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Temporal Trends in the Occurrence and Outcomes of Atrial Fibrillation in Patients with Acute Myocardial Infarction (From the Atherosclerosis Risk in Communities Surveillance Study)

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Abstract

Atrial fibrillation (AF) frequently coexists in the setting of myocardial infarction (MI), being associated with increased mortality. Nonetheless, temporal trends in the occurrence of AF complicating MI and in the prognosis of these patients are not well described. We examined temporal trends in prevalence of AF in the setting of MI and the effect of AF on prognosis in the community. We studied a population-based sample of 20,049 validated first incident nonfatal hospitalized MIs among 35- to 74-year old residents of 4 communities in the ARIC Study from 1987 through 2009. Prevalence of AF in the setting of MI increased from 11% to 15% during the 23-year study period. The multivariable adjusted odds ratio for prevalent AF, per 5-year increment, was 1.11 (95% confidence interval [CI]: 1.04–1.19). Overall, in patients with MI, AF was associated with increased 1-year case fatality (OR 1.47, 95% CI 1.07–2.01) compared to those without AF. However, there was no evidence that the impact of AF on MI survival changed over time or differed over time by sex, race or MI classification (all p-values > 0.10). In conclusion, co-occurrence of AF in MI slightly increased between 1987 and 2009. The adverse impact of AF on survival in the setting of MI was consistent throughout. In the setting of MI, co-occurrence of AF should be viewed as a critical clinical event, and treatment needs unique to this population should be explored further.

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Keywords

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Despite the significant decline in the incidence rate of myocardial infarction (MI) since the end of the 20th century,[1–3] the estimated annual incidence of MI in the US remains high at 525,000 cases.[4] A recent systematic review and meta-analysis reported that approximately 1 in 10 MI patients had concomitant AF,[5] which was associated with a significantly increased risk of death.[5] However, little is known about the temporal trends related to the association of AF with prognosis of MI patients. Two studies reported a significantly higher mortality rate among MI patients who developed AF compared to those who did not, with no evidence of a clinically meaningful improvement in survival during the study period among those with coexisting AF and MI.[6,7] Both studies were relatively small and lacked precision in trend analyses. Furthermore, the prior studies on prognosis of patients with co-occurring AF and MI have been conducted in predominately white communities, which is a limitation because the decline in incidence and mortality rates for MI have been slower among blacks compared to whites, especially among men,[1] and blacks have a lower risk of AF compared to whites.[8] Our aims were to estimate the prevalence of AF in the setting of MI over time as well as by sex, race and MI classification; to describe the impact of AF on mortality; and to assess the temporal trends in mortality among MI patients with and without concomitant AF overall and among subgroups utilizing a large community-based biracial study.

METHODS

The community surveillance component of the ARIC Study, described previously, was designed to provide knowledge about the burden of and trends in CHD morbidity and mortality in 4 US communities (details included in supplemental material).[9,10]

Presence of AF during the MI hospitalization was defined by the presence of AF *International Classification of Diseases, 9th revision, Clinical Modification,* (ICD-9-CM) hospital discharge diagnosis codes of 427.3x in any position. Validity of ICD codes for the identification of AF has been described elsewhere.[11] We did not distinguish between AF that started before versus during the MI hospitalization.

All-cause mortality, at 28-days and 1-year, was determined by medical record review, state death records linkage, and linkage with the National Death Index. Deaths were classified based on the duration from date of hospital admission until date of death.

Patient characteristics, including age, sex, and race were abstracted from medical records by trained and certified study staff as were data on cardiovascular-related comorbidities, including a history of hypertension, stroke and diabetes. Prescription medications at admission, during hospitalization or at discharge and procedures were classified as yes or no. New therapies have been introduced during the study period and the impact of these therapies was estimated beginning in the year for which complete treatment information was available: ACE or angiotensin II inhibitors, 1992; Antiplatelet agents other than aspirin, 1997; and lipid-lowering agents, 1999.

Adjustment for disease severity and clinical comorbidities was performed with a modified Predicting Risk of Death in Cardiac Disease Tool (PREDICT) score.[12] The PREDICT score, developed in a community-based study, utilizes information routinely collected during a hospitalization with MI, including cardiogenic shock, clinical history (cardiac events and procedures), age, severity of ECG changes, congestive HF, kidney function, and the Charlson Comorbidity Index, to determine mortality risk. Data on renal function has not always been collected in ARIC community surveillance, so a validated modification of the PREDICT score, ranging from 0 to 21, was used.[13,14]

Hospitalized non-fatal first incident definite and probable MIs were eligible for inclusion. Patients whose race was not white or black as well as nonwhites from the Minneapolis and Washington County field centers were excluded (n = 442) due to insufficient sample size. Patients with unknown mortality status at 28-days or 1-year (n = 342) or with incomplete covariate data (n = 91) were also excluded.

The temporal trend in prevalence of coexisting AF among MI patients was assessed with a logistic regression model using year (continuous) as the main independent variable adjusted for age (5-year groups), sex, a composite race and field center variable, number of ICD-9-CM diagnosis codes, MI classification (STEMI/NSTEMI/Unclassified) and severity (PREDICT). The impact of AF on survival overall was assessed with logistic regression models adjusted for age, sex, race, field center, MI classification, number of ICD-9-CM codes, severity (PREDICT), presentation characteristics (first systolic blood pressure and first pulse), medications, and therapeutic procedures, and within subgroups defined by sex, race, and MI classification. Trends in the association of AF with 1-year case fatality among MI patients were examined with multivariable logistic regression models. Pre-specified 2-way multiplicative interactions of trends in prevalence and mortality with sex, race, and MI classification were examined. A $p<0.10$ was considered evidence of effect modification.

All analyses weighted the contribution of each hospitalization by the inverse of its sampling probability to generate point, variance and 2-tailed P values that account for the sampling design. All statistical analyses were performed using survey procedures in SAS (version 9.2; SAS Institute, Inc, Cary, NC).

RESULTS

Our final analytic sample included 13,155 definite and probable first incident MIs, for a weighted sample of 20,049. Baseline patient characteristics over time, in 4-year intervals, are shown in Table 1, while Table 2 shows prevalence of medications and therapeutic procedures. The age and sex distributions of the sample were stable over the study period, with an overall mean age of 59 years at the time of hospitalization; women accounted for 36% of the sample. The prevalence of AF accompanying MI increased slightly over the 23-year study period (Table 1), although this was due primarily to a low prevalence of concomitant AF in the first few years. The proportion of MIs classified as NSTEMI increased during the study period.

The prevalence of coexisting AF in the setting of MI increased over the study period. After adjustment there was no evidence that the time trend in prevalence of co-occurring AF and MI differed by sex (p for interaction = 0.43) or race (p for interaction = 0.69); however, there was evidence of a different AF time trend by MI classification (p for interaction = 0.005) (Figure 1). The prevalence of AF in patients with NSTEMI or unclassified MI (neither STEMI nor NSTEMI) increased during the study period, while among STEMI patients the prevalence of AF decreased.

Overall, the presence (versus absence) of AF complicating MI was associated with more than a 2-fold increased odds of post-MI death at 28-days and 1-year, after adjustment for age group, sex, race, field center and year (Table 3). This association did not differ by sex, race or MI classification.

Among those with AF and MI, there was no evidence of improved 1-year survival over time (Table 4). Conversely, among those without AF, 1-year survival improved over time. There was no statistical evidence that the trend in 1-year MI survival differed for those with versus without AF (p for interaction = 0.45). The impact of AF on 1-year case fatality did not differ by sex, race or MI classification. Within strata defined by AF status as well as sex, race or MI classification, respectively, temporal trends in survival were similar; the point estimates suggested improved survival among all strata, except men with AF, over the study period. A sensitivity analysis, excluding those who had a cardiac operative procedure performed during the index hospitalization, was performed and results were consistent with the primary analysis.

DISCUSSION

In this population-based sample of validated MI hospitalizations, the prevalence of concomitant AF in MI increased slightly from 1987 to 2009 and was approximately 15% in the most recent years. The secular trend in the prevalence of AF in the setting of MI differed by MI classification; the prevalence of coexisting AF increased over time among NSTEMI and unclassified MIs and decreased among STEMIs. Co-occurrence of AF in the setting of MI was associated with an increased risk of death and this association did not differ by sex, race or MI classification. Finally, improvements over time in 1-year survival among MI patients were greater in those without AF compared to those with AF, but this difference was not statistically significant.

The percent of patients with co-occurring AF increased over time among those with NSTEMI and unclassified MIs, while simultaneously decreasing among STEMIs. It is not surprising that AF was more common among NSTEMIs as these patients tend to be older and have more comorbidities.[15–17] However, we adjusted for age group, sex, race, field center, MI classification, severity of MI and number of ICD-9-CM diagnosis codes. This is not the first study to report an increasing prevalence of AF complicating NSTEMI; in the Worcester Heart Attack Study, the adjusted OR of having AF in the setting of NSTEMI was 1.96 (95% CI: 1.38 – 2.79) in 2005 compared to 1997, while in STEMI the corresponding OR was 1.53 (95% CI: 0.97 – 2.44).[2] In addition to the aging population, the prevalence of comorbidities, including known risk factors for AF, has increased over time, especially

among NSTEMIs, and could be driving the trend of increasing co-occurrence of AF and NSTEMI.[18] Potential explanations for the difference between STEMI and NSTEMI include changes in patient characteristics over the study period, changes in treatment strategies resulting in STEMI patients undergoing catheterization and subsequently reducing AF risk, or the impact of AF on the ECG ST segments, making it more difficult to classify an event as STEMI in the presence of AF.

Regardless of the temporal trends, AF complicating MI is consistently associated with worse survival;[5–7,19,20] in a meta-analysis of 23 studies that provided multivariable adjusted analyses, the pooled mortality OR associated with AF in MI patients was 1.46 (95% CI 1.35 – 1.58).[5] Our results are consistent with previous studies. Given the independent negative impact of AF on survival following MI, the occurrence of AF in MI should be viewed as a minor event relative to more severe complications like ventricular tachycardia, but should be recognized as a critical condition. To date, prognostic risk scores for MI ignore AF in determining the risk of death and therapeutic decisions.[21,22] Further consideration of AF in prognostic scores is warranted, especially because prevalence of AF in the community is estimated to increase as the population ages,[23,24] and because AF often complicates MI.[5,20]

Moreover, patients with AF complicating MI have unique treatment needs that are not fully understood. Aspirin is a cornerstone of acute MI therapy and dual antiplatelet therapy (aspirin and clopidogrel) is considered the gold standard following percutaneous coronary intervention.[25] However, the combination of oral anti-coagulants and antiplatelets is associated with a high frequency of major bleeding.[26] Thus, the optimal treatment strategy is unclear when the risks of thromboembolism and bleeding are considered. The introduction of new direct oral anticoagulant agents for the prevention of thromboembolic complications in AF as well as for the treatment of acute coronary syndromes raises additional questions about the optimal treatment strategy.[27,28]

There are several limitations of this study. The diagnosis of AF relied on ICD-9-CM hospital discharge codes and is not otherwise adjudicated. Nonetheless, this method has been found to have acceptable validity in epidemiologic studies.[8,11] Temporal trends in co-occurrence of AF and MI are based on the proportion of MIs in a given time with documented AF. It is possible that the trends would change if this analysis were based on rates of co-occurrence, which would scale the results to account for changes in the size of the population. The onset of AF was unknown and we included both AF occurring before and during the MI hospitalization. However, in a prior study the occurrence of AF before or after MI was associated with an increase in mortality over no AF in MI patients.[6] In our study, patients who developed AF after hospital discharge were not identified and would be misclassified. Nevertheless, there is a positive association between time from incident MI to first-detected AF and risk of death;[6] consequently, our reported association likely was underestimated. Coding practices likely have changed over time. In an effort to account for these changes, analyses were adjusted for the number of ICD-9-CM codes. A previous analysis in ARIC reported greater declines over time in first myocardial infarction after accounting for trends in cardiac biomarker utilization.[1] The advent of more sensitive biomarkers has particularly impacted the diagnosis of NSTEMI, with less severe cardiac events being classified as NSTEMI. However, it is unclear if the net effect would increase or decrease the co-

occurrence of AF; it is possible that transient increases in cardiac biomarkers associated with rapidly conducting AF would result in a small increase in concomitant AF. It is also plausible that classification of less severe cardiac events would result in fewer events of co-occurring AF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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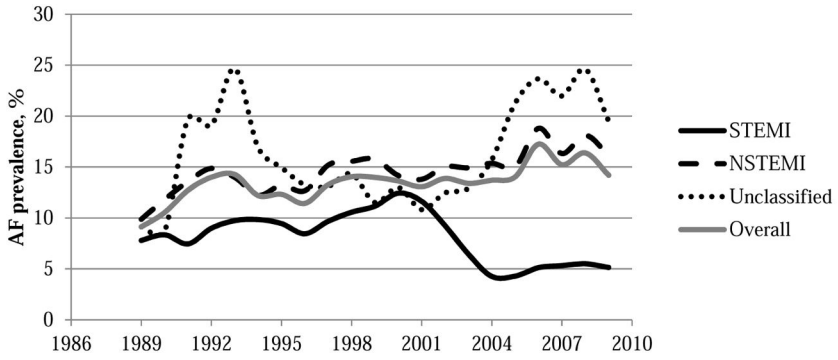

Figure 1.

Three-year moving average of AF prevalence in hospitalizations with incident definite or probable myocardial infarction overall and by subtypes (ST-Elevation myocardial infarction [STEMI], non-ST-Elevation myocardial infarction [NSTEMI], and unclassified) in the Community Surveillance component of the Atherosclerosis Risk in Communities Study, 1987 – 2009

Table 1

Baseline characteristics of patients hospitalized with incident definite or probable myocardial infarction by event year groups in the Community Surveillance component of the Atherosclerosis Risk in Communities Study, 1987 – 2009

Variable	1987 – 1990 (n = 3330)	1991 – 1994 (n = 3735)	1995 – 1998 (n = 3770)	1999 – 2002 (n = 3501)	2003 – 2006 (n = 3215)	2007– 2009 (n = 2499)
Age (years)	59.8	59.9	59.6	59.0	58.9	58.8
Women	1140 (34%)	1313 (35%)	1380 (37%)	1276 (36%)	1144 (36%)	955 (38%)
Community and race groups						
Forsyth County, NC blacks	271 (8%)	325 (9%)	459 (12%)	364 (10%)	369 (11%)	420 (17%)
Forsyth County, NC whites	966 (29%)	1124 (30%)	1174 (31%)	975 (28%)	899 (28%)	763 (31%)
Jackson, MS blacks	286 (9%)	388 (10%)	432 (11%)	579 (17%)	582 (18%)	397 (16%)
Jackson, MS whites	496 (15%)	537 (14%)	367 (10%)	289 (8%)	181 (6%)	151 (6%)
Minneapolis, MN whites	701 (21%)	724 (19%)	668 (18%)	743 (21%)	749 (23%)	433 (17%)
Washington County, MD whites	610 (18%)	637 (17%)	670 (18%)	551 (16%)	435 (14%)	336 (13%)
Comorbidities						
Hypertension	1807 (54%)	2138 (57%)	2215 (59%)	2240 (64%)	2053 (64%)	1855 (74%)
Stroke	155 (5%)	259 (7%)	301 (8%)	280 (8%)	219 (7%)	198 (8%)
Diabetes mellitus	--	641 (17%)	1076 (29%)	1043 (30%)	1139 (35%)	946 (38%)
PREDICT score*	6.2	6.5	6.5	5.7	5.7	6.8
Presentation characteristics						
Hospital arrival < 2 hours†	995 (30%)	1113 (30%)	1143 (30%)	1064 (30%)	798 (25%)	623 (25%)
First systolic blood pressure (mm Hg)	144.2	148.3	147.4	149.2	145.5	148.0
First pulse rate (bpm)	84.1	85.3	85.8	86.9	87.6	89.5
Atrial fibrillation	351 (11%)	489 (13%)	513 (14%)	471 (13%)	527 (16%)	366 (15%)
Myocardial infarction classification						
ST-elevation myocardial infarction	793 (24%)	1071 (29%)	1038 (28%)	689 (20%)	512 (16%)	517 (21%)
Non ST-elevation myocardial infarction	2214 (66%)	2157 (58%)	2221 (59%)	2373 (68%)	2326 (72%)	1789 (72%)
Unclassified	323 (10%)	506 (14%)	510 (14%)	438 (13%)	377 (12%)	194 (8%)

Continuous variables presented as mean

Categorical variables presented as count (%)

History of diabetes not routinely collected until 1991

* Modified PREDICT score did not include kidney function

† Hospital arrival < 2 hours was determined based on duration from earliest symptom onset time to hospital arrival time

Table 2

Medication* and therapeutic procedures during hospitalization with incident definite or probable myocardial infarction by event year groups in the Community Surveillance component of the Atherosclerosis Risk in Communities Study, 1987 – 2009

Variable	1987 – 1990 (n = 3330)	1991 – 1994 (n = 3735)	1995 – 1998 (n = 3770)	1999 – 2002 (n = 3501)	2003 – 2006 (n = 3215)	2007– 2009 (n = 2499)
Medication						
Aspirin	2251 (68%)	3233 (87%)	3358 (89%)	3173 (91%)	2846 (89%)	2280 (91%)
β blockers	1549 (47%)	2252 (60%)	2671 (71%)	2832 (81%)	2796 (87%)	2236 (89%)
Calcium channel blockers	2151 (65%)	2197 (59%)	1497 (40%)	852 (24%)	702 (22%)	634 (25%)
ACE or angiotensin II inhibitors	--	664 (18%)	1724 (46%)	2162 (62%)	2115 (66%)	1624 (65%)
Warfarin	302 (9%)	545 (15%)	635 (17%)	476 (14%)	430 (13%)	338 (14%)
Lipid-lowering medications	--	--	248 (7%)	2047 (58%)	2284 (71%)	1829 (73%)
Antiplatelet agents other than aspirin	--	--	823 (22%)	1992 (57%)	2011 (63%)	1504 (60%)
Procedures						
Thrombolytic agents†	737 (22%)	998 (27%)	708 (19%)	366 (10%)	52 (2%)	52 (2%)
Percutaneous coronary intervention	538 (16%)	855 (23%)	999 (27%)	1202 (34%)	1325 (41%)	1020 (41%)
Coronary artery bypass graft	466 (14%)	478 (13%)	577 (15%)	438 (13%)	301 (9%)	189 (8%)

*On admission, during hospitalization, or at discharge

†Thrombolytic agents include intracoronary and intravenous

The following medications were not routinely collected until the year indicated in parentheses: ACE or angiotensin II inhibitors (1992), antiplatelet agents other than aspirin (1997) and lipid-lowering agents (1999)

Table 3

Odds ratios for 28-day and 1-year all-cause case fatality comparing patients with versus without atrial fibrillation in the setting of hospitalized incident definite or probable myocardial infarction in the Community Surveillance component of the Atherosclerosis Risk in Communities Study, 1987 – 2009

	Case Fatality (months)	
	1	12
Variable	**OR* (95% CI)**	**OR (95% CI)**
Number of deaths	204 (1.0%)	1431 (7.1%)
Model 1: Age, sex, race, field center and year	2.23 (1.13 – 4.42)	2.15 (1.63 – 2.83)
Model 2: Model 1 + MI classification† and # ICD-9-CM	2.13 (1.06 – 4.29)	1.93 (1.45 – 2.58)
Model 3: Model 2 + presentation characteristics‡	1.92 (0.92 – 4.02)	1.72 (1.26 – 2.35)
Model 4: Model 3 + Medication§	2.20 (0.97 – 4.99)	1.55 (1.12 – 2.12)
Model 5: Model 3 + therapeutic procedures‖	1.71 (0.84 – 3.49)	1.56 (1.15 – 2.12)
Model 6: Model 2 + presentation characteristics, medications and procedures	2.10 (0.94 – 4.70)	1.47 (1.07 – 2.01)

*OR = odds ratio; Comparison of co-occurring atrial fibrillation and myocardial infarction (MI) to MI

†MI classification = ST-Elevation MI, non ST-Elevation MI and unclassified

‡Presentation characteristics = first systolic blood pressure, first pulse and the modified PREDICT score

§Medications = aspirin, β blockers, Calcium channel blockers, ACE or angiotensin II inhibitors, warfarin, lipid-lowering medications and antiplatelet agents other than aspirin

‖Therapeutic procedures = percutaneous coronary intervention and coronary artery bypass graft

Table 4

Temporal trends in 1-year all-cause case fatality stratified by atrial fibrillation status among those hospitalized with incident definite or probable myocardial infarction in the Community Surveillance component of the Atherosclerosis Risk in Communities Study, 1987 – 2009. Results presented as odds ratios (OR)* of mortality per 5-year increment

	Atrial Fibrillation			No Atrial Fibrillation		
	n / N	**OR per 5-year Increment**	**Interaction p-value (subgroup* year)**	**n / N**	**OR per 5-year Increment**	**Interaction p-value (subgroup* year)**
Overall	367 / 2717	0.86 (0.60 – 1.21)	--	1063 / 17332	0.74 (0.62 – 0.88)	--
Men	229 / 1731	1.05 (0.64 – 1.70)	0.32	630 / 11110	0.72 (0.57 – 0.92)	0.21
Women	139 / 986	0.71 (0.43 – 1.19)		433 / 6222	0.82 (0.63 – 1.06)	
Whites	249 / 2140	0.98 (0.68 – 1.41)	0.33	621 / 13036	0.84 (0.66 – 1.05)	0.40
Blacks	119 / 577	0.79 (0.42 – 1.45)		442 / 4296	0.63 (0.48 – 0.82)	
STEMI	45 / 391	0.68 (0.32 – 1.44)	0.63	173 / 4228	0.71 (0.50 – 1.00)	0.13
NSTEMI	245 / 1945	0.84 (0.57 – 1.24)		726 / 11136	0.73 (0.58 – 0.90)	
Unclassified	77 / 381	0.68 (0.32 – 1.44)		165 / 1968	0.59 (0.35 – 1.00)	

AF = atrial fibrillation

Overall, there was no statistical evidence that 1-year survival over time differed between those with or without AF (p for interaction = 0.45)

*Adjusted for age, sex, race, field center, MI classification (STEMI/NSTEMI/Unclassified), number of ICD-9-CM codes, presentation characteristics (first systolic blood pressure, first pulse and MI severity), medications (aspirin, β blockers, Calcium channel blockers, ACE or angiotensin II inhibitors, warfarin, lipid-lowering medications and antiplatelet agents other than aspirin), and therapeutic procedures (percutaneous coronary intervention and coronary artery bypass graft