	1.00	0.92, 1.09	0.92	0.83, 1.04
Numbers of vessels with 50% stenosis				
IRR	0.99	0.92, 1.06	0.96	0.89, 1.03
Gensini angiographic score				
coefficient	-1.7	-5.28, 1.88	-3.32	-7.2, 0.57

Notes: Fully-adjusted models adjusted for age, sex, race, BMI, smoking status, education, HDL, LDL, triglycerides, diabetes, hypertension, hypercholesterolemia, eGFR, medications (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker); Multiple imputation by chained equation was used.

Supplemental Table 2. Association between AF history and incident MI in EmCAB, model using multiple imputation by chained equation (MICE)

	nonfatal MI		fatal MI		incident MI		All-cause mortality	
	without AF history	with AF history	without AF history	with AF history	without AF history	with AF history	without AF history	with AF history
Incidence rate (per 1000 Pys)	4.75	2.99	2.4	2.39	7.16	5.38	49.28	68.69
HR								
crude	ref	0.62(0.25, 1.52)	ref	0.99(0.36, 2.75)	ref	0.74(0.38, 1.46)	ref	1.66(1.37, 2.01)
fully-adjusted	ref	0.75(0.30, 1.87)	ref	0.79(0.28, 2.27)	ref	0.81(0.41, 1.60)	ref	1.26(1.03, 1.53)

Notes: Fully-adjusted models adjusted for age, sex, race, BMI, smoking status, education, HDL, LDL, triglycerides, diabetes, hypertension, hypercholesterolemia, eGFR, medications (ACE/ARB, aspirin, clopidogrel, statin, beta-blocker); Multiple imputation by chained equation was used.

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