Prediction of the Recurrence of Atrial Fibrillation After Successful Cardioversion with P Wave Signal-Averaged ECG

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Background: The recurrence of atrial fibrillation (AF) was often observed after cardioversion.

Methods: In our study, a P wave triggered P wave signal-averaged ECG (P-SAECG) was performed on 118 consecutive patients 1 day after successful electrical cardioversion in order to evaluate the utility of this method to predict AF after cardioversion. We measured the filtered P wave duration (FPD) and the root mean square voltage of the last 20 ms of the P wave (RMS 20).

Results: During a 1-year follow-up, a recurrence was observed in 57 patients (48%). Patients with recurrence of AF had a larger left atrial size (41.9 ± 4.0 vs 39.3 ± 3.1 mm, $P < 0.0003$), a longer FPD (139.6 ± 16.0 vs 118.2 ± 14.1 ms, $P < 0.0001$), and a lower RMS 20 (2.57 ± 0.77 vs 3.90 ± 0.99 μ V, $P < 0.0001$). A cutoff point (COP) of $\text{FPD} \geq 126$ ms and $\text{RMS 20} \leq 3.1$ μ V could predict AF with a specificity of 77%, a sensitivity of 72%, a positive value of 75%, a negative predictive value of 75%, and an accuracy of 75%. A stepwise logistic regression analysis of variables identified COP (odds ratio 9.97; 95% CI, 4.10–24.24, $P < 0.0001$) as an independent predictor for recurrence.

Conclusions: We conclude that the probability of recurrence of AF after cardioversion could be predicted by P-SAECG. This method seems to be appropriate to demonstrate a delayed atrial conduction that might be a possible risk factor of reinitiation of AF. **A.N.E. 2005;10(4):414–419**

P wave signal-averaged ECG; atrial fibrillation; cardioversion; recurrence

Atrial fibrillation (AF) is a very common arrhythmia which often causes strokes.^{1–3} In an attempt to reduce the formation of thrombi electrical cardioversion (EC) is generally performed^{4–6} but recurrence of AF is very high after EC.^{6–11} Antiarrhythmic drugs reduce the recurrence of AF after EC but the incidence is still above one third of patients.^{4–11} Attempts to predict which patients have a risk for recurrence in short-term or long-term outcome after EC have been disappointing.^{4–11} We investigated, on the basis of our observation¹² concerning a longer filtered P wave duration (FPD) in P wave triggered P wave signal-averaged ECG (P-SAECG) in paroxysmal AF, a prospective study

in order to examine the prediction of this method for the recurrence of AF after EC in a long-term outcome.

METHODS

The study population consisted of 141 patients with persistent nonvalvular AF (duration above 7 days, range 9–96 days) after first time EC and a sinus rhythm over 24 hours. The patients were examined between March 2000 and June 2002. All patients were evaluated by transthoracic and transesophageal echocardiography before cardioversion. Patients with an exclusion of a thrombus were

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enrolled in the study. Patients were excluded for pregnancy, known pulmonary hypertension, chronic pulmonary diseases, sleep apnoea syndrome, a chemical cardioversion, a change of antiarrhythmic therapy during the study, a history of ventricular arrhythmias, or propafenone or flecainide therapy within the last 3 months. Propafenone and flecainide led to an increase of the FPD and was therefore excluded.¹³ Demographic data, medications, and past medical history were gathered by patient interview and review of their medical record.

Antiarrhythmic drugs were given and were not withdrawn during the whole study. Direct current cardioversion was started with 100 J and was increased until 360 J and if necessary repeated three times. All patients were receiving for at least 1 week before and at least 6 months after cardioversion an effective anticoagulation.

The P-SAECG was measured one time 1 day after EC. After cardioversion, all patients were under rhythm monitoring for 24 hours. The antiarrhythmic drugs for maintaining sinus rhythm depended on the clinical judgment of the observing physician and the arrhythmia history of the patients. During the 12-month follow-up period, patients were evaluated in the outpatient department monthly or by signs of a recurrence with ECG and 24-hour Holter ECG. The recurrence of AF after EC had to be documented with ECG or 24-hour Holter ECG.

P Wave Signal-Averaged ECG

Recording of P wave triggered P-SAECG was described before.^{12,14} Orthogonal X, Y, and Z leads (Predictor, Kaiser Medizintechnik, Germany) were used with a specifically designed software that retained the P wave as a trigger of the averaging process. Signals were digitized at a frequency of 1000 samples/s with 16-bit accuracy. After eliminating supraventricular and ventricular extrasystole, signals from each lead were then amplified and filtered between 40 and 250 Hz by using a bidirectional filter. A P wave template was selected by detection of the first peak of the filtered P wave and P wave complexes not matching the template with a 99% correlation coefficient were automatically rejected to minimize P wave jitter. P waves were recorded until a noise end point of $0.5 \mu\text{V}$ was achieved in the P-Q interval. The P wave complexes of filtered X, Y, and Z leads were combined to a vector magnitude $\sqrt{X^2 + Y^2 + Z^2}$. The FPD of the vector magnitude was defined as the interval be-

tween the onset and offset point, and the root mean square voltage of the last 20 ms of the P wave (RMS 20) could also be measured with the software.

Echocardiography

An M-mode and two-dimensional echocardiography (Model SSH-160 A, Toshiba Corp., Japan) was performed in all patients in order to determine left atrial size.

Statistics

All data are presented as mean values $\pm$ SD. Differences between the values were evaluated for statistical significance using Fisher's Exact test and chi-square test for baseline characteristics. In the analysis of continuous variables, Kruskal-Wallis analysis of variance with post hoc Student's *t*-test were used for variables with normal distribution and the Mann-Whitney *U* test was used for variables with nonnormal distribution. A measure of the linear association between two variables was evaluated using Pearson's correlation coefficient and all statistical tests were 2-tailed. A multivariate Cox regression analysis was performed on variables found to be significant predictors for recurrence of AF with univariate analysis. For all variables with at least a moderate level of association, we estimated the individual odds ratios with confidence intervals. Kaplan-Meier analysis with log-rank test was used to compare the probability of recurrence of AF. A *P* value of ≤ 0.05 was considered significant.

RESULTS

Twenty-three patients had to be excluded from the study because of an alteration of antiarrhythmic therapy. During the follow-up among 118 subjects, we could document 57 (48%) recurrences of AF after EC. There was no difference in demographic data. The left atrial size was larger in patients with a recurrence of AF (41.9 ± 4.0 vs 39.3 ± 3.1 mm, $P < 0.0003$). The clinical characteristics of the patients are shown in Table 1. The duration of AF was not different between both groups (39.1 ± 21.7 vs 37.7 ± 24.5 days, $P = \text{ns}$). There was also no difference in energy (237.2 ± 88.7 vs 243.6 ± 90.9 J, $P = \text{ns}$) or attempts (3.0 ± 1.4 vs 2.8 ± 1.4 , $P = \text{ns}$) for EC. A recurrence was observed after a mean of 25.7 ± 60.6 days (range 2–349 days).

Table 1. Patients Clinical Characteristics

Characteristics	Recurrence	Sinus Rhythm	P value
Number (males/females)	57 (35/22)	61 (37/24)	ns
Age (years)	63.5 ± 10.7	63.6 ± 9.9	ns
Mean body mass index (kg/m ²)	27.7 ± 4.3	27.7 ± 3.8	ns
Heart rate (beats/min)	68.7 ± 13.0	68.0 ± 11.1	ns
NYHA classification	1.5 ± 0.6	1.4 ± 0.6	ns
I	32 (56%)	40 (66%)	ns
II	21 (37%)	18 (30%)	ns
III	4 (7%)	3 (4%)	ns
Angiographic results			
Ejection fraction (%)	54.1 ± 9.0	55.8 ± 11.1	ns
Echocardiographic results			
LVEDD (mm)	52.1 ± 3.5	51.7 ± 4.6	ns
Left atrial diameter (mm)	41.9 ± 4.0	39.3 ± 3.1	<0.0003
Left atrial diameter ≥40 mm (n)	39 (68%)	29 (48%)	<0.03
Diseases			
Coronary heart disease (n)	32 (56%)	37 (61%)	ns
Hypertension (n)	31 (54%)	28 (46%)	ns
Left ventricular hypertrophy (n)	7 (23%)	5 (18%)	ns
Dilated cardiomyopathy (n)	5 (9%)	8 (13%)	ns
Diabetes mellitus (n)	6 (11%)	7 (11%)	ns
No cardiac disease (n)	0	0	ns
Medication			
β-blockers (n)	29 (51%)	35 (57%)	ns
Verapamil (n)	14 (25%)	10 (16%)	ns
Amiodarone (n)	6 (11%)	11 (18%)	ns
Sotalolol (n)	10 (18%)	15 (25%)	ns

LVEDD = left ventricular enddiastolic diameter.

P Wave Signal-Averaged ECG

The FPD was significantly longer (139.6 ± 16.0 vs 118.2 ± 14.1 ms, $P < 0.0001$) and the RMS 20 lower (2.57 ± 0.77 vs 3.90 ± 0.99 μ V, $P < 0.0001$) in patients with a recurrence of AF. Figure 1 shows two original tracings of the P-SAECG of representative patients with and without a recurrence of AF after EC.

Chi-square test showed that a cutoff point (COP) of FPD ≥ 126 ms and RMS 20 ≤ 3.1 had the best predictive power for recurrence after cardioversion (Table 2). The COP had a significant higher incidence in patients with a recurrence of AF after EC than in sinus rhythm (41 patients (72%) vs 14 pa-

tients (23%), $P < 0.0001$) The Kaplan-Meier analysis is shown in Figure 2. The multivariate stepwise regression analysis showed that COP and left atrial diameter ≥ 40 mm were independent variables of a recurrence after cardioversion (Table 3).

DISCUSSION

The results of our study supported in a large homogeneous collective with AF and successful EC that the COP is a risk factor for recurrence of AF after EC. In addition, COP was the best predictor of the prognosis for the maintenance of sinus rhythm than the other parameters.

Table 2. Specificity, Sensitivity, and Predictive Value of the Measurements of Signal-Averaged ECG and Echocardiography

	Specificity	Sensitivity	PPV	NPV	Accuracy
COP	77	72	75	75	75
Left atrial diameter ≥ 40 mm	52	68	57	64	60

NPV = negative predictive value; PPV = positive predictive value; COP = cutoff point. COP was defined as FPD ≥ 126 ms and RMS 20 ≤ 3.1 μ V.

Figure 1. Original tracings of a patient with (B) and without (A) a recurrence of AF after cardioversion.

Antiarrhythmic Drugs

The influence of antiarrhythmic drugs on the variables of P-SAECG could not be fully excluded.

Sotalol, a β -blocker or verapamil did not have an effect on the measurements.^{15,16} Amiodarone influenced the FPD and RMS 20 only in the case of an effective therapy of AF.¹⁷

Figure 2. Kaplan–Meier analysis of percentages of patients remaining free of atrial fibrillation after cardioversion.

P Wave Signal-Averaged ECG

The FPD was significantly longer and the RMS 20 was significantly lower in patients with a recurrence of AF after EC. Other studies also found a longer FPD and a lower RMS 20 among patients with a recurrence but they had another COP.^{18–23} The antiarrhythmic therapy was discontinued for 5 half-lives in the study of Opolski et al.¹⁸ They found a longer FPD (145 vs 130 ms, $P < 0.001$), a lower RMS 20 (1.6 vs 2.2 μV , $P < 0.02$), and a COP with a FPD of 137 ms and a RMS 20 of 1.9 μV . This value reached a specificity of 71%, a sensitivity of 73%, and a negative predictive and positive value of 85% and 53% in 11 patients (31%) with a recurrence. AF was cardioverted by electrical or chemical means in a group of 73 patients with AF in the study of Aytemir et al.¹⁹ They used, for instance, propafenone for chemical cardioversion which led to a longer FPD.¹³ It was remarkable that the FPD (138.3 vs 112.4 ms, $P = 0.001$) and the COP (128 ms, 2.1 μV) was lower and the RMS 20 (1.9 vs 2.5 μV , $P = 0.001$) was higher than that in the study of Opolski et al.¹⁸ They achieved a specificity of 76%, a sensitivity of 70%, and a negative predictive and positive value of 78% and 69% in 31 patients with a

recurrence of AF after EC.¹⁹ Guo et al.²⁰ examined 60 patients after EC and observed a high incidence (77%) of recurrence of AF after EC. The FPD was longer (157 vs 143 ms, $P < 0.0001$) and the RMS 20 was lower (3.6 vs 5.2 μV , $P < 0.0001$) in patients with a recurrence of AF. Because of the missing definition of COP, they could not calculate specificity, sensitivity, negative predictive, or positive value of patients with recurrence of AF. Turitto et al.²¹ and Stafford et al.²² could not predict the recurrence of AF after EC with P-SAECG. Turitto et al.²¹ examined patients with paroxysmal AF or flutter which did not represent patients after a cardioversion because of different kinds of atrial electrophysiological properties. There are possible reasons for the negative result in the study of Stafford et al.²² On the one hand, high-risk patients for recurrence were included and on the other hand, a P wave triggered P-SAECG was not performed which led to longer FPD and a consecutive lower predictive power of the results of the measurements.²² Raitt et al.²³ found a slower atrial conduction in an electrophysiologic study and a concordant longer FPD (148 vs 133 ms, $P < 0.015$) in 39 patients with a recurrence of AF after EC. This study showed the reflection of slow atrial conduction due to P-SAECG. However, the consensus of all studies which could predict a recurrence with P-SAECG is a longer FPD and a lower RMS 20 among patients with a recurrence of AF after EC.

Properties of AF

The multiple wavelet hypothesis of AF states that AF is the result of multiple simultaneous wavefronts of reentry in the atria.²⁴ The onset of AF depends on atrial conduction velocity and refractory period. The predictive value of signal-averaged FPD of patients with recurrence of AF after EC is probably the result of reflecting the intraatrial conduction delay by a longer FPD.^{12,25–27}

Table 3. Univariate and Multivariate Predictors of AF Recurrence After Cardioversion

	Univariate			Multivariate		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P Value
COP	8.60	3.75–19.74	<0.0001	9.97	4.10–24.24	<0.0001
Left atrial diameter ≥ 40 mm	2.39	1.13–5.07	<0.03	3.16	1.29–7.78	<0.012

COP was defined as FPD ≥ 126 ms and RMS 20 ≤ 3.1 μV .

Limitation

A problem of all studies^{18–23} was the documentation of AF after EC because of a high number of asymptomatic episodes of AF.^{28,29} Therefore, our patients could have had asymptomatic nondetected episodes of AF which might have influenced our results.

The results of our study suggest that the probability of recurrence of AF after cardioversion could be predicted by P-SAECG. This method seems to be appropriate to show a delayed atrial conduction that was a risk factor for reinitiation of AF.

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