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Atrial Fibrillation in the Setting of Acute Myocardial Infarction: The GUSTO-I Experience

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Objectives. **We examined the clinical predictors and angiographic and clinical outcomes associated with atrial fibrillation in the setting of acute myocardial infarction (MI).**

Background. **This condition has been studied primarily in prethrombolytic era small trials.**

Methods. **We compared baseline clinical characteristics, short-term clinical and angiographic outcomes and 1-year mortality of patients enrolled in the Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (GUSTO-I) trial with atrial fibrillation on admission electrocardiography (n = 1,026 [2.5%]) or after enrollment (n = 3,254 [7.9%]) and those without atrial fibrillation (n = 36,611 [89.6%]). Univariable and multivariable analyses were used to assess relations between baseline factors and the development of atrial fibrillation.**

Results. **Patients with any atrial fibrillation more often had three-vessel coronary artery disease and initial Thrombolysis in Myocardial Infarction (TIMI) grade <3 flow than those without the arrhythmia. In-hospital stroke was increased in patients with atrial fibrillation (3.1% vs. 1.3%, p = 0.0001), mainly ischemic stroke (1.8% vs. 0.5%, p = 0.0001). Significant multivariable predictors of later atrial fibrillation included advanced age, higher peak creatine kinase levels, worse Killip class and increased heart rate. The unadjusted mortality rate was significantly higher at 30 days (14.3% vs. 6.2%, p = 0.0001) and at 1 year (21.5% vs. 8.6%, p < 0.0001) in patients with atrial fibrillation. The adjusted 30-day mortality rate remained significantly higher with any (odds ratio [OR] 1.3, 95% confidence interval [CI] 1.2 to 1.4) or later (OR 1.4, 95% CI 1.3 to 1.5) atrial fibrillation but not with baseline atrial fibrillation (OR 1.1, 95% CI 0.88 to 1.3).**

Conclusions. **Atrial fibrillation in the setting of acute MI independently predicts stroke and 30-day mortality. More aggressive treatment strategies in this subgroup may be warranted and deserve further study.**

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Atrial fibrillation is a common complication of acute myocardial infarction (MI), with a reported incidence of 7% to 18% (1–12). Its etiology may include left ventricular dysfunction with hemodynamic disturbances (1–6), pericarditis (7), metabolic abnormalities, excess catecholamine release or iatrogenic factors (e.g., use of sympathomimetic drugs) (8). Left atrial ischemia or infarction may also be a cause, particularly in patients who develop atrial fibrillation within 3 h of MI onset (9).

Advanced age and congestive heart failure are two factors associated with atrial fibrillation after MI (10–12). Female gender has been implicated, but MI location and enzyme levels have proven less helpful (2,6,10–12). Although angiographic data are few, this population may also have more severe coronary artery disease (13).

The relation of atrial fibrillation to patient outcomes has been evaluated (14–16). Although some studies have shown increased in-hospital mortality with this arrhythmia (6,10), this finding has not been consistent (7), especially after adjustment for congestive heart failure, previous MI, cardiogenic shock, ventricular tachycardia and ventricular fibrillation (11,12). Atrial fibrillation may simply reflect an overall poorer clinical status—hemodynamic instability, decreased left ventricular function and larger infarction. Thus, despite the prevalence of this complication, many issues remain unresolved.

Most studies of atrial fibrillation in acute MI have been relatively small and were performed in the prethrombolytic era in only a few tertiary centers. The large Global Utilization of Streptokinase and TPA (alteplase) for Occluded Coronary Arteries (GUSTO-I) trial allows an exploration of this topic in the thrombolytic era (17,18). We assessed the incidence of atrial fibrillation in acute MI, the clinical and angiographic risk factors related to its development and its association with in-hospital, 30-day and 1-year outcomes.

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Abbreviations and Acronyms

aPTT	=	activated partial thromboplastin time
CABG	=	coronary artery bypass graft surgery
CI	=	confidence interval
CK	=	creatine kinase
ECG	=	electrocardiogram, electrocardiographic
GUSTO-I	=	Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (trial)
MI	=	myocardial infarction
OR	=	odds ratio
PTCA	=	percutaneous transluminal coronary angioplasty
TIMI	=	Thrombolysis In Myocardial Infarction

Methods

Patients. Enrollment criteria for GUSTO-I included presentation to the hospital within 6 h of symptom onset, with chest pain lasting ≥20 min and accompanied by electrocardiographic (ECG) signs of ≥0.1-mV ST segment elevation in two or more limb leads or ≥0.2 mV in two or more contiguous precordial leads (17). Exclusion criteria included previous stroke, active bleeding and recent trauma or major surgical intervention. Data from 40,891 patients (99.7%) were complete for analysis; other patients (n = 130) were excluded.

We reviewed case report form and baseline ECG data on all patients to obtain information about atrial fibrillation. Patients who had "Yes" checked on the case report form were included in the "Any" category (n = 4,278), as were patients with missing case report form data whose baseline ECG showed the arrhythmia (n = 2). This group was further classified into those who had atrial fibrillation at "Entry" and those who developed the arrhythmia "Post-admission." The "Entry" group included patients whose baseline ECG showed atrial fibrillation (reviewed by the ECG core laboratory and defined as the absence of P waves, atrial activity represented by fibrillatory waves and irregular RR intervals [n = 1,026]). All other patients who had "Yes" checked on the case report form were counted in the "Post-admission" category (n = 3,254). This classification was an attempt to separate patients with acute versus chronic atrial fibrillation and to determine whether this difference had any further effect on outcomes. Patients who had "No" checked on the form and whose baseline ECG showed no atrial fibrillation were counted in the "None" group.

Treatment strategies. Patients were randomized to receive streptokinase with subcutaneous heparin, streptokinase with intravenous heparin, accelerated alteplase with intravenous heparin or the combination of alteplase and streptokinase with intravenous heparin (17). Subcutaneous heparin (12,500 U twice daily) was continued for 7 days or until discharge; intravenous heparin (5,000-U bolus, 1,000 U/h, adjusted to keep the activated partial thromboplastin time [aPTT] between 60 and 85 s) was given for 48 h or longer at the investigator's discretion. Chewable aspirin (≥160 mg) was given at enrollment and daily thereafter (160 to 325 mg/day). Patients with no contraindications were to receive intravenous atenolol, 10 mg, in two doses, then 50 to 100 mg orally daily. The use of other medications or procedures was at the discretion of the attending physician.

Angiography. In patients not randomized to the angiographic substudy (18), angiography was performed per institution protocol. Ejection fraction was calculated using the area–length method (19).

End points. The primary end point of the study was death from any cause at 30 days. Other major clinical outcomes assessed included the combined end point of death and disabling stroke. Hemorrhagic and ischemic stroke, reinfarction, ischemia, shock and congestive heart failure or pulmonary edema were also assessed (17).

Statistical analysis. Categoric baseline characteristics of patients with no atrial fibrillation, those with atrial fibrillation at entry, those developing it after admission and those with any atrial fibrillation were compared by summarizing frequencies and percentages. Continuous data were compared after summarizing them as percentiles or mean value ± SD. Binary outcome variables also were reported as percentages.

We performed univariable chi-square analyses of the risk of atrial fibrillation associated with peak creatine kinase (CK) level and the 15 baseline clinical predictors of 30-day mortality in this cohort (20). For continuous variables, transformations or spline functions were used as appropriate. Variables with some predictive value were then tested in a multiple logistic regression model to identify independent predictors of later atrial fibrillation. We calculated adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the ability of these variables to predict the arrhythmia.

Results

Clinical characteristics. The overall incidence of atrial fibrillation in this population was 10.4%. The most important univariable predictors of atrial fibrillation were older age, increased heart rate, Killip class, no current smoking and lower systolic blood pressure (Table 1). Other variables associated with this arrhythmia included previous hypertension or cerebrovascular disease, no previous smoking, diabetes mellitus and female gender. Although their relative importance varied slightly, these factors remained predictive when the timing of atrial fibrillation was considered (at entry vs. after admission). Location of infarction and time to thrombolytic therapy were less helpful in all groups.

Angiographic characteristics. Patients with atrial fibrillation had more severe coronary artery disease, more right coronary involvement, poorer reperfusion and a lower ejection fraction than those without the arrhythmia (Table 2). These angiographic patterns held when patients with atrial fibrillation were classified into those with the arrhythmia at entry and those who developed it after hospital admission.

Treatment. Patients with atrial fibrillation were more commonly treated with digoxin and calcium channel antagonists but were less likely to receive beta-adrenergic blocking agents

Table 1. Baseline Clinical Characteristics

Characteristic	Atrial Fibrillation			Timing of Atrial Fibrillation	
	None (n = 36,611)	Any (n = 4,280)	Chi-Square*	At Entry (n = 1,026)	After Admission (n = 3,254)
Age (yr)	60 ± 12	67 ± 11	1,357	67 ± 11	68 ± 10
HR (beats/min)	75 ± 17	80 ± 23	393	87 ± 28	77 ± 20
Killip class			344		
I	31,551 (86.6)	3,189 (75.0)		778 (76)	2,413 (75)
II	4,256 (11.7)	854 (20.1)		202 (20)	652 (20)
III	409 (1.1)	139 (3.3)		27 (3)	112 (4)
IV	238 (0.7)	73 (1.7)		16 (2)	57 (2)
Current smoker	16,088 (44.1)	1,387 (32.7)	214	351 (35)	1,038 (32)
SBP (mm Hg)	129.4 ± 23.2	125.3 ± 24.6	119	126 ± 24	123 ± 25
DBP (mm Hg)	78.3 ± 14.8	75.9 ± 15.7	85	76 ± 15	76 ± 17
Hypertension	13,621 (37.3)	1,895 (44.5)	78	445 (44)	1,451 (45)
Former smoker	25,480 (70.2)	2,678 (63.5)	73	629 (63)	2,051 (64)
Female	8,983 (24.5)	1,305 (30.5)	61	318 (31)	989 (30.4)
Previous MI	5,818 (15.9)	867 (20.3)	50	191 (19)	676 (21)
Diabetes	5,244 (14.4)	752 (17.6)	29	163 (16)	589 (18)
Weight (kg)	79.6 ± 15.6	78.3 ± 15.9	25	79 ± 17	78 ± 16
Height (cm)	171.3 ± 9.3	171.0 ± 9.8	16	171 ± 10	171 ± 10
Location of MI			9		
Anterior	14,211 (38.9)	1,708 (40.0)		343 (33)	1,366 (42)
Inferior	21,014 (57.6)	2,437 (57.1)		645 (63)	1,793 (55)
Other	1,226 (3.4)	122 (2.9)		38 (4)	84 (3)
Time to thrombolytic therapy (h)	3.1 ± 1.6	3.2 ± 1.7	7	3.1 ± 1.7	3.3 ± 1.5
Treatment					
Accelerated alteplase	9,354 (25.6)	1,013 (23.7)		250 (24)	764 (24)
SK+IV heparin	9,232 (25.2)	1,152 (26.9)		265 (26)	887 (27)
Combination alteplase+SK	9,291 (25.4)	1,039 (24.3)		251 (25)	789 (24)
SK+SQ heparin	8,734 (23.9)	1,074 (25.1)		260 (25)	814 (25)

*For univariable logistic regression model for relation of each variable with occurrence of any atrial fibrillation. Data presented are mean value ± SD or number (%) of patients. DBP = diastolic blood pressure; HR = heart rate; IV = intravenous; MI = myocardial infarction; SBP = systolic blood pressure; SK = streptokinase; SQ = subcutaneous.

(Table 3). Cardioversion was more frequent in patients with any atrial fibrillation.

In-hospital outcomes. Death, reinfarction, cardiogenic shock, heart failure, ventricular fibrillation and asystole occurred more often in patients with (overall and by time of arrhythmia) than without this arrhythmia (all $p < 0.0001$) (Table 4). In-hospital stroke was also significantly increased in patients with the arrhythmia (overall and by time of arrhythmia, all $p < 0.001$), mostly related to ischemic events. Although more intracranial hemorrhages occurred in patients with atrial fibrillation ($p = 0.037$), this difference was not significant after adjustment for baseline predictors of this event ($p = 0.10$) (21). The length of stay (both intensive care unit and total hospital stay) was longer in patients with atrial fibrillation, particularly if they developed it after enrollment.

Outcomes at 30 days and 1 year. The unadjusted 30-day mortality rate was higher in patients with than without atrial fibrillation (Fig. 1), regardless of when the arrhythmia developed. After adjustment for baseline differences, the 30-day mortality rate remained significantly higher in the group with any atrial fibrillation (OR 1.3, 95% CI 1.2 to 1.4) and in patients who developed the arrhythmia after admission (OR 1.4, 95% CI 1.3 to 1.5) but not in those with the arrhythmia at entry (OR 1.1, 95% CI 0.88 to 1.3).

Patients who underwent coronary artery bypass graft surgery (CABG) developed atrial fibrillation more often than patients who did not (20.9% vs. 6.7%). Of all patients who developed atrial fibrillation, 22% had CABG. Although we could not determine the timing of the arrhythmia in relation to CABG, patients who did and did not undergo CABG had similar rates of atrial fibrillation at entry (2.1% and 2.5%, respectively). The development of atrial fibrillation was somewhat less predictive of mortality among patients undergoing CABG (OR 1.25, 95% CI 0.85 to 1.82 vs. OR 1.51, 95% CI 1.33 to 1.72 for no CABG).

The unadjusted 1-year mortality rate was significantly higher (and similar) in patients who presented with or developed atrial fibrillation than in those without the arrhythmia (Fig. 2).

Multivariable model. The most important predictor of developing atrial fibrillation was age (adjusted OR 3.20, 95% CI 2.99 to 3.43) (Table 5, Fig. 3). Other significant predictors (in decreasing order) included peak CK level, Killip class, heart rate, systolic blood pressure and height. Patients treated

Table 2. Angiographic Characteristics*

Characteristic	Atrial Fibrillation		p Value	Timing of Atrial Fibrillation	
	None (n = 36,611)	Any (n = 4,280)		At Entry (n = 1,026)	After Admission (n = 3,254)
Angiography	20,343 (55.7)	2,309 (54.1)	0.051	467 (45.7)	1,843 (56.8)
Infarct-related artery					
LAD	7,382 (36.7)	779 (34.1)	0.001	116 (25.0)	664 (36.4)
LCx	2,372 (11.8)	252 (11.0)		64 (13.8)	188 (10.3)
RCA	9,074 (45.1)	1,091 (47.7)		243 (52.3)	848 (46.5)
LMCA	72 (0.4)	20 (0.9)		6 (1.3)	14 (0.8)
Bypass graft	341 (1.7)	41 (1.8)		6 (1.3)	35 (1.9)
Unknown	864 (4.3)	103 (4.5)		29 (6.2)	74 (4.1)
No. diseased vessels					
0	1,541 (9.0)	105 (5.4)	0.0001	39 (10.2)	66 (4.2)
1	8,043 (47.2)	696 (35.8)		168 (44.0)	528 (33.8)
2	4,674 (27.4)	595 (30.6)		101 (26.4)	494 (31.6)
3	2,801 (16.4)	548 (28.2)		74 (19.4)	474 (30.4)
TIMI flow grade					
<3	6,146 (50.9)	737 (58.1)	0.0001	157 (58.6)	580 (57.9)
3	5,933 (49.1)	532 (41.9)		111 (41.4)	421 (42.1)
LVEF (%)	52.2 ± 12.9	49.1 ± 13.5	0.001	48.7 ± 13.2	49.1 ± 13.5

*Includes patients in angiographic substudy. Data presented are mean value ± SD or number (%) of patients. LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; RCA = right coronary artery; TIMI = Thrombolysis in Myocardial Infarction.

with accelerated alteplase were less likely to develop atrial fibrillation. Although significant, previous hypertension and inferior location of infarction were less important in the multivariable analysis.

Discussion

Atrial fibrillation continues to be a significant complication of acute MI, with an incidence of 10.4% in the present study. Atrial fibrillation is also a marker of higher risk baseline clinical and angiographic features. As with previous studies (10–12), age was found to be an important independent predictor of this arrhythmia. Patients treated with accelerated alteplase were less likely to develop atrial fibrillation. Although we could not ascertain the precise etiology of this rhythm disturbance, the observation that worse Killip class, increased heart rate and lower blood pressure were associated with atrial fibrillation suggests that hemodynamic compromise is the most likely mechanism. This is consistent with other studies (3,6) that found more unfavorable invasive hemodynamic measures in patients who later developed atrial fibrillation than in those who did not.

Table 3. Treatments

Therapy	Atrial Fibrillation*		Timing of Atrial Fibrillation	
	None (n = 36,611)	Any (n = 4,280)	At Entry (n = 1,026)	After Admission (n = 3,254)
Digoxin	2,999 (8.2)	2,488 (58.3)	431 (42.1)	2,058 (63.4)
Beta-blockers				
Intravenous	16,464 (45.0)	1,710 (40.0)	402 (39.2)	1,308 (40.2)
Oral	26,516 (72.5)	2,557 (59.9)	601 (58.6)	1,957 (60.3)
Ca-channel antagonists	10,885 (29.8)	1,550 (36.4)	312 (30.4)	1,239 (38.2)
Cardioversion	702 (2.1)	264 (7.9)	53 (6.4)	211 (8.4)

*p = 0.0001 for all comparisons. Data presented are number (%) of patients. Ca = calcium.

Angiographic characteristics. The most important angiographic finding is that atrial fibrillation denoted more extensive coronary artery disease and poorer reperfusion of the infarct-related artery. This may have important patient management implications. Because these patients more often have three-vessel disease and impaired left ventricular function, they may derive benefit from early catheterization with appropriate triage to revascularization if the situation warrants. Finally, this study, with a sample size adequate to estimate infarct-related artery location reliably (5,9,22), only weakly implicates right coronary artery involvement, suggesting that actual territories at risk—including the sinoatrial node, the atrioventricular node, and the atria—are less important in the pathogenesis of atrial fibrillation than inadequate reperfusion with resultant derangement in local and global hemodynamics.

In-hospital complications. Patients with atrial fibrillation, particularly those with later onset, had a more complicated hospital course than those without the arrhythmia. Reinfarction and recurrent ischemia were more common in this group, which correlates with the angiographic findings of lesser reperfusion and more extensive coronary artery disease. Heart failure and cardiogenic shock were also more frequent in this

Table 4. Clinical Outcomes

	Atrial Fibrillation			Timing of Atrial Fibrillation	
	None (n = 36,611)	Any (n = 4,280)	p Value	At Entry (n = 1,026)	After Admission (n = 3,254)
Mortality (unadjusted)					
In-hospital	2,104 (5.8)	591 (13.8)	0.0001	149 (14.6)	442 (13.6)
30 d	2,219 (6.1)	611 (14.3)	0.0001	149 (14.6)	462 (14.2)
1 yr	(8.4)*	(21.5)*	< 0.0001	(22.2)*	(21.2)*
Stroke	467 (1.3)	133 (3.1)	0.0001	30 (2.9)	103 (3.2)
Hemorrhagic	230 (0.6)	38 (0.9)	0.037	10 (1.0)	28 (0.9)
Hemorrhagic conversion	26 (0.07)	8 (0.19)		2 (0.2)	6 (0.2)
Ischemic	172 (0.5)	75 (1.8)	0.0001	14 (1.4)	61 (1.9)
Unknown	31 (0.08)	12 (0.28)		4 (0.4)	8 (0.3)
Time to ischemic stroke from symptom onset (d)	3.0	5.3		17	5.7
Death or disabling stroke	2,374 (6.5)	663 (15.5)	0.0001	158 (15.4)	505 (15.5)
Peak total CK (IU/liter)	1,883 ± 1,809	2,348 ± 2,092	0.0001	2,086 ± 2,248	2,430 ± 2,034
CK-MB fraction	178 ± 214	217 ± 254	0.0001	185 ± 189	226 ± 269
Reinfarction	1,306 (3.6)	319 (7.5)	0.0001	45 (4.4)	274 (8.4)
Recurrent ischemia	6,989 (19.1)	1,131 (26.5)	0.0001	166 (16.2)	965 (29.7)
Cardiogenic shock	1,786 (4.9)	649 (15.2)	0.0001	134 (13.1)	515 (15.9)
CHF or pulmonary edema	5,058 (13.8)	1,560 (36.5)	0.0001	299 (29.2)	1,261 (38.8)
Angioplasty	6 (0.04)	2 (0.1)	0.0001	181 (17.8)	564 (17.4)
Bypass surgery	2,702 (7.4)	813 (19.1)	0.0001	77 (7.5)	736 (22.7)
Arrhythmias					
Sustained VT	1,888 (5.2)	633 (14.8)	0.0001	126 (12.3)	507 (15.6)
Ventricular fibrillation	2,110 (5.8)	628 (14.7)	0.0001	139 (13.6)	489 (15)
AV block†	2,595 (7.1)	789 (18.5)	0.0001	127 (12.4)	662 (20.4)
Asystole	1,762 (4.8)	579 (13.6)	0.0001	130 (12.7)	449 (13.8)
ICU stay (d)	4 ± 3	6 ± 4	0.0001	5.0 ± 3.8	6.2 ± 4.6
Hospital stay (d)	10 ± 9	13 ± 11	0.0001	10.9 ± 13.0	14.3 ± 10.0

*Kaplan-Meier estimates. †Second or third degree. Data presented are mean value ± SD or number (%) of patients. AV = atrioventricular; CK = creatine kinase; CHF = congestive heart failure; d = days; ICU = intensive care unit; VT = ventricular tachycardia.

group, which may relate to the altered hemodynamic variables from the loss of atrial contraction and more severe ischemia (supported by angiographic findings and higher CK levels in those with atrial fibrillation). Finally, patients with atrial fibrillation more often developed other arrhythmias, such as advanced atrioventricular conduction disturbances, ventricular

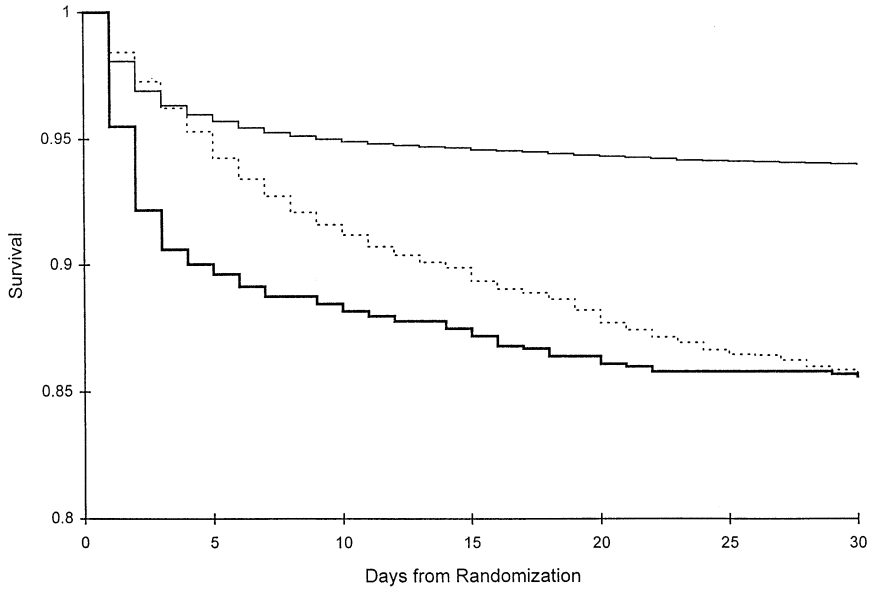

Figure 1. Kaplan-Meier estimate of 30-day mortality rate among patients with no atrial fibrillation **(thin solid line)** and among those with this arrhythmia at entry **(thick solid line)** or after admission **(dotted line).**

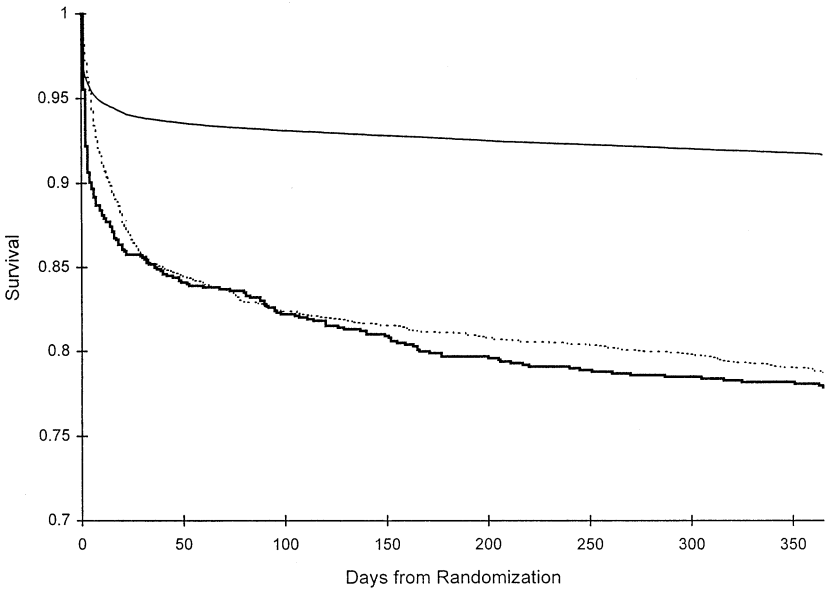

Figure 2. Kaplan-Meier estimate of 1-year mortality rate among patients with no atrial fibrillation **(thin solid line)** and among those with this arrhythmia at entry **(thick solid line)** or after admission **(dotted line).**

tachycardia and ventricular fibrillation. Although this finding could reflect many factors, the more prevalent use of digoxin, calcium-channel antagonists and antiarrhythmic agents is most likely important.

Patients with chronic atrial fibrillation have a higher risk of ischemic cerebrovascular events than those with normal sinus rhythm (23,24). Oral anticoagulants and the maintenance of sinus rhythm can reduce the later incidence of stroke and can particularly benefit high risk patients (23,24). This study shows that atrial fibrillation occurring in the peri-infarct period is independently associated with stroke (in-hospital incidence of 3.1% for any atrial fibrillation vs. 1.3% for no atrial fibrillation), driven primarily by an increase in ischemic events (1.8% vs. 0.5%). More aggressive therapy in this population (anticoagulation and early cardioversion) may improve outcomes, but this issue needs further study before implementation.

Table 5. Independent Clinical Predictors of Atrial Fibrillation After Acute Myocardial Infarction

Characteristic	Adjusted Chi-Square	OR (95% CI)
Age (yr)	1,116	3.20 (2.99–3.43)
Peak CK (IU/liter)	384 (4 df)	1.88 (1.69–2.09)
Killip class (IV vs. I)	154 (3 df)	3.28 (2.28–4.71)
HR (beats/min)	137 (4 df)	1.16 (1.05–1.27)
SBP (mm Hg)	108	0.77 (0.73–0.81)
Height (cm)	63	1.32 (1.23–1.41)
Female gender	27	1.35 (1.20–1.51)
Previous MI	23	1.27 (1.15–1.39)
Time to treatment (h)	22 (4 df)	0.84 (0.76–0.92)
Previous hypertension	21	1.20 (1.11–1.3)
Previous CVD	17	1.53 (1.25–1.88)
Thrombolytic regimen*	15 (3 df)	0.82 (0.74–0.92)
Inferior MI	9.8 (2 df)	0.79 (0.63–0.99)
Diabetes mellitus	8.3	1.16 (1.05–1.28)

*Accelerated alteplase versus streptokinase with intravenous heparin. CI = confidence interval; CVD = cerebrovascular disease; df = degrees of freedom; OR = odds ratio; other abbreviations as in Tables 1 and 4.

Mortality. Studies have attempted to determine the relation between atrial fibrillation and mortality in patients with acute MI (1–10). Two recent, large studies found a higher incidence of in-hospital and long-term mortality in patients with than without atrial fibrillation (11,12). However, after adjustment for other variables known to affect prognosis, no independent relation of atrial fibrillation with in-hospital mortality was shown by either group. The results differed for long-term mortality; with multivariable analysis, Behar et al. (11) found that it independently predicted long-term mortality, whereas Goldberg et al. did not (12).

In the present study, the mortality rate was much lower than that reported previously (in-hospital mortality rate in patients with and without atrial fibrillation 13.8% and 5.9%, respectively, vs. 25.5% and 16.2% in the Secondary Prevention Reinfarction Israeli Nifedipine Trial [SPRINT] registry) (11). This finding reflects in part the changing management of patients with acute MI, including improved technology and medical regimens (e.g., thrombolytic agents, aspirin, beta-blockers and angiotensin-converting enzyme inhibitors). It is also a function of the population studied; all patients enrolled in GUSTO-I were thrombolytic eligible and would be expected to have a better prognosis than those from prethrombolytic era studies.

The unadjusted mortality rate in this trial was significantly higher at both 30 days and 1 year in patients with atrial fibrillation (at entry, after admission and overall) than in those with normal sinus rhythm. However, after correction for baseline risk, only postadmission and overall atrial fibrillation were independently associated with increased 30-day mortality; those with atrial fibrillation at entry were not at significantly increased risk. This could relate to patients with chronic atrial fibrillation being included in the entry group, which would not have been as related to size and consequence of the

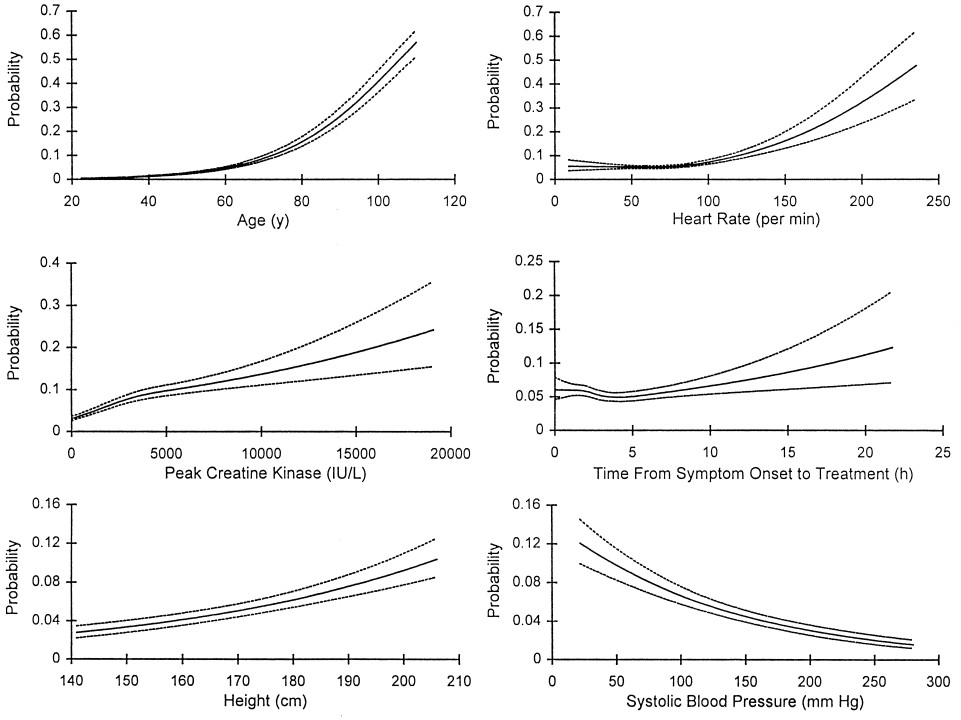

Figure 3. Adjusted (multivariable) probabilities for development of atrial fibrillation **(solid lines)** with 95% CIs **(dotted lines)** as a function of selected continuous baseline variables.

acute MI as later atrial fibrillation would. Nevertheless, any atrial fibrillation remains a useful marker of patients who are more critically ill. These patients should be monitored carefully in the peri-infarct period.

Study limitations. One limitation of our study concerns the lack of precise timing of onset and duration of atrial fibrillation. Patients in the entry group may have developed atrial fibrillation during the acute MI but before enrollment. We had no information about the duration of atrial fibrillation after discharge and thus cannot comment about the effects of paroxysmal versus long-term atrial fibrillation. In addition, although we adjusted for known baseline predictors of death, our mortality results may have been affected by other factors, including events that occurred from enrollment to development of atrial fibrillation, such as CABG.

Certain patient management issues remain ill-defined. Because we did not have detailed information about the use of antiarrhythmic therapy, the relation between these agents and patient outcomes could not be evaluated. Similar questions about elective cardioversion, anticoagulation and medications used for rate control need to be addressed. The data being prospectively collected from patients with atrial fibrillation in the GUSTO-III trial should provide insight into these important issues.

Conclusions. Atrial fibrillation remains a common complication of acute MI in the thrombolytic era. Because of their lower ejection fraction, more severe coronary artery disease and greater frequency of incomplete reperfusion, patients with this arrhythmia should be considered for early angiography and revascularization. These patients, particularly those who develop atrial fibrillation after admission, also have a more complicated hospital course and tend to have worse outcomes (including stroke and overall mortality). A more aggressive approach to management, including close monitoring, anticoagulation and cardioversion, may be warranted.

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