Effects of P-wave Dispersion on Atrial Fibrillation in Patients with Acute Anterior Wall Myocardial Infarction

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Background: P-wave dispersion (P dispersion), defined as the difference between the maximum and the minimum P-wave duration (P minimum), and maximum P-wave duration (P maximum) have been used to evaluate the discontinuous propagation of sinus impulse and the prolongation of atrial conduction time respectively. The aim of this study was to investigate whether early assessment of P dispersion predicts paroxysmal atrial fibrillation (AF) in patients with acute anterior wall myocardial infarction (MI).

Methods: We prospectively evaluated 147 consecutive patients (45 women, 102 men; aged 55 ± 9 years) with a first acute anterior wall MI. All patients were evaluated by echocardiography to measure the left atrial diameter and left ventricular ejection fraction (LVEF). Electrocardiography was recorded from all patients on admission and every day during hospitalization.

Results: AF occurred in 25 patients. In 122 patients, AF did not occur. P maximum was found to be significantly higher in patients with AF than in patients without AF (115 ± 17.3 ms vs 101 ± 14.7 ms, $P = 0.001$). P dispersion also was significantly higher in patients with AF than in patients without AF (50 ± 12.5 ms vs 43 ± 10.1 ms, $P = 0.01$). There was no significant difference between the two groups in P minimum (64 ± 12.5 ms vs 59 ± 11.7 ms, $P = 0.057$). The echocardiographically left atrial diameters were not significantly higher in the patients with AF than those without (25 ± 3.38 mm and 23 ± 3.36 mm, respectively, $P = 0.76$). LVEF was found to be significantly different in the patients who developed AF and in those who did not ($37.96 \pm 6.18\%$ vs $47.70 \pm 6.01\%$, $P = 0.0001$).

Conclusions: Although P maximum and P dispersion are significant predictive factors of AF in patients with acute anterior wall MI in the univariate analysis, on the basis of multivariate analysis, only age and LVEF were independent predictive parameters for AF. **A.N.E. 2003;8(2):101–106**

P-wave dispersion; P-wave duration; acute anterior wall myocardial infarction

Atrial fibrillation (AF) is a common arrhythmia in patients with acute myocardial infarction (MI) and observed ranges are between 5% and 23% in previous studies.¹ AF is usually transient, and spontaneous reversion is quite common. AF occurs more frequently following anterior than inferior wall MI. AF tends to occur in patients with left ventricular failure and is observed in patients with pericarditis and ischemic injury to the atria.² The presence of AF further compromises cardiac function in addition to damage to the myocardium caused by the MI.³

Atrial fibrillation is more common during the first 24 hours after MI.² Advanced age, hyperten-

sion, congestive heart failure, diabetes mellitus, and pulmonary disease seem to promote AF/flutter in patients with acute MI.^{1,4–6} AF during acute MI is associated with increased in-hospital and long-term mortality and complications such as cardiogenic shock, ventricular arrhythmias, congestive heart failure, and thromboembolic events, particularly in patients with anterior MI.^{1,3,7,8}

P-wave dispersion (P dispersion) is defined as the difference between the maximum and the minimum P-wave duration (P minimum) in 12-leads of the surface ECG.^{9,10} Inhomogeneous propagation of sinus impulses and the prolongation of intraatrial and interatrial conduction time are well-known

electrophysiological characteristics of atria prone to fibrillation.^{9–13} P dispersion has been studied in patients with essential hypertension, idiopathic paroxysmal AF, and spontaneous angina episodes.^{12,14,15} To our knowledge, P dispersion has not yet been evaluated in patients with acute anterior wall MI.

The aim of this study was to investigate whether early assessment of P dispersion predicts paroxysmal AF in patients with acute anterior wall MI.

METHODS

Patients

We prospectively evaluated 147 consecutive patients (45 women, 102 men; aged 55 ± 9 years) who were admitted to our hospital with a first acute anterior wall MI who met the following criteria: (1) chest pain lasting >30 min; (2) ST segment elevation >2 mm at least in two anterior electrocardiographic leads; and/or (3) transient elevation of creatin kinase and/or MB isoenzyme levels. All patients who were admitted to the hospital within 12 hours of the onset of symptoms were included in this study.

All patients were hospitalized and evaluated with electrocardiography (ECG) and echocardiography. ECG recordings were performed on admission and every day. Echocardiographies were performed on the third day during hospitalization. Maximum P-wave duration (P maximum), P minimum, and P dispersion were calculated in all patients. The diagnosis of AF was performed according to the following criteria: absence of P waves, coarse or fine fibrillatory waves, and completely irregular R-R intervals according to the available 12-lead ECG recordings and reports of monitoring.

All the patients were examined by careful auscultation at least twice daily. Detection of pericardial rub during the first 72 hours after admission was considered diagnostic of infarction-related pericarditis. The diagnosis of pericardial rub was made after confirmation by at least two cardiologists. Thyroid function tests were studied in all patients.

Patients with atrioventricular block, right or left bundle branch block, history of paroxysmal or permanent AF, ventricular preexcitation, congenital heart disease, prior pacemaker implantation, hyperthyroidism, pulmonary embolism, valvular heart disease, chronic obstructive pulmonary dis-

ease, cardiomyopathy, open heart surgery, abnormal serum electrolyte values, and patients with receiving digitalis, or any antiarrhythmic drugs were excluded from this study.

12-Lead Surface Electrocardiography

A 12-lead surface ECG was obtained from all patients in the supine position using Hewlett-Packard Electrocardiograph Sanborn Series (Chine) machine. The 12-lead ECG was recorded at a paper speed of 50 mm/s and 1-mV/cm standardization on admission and every day. All patients were breathing freely but not allowed to speak during the ECG recordings.

P-Wave Duration Measurements

The P-wave duration was calculated in all 12-leads of the surface ECG and simultaneously recorded. Two investigators without knowledge of the patients' clinical status calculated the measurements of the P-wave duration manually.

Electrocardiographies with measurable P waves in nine or less leads were excluded from the study. P maximum in any of the 12-lead surface ECGs was calculated and used as a marker of prolonged atrial conduction time. P dispersion, defined as the difference between P maximum and P minimum, was calculated from the 12-lead ECG. This difference was defined as P-wave dispersion ($P \text{ dispersion} = P \text{ maximum} - P \text{ minimum}$). To improve accuracy, measurements were performed with calipers and magnifying lens for defining the ECG deflection. Many investigators have previously used this method.^{16–18} The onset of P wave was defined as the junction between the isoelectric line and the start of P-wave deflection and the offset of the P waves as the junction between the end of the P-wave deflection and the isoelectric line.¹⁹ Normal sinus rhythm was diagnosed when the following five criteria were present: (1) P wave of sinus origin (normal mean axis of P wave); (2) constant and normal PR interval (of 0.12–0.20 s); (3) constant P-wave configuration in a given lead; (4) rate between 60 and 100 bpm; and (5) constant PP (or RR) interval.²⁰

The intraobserver and interobserver reproducibility of P-wave duration and dispersion of P measurements were 2 ± 3 ms, 0.3 ± 2 ms, 4 ± 3 ms, 0.4 ± 4 ms, respectively.

Echocardiography

Patients were evaluated by two-dimensional and Doppler echocardiography on the third day by using a Hewlett-Packard Sonos 5500 machine with 2.5 MHz transducer. Left ventricular ejection fraction (LVEF) was determined in parasternal long-axis views using the Teichholz method.²¹ Two echocardiographers who were blind to the patients' clinical and laboratory data interpreted each echocardiographic examination independently.

Therapy

Thrombolytic therapy was administered to 98 patients. Of these, 48 received streptokinase (1500000 IU IV, over 1 hour) and 50 had *t*-PA (100 mg IV, over 90 minutes). The administration of thrombolytics was immediately followed by heparin. Forty-nine patients did not receive thrombolytic therapy due to some contraindication for thrombolysis or late admission after the onset of the pain. ACE inhibitors and beta-blockers were administered to 132 patients and 93 patients, respectively.

Statistical Analysis

Data are presented as mean $\pm$ SD. Comparisons between the two groups were performed by means of an unpaired *t*-test for continuous variables and Mann-Whitney U test, where appropriate. Categorical variables were analyzed with contingency tables using the chi-square test and the Fisher's exact test when appropriate. Multivariate logistical regression analysis was performed to identify the independent predictors of AF. For multiple regression, factors showing a value $P < 0.1$ in univariate analysis were selected. A P value of <0.05 was considered statistically significant.

RESULTS

The characteristics of the patients are shown Table 1. In the comparison of the patients with and without P dispersion, there was a significant difference in age. There were no significant differences due to hypertension, diabetes mellitus, hyperlipidemia, smoking, pericarditis, and therapy including beta-blockers and ACE inhibitors. Twelve of the 25 patients with AF and 86 of the 122 patients without AF received thrombolytic therapy (Table 1). No significant differences in the heart rate and respiratory rate were noticed between patients with AF

Table 1. Clinical Characteristics of Study Population

	AF (n = 25)	Non-AF (n = 122)	P
Age (years)	62 $\pm$ 9	53 $\pm$ 8	0.0001
Sex (males/females)	17/8	87/35	0.74
Hypertension	9 (36%)	49 (40%)	0.61
Diabetes mellitus	3 (12%)	24 (20%)	0.36
Hyperlipidemia	10 (40%)	66 (54%)	0.19
Smoking history	12 (48%)	68 (56%)	0.47
Pericardial rub	8 (32%)	34 (28%)	0.48
Beta-blocker	13 (52%)	80 (66%)	0.22
ACE inhibitor	23 (92%)	109 (89%)	0.91
Thrombolytic therapy	12 (48%)	86 (70%)	0.03

AF: atrial fibrillation.

and without AF. Thyroid function tests were normal in all patients.

In most of the patients, AF occurred on the first and second days of MI during hospitalization. AF occurred in 17 patients (68%) on day 1, 5 patients (20%) on day 2, and 3 patients (12%) on day 3. AF was usually transient and spontaneous reversion to sinus rhythm occurred in 17 of the patients. Medical treatment was administered to 7 patients, and cardioversion was performed on 1 patient.

There was no significant difference between the two groups in the left atrial diameter. Left ventricular ejection fraction was significantly lower in patients with AF than in patients without AF. (Table 2). P maximum and P dispersion were significantly higher in the group with AF than in the group without AF ($P = 0.001$ and $P = 0.01$, respectively) (Table 2). There was no significant difference between the two groups for P minimum ($P = 0.057$).

By univariate analysis, P dispersion and P maximum were found to be significantly higher in patients with AF than those without (Fig. 1). Six clinical, electrocardiographic, and echocardiographic variables entered the multivariate logistic regression analysis at $P < 0.1$ (Tables 1 and 2). Multivariate analysis showed that age and LVEF were independent predictors of AF in patients with acute anterior wall MI (Table 3).

DISCUSSION

The clinical significance of P-wave duration has been investigated in many clinical conditions such as left atrial enlargement,^{19,22,23} left atrial hypertension,^{24–26} exercise, or angioplasty-induced myocardial ischemia,^{27–29} acute MI,^{25,30,31} stable angina

Table 2. Mean Values of the Studied Parameters in the Groups of the Study Population

	AF (n = 25)	Non-AF (n = 122)	P
P maximum (ms)	115 ± 17.3	101 ± 14.7	0.001
P minimum (ms)	64 ± 12.5	59 ± 11.7	0.057
P dispersion (ms)	50 ± 12.5	43 ± 10.1	0.01
LAD (mm)	25 ± 3.38	23 ± 3.36	0.76
LVEF (%)	37.96 ± 6.18	47.70 ± 6.01	0.0001

AF: atrial fibrillation; LAD: left atrial dimension; LVEF: left ventricular ejection fraction.

pectoris,^{25,32–34} and in patients with paroxysmal AF.^{9,10,17,35}

P-maximum values may be influenced by diffuse myocardial ischemia probably due to left atrial distention, left atrial wall ischemia, ischemia-induced increase in left atrial pressure, and volume that prolongs atrial conduction time. Josephon et al.³⁶ reported that the electrocardiographic pattern of left atrial dilatation was unrelated to left atrial pressure or volume in patients with coronary artery disease. This was related to prolongation of interatrial conduction time due to multiple factors. Rios et al.³⁷ reported an increased incidence of P-wave abnormalities with more severe coronary artery disease and more severe left ventricular dysfunction. In our study, P maximum was significantly higher between the patients who developed AF and those who did not in anterior wall MI.

In patients with coronary artery disease, the multiple etiological factors of atrial arrhythmias have been documented.³⁸ The difference in the conduction properties between the ischemic atrial

myocardium and the adjacent nonaffected tissue may lead to discontinuous propagation of sinus impulses. The heterogeneity of structural and electrophysiological properties of the atrial myocardium plays a major role in the initiation of atrial reentry because of the increased likelihood of unidirectional block of premature impulses.³⁹ The discontinuous and inhomogeneous propagation of sinus impulse in patients with paroxysmal lone AF has been recently evaluated with a new simple ECG marker, P dispersion.^{9,10} Ischemia-induced discontinuous and inhomogeneous propagation of sinus impulses and preexisting left atrial dilatation, distension, overload, and atrial wall fibrosis may lead to increase of P dispersion in patients with acute anterior wall MI.

Dilaveris et al.,¹² reported an increased P dispersion and P maximum during spontaneous anginal episodes. Weber et al.¹¹ studied P dispersion in patients who underwent bypass surgery to predict AF developed after bypass surgery and found a significant difference in P dispersion between patients who developed AF and those who did not. Myrianthefs et al.,²⁹ showed significant P-wave duration prolongation during angioplasty-induced myocardial ischemia in patients with single-vessel left anterior descending artery disease.

Figure 1. The graph depicts the mean duration of P dispersion and P maximum.**Table 3.** Independent Predictor Parameters for Atrial Fibrillation

	P
Age	0.002
P minimum (ms)	0.325
P maximum (ms)	0.234
P dispersion (ms)	0.642
LVEF (%)	0.0001
Thrombolytic therapy	0.075

LVEF: left ventricular ejection fraction.

The increase in P dispersion during myocardial ischemia may be a consequence of ischemia-induced inhomogeneous and discontinuous atrial conduction and is not only related to P maximum but may also be related to P minimum.¹² We did not find a significant difference between the two groups for P minimum.

Previous studies have shown that increasing age, hypertension, diabetes mellitus, pulmonary disease, left ventricular dysfunction, left atrial dimension, history of paroxysmal AF, and organic heart disease^{1,4,5,40-47} could predict AF. Age-related structural changes such as increased atrial fibrosis, and atrial dilatation may explain the increased incidence of AF in old patients. Paroxysmal AF is considered a complication of acute MI associated with increased in-hospital and long-term mortality rates.^{1,3,7,8}

In our study, P dispersion and P maximum were found to be significant univariate predictors in patients with acute anterior wall MI, where only age and LVEF remained significant independent predictors of AF in the multivariate analysis. To our knowledge, this study is the first to investigate a relation between the P dispersion and AF in patients with acute anterior wall MI.

Study Limitations

It is known that changes in autonomic tone may affect P-wave duration mainly through the effects on atrial conduction velocity. Since respiratory rate and heart rate were similar between two groups, we believed that possible fluctuations of the autonomic cardiac control did not significantly influence our results.

Left atrial maximal diameter measured in this study may not accurately reflect left atrial size and volume in patients with AF, because atrial dilatation can be eccentric.⁴⁸ The role of the right atrium in the onset of AF was not evaluated in this study.

CONCLUSIONS

Age and LVEF are found to be significant independent predictors of the onset of AF in multivariate analysis, whereas P-wave maximal duration and particularly P dispersion are significant predictive factors of AF in patients with acute anterior wall MI in the univariate analysis. In our opinion, the reliability of the parameters highlighted in this study should be tested in larger prospective studies.

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