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Management and outcome of patients with atrial fibrillation during acute myocardial infarction: the GUSTO-III experience

C-K Wong, H D White, R G Wilcox, D A Criger, R M Califf, E J Topol, E M Ohman, for the GUSTO-III Investigators

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See end of article for authors' affiliations

Correspondence to: Professor Harvey D White, Department of Cardiology, Green Lane Hospital, Private Bag 92-189, Auckland 1030, New Zealand; harveyw@adhb.govt.nz

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Objective: To investigate the use of antiarrhythmic agents and electrical cardioversion in the management of patients with atrial fibrillation complicating acute myocardial infarction, and their relation to 30 day and one year mortality.
Design: Prospective study of 1138 patients with atrial fibrillation from the GUSTO-III trial.
Interventions: Of the 1138 study patients, 317 (28%) received antiarrhythmic treatment, including class I antiarrhythmic agents (12%), sotalol (5%), and amiodarone (15%); electrical cardioversion was attempted in 116 (10%).
Results: Sinus rhythm was restored in 72% of patients receiving class I antiarrhythmic agents, 67% of those receiving sotalol, 79% of those receiving amiodarone, and 64% of those having electrical cardioversion. After adjusting for baseline characteristics and complications occurring before the onset of atrial fibrillation, there was no difference among the treatment groups in the incidence of sinus rhythm at the time of discharge or before deterioration to hospital death. However, the use of class I antiarrhythmic drugs or sotalol was associated with a lower unadjusted 30 day and one year mortality. After adjustment for baseline factors and pre-atrial fibrillation complications, the odds ratios for 30 day and one year mortality were 0.42 (95% confidence interval (CI) 0.19 to 0.89) and 0.58 (95% CI 0.33 to 1.04) with class I agents, and 0.31 (95% CI 0.07 to 1.32) and 0.31 (95% CI 0.09 to 1.02) with sotalol. In contrast, there was no association between the use of amiodarone or electrical cardioversion and 30 day or one year mortality.
Conclusions: There was a strong trend towards lower mortality associated with the use of class I antiarrhythmic agents or sotalol in managing patients with atrial fibrillation after acute myocardial infarction. Randomised trials are indicated.

Atrial fibrillation during acute myocardial infarction can occur secondary to postinfarction complications but when it occurs independently it carries a worse prognosis.[1] Of 13 858 patients who were in sinus rhythm when enrolled in the GUSTO-III trial (global use of strategies to open occluded coronary arteries), the odds ratio for 30 day mortality in the 906 patients with versus those without the development of new atrial fibrillation was 1.49 (95% confidence interval (CI) 1.17 to 1.89), after adjusting for baseline differences and prespecified postmyocardial infarction complications occurring before the onset of atrial fibrillation.[1] There is, however, scant information about whether treatment of atrial fibrillation after thrombolysis in patients with acute myocardial infarction alters mortality.

Although antiarrhythmic drugs may prevent the development of atrial fibrillation or restore sinus rhythm if atrial fibrillation has occurred, the proarrhythmic and negative inotropic effects of these drugs may have harmful sequelae. Meta-analysis of randomised controlled trials of quinidine for maintaining sinus rhythm after electrical cardioversion showed that it was more effective than placebo in suppressing recurrent atrial fibrillation. However, quinidine was also associated with higher mortality.[2] Various antiarrhythmic drugs have been compared in the management of atrial fibrillation, and recently amiodarone was reported to be more effective than sotalol or propafenone in preventing recurrence of atrial fibrillation.[3] In the postinfarction setting, however, published reports on the treatment of atrial fibrillation are limited, despite the many investigations of antiarrhythmic agents for preventing ventricular arrhythmias and sudden cardiac death.[4–6]

In this prospective substudy of the GUSTO-III trial, we investigated the effects of different early management strategies for atrial fibrillation on 30 day and one year mortality, including the use of drugs and electrical cardioversion. Complications of myocardial infarction occurring before the development of atrial fibrillation were analysed in detail[1] in order to determine the real impact of the antiarrhythmic treatment on outcome.

METHODS

Patients

The enrolment criteria for the GUSTO-III trial[7] included presentation within six hours with prolonged ischaemic symptoms of acute myocardial infarction and ST segment elevation or new onset left bundle branch block on the ECG. There were no exclusions on account of age. Patients were randomised to receive either recombinant plasminogen activator (reteplase) or tissue plasminogen activator (alteplase). All patients received aspirin and heparin. The primary end point was mortality within 30 days; the secondary end point was mortality at one year follow up. Prespecified complications of myocardial infarction were recorded.[1 7]

Abbreviations: CAST, cardiac arrhythmia suppression trial; CI, confidence interval; GUSTO, global use of strategies to open occluded coronary arteries; NS, non-significant; SWORD, survival with oral d-sotalol

Table 1 Baseline characteristics and mortality in patients with atrial fibrillation in the GUSTO-III trial

	All patients (n=1138)	Patients with no history of previous AF (n=883)	Patients with history of paroxysmal AF (n=117)	Patients with history of chronic AF (n=138)
Age (years)*	71 (63, 77)	70 (63, 77)	72 (65, 78)	72 (67, 78)‡
Male sex	749 (66%)	596 (67%)	64 (55%)†	89 (64%)
Height (cm)*	170 (163, 177)	170 (163, 177)	170 (160, 177)	170 (165, 178)
CHD risk factors				
Smoking				
Current	297 (26%)	240 (27%)	33 (28%)	24 (18%)
Previous	426 (38%)	330 (38%)	38 (32%)	58 (42%)
Never	408 (36%)	307 (35%)	46 (39%)	55 (40%)
Hypertension	561 (49%)	423 (48%)	57 (49%)	81 (59%)*
Diabetes mellitus	218 (19%)	168 (19%)	20 (17%)	30 (22%)
Hypercholesterolaemia	352 (31%)	284 (33%)	35 (30%)	33 (24%)
History of:				
MI	266 (23%)	189 (21%)	31 (26%)	46 (33%)†
Angina	521 (46%)	392 (44%)	58 (50%)	71 (51%)
Cerebrovascular disease	40 (4%)	23 (3%)	8 (7%)*	9 (7%)*
CABG	44 (4%)	28 (3%)	4 (3%)	12 (9%)†
PTCA	60 (5%)	45 (5%)	7 (6%)	8 (6%)
CHF	78 (7%)	42 (5%)	12 (10%)*	24 (17%)‡
Thrombolytic treatment	59 (5%)	37 (4%)	10 (9%)*	12 (9%)*
Systolic BP (mm Hg)*	130 (113, 150)	130 (113, 149)	130 (115, 150)	133 (116, 157)
Diastolic BP (mm Hg)*	80 (68, 90)	78 (67, 90)	80 (70, 92)	80 (70, 90)†
Pulse (beats/min)*	77 (64, 92)	76 (63, 90)	80 (66, 107)‡	82 (66, 100)†
Killip class				†
I	845 (75%)	668 (76%)	85 (73%)	92 (67%)
II	239 (21%)	179 (20%)	26 (22%)	34 (25%)
III	28 (2%)	16 (2%)	3 (3%)	9 (7%)
IV	19 (2%)	13 (1%)	3 (3%)	3 (2%)
Infarct location				
Anterior	558 (49%)	424 (48%)	54 (46%)	80 (58%)
Inferior	530 (47%)	426 (48%)	54 (46%)	50 (36%)
Other	46 (4%)	31 (4%)	8 (7%)	7 (5%)
Time to treatment (hours)*	3 (2, 4)	3 (2, 4)	3 (2,4)	3 (2, 4)
Mortality				
24 hours	35 (3%)	28 (3%)	2 (2%)	5 (4%)
48 hours	50 (4%)	37 (4%)	4 (3%)	9 (7%)
In-hospital	169 (15%)	125 (14%)	17 (15%)	27 (20%)
30 days	186 (16%)	137 (16%)	18 (15%)	31 (22%)*
1 year	272 (24%)	195 (22%)	28 (24%)	49 (36%)‡

*Data are presented as median (25th, 75th centiles); all others are actual patient numbers with percentages.
*p < 0.05, †p < 0.01, ‡p < 0.001 *v* patients with no history of previous AF.
AF, atrial fibrillation; BP, blood pressure; CABG, coronary artery bypass grafting; CHF, congestive heart failure; CHD, coronary heart disease; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

This prospective substudy of atrial fibrillation began two months after the main trial was launched,[7] and by eight months all GUSTO-III study sites were participating in it. A separate clinical report form recorded data on the occurrence and treatment of the first episode of atrial fibrillation occurring after the time of enrolment. The site investigator enrolled all patients with any clinically significant atrial fibrillation diagnosed from the time of GUSTO-III study recruitment to hospital discharge or 30 days.

In all, 1138 patients with atrial fibrillation were enrolled. The following data were recorded:

- history of paroxysmal or chronic atrial fibrillation (including persistent atrial fibrillation for prolonged periods) before myocardial infarction
- the use of ventricular rate controlling agents (β blockers, calcium antagonists, or digitalis) during the atrial fibrillation episode
- the use of class I antiarrhythmic drugs[8] (procainamide, quinidine, disopyramide, encainide, flecainide, and propafenone), sotalol, and amiodarone for medical cardioversion, as well as the use of electrical cardioversion, and whether cardioversion to sinus rhythm was successful
- cardiac rhythm at discharge or the last stable rhythm recorded before deterioration to in-hospital death
- the list of antiarrhythmic agents prescribed at discharge.

Data management and quality assurance

All case report forms were forwarded to the coordinating centres (Duke Clinical Research Institute, Durham, North Carolina, USA, or the Nottingham Clinical Research Centre, Nottingham, UK) where the data were entered.[7] Missing or incongruent data were identified. A random sample of 10% of the case report forms was verified against source medical records, including at least one form at each enrolling site.[7] The percentage of complete follow up was 99.7% at 30 days and 97.7% at one year.

Recorded complications

The recorded complications included recurrent ischaemia, reinfarction, worsening heart failure, hypotension, cardiogenic shock, electromechanical dissociation, acute mitral regurgitation, acute ventricular septal defect, cardiac rupture or tamponade, second or third degree heart block, asystole, sustained ventricular tachycardia, ventricular fibrillation, transient ischaemic attack, stroke, pulmonary embolism, peripheral vascular embolism, and severe bleeding.[1]

Statistical analysis

Patients were classified into three groups according to whether they had paroxysmal or chronic atrial fibrillation before enrolment, or no history of atrial fibrillation. Continuous variables are presented as medians with 25th and 75th centiles (end points of the interquartile range), and discrete variables are presented as frequencies and percentages. Group

Table 2 Rate limiting dugs and heparin in the management of atrial fibrillation

	All patients (n=1138)	Patients with no history of previous AF (n=883)	Patients with history of paroxysmal AF (n=117)	Patients with history of chronic AF (n=138)
Digitalis	558 (49%)	422 (48%)	60 (51%)	76 (55%)
Diltiazem	146 (13%)	117 (13%)	18 (15%)	11 (8%)
Verapamil	78 (7%)	51 (6%)	16 (14%)*	11 (8%)
Diltiazem and/or verapamil	207 (18%)	157 (18%)	30 (26%)†	20 (14%)
Metoprolol	238 (21%)	194 (22%)	27 (23%)	17 (12%)†
Atenolol	170 (15%)	137 (16%)	18 (15%)	15 (11%)
Esmolol	13 (1%)	11 (1%)	1 (<1%)	1 (<1%)
Other β blocker	111 (10%)	84 (10%)	14 (12%)	13 (9%)
Any β blocker	329 (29%)	262 (30%)	39 (33%)	28 (20%)†
Heparin	552 (49%)	444 (50%)	58 (50%)	50 (36%)*

Data are presented as actual patient numbers with percentages.
*p < 0.01, †p < 0.05 *v* patients with no history of previous AF.
AF, atrial fibrillation.

comparisons were performed by using logistic models for categorical data and general linear models for continuous data. Baseline characteristics and prespecified in-hospital complications that occurred before the onset of atrial fibrillation were analysed, as were the drugs taken in the two weeks before enrolment. Outcomes of the three groups were analysed by using multivariable analysis with stepwise logistic modelling, with adjustments for the baseline differences.

For the index atrial fibrillation episode, we analysed the use of rate limiting drugs, antiarrhythmic drugs, and electrical cardioversion. Multivariable analysis was performed to determine whether class I antiarrhythmic agents, sotalol, amiodarone, or electrical cardioversion had independent effects on the presence of sinus rhythm at the time of discharge or the time before hospital death, and on 30 day and one year mortality. Stepwise adjustments were done for the grouping of atrial fibrillation, the baseline differences, the prespecified pre-atrial fibrillation complications, and the concurrent use of antiarrhythmic treatments. For hospital survivors, we also performed stepwise logistic regression to determine whether maintenance treatment with class I antiarrhythmic agents, sotalol, and amiodarone altered one year survival. Adjusted odds ratios and 95% confidence intervals were calculated.

RESULTS

Of the 1138 patients enrolled in the substudy, 883 had no history of previous atrial fibrillation, 117 had a history of paroxysmal atrial fibrillation, and 138 had a history of chronic atrial fibrillation. Table 1 shows the baseline characteristics of the three groups. When compared with patients who had no history of atrial fibrillation, those with a history of chronic atrial fibrillation had worse baseline characteristics and higher 30 day and one year mortality (table 1). After adjusting for the significant baseline factors (including pulse rate, systolic blood pressure, age, history of previous infarction or angina, and Killip class), the odds ratios for 30 day and one year mortality in patients with chronic atrial fibrillation were 1.10 (95% CI 0.68 to 1.79) and 1.46 (95% CI 0.95 to 2.25). The adjusted odds ratios for 30 day and one year mortality in patients with a history of paroxysmal atrial fibrillation were 0.80 (95% CI 0.45 to 1.42) and 0.92 (95% CI 0.56 to 1.51).

Use of rate limiting drugs

In the two weeks before enrolment, digitalis was used in 12% of patients, β blockers in 20%, and diltiazem or verapamil in 12%. With the index atrial fibrillation episode, digitalis was used in 49%, β blockers in 29%, and diltiazem or verapamil in 18% of patients (table 2).

Table 3 Antiarrhythmic drugs and percentages of successful conversion

	All patients (n=1138)	Patients with no history of previous AF (n=883)	Patients with history of paroxysmal AF (n=117)	Patients with history of chronic AF (n=138)
Use of drugs				
Any class I agent	132 (12%)	112 (13%)	14 (12%)	6 (4%)†
Procainamide	92 (8%)	85 (10%)	3 (3%)*	4 (3%)*
Quinidine	23 (2%)	16 (2%)	4 (3%)	3 (2%)
Disopyramide	8 (1%)	3 (<1%)	2 (2%)	3 (2%)*
Encainide	4 (<1%)	2 (<1%)	0%	2 (1%)
Flecainide	6 (1%)	4 (<1%)	0%	2 (1%)
Propafenone	24 (2%)	16 (2%)	5 (4%)	3 (2%)
Sotalol	55 (5%)	41 (5%)	8 (7%)	6 (4%)
Amiodarone	168 (15%)	137 (16%)	16 (14%)	15 (11%)
Any antiarrhythmic agent	317 (28%)	262 (30%)	32 (27%)	23 (17%)†
Successful conversion to sinus rhythm				
Any class I agent	72%	74%	64%	50%
Procainamide	70%	72%	33%	50%
Quinidine	61%	69%	50%	33%
Disopyramide	13%	0%	50%	0%
Encainide	0%	0%	0%	0%
Flecainide	17%	25%	0%	0%
Propafenone	67%	69%	100%	0%
Sotalol	67%	73%	63%	33%
Amiodarone	79%	85%	63%†	6%‡
Any antiarrhythmic agent	80%	84%	72%	48%‡

Data are presented as actual patient numbers with percentages in the first half and percentages only in the second half.
*p < 0.05, †p < 0.01, ‡p < 0.001 *v* patients with no history of previous AF.
AF, atrial fibrillation.

Table 4 Presence of sinus rhythm, and antiarrhythmic drugs prescribed at hospital discharge

	All patients (n=1138)	Patients with no history of previous AF (n=883)	Patients with history of paroxysmal AF (n=117)	Patients with history of chronic AF (n=138)
Normal sinus rhythm at time of discharge or before in-hospital death	795 (70%)	698 (79%)	76 (65%)‡	21 (15%)‡
Antiarrhythmic agents prescribed at discharge				
Procainamide	38 (3%)	36 (4%)	0	2 (1%)
Quinidine	8 (<1%)	5 (<1%)	1 (<1%)	2 (1%)
Disopyramide	5 (<1%)	2 (<1%)	2 (2%)‡	1 (<1%)
Encainide	0	0	0	0
Flecainide	1 (<1%)	1 (<1%)	0	0
Propafenone	13 (1%)	9 (1%)	3 (3%)	1 (<1%)
Any class I antiarrhythmic agent	65 (6%)	53 (6%)	6 (5%)	6 (4%)
Sotalol	58 (5%)	40 (5%)	10 (9%)	8 (6%)
Amiodarone	102 (9%)	78 (9%)	14 (12%)	10 (7%)
Any antiarrhythmic agent	221 (19%)	168 (19%)	30 (26%)	23 (17%)

Data are presented as actual numbers with percentages.
‡p < 0.001 *v* patients with no history of previous AF.
AF, atrial fibrillation.

Medical and electrical cardioversion

Of the 1138 patients, 317 (28%) received antiarrhythmic drugs for cardioversion, class I antiarrhythmic agents being used in 12%, sotalol in 5%, and amiodarone in 15% (table 3). The three groups of drugs were associated with successful cardioversion in 72%, 67%, and 79% of patients, respectively. Patients with a history of chronic atrial fibrillation less often received antiarrhythmic agents than patients who had no history of atrial fibrillation (17% *v* 30%, p < 0.01) and had a lower rate of successful cardioversion (48% *v* 84%, p < 0.001). Of patients with a history of paroxysmal atrial fibrillation, 27% received antiarrhythmic agents and 72% had successful cardioversion (non-significant (NS) for both groups *v* patients who had no history of atrial fibrillation, table 3).

Electrical cardioversion was attempted in 116 patients (10%), with about half also receiving antiarrhythmic drugs, and normal sinus rhythm was restored in around two thirds of these patients (67% in those with no history of atrial fibrillation, 54% in those with previous paroxysmal atrial fibrillation, and 44% in those with previous chronic atrial fibrillation; NS). Less than 1% (nine patients) had asystole, and 5% had sinus bradycardia following cardioversion. At the time of discharge or before in-hospital death, 795 patients (70%) had normal sinus rhythm, while 221 (19%) were taking antiarrhythmic drugs, including class I antiarrhythmic agents (6%), sotalol (5%), and amiodarone (9%) (table 4).

Relation between the use of in-hospital antiarrhythmic drugs or electrical cardioversion and clinical outcome

There were 169 hospital deaths (15%) and 969 patients were discharged. Of the hospital survivors, the patients who were most likely to be in sinus rhythm at discharge were those with no previous history of atrial fibrillation (87%), followed by those with a history of paroxysmal atrial fibrillation (75%, p < 0.01), and by those with a history of chronic atrial fibrillation (15%, p < 0.001). The odds ratios for having normal sinus rhythm at the time of discharge (the hospital survivors) or before hospital death (including the non-survivors) with the different treatments are shown in table 5. After adjusting for baseline factors, including the grouping of atrial fibrillation and pre-atrial fibrillation complications, the odds ratios were not significant. There was a trend favouring the use of sotalol.

The use of class I antiarrhythmic agents or sotalol was associated with lower 30 day and one year mortality (table 6), with adjusted odds ratios of 0.42 (95% CI 0.19 to 0.89) and 0.58 (95% CI 0.33 to 1.04) with class I agents, and 0.31 (95% CI 0.07 to 1.32) and 0.31 (95% CI 0.09 to 1.02) with sotalol. There was no association between the use of amiodarone or electrical cardioversion and mortality. Further analysis incorporating the use of any β blockers into the multivariable model was performed. The odds ratios for 30 day and one year mortality, and for one year survival in the hospital survivors, were similar to the original results.

Maintenance treatment with different antiarrhythmic drugs at the time of hospital discharge did not affect the one

Table 5 Odds ratios and 95% confidence intervals for normal sinus rhythm at the time of discharge or before hospital death

	Unadjusted	Adjusted for baseline characteristics*	Adjusted for baseline characteristics and pre-AF complications†
Excluding in-hospital deaths			
Class I antiarrhythmic agents‡	1.33 (0.83 to 2.15)	0.83 (0.48 to 1.42)	0.83 (0.48 to 1.43)
Sotalol	2.09 (0.88 to 4.99)	2.05 (0.75 to 5.59)	2.10 (0.77 to 5.75)
Amiodarone	1.60 (0.99 to 2.57)	1.40 (0.80 to 2.44)	1.47 (0.84 to 2.57)
Electrical cardioversion	1.18 (0.70 to 2.00)	0.95 (0.52 to 1.75)	0.96 (0.52 to 1.77)
At discharge or before in-hospital death			
Class I antiarrhythmic agents‡	1.67 (1.08 to 2.60)	1.10 (0.68 to 1.78)	1.10 (0.68 to 1.79)
Sotalol	2.75 (1.22 to 6.16)	2.31 (0.96 to 5.57)	2.30 (0.95 to 5.57)
Amiodarone	1.44 (0.99 to 2.09)	1.38 (0.89 to 2.14)	1.45 (0.94 to 2.25)
Electrical cardioversion	1.15 (0.75 to 1.76)	1.01 (0.62 to 1.65)	1.05 (0.64 to 1.72)

*Adjusted for grouping of atrial fibrillation (AF) including paroxysmal AF, chronic AF, and no previous AF; baseline pulse rate; baseline systolic blood pressure; age; hypercholesterolaemia; and Killip class.
†In addition to the above demographics, adjusted for significant pre-AF complications including recurrent ischaemia, reinfarction, and acute ventricular septal defect.
‡Includes procainamide, quinidine, disopyramide, encainide, flecainide, and propafenone.

Table 6 Odds ratios (and 95% confidence intervals) for 30 day and one year mortality, comparing the different in-hospital treatment of atrial fibrillation

	Unadjusted	Adjusted for baseline characteristics*	Adjusted for baseline characteristics and pre-AF complications†
30 day mortality			
Class I antiarrhythmic agents‡	0.30 (0.15 to 0.63)	0.38 (0.18 to 0.81)	0.42 (0.19 to 0.89)
Sotalol	0.21 (0.05 to 0.85)	0.26 (0.06 to 1.12)	0.31 (0.07 to 1.32)
Amiodarone	1.23 (0.81 to 1.87)	1.21 (0.77 to 1.90)	1.08 (0.68 to 1.74)
Electrical cardioversion	1.22 (0.75 to 2.01)	1.24 (0.73 to 2.10)	1.16 (0.66 to 2.03)
1 year mortality			
Class I antiarrhythmic agents‡	0.41 (0.24 to 0.70)	0.54 (0.30 to 0.95)	0.58 (0.33 to 1.04)
Sotalol	0.19 (0.06 to 0.63)	0.26 (0.08 to 0.85)	0.31 (0.09 to 1.02)
Amiodarone	1.12 (0.78 to 1.63)	1.14 (0.75 to 1.73)	1.03 (0.67 to 1.57)
Electrical cardioversion	1.24 (0.81 to 1.91)	1.33 (0.82 to 2.16)	1.27 (0.78 to 2.09)

*Adjusted for grouping of atrial fibrillation (AF) including paroxysmal AF, chronic AF, and no previous AF; pulse rate; systolic blood pressure; age; history of myocardial infarction; angina; percutaneous transluminal coronary angioplasty; Killip class; and smoking class (previous, current, never).
†In addition to the above demographics, adjusted for significant pre-AF complications including worsening heart failure, shock, acute ventricular septal defect, and stroke.
‡Includes procainamide, quinidine, disopyramide, encainide, flecainide, and propafenone.

year survival rate in various multivariable models adjusted for baseline characteristics and the use of similar or different antiarrhythmic drugs during the hospital stay.

DISCUSSION

In this prospective study, we report the use of antiarrhythmic treatment for atrial fibrillation and the outcome in patients who received thrombolysis early after an acute myocardial infarct. Although only 28% of patients received antiarrhythmic drugs and 10% received electrical cardioversion, most patients (70%) were in sinus rhythm at the time of hospital discharge or in the period before hospital death. Our study reveals wide variations in the management of atrial fibrillation after thrombolytic treatment for acute myocardial infarction (different class I antiarrhythmic drugs, sotalol, amiodarone, and electrical cardioversion). Sinus rhythm was restored in a similar proportion (~70%) of patients treated by the different approaches. The use of class I antiarrhythmic drugs was associated with lower 30 day mortality and a trend towards lower one year mortality. The use of sotalol was associated with a trend towards lower 30 day and one year mortality.

Previous reports[1 9–11] have shown that patients with atrial fibrillation had worse baseline characteristics, more in-hospital complications, and worse outcomes than those without atrial fibrillation. In our earlier study analysing complications preceding the onset of atrial fibrillation in GUSTO-III patients who were in sinus rhythm at recruitment,[1] we found that worsening heart failure, hypotension, third degree heart block, and ventricular fibrillation independently predicted the development of atrial fibrillation, and that new onset atrial fibrillation independently carried a worse prognosis, with 30 day mortality of 15% in those with new onset atrial fibrillation *v* 6% in those without ($p < 0.001$). In the current study of unselected patients with atrial fibrillation during acute myocardial infarction, the adjusted 30 day mortality rates were similar, regardless of whether atrial fibrillation was new or whether it was preceded by earlier episodes of paroxysmal or chronic atrial fibrillation. There was, however, a trend towards higher one year mortality in patients with a previous history of chronic atrial fibrillation, which was not fully explained by their worse baseline characteristics.

Despite the high initial success rate of treatment in restoring sinus rhythm, the treatment of atrial fibrillation with antiarrhythmic drugs and electrical cardioversion did not predict the presence of sinus rhythm at the time of hospital discharge or before deterioration to in-hospital death. Although the antiarrhythmic effects of the drugs could have differed between survivors and patients who died, subgroup analysis in the hospital survivors showed similar results. However, antiarrhythmic treatment could have reduced the total duration of atrial fibrillation during the hospital period. A shorter duration of atrial fibrillation may limit heart failure progression and recurrent ischaemia, or the occurrence of other complications such as stroke. This could help to explain our observation that acute treatment of atrial fibrillation with class I antiarrhythmic drugs and sotalol was associated with improved prognosis, but continued use of these drugs at hospital discharge was not associated with lower mortality.

Although about 30% of patients received antiarrhythmic drugs or electrical cardioversion for treatment of atrial fibrillation, only class I antiarrhythmic drugs and sotalol were associated with better outcomes, and not amiodarone or electrical cardioversion. This observation held true regardless of whether or not patients were treated with β blockers. Our findings should not be compared with the negative findings in the CAST (cardiac arrhythmia suppression trial)[4 12] and SWORD (survival with oral d-sotalol) trials,[13] which investigated the longer term use of class I antiarrhythmic drugs (flecainide, encainide, and moricizine) or d-sotalol for preventing ventricular arrhythmia and sudden death; nor should they be compared with the previous meta-analysis on the prophylactic use of antiarrhythmic drugs after acute myocardial infarction.[14] What we have shown is a potential benefit with short term early treatment of atrial fibrillation complicating acute myocardial infarction, and no further benefit with prolonged use after hospital discharge. This provides the rationale for large scale randomised trials comparing short term use of class I antiarrhythmic drugs (and sotalol) with rate control alone in management of atrial fibrillation occurring after myocardial infarction.

Limitations

Despite being prospective, this study was observational in nature and was therefore subject to biases not present in a randomised trial. During the postinfarction period, many dynamic changes occur and some postinfarct complications independently predict the development of new onset atrial fibrillation.[1] Thus in any randomised trial, careful attention should be given to the timing of atrial fibrillation relative to the occurrence or management of complications occurring before atrial fibrillation develops. The current observational study included all patients with atrial fibrillation, and was adjusted not only for baseline differences—including a history of previous atrial fibrillation—but also for prespecified postinfarction complications that occurred before atrial fibrillation,

and for the concurrent use of different antiarrhythmic treatments or β blockers. The findings are therefore relevant in contemporary practice.

Measurements of left ventricular function were not recorded. The left ventricular ejection fraction and other investigation results may have influenced the choice of antiarrhythmic drugs given to the patients. Despite detailed adjustments in the multivariable model, the better prognosis in patients who received class 1 drugs or sotalol may have been related to the fact that these patients were at lower risk than the others. We observed an association between the use of class 1 drugs or sotalol and better survival. Whether this represents a cause and effect relation can only be addressed in a randomised trial.

Finally, we analysed class I antiarrhythmic drugs as a single group, but the results mainly reflect those of procainamide, the class I agent used most commonly in this study.

Conclusions

The current use of antiarrhythmic drugs and electrical cardioversion in the management of atrial fibrillation during acute myocardial infarction is highly variable. There appears to be an association between the short term use of class I antiarrhythmic agents or sotalol and more favourable outcomes, which is not observed with the use of amiodarone or electrical cardioversion. The hypothesis that some but not all antiarrhythmic agents improve the outcome of atrial fibrillation during acute myocardial infarction needs to be tested in future randomised trials.

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Authors' affiliations

***C-K Wong, H D White,** Cardiovascular Research Unit, Green Lane Hospital, Auckland, New Zealand
R G Wilcox, University Hospital-Nottingham, Nottingham, UK
D A Criger, R M Califf, Duke Clinical Research Institute, Durham, North Carolina, USA
E J Topol, Cleveland Clinic, Cleveland, Ohio, USA
E M Ohman, University of North Carolina, Chapel Hill, North Carolina, USA

*Also Department of Medicine and Therapeutics, Chinese University of Hong Kong, Hong Kong, China

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ELECTRONIC PAGES

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The following electronic only article is published in conjunction with this issue of *Heart*.

Continuous left hemidiaphragm sign revisited: a case of spontaneous pneumopericardium and literature review

L Brander, D Ramsay, D Dreier, M Peter, R Graeni

In pneumopericardium, a rare but potentially life threatening differential diagnosis of chest pain with a broad variety of causes, rapid diagnosis and adequate treatment are crucial. In upright posteroanterior chest radiography, the apical limit of a radiolucent rim, outlining both the left ventricle and the right atrium, lies at the level of the pulmonary artery and ascending aorta, reflecting the anatomical limits of the pericardium. The band of gas surrounding the heart may outline the normally invisible parts of the diaphragm, producing the continuous left hemidiaphragm sign in an upright lateral chest radiograph. If haemodynamic conditions are stable, the underlying condition should be treated and the patient should be monitored closely. Acute haemodynamic deterioration should prompt rapid further investigation and cardiac tamponade must be actively ruled out. Spontaneous pneumopericardium in a 20 year old man is presented, and its pathophysiology described.

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