EFFECT OF LEFT ATRIA SIZE ON P-WAVE DISPERSION: A STUDY IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION

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Abstract

INTRODUCTION: Paroxysmal atrial fibrillation (AF) is a common arrhythmia encountered in clinical practice. Experimental and human mapping studies have demonstrated that perpetuation of AF is due to the presence of multiple reentrant wavelets with various sizes in the right and left atria. P-wave dispersion (PWD), defined as the difference between the maximum and minimum P-wave duration, has been proposed as being useful for the prediction of paroxysmal atrial fibrillation (AF). This study was undertaken to examine the effect of left atria (LA) dimension on P-wave dispersion in unselected patients with PAF compared to healthy controls.

METHODS: In this study, 40 consecutive patients with PAF (25 male, 15 female, mean age 45 ± 9 years) and 40 age and gender matched healthy controls (25 male, 15 female, mean age 46 ± 10 years) were studied. The P wave duration was calculated in all 12 leads of the surface ECG. The difference between the maximum and minimum P wave duration was calculated and defined as P wave dispersion (PWD = Pmax - Pmin). All patients and controls were also evaluated by echocardiography to measure the left atrial diameter and left ventricular ejection fraction (LVEF).

RESULTS: P-wave dispersion in patients with PAF and normal LA diastolic diameter (LAD) was longer than in controls with normal LA size (51±9 vs. 34±8 ms, $P < 0.002$). P-wave dispersion increased in patients with PAF (60±14 vs. 50±7 ms, $P < 0.001$) and controls (39 ± 9 vs. 33 ± 9 ms, $P < 0.004$) with increased LAD. In the PAF group, P-wave dispersion correlated with LAD ($r = 0.40$, $P = 0.001$) and LA diastolic volume ($r = 0.62$, $P < 0.001$). On multivariate logistic regression analysis, only P-wave dispersion retained significance on development of PAF.

CONCLUSION: P-wave dispersion increased in patients with PAF and normal LA size. In controls with increased LA size, P-wave dispersion increased but did not reach the levels attained in patients with PAF. These findings can be explained by the changes in LA microarchitecture which concurrently decreased atrial myocardial contraction, increased P-wave dispersion and predisposed to PAF.

Keywords: coronary calcification, inflammation, risk factors, h-CRP.

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia and an important prognostic indicator encountered in clinical practice.[1,2] Experimental and human mapping studies have demonstrated that perpetuation of AF is due to the presence of multiple reentrant wavelets with various sizes in the right and left atria.[3] The prolongation of intraatrial and interatrial conduction time and the inhomogeneous propagation of sinus impulses are well known electrophysiologic characteristics in patients with paroxysmal atrial fibrillation (AF). Previous studies have demonstrated that individuals with a clinical history of paroxysmal AF show a significantly increased P-wave duration in 12-lead surface electrocardiograms (ECG) and signal-averaged ECG recordings. P-wave dispersion is defined as the difference between the longest and the shortest P-wave duration recorded from multiple different surface ECG leads.[4]

It is evident that invasive electrophysiologic studies are needed to evaluate the electrophysiologic properties of the atrium that contribute to the initiation and the perpetuation of fibrillation.[5] However, electrophysiologic studies are highly complex, time consuming and expensive, and could not be used as a screening test for

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the general population. Consequently, the identification of simple electrocardiographic predictors for the development of atrial fibrillation appears to be the most practical approach.[6]

The purpose of this study was to search for simple electrocardiographic markers derived from the 12-lead surface electrocardiogram that could be used for the best separation between patients with idiopathic PAF and healthy control subjects and as possible indicators for the development of PAF.

Materials and Methods

Study population

Forty consecutive patients, 25 men and 15 women aged 45 ± 9 years with a history of idiopathic PAF, were studied. The diagnosis of atrial fibrillation was made when visible P waves on all 12 leads of the electrocardiogram were absent and an irregular random ventricular response was present. Atrial fibrillation was considered paroxysmal if the fibrillatory process ended spontaneously after some seconds, minutes, hours, or up to 2 days. Atrial fibrillation was defined as idiopathic when the patient's history, physical examination, chest radiograph, 12-lead surface electrocardiogram, and echocardiogram (M-mode, two-dimensional, Doppler) revealed no detectable cardiovascular or other disease.[7,8] Thus, excluded from the study were patients with history of PAF who had coronary artery disease, valvular heart disease, hypertension, hyperthyroidism, cardiomyopathy, congenital heart diseases, congestive heart failure, pericarditis, chronic obstructive pulmonary disease, pulmonary emboli, preexcitation syndromes, sick sinus syndrome, bundle branch block, atrioventricular block and open heart surgery.

The control group consisted of 40 age and sex-matched healthy subjects. No evidence of cardiac or other disease was apparent in this group from history, physical examination, electrocardiogram, chest radiograph and echocardiogram. The baseline characteristics of patients and control subjects are shown in Table 1.

Data acquisition

A 12-lead surface electrocardiogram was obtained from all patients and control subjects in the supine position. During the electrocardiographic recording all participants were breathing freely but not allowed to speak. The 12-lead electrocardiogram was recorded at a paper speed of 50 mm/sec and 1 mV/cm standardization. The P-wave duration was calculated in all 12 leads of the surface electrocardiogram simultaneously recorded. The measurements of the P-wave duration were performed manually by two of the investigators without knowledge of patient assignment by using calipers and a magnifying lens (10-fold magnification) for defining the electrocardiogram deflections. This method has also been used by other investigators.[9-11] The onset of the P-wave was defined as the junction between the isoelectric line and the beginning of P-wave deflection and the offset of the P-wave as the junction between the end of the P-wave deflection and the isoelectic line.[12,13] The maximum P-wave duration (P maximum) in any of the 12 electrocardiographic leads was calculated and used as a marker of prolonged atrial conduction time. The difference between the maximum P-wave duration and the minimum P-wave duration (P minimum) was also calculated from the 12-lead electrocardiogram. This difference which was defined as P-wave dispersion (P dispersion) was used as a marker of the nonuniform anisotropic inhomogeneous atrial conduction.

Statistical analysis

Data are presented as mean values ± SD. Continuous variables were compared by Mann-Whitney U test and categorical variables were compared by means of chi-square test. All statistical calculations were performed with commercially available computer software. Statistical significance was assumed for a p value < 0.05.

Table 1. Baseline characteristics of patients and healthy control subjects

	Patients	Controls	p Value
No.	40	40	NS
Men/women	25/15	25/15	NS
Age (years)	45 ± 9	46 ± 10	NS
Heart rate (beats/min)	72 ± 4	70 ± 3	NS
Respiratory rate (breaths/min)	12 ± 1	12 ± 2	NS
QRS duration (msec)	80 ± 17	80 ± 14	NS
PQ duration (msec)	160 ± 19	162 ± 20	NS
Left ventricular ejection fraction (%)	65 ± 7	64 ± 6	NS

LA: Left atrium, LVEF: left ventricular ejection fraction, NS: not significant.

Results

Forty patients and 40 control subjects participated in this study. There were no significant differences between patients and control subjects concerning age, sex, heart rate, respiratory rate, QRS duration, PQ duration and the echocardiographically determined left atrial maximal dimension and left ventricular ejection fraction (table 1). P-wave dispersion in patients with PAF and normal LA diastolic diameter (LAD) was longer than that in controls with normal LA size (51 ± 9 vs. 34 ± 8 ms, $P < 0.002$). P-wave dispersion increased in patients with PAF (60 ± 14 vs. 50 ± 7 ms, $P < 0.001$) and controls (39 ± 9 vs. 33 ± 9 ms, $P < 0.004$) with increased LAD. In the PAF group, P-wave dispersion correlated with LAD ($r = 0.40$, $P = 0.001$), LA diastolic volume ($r = 0.62$, $P < 0.001$). On multivariate logistic regression analysis, only P-wave dispersion retained significance on development of PAF.

Discussion

The principal new findings of this study suggest that there are simple electrocardiographic markers, which can best separate patients with idiopathic PAF from healthy control subjects and can be used for the prediction of idiopathic PAF. Increased P-wave duration was found to significantly separate patients with idiopathic PAF from healthy subjects. This is in accordance with previously reported studies.[14-17] P-wave dispersion is a simple, noninvasive, electrocardiographic marker that best separated patients with idiopathic PAF from healthy control subjects and could be used as a significant predictor of idiopathic PAF.

Mechanism of atrial fibrillation

Atrial fibrillation is a common arrhythmia that can be encountered in patients with and without structural heart disease. Recent evidence suggests that randomly reentrant wavelets are responsible for the genesis of this arrhythmia.[18] Electrophysiological studies by programmed atria stimulation have shown that intraatrial conduction delay8, fragmented atria activity[19,20] and anisotropic conduction[2,6] are associated with paroxysmal atria fibrillation. Besides, right atria mapping studies during sinus rhythm have demonstrated that prolonged, fractionated atria electrocardiograms are more frequent and more distributed within the entire right atrium in these patients.

Atrial vulnerability or atrial propensity to sustain atrial fibrillation is determined by atrial surface area (size), morphology, anatomic obstacles and spatial distribution of non-homogeneous electrophysiologic characteristics.[21]

Electrocardiographic predictors of paroxysmal lone atrial fibrillation

P-wave prolongation

Slow inhomogenous conduction of atria impulse and prolonged fractionated atria electrocardiogram can be reflected by prolongation of p-wave duration. Prolonged p-wave duration in 12-lead surface ECG and signal averaged ECG were commonly used for prediction of paroxysmal atria fibrillation and considered to represent intra- and interatrial conduction delays predisposing to atria fibrillation.[22]

In this study, the maximum P-wave duration was calculated from a 12-lead surface electrocardiogram in patients with idiopathic PAF.[19] We found that P-wave duration was significantly longer in patients with idiopathic PAF than in healthy control subjects. This is in accordance with previously reported studies.[16,23,24] A P maximum value of 110 msec proved to have good sensitivity and specificity for the separation of patients with idiopathic PAF from control subjects. Patients with a P maximum 110 msec proved to have a twofold risk to experience recurrences of PAF in a 12-month follow-up period.[16,25] Therefore we suggest that prolonged P-wave duration may be a useful predictor of idiopathic PAF, although the P-wave duration in our study was assessed in a selected group of patients already known to have idiopathic PAF.

P-wave dispersion

The heterogeneity of structural and electrophysiologic properties of the atrial myocardium is believed to play a major role in the initiation of reentry, because of the increased likelihood of unidirectional block of premature impulses.[26] It is suggested that the inhomogeneous and anisotropic distribution of connections between fibers and bundles of fibers results in the discontinuous anisotropic propagation of sinus impulses.[27] Other intracellular or intercellular factors, such as the presence of a particular spatial expression of membrane structures such as connexions, ion channels, or regulatory proteins, may influence intercellular connections and impulse propagation, thus conferring the highly anisotropic properties of the atrial tissue.

In addition to the proposed effect on impulse propagation by the atrial microarchitecture, fixed anatomic obstacles and site-specific conduction delays in the atrial myocardium might also account for the nonuniform and inhomogeneous atrial conduction. The role of major discontinuities in the atrial structural millieu such as the superior vena cava, inferior vena cava and pulmonary veins for the provocation of intraatrial and interatrial conduction delay has already been proposed.[28] The presence of site-dependent

conduction delays in the atrial myocardium prone to fibrillation was suggested by Papageorgiou et al,[2] who found that during high right atrium stimulation, patients with atrial fibrillation inducibility exhibited significant prolongation of conduction to the posterior triangle of Koch compared with coronary sinus stimulation. They finally proposed that slow conduction in the low right atrium may be required for reentry and may initiate atrial fibrillation.

Moreover P dispersion is a relatively novel ECG index in noninvasive electrocardiology and seems to be quiet useful in prediction of atria fibrillation in various clinical settings.[27-30] It is believed that increased p-dispersion simply reflects inhomogenous and discontinuous propagation of sinus impulses.[4,29,30]

As a marker of this variation in P-wave duration measurements, we used the difference between the maximum and the minimum P-wave durations (P dispersion) measured in the 12-lead electrocardiogram.[20] We found that P dispersion was significantly higher in patients with idiopathic PAF compared to healthy control subjects. A P dispersion value of 40 msec separated patients with idiopathic PAF from control subjects, with a very good sensitivity, specificity and positive predictive accuracy.[31] P dispersion was able to complement and strengthen the role of P maximum for the best separation between patients with history of idiopathic PAF and healthy control subjects.[32,33] Patients with P dispersion 40 msec proved to have a two-fold risk to experience recurrences of PAF in a 12-month follow-up period.[31] Our data suggest that P dispersion is a valuable index that can separate patients with idiopathic PAF from healthy subjects and may be used to predict the development of PAF.

Study limitations

Biopsy studies have documented that occult myocardial diseases (myocarditis, cardiomyopathy, and so forth) can underlie the so-called idiopathic atrial fibrillation and be responsible for the arrhythmic phenomena.[34] Cardiac biopsy to exclude these myocardial diseases was not performed in our study.

It is well known that changes in autonomic tone may affect P-wave duration through effects on either conduction velocity or changes in atrial size or pressure that may arise from the associated change in heart rates.[35] We believe that autonomic nervous system activity had no significant effects on our results because patients with idiopathic PAF and healthy control subjects had similar heart and respiratory rates during electrocardiographic recordings and because the duration of the PQ segment was similar in both groups.

Conclusions

The results of our study suggest that P maximum and P dispersion are simple electrocardiographic markers that are significantly different between patients with idiopathic PAF and healthy control subjects. Prolongation of P wave time and increase of its dispersion are independent predictors of atrial fibrillation. Further studies, however, are required to determine whether these simple markers may be used as indicators of the recurrence of PAF.

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