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Likelihood of Spontaneous Conversion of Atrial Fibrillation to Sinus Rhythm

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Objectives. **We sought to determine the likelihood and predictors of spontaneous conversion to sinus rhythm of recent-onset atrial fibrillation (symptoms <72 h).**

Background. **Although spontaneous conversion of recent-onset atrial fibrillation is common, the likelihood and clinical and echocardiographic predictors have not been fully defined. Such data would be important for management of patients in whom early cardioversion is desired: Cardioversion could be delayed in patients with a high likelihood of spontaneous conversion, and it could be expeditiously pursued if spontaneous conversion is unlikely.**

Methods. **We screened 1,822 consecutive adults admitted to the hospital with atrial fibrillation and prospectively identified 356 patients (45% male, mean age ± SD 68 ± 16 years) with atrial fibrillation of <72-h duration. The occurrence of spontaneous conversion to sinus rhythm and clinical and echocardiographic data were identified through retrospective chart review.**

Results. **Spontaneous conversion to sinus rhythm occurred in 68% of the study group (n = 242; 95% confidence interval [CI] 63% to 73%). Among patients with spontaneous conversion, the total duration of atrial fibrillation was <24 h in 159 (66%), 24 to 48 h in 42 (17%) and >48 h in 41 (17%) ($p < 0.001$). Logistic regression analysis of clinical data identified presentation <24 h from onset of symptoms as the only predictor of spontaneous conversion (odds ratio 1.8, 95% CI 1.4 to 2.4, $p < 0.0001$). Normal left ventricular systolic function was more common among patients with spontaneous conversion ($p = 0.03$), but it was not an independent predictor of conversion. Left atrial dimension was similar between groups.**

Conclusions. **Spontaneous conversion to sinus rhythm occurs in almost 70% of patients presenting with atrial fibrillation of <72-h duration. Presentation with symptoms of <24-h duration is the best predictor of spontaneous conversion.**

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Atrial fibrillation is the most commonly encountered sustained arrhythmia, occurring in 0.4% to 2.0% of the population (1) and increasingly prevalent with advancing age (2). It has been estimated that >260,000 hospital admissions annually are related to atrial fibrillation (3). For patients who are in hemodynamically stable condition, initial therapy for this arrhythmia includes ventricular rate control with subsequent consideration of pharmacologic or direct current (DC) cardioversion to relieve symptoms and improve cardiac output (4–6). If the duration of atrial fibrillation is <48-h, early cardioversion has been advocated (4–6) and shown to be safe (7). Although data from small series (8–13) have suggested that a significant proportion of patients presenting with atrial fibrillation will have spontaneous conversion to sinus rhythm, to our knowledge, no data from large consecutive series have been reported. In addition, clinical and echocardiographic indexes predictive of spontaneous conversion have not been fully examined. Because both pharmacologic and electrical cardioversion are expensive, time-consuming and potentially hazardous interventions (14–18), the ability to identify patients in whom spontaneous conversion is likely would help in the clinical management of atrial fibrillation. For patients in whom cardioversion is desired, active cardioversion could be delayed for those with a high likelihood of spontaneous conversion, whereas patients with a low likelihood of spontaneous conversion could be directed to expeditious pharmacologic or electrical cardioversion.

Accordingly, we studied a consecutive series of patients admitted to the hospital with new-onset (<72 h) atrial fibrillation to determine the likelihood of spontaneous conversion to sinus rhythm and to identify clinical and echocardiographic indexes predictive of such conversion.

Methods

Patients. We prospectively screened 1,214 consecutive adult patients admitted to the Beth Israel Hospital from January 1, 1990 through September 25, 1995 and 608 consec-

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Abbreviations and Acronyms

AV = atrioventricular
CHF = congestive heart failure
CI = confidence intervals
DAAF = Digitalis in Acute Atrial Fibrillation (trial)
DC = direct current
OR = odds ratio

utive patients admitted to the University of Connecticut Health Center from September 28, 1991 through April 29, 1996 with a diagnosis that included atrial fibrillation to identify those with a clinically estimated duration of atrial fibrillation of <72 h. We have previously reported data from a subset of this 1,822-patient cohort to assess for occurrence of cardioversion-related thromboembolic events in patients with atrial fibrillation of <48-h duration (7). Case identification criteria and methodology of that analysis have been described elsewhere and were different from those of the present report. For the present analysis, onset of atrial fibrillation was defined as a new, abrupt and clearly recognizable onset of symptoms, including palpitation, dyspnea, angina or dizziness alone or in combination. Exclusion criteria included 1) atrial fibrillation of uncertain duration or clinically suggestive of >72-h duration, 2) concomitant antiarrhythmic therapy at the time of presentation (e.g., quinidine, procainamide, flecainide, propafenone, sotalol or amiodarone), and 3) performance of a transesophageal echocardiography–guided approach for active cardioversion. There were 356 patients who met entry criteria, and data from a retrospective review of their hospital and clinic records are included in this report.

Clinical and echocardiographic indexes. Clinical and echocardiographic data retrieved from the patient's hospital and clinic records included age, gender, condition predisposing to atrial fibrillation (hypertension, coronary artery disease, excessive alcohol consumption, rheumatic heart disease, pulmonary embolism, hyperthyroidism, infection), history of previous atrial fibrillation, history of previous myocardial infarction, and congestive heart failure (CHF) on presentation. Cardiovascular medications, including beta-adrenergic receptor antagonists, calcium channel blocking agents or digoxin taken before presentation as well as those added during the index hospital stay were noted. When available, echocardiographic data, including M-mode left atrial dimension (19) and left ventricular systolic function (defined as abnormal if there were regional or global wall motion abnormalities), were also recorded.

Conversion of atrial fibrillation. For patients with conversion to sinus rhythm, the duration of atrial fibrillation was estimated from the initial onset of the acute symptoms until the time of the in-hospital conversion, as documented by 12-lead electrocardiography or rhythm strip. Conversion was defined as *spontaneous* if it occurred before or after the administration of only rate-controlling medications (beta-adrenergic receptor antagonists, calcium channel blockers or digoxin). Conversion was defined as *active* if it occurred after administration of one or more antiarrhythmic medications (e.g., quinidine, procainamide, flecainide, propafenone, sotalol or amiodarone) or after DC countershock. Patients with *nonspontaneous conversion* included those who underwent active cardioversion (electrical or pharmacologic) and those who had sustained atrial fibrillation throughout the index hospital admission.

Data analysis. All data are reported as mean value ± 1 SD. A forward logistic regression analysis model was constructed to assess the predictive value of individual clinical and echocardiographic indexes for spontaneous conversion of atrial fibrillation (SPSS for Windows, version 6.0, SPSS Inc.). In this forward stepwise selection of covariates, removal testing is based on the probability of the likelihood-ratio statistic based on the maximal partial likelihood estimates. For entry in the model a cutoff p value of 0.05 was used and for removal from it a cutoff value of 0.1. The model allowed for a maximum of 20 iterations. The dependent variable was spontaneous conversion to sinus rhythm; covariates included age, gender, predisposing condition, history of previous atrial fibrillation, history of previous myocardial infarction, class of ventricular rate-controlling agent used (before or during the index admission), presence of CHF on presentation and duration of atrial fibrillation <24 h at presentation. For patients with transthoracic echocardiographic data, a separate analysis included left ventricular systolic dysfunction and left atrial enlargement as covariates together with those listed previously. On the basis of results of the logistic regression analysis, the odds ratio (OR) and 95% confidence interval (CI) were calculated.

Results

Patients. The study group included 356 adults (159 [45%] male, 197 [55%] female) with a mean age of 68 ± 16 years. The clinical characteristics and echocardiographic data for the entire group are summarized in Table 1. An underlying systemic condition predisposing to atrial fibrillation was identified in 275 patients (79%), no underlying condition was identified in 81 patients (23%). Forty percent of patients had a history of prior atrial fibrillation, and the clinically estimated duration of atrial fibrillation was <24 h in 292 patients (82%). Two hundred thirty-three patients (65%) were receiving atrioventricular (AV)-node blocking agents at the time of presentation to the hospital. After admission, digoxin (n = 138, 39%), calcium channel blockers (n = 105, 30%) or beta-adrenergic receptor antagonists (n = 82, 23%) were added. Transthoracic echocardiographic data were available for 275 patients (77%) and are also summarized in Table 1. Left ventricular systolic dysfunction was present in 70 patients (25%), and 49% of patients had left atrial enlargement (long axis dimension >4.0 cm).

Clinical outcomes and predictors of spontaneous conversion. Spontaneous conversion to sinus rhythm occurred in 68% (n = 242; 95% CI 63% to 73%) of the study group. Among patients with spontaneous conversion, the total duration of atrial fibrillation was <24 h in 159 patients (66%), 24 to

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Table 1. Comparison of Clinical and Echocardiographic Indexes Among Patients Who Did and Did Not Have Spontaneous Conversion to Sinus Rhythm

	Patients With Spontaneous Conversion (n = 242)	Patients With Nonspontaneous Conversion (n = 114)	Chi-Square	p Value
Age (yr)	68 ± 17	69 ± 16		0.69
Female	138 (57%)	59 (52%)	0.90	0.34
Underlying systemic disorder				
Hypertension	105	48	0.01	0.91
Ischemic heart disease	70	33	0.02	0.90
Prior myocardial infarction	23	12	0.01	0.91
Infection	14	13	2.74	0.10
Rheumatic heart disease	2	4	1.94	0.16
Pericarditis	1	2	0.45	0.50
Pulmonary embolus	2	0	0.33	0.57
Hyperthyroidism	2	0	0.05	0.83
History of prior atrial fibrillation	97	47	0.01	0.93
Duration of atrial fibrillation <24 h at presentation	213	79	17.16	< 0.001
AV node blocking agent				
At presentation				
Beta-adrenergic receptor antagonist	52	32	1.52	0.22
Calcium channel blocker	52	28	0.26	0.61
Digoxin	42	27	1.60	0.21
Added after presentation				
Beta-adrenergic receptor antagonist	57	25	0.04	0.84
Calcium channel blocker	73	32	0.08	0.78
Digoxin	97	41	0.39	0.53
Transthoracic echocardiographic data (n = 275)				
Left atrial dimension (n = 246) (cm)	4.1 ± 0.7	4.2 ± 0.8		0.25
Left atrial dimension >4.0 cm	82 (47%)	38 (54%)	0.90	0.34
Left ventricular systolic dysfunction	40 (21.3%)	30 (34%)	4.79	0.03

Data are presented as mean value ± SD or number (%) of patient group. AV = atrioventricular.

48 h in 42 (17%) and >48 h in 41 (17%) ($p < 0.001$). Of 292 patients presenting with atrial fibrillation of <24-h duration, spontaneous conversion to sinus rhythm occurred in 213 (73%). In contrast, only 45% (29 of 64) of those with onset of atrial fibrillation between 24 and 72 h before presentation had spontaneous termination of the arrhythmia ($p < 0.001$).

Logistic regression analysis of clinical data identified duration of atrial fibrillation <24 h at presentation as the only clinical predictor of spontaneous conversion to sinus rhythm (OR 1.8; 95% CI 1.4 to 2.4, $p < 0.0001$). Age, gender and predisposing systemic condition for atrial fibrillation were not predictive of spontaneous conversion. The use of digoxin, beta-blockers or calcium channel blockers at the time of presentation or the subsequent administration of these agents was not predictive of spontaneous conversion. When echocardiographic data were also included, the duration of atrial fibrillation <24 h at presentation remained the best predictor of spontaneous conversion (OR 2.2; 95% CI 1.6 to 3.1, $p < 0.0001$).

Echocardiographic left atrial enlargement was not predictive of spontaneous conversion to sinus rhythm. Preserved left ventricular systolic function was more common among patients with spontaneous conversion ($p = 0.03$) but was also not an independent predictor of such conversion.

Ninety-five patients (27%) in the study group received therapies for active cardioversion; specific antiarrhythmic treatment was instituted in 82 patients, including quinidine (n = 43), procainamide (n = 29) or other antiarrhythmic agents (n = 10). Fifteen patients continued to have atrial fibrillation throughout the hospital stay.

Discussion

Immediate electrical cardioversion is indicated whenever atrial fibrillation is associated with hemodynamic compromise. In patients in stable condition, however, a less aggressive strategy is generally used, beginning with ventricular rate control and followed by elective pharmacologic or electrical cardioversion to relieve symptoms and improve cardiac output (4–6). Because both pharmacologic and electrical cardioversion have associated risks (14–17), identifying patients in whom spontaneous conversion is likely to occur and avoiding active intervention might decrease cardioversion-related morbidity. In this consecutive study of 356 patients with atrial fibrillation, almost 70% of patients had spontaneous conversion to sinus rhythm, and a duration of atrial fibrillation <24 h at presentation was identified as the best clinical predictor of spontaneous conversion. Other clinical and echocardiographic

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variables such as age, gender, left atrial enlargement, left ventricular systolic dysfunction or use of ventricular rate–controlling agents were not predictive of spontaneous conversion.

Comparison with previous studies. Previous data on spontaneous conversion of atrial fibrillation to sinus rhythm have been derived from smaller series that focused on the utility of specific AV node blocking agents or antiarrhythmic medications for promoting cardioversion. With the possible exception of sotalol, agents such as digoxin, beta-adrenergic receptor antagonists or calcium channel blockers are effective for ventricular rate control but ineffective for converting atrial fibrillation to sinus rhythm (20–25). Previously, Falk and colleagues (8), examining the efficacy of digoxin for converting atrial fibrillation in a study of 36 patients, reported that 44% of the patients in the placebo arm had spontaneous conversion, compared with 50% of patients randomized to digoxin. Similar results were recently reported by the Digitalis in Acute Atrial Fibrillation (DAAF) investigators (12). In that multicenter prospective study of digoxin versus placebo for conversion of recent atrial fibrillation, there was no significant difference (51% vs. 46%, respectively) in the rate of conversion to sinus rhythm. The finding of both studies that digoxin does not promote conversion to sinus rhythm is consistent with our data. The slightly lower spontaneous conversion rates reported both by Falk et al. (8) and the DAAF investigators (12) (as compared with those in the current study) is probably related to differences in patient population. The previous studies included patients with atrial fibrillation of up to 7 days' duration, whereas our study included only those with atrial fibrillation of <72-h duration. We chose to study patients with atrial fibrillation of shorter duration as they represent the clinical population for whom early cardioversion is advocated (4–6). For those with atrial fibrillation of >72-h duration, active conversion is advocated either after the patient has had 3 to 4 weeks of warfarin therapy or after the patient has been treated with heparin and results of a transesophageal echocardiogram are negative for intracardiac thrombi (26–28).

Galve and colleagues (9) examined the utility of amiodarone versus placebo for acute short-term conversion of atrial fibrillation to sinus rhythm in 50 patients. Conversion occurred in 68% of those receiving amiodarone versus 60% of patients given placebo (p = NS). In concert with our results, these investigators noted that shorter duration of atrial fibrillation was associated with conversion (duration of 12 h for patients with spontaneous conversion vs. 41 h for patients without conversion). In contrast to our data, however, they also found that younger age, smaller left atrial size and absence of heart failure were predictive of spontaneous conversion.

Weiner and colleagues (11), reported data from a 50-patient randomized study comparing propafenone with verapamil (as a control) in the treatment of recent onset atrial fibrillation (<2 weeks' duration). In the verapamil arm, 9 (41%) of 22 patients had spontaneous conversion to sinus rhythm after 48 h. Among a subset of patients in their study with atrial fibrillation for <24 h, 7 (58%) of 12 patients had spontaneous conversion, a rate similar to the 73% rate in our study. When the duration of atrial fibrillation was >24 h, only 2 (20%) of 10 patients had spontaneous conversion. In another study (13) comparing short-term (3 and 8 h) conversion rates in patients with recent onset atrial fibrillation (<7 days) receiving propafenone or placebo, >50% of the patients receiving placebo had conversion to sinus rhythm. Although propafenone was more efficacious than placebo for conversion to sinus rhythm (78% vs. 56%, p = 0.02), among those with conversion the mean duration of atrial fibrillation from oral ingestion of therapy to arrhythmia conversion was identical in the two groups (181 min). Presence of heart disease (including cardiomyopathy, valvular, congenital and coronary disease) was associated with lower rates of short-term spontaneous conversion.

Our finding that atrial fibrillation of <24 h duration at presentation was the best predictor of conversion to sinus rhythm is consistent with the recently described, elegant goat model of atrial fibrillation reported by Wijffels and co-workers (29). They reported that the length of artificially induced atrial fibrillation correlated with the duration of sustained atrial fibrillation once artificial atrial fibrillation was terminated. After 2 weeks of induced atrial fibrillation, long-term sustained atrial fibrillation was the most likely outcome. In contrast, short episodes of induced atrial fibrillation led to prompt spontaneous conversion once atrial fibrillation was terminated. Electrophysiologic investigation in that animal model revealed a direct correlation between atrial effective refractory period and duration of the arrhythmia. As suggested by these authors (29), atrial fibrillation "begets atrial fibrillation" by promoting electrophysiologic conditions favorable for propagation of the arrhythmia, providing a compelling explanation for the relation between likelihood of spontaneous conversion to sinus rhythm and duration of atrial fibrillation.

Our study, in contrast to that of Galve et al. (9), did not identify left atrial size as a predictor for spontaneous conversion. However, our findings agree with those of Dittrich et al. (30), who also found no relation between age or left atrial size and spontaneous conversion.

Limitations of the study. In our study cohort, many patients who did not have spontaneous conversion to sinus rhythm in a timely manner received active therapies (pharmacologic or electrical cardioversion) to restore sinus rhythm. By the definition employed in our study, these patients were classified as having nonspontaneous conversion. It is possible, however, that some of these patients would have had spontaneous conversion if they had not received these active therapies. Because of the retrospective nature of our analysis, we could not adjust for this confounder. Thus, our data may underestimate the true incidence of spontaneous conversion, a possibility that further underscores the need to have a placebo group in trials of antiarrhythmic agents for conversion of atrial fibrillation to sinus rhythm.

Conclusions. Spontaneous conversion to sinus rhythm occurs in almost 70% of patients with atrial fibrillation of <72-h duration, and a clinical duration of atrial fibrillation of <24 h

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at presentation is the best predictor of spontaneous conversion. The high rate of spontaneous conversion highlights the importance of having a control group when assessing the efficacy of active cardioversion strategies.

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