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Advanced interatrial block is an electrocardiographic marker for recurrence of atrial fibrillation after electrical cardioversion

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ABSTRACT

Background: Early recurrence of atrial fibrillation (AF) is common following a successful electrical cardioversion (ECV). The purpose of this study was to investigate the hypothesis that AF recurrence is related to atrial electrical inhomogeneity, which may influence the P wave characteristics.
Methods: Two hundred ninety-one consecutive persistent AF patients who underwent ECV were enrolled, and evaluated for AF recurrences one month after the ECV. Patients with open-heart surgery, a history of catheter ablation, and an unsuccessful ECV were excluded. The P wave duration, dispersion and P wave morphology were evaluated by 12 lead ECGs 30 min after the ECV.
Results: In total, 141 patients were investigated. One month after the ECV, 60 (43%) patients maintained sinus rhythm. The advanced interatrial block (aIAB; P wave duration >120 ms and biphasic P waves in the inferior leads) (Hazard ratio [HR], 4.51; 95% confidence interval [CI] 1.45–14.01, P = 0.009), P wave dispersion (HR, 1.06; 95%CI 1.02–1.09, P = 0.001), and duration of AF per month (HR, 1.03; 95%CI 1.01–1.04, P = 0.004) were independent predictors of AF recurrence. An aIAB was not associated with structural parameters such as the left atrial volume index or right atrial area. There were no differences in the serum BNP level and frequency of administering anti-arrhythmic drugs between the patients with and without recurrence.
Conclusions: The risk of AF recurrence after the ECV can be predicted by the P wave characteristics. A longer P wave dispersion and the duration of AF also had a tendency for recurrence.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the general population. AF is associated with an increased risk of mortality, strokes, and left ventricular (LV) dysfunction. Restoration of sinus rhythm (SR) may relieve the symptoms and improve the LV function, thus, electrical cardioversion (ECV) of persistent AF to normal sinus rhythm is an accepted strategy of therapy. However, maintenance of sinus rhythm after a successful ECV is difficult, with a high incidence of AF recurrences despite the use of potent anti-arrhythmic drugs. It has been reported that relapses are most frequent during the first 2 weeks after the cardioversion [1], thus the identification of patients with an increased risk of an early AF recurrence is important for a rational clinical therapeutic strategy.

The aim of this study was to demonstrate the association between the P wave characteristics that might be influenced by atrial electrical inhomogeneity and the incidence of AF recurrences after a successful ECV.

2. Methods

2.1. Study protocol

The present study was conducted as a single-center prospective observational study. The study protocol was approved by the institutional review board of Nippon Medical School. Since 2012, we enrolled continuous patients, who gave their informed consent and underwent an initial electrical cardioversion procedure at Nippon Medical School Teaching Hospital into the study and followed them in the outpatient clinic periodically. The data from January 2012 to December 2017 were analyzed. Patients were excluded if they were <20 years old, suffered from congestive heart failure, had a history of open-heart surgery, underwent radiofrequency catheter ablation, or underwent hemodialysis. The patients who could not return to sinus rhythm or had an immediate recurrence of atrial fibrillation after a successful ECV were excluded. The clinical data were recorded, and echocardiography was performed before the ECV.

2.2. Electrical cardioversion protocol

After obtaining written informed consent, the ECV was performed under sedation with intravenous midazolam (0.01 mg/kg). A biphasic R-wave synchronized shock

Abbreviations: aIAB, advanced interatrial block; AF, atrial fibrillation; BNP, brain natriuretic peptide; CI, confidence interval; ECV, electrical cardioversion; LVEF, left ventricular ejection fraction; SR, sinus rhythm.

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(Cardiolife model TEC-8300; Nihon Kohden, Inc., Tokyo, Japan) was applied in the patients via self-adhesive skin electrodes (P-511; Nihon Kohden) in the anterior-posterior position. An initial ECV was delivered with 100 J and if the initial shock failed to terminate the AF, the biphasic shock energy was gradually increased to 150 and then 270 J. If the ECV successfully terminated the AF, the patients were monitored for 2 h whether there were any AF recurrences or not. The patients who remained in AF even after a 270 J CV or exhibited AF within 2 h were defined as a failure of the ECV.

2.3. ECG analysis

Standard 12-lead ECGs were recorded in the supine position with an electrocardiographic recorder (ECCG-1460, Nihon Kohden) 30 min after the ECV. All digital data from the standard 12 lead ECG signals were instantaneously processed at a sampling rate of 1 kHz. The electrocardiographic data were subsequently transferred to an ECG diagnostic information system (PRM-3000, Nihon Kohden) for analysis. P waves of >120 ms with a biphasic morphology in the inferior leads has been defined as advanced interatrial block (aIAB), which were referred in a recent consensus report. [2,3] The P wave dispersion was calculated as the difference between the maximum and minimum P wave duration in all 12 ECG leads after sinus rhythm conversion.

2.4. Transthoracic echocardiographic analysis

The patients underwent a comprehensive transthoracic echocardiographic examination within 1 month before the ECV. The left atrial diameter (LAD) was obtained in the parasternal long axis view. The LA volume was calculated using the biplane area-length method. Measurements were obtained during end-systole from the frame preceding mitral valve opening. The LA volume index (LAVI) was calculated as the ratio of the LA volume to the body surface area (mL/m^2). Pulse wave Doppler samples were placed in the apical 4-chamber view at the mitral inflow to measure the early transmitral flow velocity (E), and early diastolic septal and lateral mitral annulus velocity (E'). The left ventricular ejection fraction (LVEF) was assessed using Simpson's method.

2.5. Laboratory analysis

The plasma B-type natriuretic peptide (BNP) concentrations and serum creatinine were measured in all patients before the ECV. The plasma BNP concentrations were determined with a specific immunoradiometric assay for human BNP with commercial kits (Shionoria kit; Shionogi and Kyowa Medex, Tokyo, Japan).

2.6. Follow-up of the patients

After a successful ECV, the patients were followed-up at the outpatient hospital at 1, 2, and 4 weeks. An ECG was recorded at every visit or anytime the patients had palpitations. A 24-h Holter electrocardiogram was evaluated at 1 month in the patients with no recurrences.

2.7. Statistical analysis

The data are expressed as the mean ± standard deviation for continuous variables, and as absolute frequencies and percentages for categorical variables. For the continuous and categorical variables, the differences between the groups were compared using a Student *t*-test and Fisher's exact test, respectively. To find the independent predictors of a recurrence of AF, a stepwise logistic regression procedure was performed.

P-values of <0.05 were considered statistically significant. All statistical analyses were conducted using SPSS for Windows 21.0 J software (SPSS Inc., Chicago, Illinois, USA).

3. Results

3.1. Study subjects

Enrollment of the patients was started in January 2012, and 291 consecutive patients who were referred for an initial ECV of persistent AF were screened. After the exclusion of 150 patients, 141 patients (64 ± 11 years old, 113 males) were enrolled into the study (Supplemental Fig. 1). At 1 month after the ECV, 81 (57%) patients had returned to AF rhythm. Table 1 shows the clinical characteristics of the patients with and without AF recurrences. The prevalence of patients with biphasic P wave morphologies in leads II, III and aVF (Fig. 1) with prolongation (aIAB) was higher in the recurrence group than in the non-recurrent group (23 of 81 [28%] vs. 8 of 60 patients

Table 1
Comparison of the parameters between the patients with and without recurrence.

	Total	Recurrence	Non-recurrence	P-value
	(n = 141)	(n = 81)	(n = 60)	
Age, y	64 ± 11	65 ± 11	61 ± 11	0.02
Male, gender, n	113 (80%)	62 (77%)	51 (85%)	0.29
AF duration, y	2.7 ± 3.0	3.4 ± 4.0	1.9 ± 2.4	0.01
Concomitant drug use during the follow-up				
ACEi/ARB, n	54 (38%)	29 (36%)	25 (42%)	0.49
Beta-blocker, n	78 (55%)	43 (53%)	35 (58%)	0.61
Anti-arrhythmic drug use	128 (91%)	73 (90%)	55 (92%)	1.00
Bepridil, n	91 (65%)	52 (64%)	39 (65%)	1.00
Amiodarone, n	27 (19%)	13 (16%)	14 (23%)	0.29
Comorbidities				
History of stroke, n	10 (7%)	5 (6%)	5 (8%)	0.74
Hypertension, n	83 (59%)	50 (62%)	33 (55%)	0.49
Sleep apnea, n	10 (7%)	5 (6%)	5 (8%)	0.74
Diabetes melitus, n	21 (15%)	9 (11%)	12 (20%)	0.16
COPD, n	1 (1%)	0 (0%)	1 (2%)	0.43
Ischemic heart disease, n	7 (5%)	6 (7%)	1 (2%)	0.24
Body mass index, kg/m^2	24.8 ± 3.8	24.8 ± 3.3	24.8 ± 4.5	0.97
Echocardiographic parameters				
Left atrial diameter, mm	43.1 ± 6.4	44.0 ± 6.1	42.0 ± 6.7	0.11
Left atrial volume index, mL/m^2	53.7 ± 16.3	55.7 ± 17.7	51.1 ± 13.8	0.10
LVEF, %	61.5 ± 12.9	61.7 ± 12.3	61.1 ± 13.7	0.75
E/E' ratio	11.9 ± 5.6	12.1 ± 6.4	11.8 ± 4.3	0.79
Serum BNP, pg/mL	168.2 ± 172.9	176 ± 158	158 ± 192	0.57
Serum creatinine, mg/dL	0.95 ± 0.22	0.95 ± 0.22	0.95 ± 0.22	0.93
Electrocardiographic parameters				
PR interval, ms	193 ± 26	195 ± 25	189 ± 27	0.17
Maximum P wave duration, ms	155 ± 16	158 ± 17	151 ± 14	0.02
Minimum P wave duration, ms	104 ± 15	103 ± 15	106 ± 14	0.37
P wave dispersion, ms	51 ± 17	58 ± 26	45 ± 12	0.001
Advanced interatrial block, n	31 (22%)	23 (28%)	8 (13%)	0.04

Values are given as the mean ± standard deviation or as the number (%).
AF, atrial fibrillation; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction.
BNP, brain natriuretic peptide.

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