

Trends in Atrial Fibrillation in Patients Hospitalized with an Acute Coronary Syndrome

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ABSTRACT

BACKGROUND: Atrial fibrillation is common among patients with cardiovascular disease and is a frequent complication of the acute coronary syndrome. Data are needed on recent trends in the magnitude, clinical features, treatment, and prognostic impact of preexisting and new-onset atrial fibrillation in patients hospitalized with an acute coronary syndrome.

METHODS: The study population consisted of 59,032 patients hospitalized with an acute coronary syndrome at 113 sites in the Global Registry of Acute Coronary Events Study between 2000 and 2007.

RESULTS: A total of 4494 participants (7.6%) with acute coronary syndrome reported a history of atrial fibrillation and 3112 participants (5.3%) developed new-onset atrial fibrillation during their hospitalization. Rates of new-onset atrial fibrillation (5.5%-4.5%) and preexisting atrial fibrillation (7.4%-6.7%) declined during the study. Preexisting atrial fibrillation was associated with older age and greater cardiovascular disease burden, whereas new-onset atrial fibrillation was closely related to the severity of the index acute coronary syndrome. Patients with atrial fibrillation were less likely than patients without atrial fibrillation to receive evidence-based therapies and more likely to develop in-hospital complications, including heart failure. Overall hospital death rates in patients with new-onset and preexisting atrial fibrillation were 14.5% and 8.9%, respectively, compared with 1.2% in those without atrial fibrillation. Short-term death rates in patients with atrial fibrillation declined over the study period.

CONCLUSIONS: Despite a reduction in the rates of, and mortality from, atrial fibrillation, this arrhythmia exerts a significant adverse effect on survival among patients hospitalized with an acute coronary syndrome. Opportunities exist to improve the identification and treatment of patients with acute coronary syndrome with, or at risk for, atrial fibrillation to reduce the incidence and resultant complications of this dysrhythmia.

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Atrial fibrillation is one of the most common cardiovascular diseases worldwide, and the global burden of atrial fibrillation is increasing.^{1,2} The acute coronary syndrome is a potent risk factor for atrial fibrillation, with atrial fibrillation occurring in up to 1 in every 5 patients hospitalized with an acute coronary syndrome.^{3,4}

To date, most investigations into the magnitude and impact of atrial fibrillation in the setting of an acute coronary syndrome have been limited by modest sample sizes, short duration of follow-up, or inclusion of less-generalizable patient populations.⁵⁻⁷ Perhaps because of the heterogeneous nature of these investigations, there remains a lack of consensus as to whether the development of atrial fibril-

lation confers an increased risk of dying in patients with an acute coronary syndrome independently of underlying risk factors.^{5,8-12} Moreover, because studies have focused largely on patients who develop new-onset atrial fibrillation during hospitalization for an acute coronary syndrome,¹³⁻¹⁵ the impact of preexisting atrial fibrillation on prognosis in this setting is poorly defined.¹⁶

Despite significant changes in the demographics, treatment, and prognosis of patients hospitalized with an acute coronary syndrome during the last 30 years,^{17,18} limited data are available describing recent trends in the magnitude, treatment, and prognosis of patients with acute coronary syndrome and new-onset¹⁹ or preexisting atrial fibrillation.²⁰ The purpose of this study was to describe changing trends in patients with and without atrial fibrillation who were enrolled in the Global Registry of Acute Coronary Events (GRACE) study between 2000 and 2007.

MATERIALS AND METHODS

Details of the design of and data-collection methods used in the GRACE Registry have been published.²¹ In brief, GRACE was a large, multinational, observational study of patients hospitalized with an acute coronary syndrome.²² A total of 113 hospitals from 14 countries contributed data to this investigation.

Adult patients admitted with a presumptive diagnosis of acute coronary syndrome at any of the 113 participating GRACE hospitals were considered eligible for study inclusion, and patients' eligibility status was assessed on the basis of predetermined criteria.^{21,22} Trained staff abstracted patients' demographic, clinical, biochemical, and electrocardiographic characteristics, as well as treatment practices and hospital outcomes, from hospital medical records using standardized case reporting forms. Standardized definitions of patient-related variables and outcomes were used (www.outcomes.org/grace).²¹ As previously described, atrial fibrillation was defined on the basis of atrial fibrillation or atrial flutter on the admission 12-lead electrocardiogram.²⁰ Patients were categorized into those with preexisting atrial fibrillation and those with new-onset atrial fibrillation according to the presence of a history of atrial fibrillation in hospital medical records.²⁰ A GRACE risk score was calculated on the basis of a validated 8-variable model.²³ All acute coronary syndrome events were assigned to 1 of 3 categories using pre-established criteria: ST-segment eleva-

tion myocardial infarction, non-ST-segment elevation myocardial infarction, and unstable angina.²¹

Data Analysis

Differences in the characteristics, treatment, and outcomes of patients who developed new-onset atrial fibrillation were compared with patients who remained free of this arrhythmia using the chi-square and Kruskal-Wallis or Wilcoxon rank-sum tests for categorical and continuous variables, respectively. Variables considered for inclusion in all multivariable adjusted regression models were selected on the basis of established associations with atrial fibrillation or reduced survival in patients with an acute coronary syndrome. Candidate variables included age, sex, current smoking status, medical history, clinical characteristics on hospital presentation, and electrocardiogram characteristics (**Table 1**). Variables were retained in the final regression

model if they were associated with the development of new-onset atrial fibrillation on univariate testing ($P < .20$). The end points examined included the development of cardiogenic shock, sustained ventricular tachycardia, renal failure, major bleeding, or stroke during hospitalization, in-hospital death, and death at 30 days after hospital admission.

RESULTS

Of the 59,032 patients who were enrolled in GRACE between 2000 and 2007, 4494 (7.6%) had preexisting atrial fibrillation and 3112 developed new-onset atrial fibrillation (5.3%) during hospitalization (**Table 1**). The mean age of study participants was 66 years, 33% were women, 10% had a history of heart failure, and 37% presented with an ST-segment elevation myocardial infarction.

Baseline Characteristics of Study Sample

Patients with atrial fibrillation (new-onset or preexisting atrial fibrillation) were on average older; female; and more likely to have a left bundle branch block, a higher average GRACE risk score, a lower ejection fraction, a higher initial serum creatinine level, a longer hospital stay, and a history of heart failure, hypertension, diabetes, or major bleeding in comparison with patients without prior atrial fibrillation who remained in sinus rhythm during hospitalization (**Table 1**). Patients who did not develop atrial fibrillation had a significantly higher body mass index, higher blood pressure, higher serum cholesterol, and lower initial heart rate on hospital presentation

CLINICAL SIGNIFICANCE

- Preexisting and new-onset atrial fibrillation are common among patients hospitalized for an acute coronary syndrome.
- Rates of heart failure and death are higher among patients with new-onset and preexisting atrial fibrillation than among patients without atrial fibrillation.
- Perhaps because of better monitoring and treatment, rates of atrial fibrillation and its complications are decreasing in patients hospitalized for an acute coronary syndrome.

Table 1 Baseline Characteristics of GRACE Participants with New-Onset, Preexisting, and No Atrial Fibrillation

Variable*	New-Onset AF (n = 3112)	P Value (New vs No)	Preexisting AF (n = 4494)	P Value (Pre vs No)	No AF (n = 51,426)	P Value (New vs Pre)
Age (y)	72.1 (11.6)	<.001	75.1 (10.4)	<.001	64.5 (13.1)	<.001
Male	1953 (63.0%)	<.001	2723 (60.8%)	<.001	34,891 (68.1%)	.059
BMI (kg/m ²)	27.3 (5.3)	<.001	27.2 (5.6)	<.001	27.8 (5.4)	.45
Hospitalized in United States	870 (28%)	<.001	1573 (35%)	<.001	11,980 (23.3%)	<.001
Systolic BP (mm Hg)	136.1 (32.5)	<.001	140.2 (31.0)	<.001	141.8 (29.5)	<.001
Diastolic BP (mm Hg)	77.0 (19.6)	<.001	77.6 (19.1)	<.001	80.4 (17.7)	.32
Pulse (beats/min)	87.9 (27.5)	<.001	86.8 (27.1)	<.001	78.3 (19.9)	.02
GRACE risk score†	159.3 (39.2)	<.001	152.9 (36.3)	<.001	128.5 (36.4)	<.001
LOS (d)	11.9 (10.9)	<.001	7.7 (7.9)	<.001	7.0 (7.1)	<.001
Medical history						
Current smoker	1675 (54.0%)	<.001	2112 (47.2%)	<.001	29,994 (58.5%)	<.001
Angina	1416 (45.6%)	<.001	2730 (61.0%)	<.001	25,725 (50.1%)	<.001
MI	877 (28.2%)	.55	1933 (43.2%)	<.001	14,738 (28.7%)	<.001
HF	396 (12.8%)	<.001	1422 (31.9%)	<.001	4068 (7.9%)	<.001
PCI	395 (12.7%)	<.001	979 (21.9%)	<.001	9124 (17.8%)	<.001
CABG	267 (8.6%)	<.001	995 (22.2%)	<.001	5984 (11.7%)	<.001
Diabetes mellitus	864 (27.8%)	<.001	1370 (30.7%)	<.001	12,541 (24.4%)	.0076
Hypertension	2035 (65.6%)	<.001	3328 (74.3%)	<.001	31,201 (60.8%)	<.001
Hyperlipidemia	1243 (40.1%)	<.001	2214 (49.8%)	.24	25,064 (48.9%)	<.001
Major bleeding	45 (1.4%)	.002	112 (2.5%)	<.001	464 (0.9%)	.0016
ACS type						
UA	508 (16.3%)	<.001	1474 (32.8%)	<.001	15,534 (30.2%)	<.001
NSTEMI	1077 (34.6%)		1864 (41.5%)		16,889 (32.8%)	
STEMI	1527 (49.1%)		1156 (25.7%)		19,003 (36.9%)	
Killip class III and IV HF	361 (11.8%)	<.001	358 (8.2%)	<.001	2048 (4.1%)	<.001
Laboratory						
Creatinine (mg/dL)	1.3 (0.9)	<.001	1.4 (1.0)	<.001	1.2 (0.8)	<.001
Total cholesterol (mg/dL)	179.5 (48.4)	<.001	174.6 (48.1)	<.001	192.3 (49.5)	.0004
Troponin‡	36.0 (86.1)	<.001	14.0 (43.7)	<.001	23.1 (66.8)	<.001
Baseline EF (%)	45.0 (15.2)	<.001	46.4 (15.7)	<.001	51.0 (14.2)	.0002
LBBB	203 (6.5%)	<.001	421 (9.4%)	<.001	2216 (4.3%)	<.001

ACS = acute coronary syndrome; AF = atrial fibrillation; BP = blood pressure; BMI = body mass index; CABG = coronary artery bypass grafting; EF = ejection fraction; GRACE = Global Registry of Acute Coronary Events; HF = heart failure; LBBB = left bundle branch block; LOS = length of stay; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; UA = unstable angina.

*Mean (\pm standard deviation), laboratory values obtained from admission.

†GRACE risk score is based on patient age, presenting heart rate, systolic blood BP, serum creatinine, Killip class, cardiac arrest on presentation, ST-segment deviation, and cardiac enzymes.²³

‡Maximum value within first 24 h.

than patients with acute coronary syndrome with preexisting or new-onset atrial fibrillation.

Patients who developed new-onset atrial fibrillation were more likely than patients who remained free from atrial fibrillation to have presented with an ST-segment elevation myocardial infarction and to have a higher initial troponin level, and were less likely to have a history of myocardial infarction, angina, hyperlipidemia, percutaneous coronary intervention, or coronary artery bypass graft surgery. In contrast, patients with preexisting atrial fibrillation were more likely to have presented with a non-ST-segment elevation myocardial infarction, have a lower initial troponin level, and have a history of myocardial infarction, angina, hyperlipidemia, percutaneous coronary intervention, or coronary artery bypass

grafting than were patients without atrial fibrillation. The exclusion of patients who underwent coronary artery bypass graft surgery during hospitalization did not significantly alter our study findings.

Characteristics of Patients With New-Onset Versus Preexisting Atrial Fibrillation

Patients with new-onset atrial fibrillation were on average younger and more likely to be hospitalized with an ST-segment elevation myocardial infarction than were patients with preexisting atrial fibrillation ($P < .001$). Patients with new-onset atrial fibrillation had a lower systolic blood pressure, a higher heart rate, a higher GRACE risk score, and a longer length of stay than patients with preexisting atrial

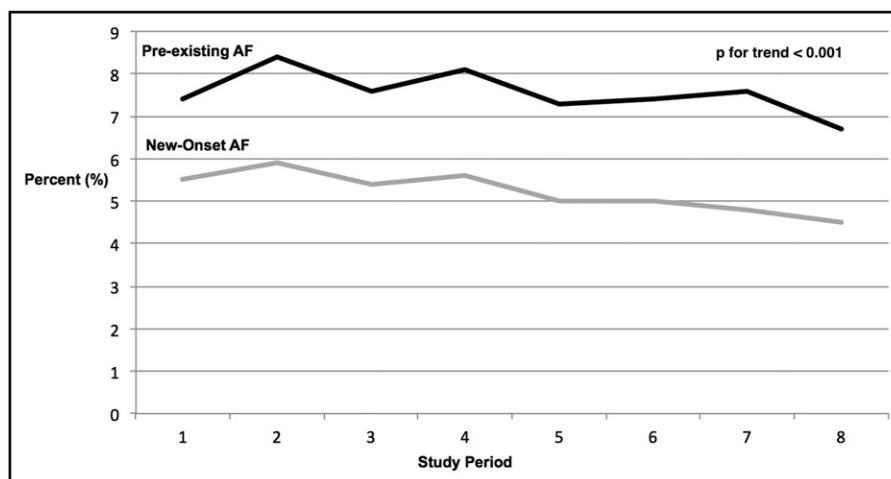


Figure 1 Rates of new-onset and preexisting atrial fibrillation in patients hospitalized with an acute coronary syndrome by study year between 2000 and 2007. AF = atrial fibrillation.

fibrillation ($P < .05$). Patients developing new-onset atrial fibrillation during their hospital stay were more likely to currently smoke but were less likely to have a history of various cardiovascular comorbidities and major bleeding than patients with preexisting atrial fibrillation ($P < .005$). Patients with new-onset atrial fibrillation were more likely to have a lower initial serum creatinine level, total cholesterol level, and baseline ejection fraction, but higher peak troponin levels, than patients with preexisting atrial fibrillation ($P < .001$).

Incidence Rates of New-Onset Atrial Fibrillation and Prevalence of Preexisting Atrial Fibrillation

Between 2000 and 2007, incidence rates of new-onset atrial fibrillation declined, albeit in an inconsistent manner, from 5.5% to 4.5% (Figure 1, P for trend $< .001$). After adjustment for several demographic and clinical factors, the multivariable adjusted odds of developing new-onset atrial

fibrillation was lower during our most recent study years (2004–2007) in comparison with our original study year (2000) (Table 2). A greater proportion of GRACE participants reported a history of atrial fibrillation than developing new-onset atrial fibrillation (7.6% vs 5.3%). The prevalence of atrial fibrillation declined from 7.4% in 2000 to 6.7% in 2007 (Figure 1, P for trend $< .001$), but the adjusted odds of having preexisting atrial fibrillation remained similar throughout the study period (Table 2).

In-Hospital Treatment and Discharge Prescription Practices

Patients with both new-onset and preexisting atrial fibrillation were significantly less likely to have received aspirin, clopidogrel, beta-blockers, angiotensin-converting enzyme inhibitors, glycoprotein IIb/IIIa antagonists, and statins (Table 3). Patients with any atrial fibrillation were more likely to have received amiodarone and warfarin during hospitalization. Use of percutaneous coronary intervention was less

Table 2 Odds of Having Preexisting Atrial Fibrillation or Developing New-Onset Atrial Fibrillation in Relation to Study Year

Study Year	New-Onset AF n (%)	Adjusted Odds New-Onset AF*	Preexisting AF n (%)	Adjusted Odds Preexisting AF
2000	441 (5.5)	—	588 (7.4)	—
2001	470 (5.9)	1.04 (0.90-1.12)	670 (8.4)	1.13 (1.00-1.29)
2002	452 (5.4)	0.96 (0.83-1.11)	712 (7.6)	1.02 (0.90-1.16)
2003	496 (5.6)	1.02 (0.88-1.17)	712 (8.1)	1.07 (0.94-1.21)
2004	408 (5.0)	0.82 (0.71-0.96)	600 (7.3)	0.90 (0.79-1.03)
2005	349 (5.0)	0.85 (0.72-0.99)	518 (7.4)	0.89 (0.78-1.02)
2006	293 (4.8)	0.82 (0.70-0.97)	467 (7.6)	0.95 (0.82-1.09)
2007	203 (4.5)	0.76 (0.63-0.91)	299 (6.7)	0.88 (0.75-1.03)

AF = atrial fibrillation.

*Referent year = 2000. Adjusted for age, sex, and GRACE risk score.

Table 3 In-Hospital Treatment Practices and Discharge Prescription According to Atrial Fibrillation Status

Treatment	New-Onset AF (n = 3112)	P Value (New vs No)	Preexisting AF (n = 4494)	P Value (Pre vs No)	No AF (n = 51,426)	P Value (New vs Pre)
In-hospital medications						
Aspirin	2902 (93.3%)	.05	3849 (86.0%)	<.001	48,377 (94.2%)	<.001
Beta-blocker	2458 (79.5%)	<.001	3390 (76.0%)	<.001	43,808 (85.7%)	<.001
ACE inhibitor	2207 (71.6%)	<.001	2837 (63.7%)	.0024	33,672 (65.9%)	<.001
Statin	1905 (61.8%)	<.001	2645 (59.3%)	<.001	36,270 (80.0%)	.031
Clopidogrel	1074 (52.6%)	<.001	1300 (43.4%)	<.001	21,371 (61.1%)	<.001
Amiodarone	1554 (50.5%)	<.001	1067 (24.1%)	<.001	2318 (4.6%)	<.001
Low-molecular-weight heparin	1870 (60.9%)	.43	2402 (54.1%)	<.001	30,614 (60.2%)	<.001
Unfractionated heparin	1746 (56.9%)	<.001	1834 (41.4%)	<.001	23,248 (45.8%)	<.001
Warfarin	556 (18.2%)	<.001	1317 (29.7%)	<.001	1768 (3.5%)	<.001
GpIIb/IIIa inhibitor	845 (27.6%)	.65	728 (16.4%)	<.001	14,185 (27.9%)	<.001
Procedures						
PCI	1011 (32.6%)	<.001	1010 (22.6%)	<.001	21,036 (41.2%)	<.001
Thrombolytics	460 (15.0%)	.0499	229 (5.2%)	<.001	6985 (13.7%)	<.001
CABG	587 (19.0%)	<.001	133 (3.0%)	<.001	2306 (4.5%)	<.001
IABP	337 (11.1%)	<.001	80 (1.8%)	.03	1173 (2.3%)	<.001
Permanent pacemaker	343 (11.3%)	<.001	200 (4.5%)	<.001	1250 (2.5%)	<.001
Discharge prescription						
Aspirin	2121 (87.4%)	<.001	2897 (79.7%)	<.001	40,338 (92.1%)	<.001
Beta-blocker	1725 (71.3%)	<.001	2593 (71.4%)	<.001	35,180 (80.6%)	.93
ACE inhibitor	1565 (65.0%)	.14	2235 (61.7%)	.03	27,675 (63.5%)	.01
Statin	1529 (63.3%)	<.001	2268 (62.6%)	<.001	32,221 (73.9%)	.57
Clopidogrel	649 (40.9%)	<.001	893 (36.7%)	<.001	16,659 (56.1%)	.008
Warfarin	476 (20.0%)	<.001	1254 (34.7%)	<.001	1632 (3.8%)	<.001

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; CABG = coronary artery bypass grafting; IABP = intra-aortic balloon pump; PCI = percutaneous intervention.

common and pacemaker implantation was more common in patients with any atrial fibrillation than in patients in normal sinus rhythm. Administration of thrombolytic medications, implantation of an intra-aortic balloon pump, and coronary artery bypass grafting were more common among patients who developed new-onset atrial fibrillation but less common in patients with preexisting atrial fibrillation, than in patients who did not have atrial fibrillation. Patients with preexisting or new-onset atrial fibrillation were more likely to have been discharged with a prescription for warfarin, but were less likely to be discharged with aspirin, beta-blockers, statins, and clopidogrel than patients without atrial fibrillation (**Table 3**).

Patients who developed new-onset atrial fibrillation were more likely to receive each of the in-hospital treatments examined, with the exception of warfarin, than were patients with preexisting atrial fibrillation ($P < .05$). Patients who developed new-onset atrial fibrillation were more likely to be discharged with aspirin and clopidogrel and less likely to receive a discharge prescription for warfarin, than hospitalized patients with preexisting atrial fibrillation ($P < .001$).

In-Hospital Complications and Thirty-Day Mortality

The frequency of most in-hospital complications was higher among patients with acute coronary syndrome and any type

of atrial fibrillation than in patients free from this arrhythmia (**Table 4**). Complication rates were highest in those with new-onset atrial fibrillation and lowest among those who did not develop atrial fibrillation. Multivariate adjustment significantly attenuated the associations between preexisting atrial fibrillation and the development of several in-hospital complications. However, preexisting atrial fibrillation remained associated with the development of heart and renal failure, sustained ventricular tachycardia, and death after multivariable adjustment (**Table 4**). New-onset atrial fibrillation retained its strong association with all in-hospital complications, including a 2-fold higher risk of dying during hospitalization, after adjustment for several potential confounding or mediating factors. Patients with new-onset atrial fibrillation were at significantly higher risk for developing in-hospital cardiogenic shock, stroke, major bleeding, and recurrent angina than patients in normal sinus rhythm.

Three percent of patients with new-onset atrial fibrillation died within 30 days of discharge, whereas 3.5% of patients with preexisting atrial fibrillation and 1.2% of patients without atrial fibrillation died during this period. However, only preexisting atrial fibrillation remained associated with an increased odds of dying within 30 days after discharge after adjustment for a number of poten-

Table 4 Clinical Complications According to the Presence and Type of Atrial Fibrillation

Complication	New-Onset AF vs No AF		Preexisting AF vs No AF		No AF
	No. (%) With New-Onset AF and Complication	Adjusted* Odds of Complication (95% CI)	No. (%) With Preexisting AF and Complication	Adjusted* Odds of Complication (95% CI)	No. (%) With No AF and Complication
Heart failure	1226 (39.7%)	3.2 (2.9-3.5)	989 (22.1%)	1.4 (1.3-1.6)	5610 (10.9%)
Cardiogenic shock	464 (15.0%)	2.8 (2.4-3.2)	217 (4.8%)	0.9 (0.8-1.1)	1695 (3.3%)
Sustained ventricular tachycardia	311 (10.0%)	3.1 (2.7-3.6)	171 (3.8%)	1.3 (1.1-1.6)	1298 (2.5%)
Renal failure	478 (15.4%)	3.1 (2.8-3.6)	334 (7.5%)	1.6 (1.4-1.8)	1491 (2.9%)
Stroke	68 (2.2%)	1.97 (1.4-2.7)	45 (1.0%)	1.2 (0.9-1.7)	312 (0.6%)
Major bleeding	212 (6.9%)	2.1 (1.8-2.5)	145 (3.3%)	1.1 (0.9-1.3)	1090 (2.1%)
In-hospital death	452 (14.5%)	2.0 (1.8-2.3)	398 (8.9%)	1.3 (1.1-1.5)	1962 (3.8%)
30-d postdischarge death	63 (3.0%)	1.2 (0.9-1.6)	116 (3.5%)	1.4 (1.1-1.8)	480 (1.2%)

AF = atrial fibrillation; CI = confidence interval.

*Adjusted for age, sex, study period, and GRACE risk score.

tially confounding prognostic factors (odds ratio [OR], 1.4; 95% confidence interval [CI], 1.1-1.8).

Trends in Major Hospital Complications

Although the rates of all major complications were higher among patients with acute coronary syndrome with any type of atrial fibrillation (new-onset or prior), rates of in-hospital heart failure, major bleeding, and death declined in a similar fashion in patients with and without atrial fibrillation between 2000 and 2007 ($P < .05$; **Figure 2**). However, rates of in-hospital stroke declined steadily in patients without atrial fibrillation or preexisting atrial fibrillation, whereas the incidence rates of stroke did not decline in patients who developed new-onset atrial fibrillation. When compared with patients who were hospitalized during 2000, patients with atrial fibrillation who were hospitalized during the most recent study year (2007) were at lower risk for developing heart failure (OR, 0.50; 95% CI, 0.39-0.64), cardiogenic shock (OR, 0.67; 95% CI, 0.45-1.01), sustained ventricular tachycardia (OR, 0.65; CI, 0.39-1.08), and in-hospital death (OR, 0.65; 95% CI, 0.43-0.99) after adjustment for potential confounders of prognostic importance (**Table 1**).

DISCUSSION

The results of this large multinational study demonstrate that preexisting and new-onset atrial fibrillation are common in patients hospitalized with an acute coronary syndrome. In contrast to atrial fibrillation trends in some communities,²⁴ the incidence rates of atrial fibrillation in patients with acute coronary syndrome declined over the 8-year study period. Atrial fibrillation was strongly associated with important adverse cardiac events, suggesting that opportunities exist for improving the treatment of patients with acute coronary syndrome and atrial fibrillation. Pa-

tients with new-onset atrial fibrillation differed from patients with preexisting atrial fibrillation, suggesting that the underlying pathophysiology of atrial fibrillation in these populations may differ.

Incidence and Prevalence of Atrial Fibrillation

Reported incidence rates of new-onset atrial fibrillation in patients hospitalized with an acute coronary syndrome vary widely, with estimates ranging from 5% to 23%.^{4,20,25,26} In the present investigation, 1 in every 13 patients reported having a history of atrial fibrillation, and 5.3% of patients developed atrial fibrillation during their acute hospitalization. Rates of new-onset atrial fibrillation in our study were slightly lower than those reported in a recent pooled analysis of 120,566 patients with acute coronary syndrome who were enrolled in clinical trials over the same period, which showed an overall incidence rate of 7.5%.²⁷ In contrast to the findings of a recent community-based study, which showed stable incidence rates of atrial fibrillation in 7513 patients hospitalized with acute myocardial infarction between 1975 and 2005, the incidence of atrial fibrillation declined during our 8-year study.⁴ Reasons for these discrepant findings might include the more contemporary nature of our study, the inclusion of a multinational sample, and the inclusion of patients with less severe types of acute coronary syndrome. This hypothesis is supported by the fact that the rates of new-onset and previous atrial fibrillation in our study were consistent with the frequency of atrial fibrillation observed in patients enrolled in the Acute Coronary Syndrome Prospective Audit Registry (4.4% new-onset, 11.4% previous atrial fibrillation).¹⁶ Because new-onset atrial fibrillation complicating myocardial infarction often results from left ventricular dysfunction and acutely increased filling pressures, greater use of coronary revascularization and effective cardiac medications may have

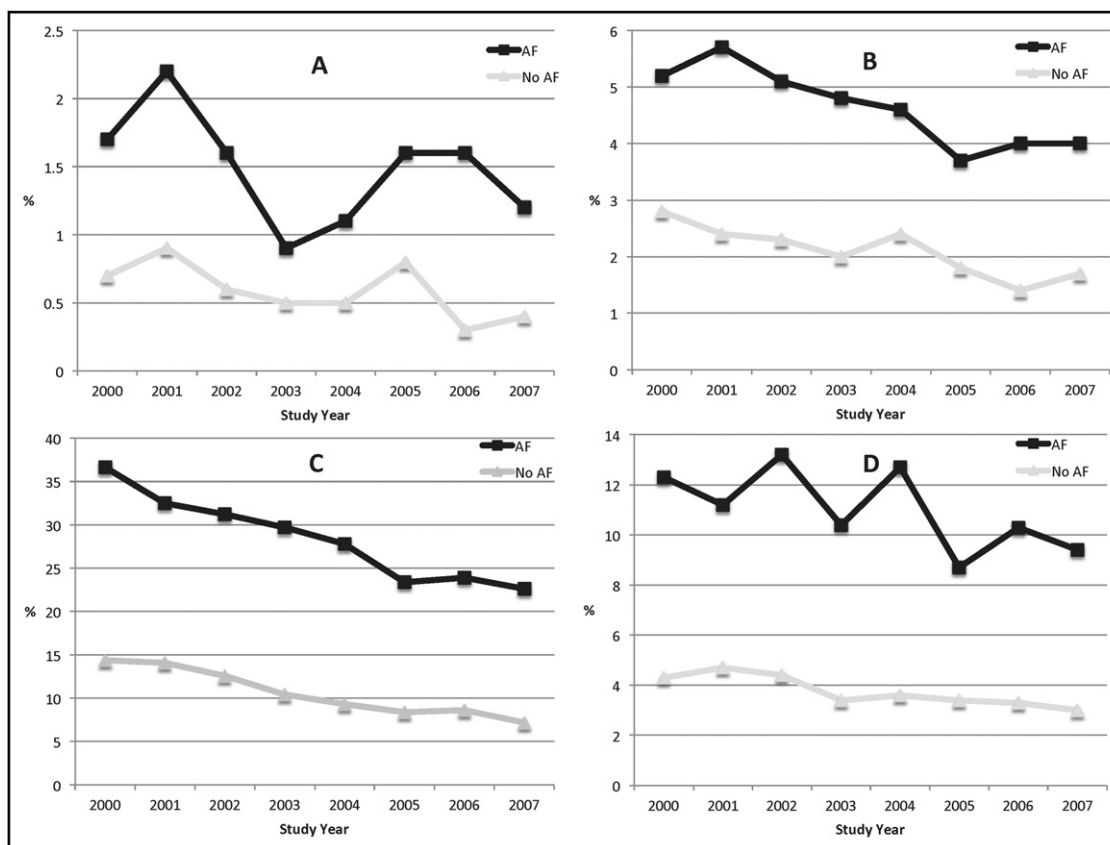


Figure 2 Rates of major in-hospital complications in patients with any type atrial fibrillation hospitalized with an acute coronary syndrome by study year between 2000 and 2007 (A = stroke, B = major bleeding, C = heart failure, D = death). AF = atrial fibrillation.

exerted a beneficial effect on the occurrence rates of new-onset atrial fibrillation in patients who were hospitalized between 2000 and 2007.

As reported in prior investigations, older age, a greater cardiovascular risk factor burden, poorer renal and left ventricular function, and disease-specific clinical status (eg, GRACE risk score) were associated with atrial fibrillation in our population.²⁰ Patients with prior atrial fibrillation also were more likely to have a history of coronary heart disease and prior coronary revascularization. New-onset atrial fibrillation was associated with greater infarct size (eg, maximum troponin level) and severity (eg, ST-segment elevation myocardial infarction), suggesting that the severity of acute coronary syndrome places patients at greater risk for developing atrial fibrillation, irrespective of their baseline cardiovascular risk factor profile.

In-Hospital Treatment and Discharge Prescription Practices

In-hospital and discharge prescription of medications known to improve prognosis from an acute coronary syndrome were lower in patients with atrial fibrillation in comparison with patients without atrial fibrillation. Although low rates of in-hospital clopidogrel and GpIIb/IIIa prescrip-

tion may be explained by provider concerns about the increased risk of bleeding associated with warfarin use, or because fewer patients with atrial fibrillation underwent percutaneous coronary intervention, the underuse of other effective cardiac medications in hospitalized patients with acute coronary syndrome and atrial fibrillation remains a perplexing but reproducible finding.²⁰ Warfarin and amiodarone were commonly used among patients with atrial fibrillation, reflecting the established efficacy of these agents in the treatment of atrial fibrillation.²⁸ However, it should be noted that rates of warfarin prescription were lower in our study than has been reported in other studies.²⁹ This finding may be secondary to provider reluctance to prescribe dual-antiplatelet therapy plus warfarin because of concerns about an increased risk for major bleeding episodes.³⁰

Despite the fact that a greater proportion of patients with atrial fibrillation presented with ST-elevation myocardial infarction, patients with any type of atrial fibrillation were less likely than patients who did not have this arrhythmia to undergo percutaneous coronary intervention. In keeping with their higher disease acuity and poorer overall clinical status, patients with new-onset atrial fibrillation were more likely to have undergone thrombolysis, placement of an

intra-aortic balloon pump, coronary artery bypass grafting, and permanent pacemaker implantation. Our findings suggest that opportunities exist for enhanced prevention of atrial fibrillation and its complications through better application of evidence-based, in-hospital acute coronary syndrome treatments.

In-Hospital Complications and Thirty-Day Mortality

As has been reported in other community-based studies of hospitalized patients with an acute coronary syndrome,²⁸ including a more limited analysis involving GRACE participants, patients with new-onset atrial fibrillation were twice as likely to die during hospitalization than were patients who did not develop atrial fibrillation.^{20,27} The relationship among new-onset atrial fibrillation, stroke, and left ventricular dysfunction likely explains a great deal of the association between atrial fibrillation and increased in-hospital mortality among GRACE participants. No excess 30-day mortality was noted among patients with new-onset atrial fibrillation compared with patients with acute coronary syndrome without atrial fibrillation. This finding could be due to a healthy survivor effect or a lack of power. In contrast to the findings of a prior study,¹⁶ patients with preexisting atrial fibrillation and an acute coronary syndrome were 30% more likely to die while hospitalized, and 40% more likely to have died by 30 days after hospital discharge, than patients without atrial fibrillation. Because atrial fibrillation occurring in the community is associated with the duration and severity of exposure to cardiovascular risk factors, the observed relation between preexisting atrial fibrillation and increased short-term mortality rates likely reflects the more advanced age and greater risk factor burden of patients with a recent or long-standing history of atrial fibrillation.

Trends in Major Hospital Complications in Patients With Atrial Fibrillation

Although the incidence rates of in-hospital stroke did not decline in patients with new-onset atrial fibrillation during the years under study, the rates of all other major in-hospital complications, including death, declined in patients with preexisting and new-onset atrial fibrillation between 2000 and 2007. These findings likely reflect the enhanced monitoring and treatment of hospitalized patients with an acute coronary syndrome in addition to the better and timelier treatment of atrial fibrillation in GRACE participants over time.

Study Strengths and Limitations

The strengths of this study include its large and diverse sample of patients hospitalized with validated acute coronary syndrome in multiple nations and its relatively contemporary perspective into the epidemiology of atrial fibrillation and acute coronary syndrome. As an observational, nonrandomized investigation, however, GRACE is subject

to certain limitations, including missing information and potential confounding by treatment indication or other unmeasured factors. Associations in a large sample such as this one may be statistically significant but not clinically meaningful. The study sample is restricted to patients with atrial fibrillation and hospitalized with an acute coronary syndrome, and findings may differ in patients with atrial fibrillation in the community. Patients who died before reaching study hospitals were excluded, left ventricular systolic function was measured in less than one half of study participants, prescription of antiarrhythmic drugs used in the treatment of atrial fibrillation was not collected, and timing of atrial fibrillation in relation to myocardial injury or receipt of cardiac medications and coronary reperfusion was not recorded.

CONCLUSIONS

In this large multinational study, atrial fibrillation was a common and serious complication in patients hospitalized with an acute coronary syndrome. We observed encouraging declines in the incidence and prevalence rates of atrial fibrillation, likely reflecting enhanced treatment efforts. Nevertheless, preexisting and new-onset atrial fibrillation remained associated with an increased risk of important cardiovascular, renal, and bleeding complications, as well as increased in-hospital mortality. Efforts remain warranted to improve the primary and secondary prevention of all patients hospitalized with an acute coronary syndrome, but particularly among those with preexisting atrial fibrillation and groups identified in this study as being at high risk for new-onset atrial fibrillation.

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